INFECTION AGE STRUCTURED VECTOR BORNE DISEASE MODEL WITH DIRECT TRANSMISSION.

by

Sunil Giri

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ABSTRACT

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Mathematical modeling is a powerful tool to study and analyze the disease dynamics prevalent in the community. This thesis studies the dynamics of two time since infection structured vector borne models with direct transmission. We have included disease induced death rate in the first model to form the second model. The aim of this thesis is to analyze whether these two models have same or different disease dynamics. An explicit expression for the reproduction number denoted by $\mathcal{R}_0$ is derived. Dynamical analysis reveals the forward bifurcation in the first model. That is when the threshold value $\mathcal{R}_0 < 1$, disease free-equilibrium is stable locally implying that if there is small perturbation of the system, then after some time, the system will return to the disease free equilibrium. When $\mathcal{R}_0 > 1$ the unique endemic equilibrium is locally asymptotically stable.

For the second model, analysis of the existence and stability of equilibria reveals the existence of backward bifurcation i.e. where the disease free equilibrium coexists with the endemic equilibrium when the reproduction number $\mathcal{R}_{02}$ is less than unity. This aspect shows that in order to control vector borne disease, it is not sufficient to have reproduction number less than unity although necessary. Thus,

the infection can persist in the population even if the reproduction number is less than unity. Numerical simulation is presented to see the bifurcation behaviour in the model. By taking the reproduction number as the bifurcation parameter, we find the system undergoes backward bifurcation at $\mathcal{R}_{02} = 1$. Thus, the model has backward bifurcation and have two positive endemic equilibrium when $\mathcal{R}_{02} < 1$ and unique positive endemic equilibrium whenever $\mathcal{R}_{02} > 1$. Stability analysis shows that disease free equilibrium is locally asymptotically stable when $\mathcal{R}_{02} < 1$ and unstable when $\mathcal{R}_{02} > 1$. When $\mathcal{R}_{02} < 1$, lower endemic equilibrium in backward bifurcation is locally unstable.

To the graduate students of Florida Atlantic University.

INFECTION AGE STRUCTURED VECTOR BORNE DISEASE MODEL WITH DIRECT TRANSMISSION.

LIST OF FIGURES

CHAPTER 1

INTRODUCTION AND BACKGROUND

Vectors are blood sucking insects like mosquitoes can transmit infectious diseases between hosts. Vector borne diseases like malaria, dengue fever, West Nile virus, Zika are illnesses caused by vectors in the human population and are a big health issue in the world today and each year 1 billion people gets infected and 1 million people dies from it [42]. Flaviviruses is responsible for all of these infectious diseases [57].

Zika is a vector borne disease and my thesis deals with time- since infection structured models to understand the transmission dynamics of Zika virus (ZIKV). Zika virus was first isolated in the Zika forest in Uganda from rhesus monkey in 1947. Between 1960s to 1980 several human infections were found in Africa and in Asia [2]. The infected individuals had a mild fever like in the case of yellow fever. Zika virus infection were limited to certain area until 2007. The outbreaks of infection in Pacific Islands in 2007 was followed by large outbreak of Zika virus infection in French Polynesia in 2013. Zika virus infection was also reported as an outbreak in Brazil in March of 2015 [27, 28, 29].

It is reported that Zika infection during pregnancy can cause serious birth defects and is associated with other pregnancy problems. Zika virus infection causes mild or no symptoms [14]. Although most Zika virus infections are characterized as mild influenza-like illness, there are evidence revealing that in the outbreak in Brazil, Zika virus infection was found to be connected with Guillain-Barre syndrome and Microcephaly. In Guillain-Barre, body's immune system mistakely attacks part of its peripheral nervous system whereas in Microcephaly, Zika affects the brain, causing swelling of the brain or spinal cord or a blood disorder which can result in bleeding, bruising or slow blood clotting [3, 46, 45]. These unfavorable health situation due to Zika infection is motivating researchers toward understanding the transmission dynamics of the disease. Zika infection is the health challenge to the world. To the date, there is no vaccine, or antiviral drug to prevent or to treat Zika disease [44]. So preventive measures is the only way to prevent the infection, especially to the pregnant women [4, 5].

In addition to vector transmission, ZIKV can be transmitted from person to person by other mode of transmission. A pregnant mother can pass ZIKV to her baby in her fetus. It can possibly be transmitted to babies during breastfeeding but this has not been confirmed [43]. Another way of transmission is blood transfusion. Direct contact is also considered a potential route of transmission among humans, probably during sex intercourse [7, 6, 40]. Zika can be transmitted from men and women to their sexual partner; most common cases involve transmission from symptomatic men to women. As of April 2016, sexual transmission of Zika have been documented in six countries Argentina, Chile, France, Italy, New Zealand and the United States- during the 2015 outbreak [41].

A mathematical model describes a system using mathematical tools. The process of developing mathematical models is called mathematical modeling. Mathematical model can be applied to different system. The principal tool used in mathematical epidemiology is the compartmental model where the total population is partitioned into different compartments and the number of compartments depends upon disease dynamics. Kermack and McKendrick in 1927 introduced probably the first known compartmental model where total the population is divided into a susceptible class, an infectious class, and a removed class [30]. The class of individuals who are healthy but can contract the disease are called susceptible individuals denoted by (S) , the class of individuals who have contracted the disease and are now sick with it, called infected individuals denoted by (I), and the class of individuals who have recovered and and are immune to the disease are called recovered individuals denoted by (R). These classes are not intersecting [30]. Using mathematical tools, infectious diseases models are analyzed to answer the questions like:

- How fast the disease spreads?
- How much of the total population is infected or will be infected?
- Under what conditions will the disease become an endemic in the population?
- Does the disease persist?
- What can be the control measures to eradicate the disease?

1.1 REPRODUCTION NUMBER AND BIFURCATION

The epidemiological model is obtained by splitting the total population into non intersecting compartments. The dynamics of such models is characterized by the reproduction number denoted by $\mathcal{R}_0$, a threshold quantity [36]. Epidemiologically, the reproduction number gives the number of secondary cases one infectious individual will produce in a population consisting only of susceptible individuals during its infectious period. Mathematically, the reproduction number $\mathcal{R}_0$ is determined by the local stability analysis of the disease free equilibrium and plays the role of a threshold value for the dynamics of the system and the disease [36].

When $\mathcal{R}_0$ is greater than one, small number of infected individual in the population will lead to the outbreak of the disease and persist in the population [1]. On the flip side, disease dies out when $\mathcal{R}_0$ is less than one. Thus, the value of reproduction number is important in determining the long time dynamics of disease and for this reason $\mathcal{R}_0 = 1$ is given as threshold value. This leads to bifurcation called as forward bifurcation. Forward bifurcation is where number as well as stability of two equilibrium for the model changes at $\mathcal{R}_0 = 1$. If the variation of parameter changes the qualitative behaviour of the steady states, we call it a bifurcation. By qualitative behaviour, we mean changes in number of steady states and stability of steady states [36, 39].

In general for many mathematical model, $\mathcal{R}_0 < 1$ is necessary and sufficient condition to eliminate disease from the population. However, there are some cases where disease does not die out even though $\mathcal{R}_0 < 1$. In those cases, $\mathcal{R}_0 < 1$ happens to be necessary but not sufficient to eliminate the disease from the population. This leads to other kind of bifurcation called as backward bifurcation. In this case, disease free and endemic equilibrium co-exist whenever $\mathcal{R}_0 < 1$ [8, 9]. In case of backward bifurcation, $\mathcal{R}_0 < 1$ is necessary but not sufficient condition to abolish the disease from the population. Thus, transmission dynamics of disease with backward bifurcation complicates in the control of the disease.

1.2 THESIS OUTLINE AND OBJECTIVES

In this study, we present a mathematical model of ZIKV incorporating both vector and direct transmission where infected individuals are structured by time-since infection. Many mathematical models dealing with the various vector borne disease has been proposed and extensively analyzed [6, 10, 22, 23, 24, 25, 26, 54]. Mathematical models helps us to understand the mechanism behind the spread of the disease and control measures required to stop the disease endemic [10]. Author in [6], suggested that reproduction number is most sensitive to the transmission form human to vectors, the ratio of humans to vectors and the vector mortality and it helps us to conclude that control measures should be taken to reduce mosquito lifespan and the mosquito bite.

The main objectives of the thesis is to do qualitative analysis of the dynamical behaviour of time since infection structured vector-borne disease mathematical model with direct transmission. Here, we form two different mathematical model representing ZIKV and do their dynamical analysis. We have included one additional parameter, disease induced death rate in the first model to from the second model. Our aim is to analyze whether these two models have same or different disease dynamics. We observed forward bifurcation in the first model and the backward bifurcation in the second model. Existence of backward bifurcation shows, in order to control this disease, it is not sufficient to have reproduction number less than unity but necessary. We shall go in details in Chapter 3 and 4.

In Chapter 1, we introduce vector borne disease featuring Zika infection. It includes history on detection of Zika infection, its mode of transmission, severity, and introduction on importance of mathematical research to understand it. Chapter 2 consists of mathematical preliminaries including mathematical theories that have been used throughout the thesis. Chapter 3 introduces epidemiological model for the vector borne disease with direct transmission and its qualitative analysis. In Chapter 4, we do qualitative analysis of the second model which include one extra biological feasible parameter disease induced death rate. In Chapter 5, we discuss the conclusion of the thesis and suggest future direction.

CHAPTER 2

MATHEMATICAL PRELIMINARIES

This chapter provides some mathematical definition, mathematical theories, theorem, lemma that has been used throughout the thesis.

2.1 STABILITY THEORY

Consider a differential equation $x' = F(x)$ for all $x \in \mathbb{R}^n$ and $t \in \mathbb{R}$.

Definition 1. *An equilibrium solution is point x^* in $\mathbb{R}^n$ such that $F(x^*) = 0$ [31].*

An equilibrium point is said to be stable if solution near to equilibrium point remains near to the equilibrium point in future time. Mathematically, it is define as below.

Definition 2. *An equilibrium point x^* is said to be stable if given $\epsilon > 0$, there exist a $\delta > 0$ depending on ϵ such that any solution $x(t)$ satisfies $|x^* - x(t)| < \delta$, whenever $|x^* - x(t_0)| < \epsilon$ and for every $t > t_0$, $t_0 \in \mathbb{R}$ [33].*

Definition 3. *The equilibrium x^* is said to be locally asymptotically stable if it is stable and there exist a constant $\delta > 0$ such that for any solution $x(t)$, if $|x^* - x(t_0)| < \delta$, then*

$$\lim_{t \to \infty} |x(t) - x^*| = 0$$

[33].

Theorem 1. *Let x^* be an equilibrium point of n- dimensional system $x' = F(x)$ and all eigenvalues of the linearlized system at x^* have neagative real parts. The x^* is locally asymptotically stable [31].*

Theorem 2. *(Gronwall's Lemma):[34] Suppose that $f(x)$ and $g(x)$ are continuous real valued functions with $f(x) \geq 0, g(x) \geq 0$ on the interval $[a, b]$.*
If $f(x) \leq c + k \int_a^x g(s)f(s)ds$, where $c, k \geq 0$, then $f(x) \leq ce^{\int_a^x g(s)ds}$.

Corollary 1. *[34] If $c = 0$ in Gronwall's inequality, then $f(x) \leq k \int_a^x g(s)f(s)ds$, implies $f(x) = 0$.*

CHAPTER 3

TIME SINCE INFECTION STRUCTURED VECTOR-BORNE DISEASE MODEL WITH DIRECT TRANSMISSION.

3.1 INTRODUCTION

Vector transmission is the primary source of ZIKV infection and direct transmission is another route. The aim of this chapter is to develop a time since infection structured nonlinear PDE model for the transmission dynamics of vector borne disease with direct transmission in the population, and to see how these two mode of transmission collaboratively contribute in the dynamics of disease in the population. The model to be develop here is an extension work of [6] where the researchers have analyzed ODE Zika model with vector borne and direct transmissions. We assume transmission rate of infection from an infected host to susceptible vector, direct transmission rate of infection from an infected host to a susceptible host, and recovery rate of infected host population varies with the time since infection. We structure the infected class by time and time since infection parameter τ.

3.2 MODEL FORMULATION

In this section, we present time since infection structured vector-host epidemic model with vector and direct transmission. In order to simulate the transmission of the mosquito borne disease, two compartmental models are combined: SI (Susceptible-Infected) model for the vector population and SIR (Susceptible-Infected-Recovered) model for the human population as in [6]. First, we discuss compartments in the host model. Total host population at time t denoted by $N(t)$ is divided into three non intersecting classes: susceptible population $S(t)$, infected host population $I(t)$ and recovered population $R(t)$. Thus,

$$N(t) = S(t) + I(t) + R(t) \quad \text{for all} \quad \text{t} \geq 0 \tag{3.1}$$

Similarly, the total mosquito population at time t denoted by $N_v(t)$ is divided into two non intersecting compartments: susceptible vector population $S_v(t)$ and infected vector population $I_v(t)$. Thus,

$$N_v(t) = S_v(t) + I_v(t) \quad \text{for all} \quad \text{t} \geq 0 \tag{3.2}$$

First we deduce an expression for total number of infected individual $I(t)$ as a function of time t [36]. After an individuals gets infected, time that passes since infection is called as time since infection and we denote time since infection by τ. Let $i(\tau, t)$ denote the density of infected individual with time since infection τ at time t. An infected individual with $\tau = 0$ accounts that the individual is just been infected and $i(0, t)$ is the density of individuals who have just been infected. Then, $i(\tau, t)\Delta\tau$ gives the number of infected individuals with the time since infection in the interval $(\tau, \tau + \Delta\tau)$ at time t. Then the total infection population at time t is the sum of all the infected individual in all infection age classes and is given as in [36] by

$$I(t) = \int_0^\infty i(\tau, t) d\tau. \tag{3.3}$$

However, number of infected individual in the infected class is always changing either by recovery or by natural death. Some leave by natural death whereas some leave the group by recovery. So we assume that the number of infected individual in the group is changing in the time interval $(t, t + \Delta t)$. Whenever disease is prevalent in the population, we assume susceptible, infected and recovered leave the group with the constant rate. Consider individuals leave all three compartments with constant per capita natural death rate μ.

Now we put our attention in forming a partial differential equation that describes the dynamics of infected class as in [36]. The number of infected individuals with the time since infection in the interval $(\tau, \tau + \Delta\tau)$ at time time t is given by $i(\tau, t)\Delta\tau$. We assume that the recovery rate depends on time since infection. Let $\gamma(\tau)$ be the per capita recovery rate. Then the $\mu + \gamma(\tau)$ gives total rate at which individual leaves the infected group due to natural death and being recovered. Thus, the number of infected individual who leaves the group due to natural death and by recovery at time t is given by $(\mu + \gamma(\tau))i(\tau, t)\Delta\tau$. Thus, at time interval $(t, t + \Delta t)$, the number of infected individuals who leave the system due to natural death and being recovered is given by

$$(\mu + \gamma(\tau))\Delta t i(\tau, t)\Delta\tau$$

For this reason, natural death rate and recovery rate brings change in the number of infected individual in the group and so the balanced dynamics caused by these changes in infected class as in [36] is given by

$$i(\tau + \Delta t, t + \Delta t)\Delta\tau - i(\tau, t)\Delta\tau = -\gamma(\tau)\Delta t i(\tau, t)\Delta\tau - \mu\Delta t i(\tau, t)\Delta\tau$$

Dividing by $\Delta\tau\Delta t$, we get,

$$\frac{i(\tau + \Delta t, t + \Delta t) - i(\tau, t)}{\Delta t} = -\left(\gamma(\tau) + \mu\right) i(\tau, t)$$
$$\frac{i(\tau + \Delta t, t + \Delta t) - i(\tau, t + \Delta t) + i(\tau, t + \Delta t) - i(\tau, t)}{\Delta t} = -\left(\gamma(\tau) + \mu\right) i(\tau, t)$$

If the partial derivative of the function $i(\tau, t)$ exist and is continuous, then taking $\Delta t \to 0$, we can rewrite above equation as

$$\frac{\partial i}{\partial \tau} + \frac{\partial i}{\partial t} = -\left(\gamma\left(\tau\right) + \mu\right) i\left(\tau, t\right) \tag{3.4}$$

Boundary condition along the boundary $\tau = 0$ and initial condition is required to complete the partial differential equation above. We are forming a model with two different mode of transmission i.e. vector transmission and direct transmission. We know, $i(0, t)$ is the density of newly infected individual by two mode of transmission at time since infection equal to zero.

In disease modeling, there has been defined a function $\pi(\tau)$ of τ called as probability that an infectious individual survives to the time since infection τ after being infected [36]. Number of infected individuals survived up to the time since infection τ is given by $\pi(\tau)I$. Similarly, number of infected individuals survived up to the time since infection $\tau+\Delta\tau$ is given by $\pi(\tau+\Delta\tau)I$. Then the difference $\pi(\tau+\Delta\tau)I-\pi(\tau)I$ gives the number of infected individuals who have left the infected class in the time since infection $\Delta\tau$. For our model, these infected individuals are leaving the infected class by natural death and those who have recovered from the disease. Thus, number of infected individual leaving the infected class at time since infection $\Delta\tau$ is$(\gamma(\tau)+\mu)\Delta\tau\pi(\tau)I$. This dynamical moment can be written in the form of equation as

$$\pi(\tau+\Delta\tau)I-\pi(\tau)I=-(\gamma(\tau)+\mu)\Delta\tau\pi(\tau)I$$

negative sign represents number of infected individuals moving out of the infected class. Dividing both sides of above equation by $\Delta\tau I$, we get

$$\frac{\pi(\tau+\Delta\tau)-\pi(\tau)}{\Delta\tau}=-(\gamma(\tau)+\mu)\pi(\tau)$$

As $\Delta\tau\to 0$, we get a differential equation for probability that an infectious individual survives to the time since infection τ after being infected given as

$$\frac{d\pi(\tau)}{d\tau}=-(\gamma(\tau)+\mu)\pi(\tau) \tag{3.5}$$

Solving the differential equation (3.5), we get the solution as

$$\pi(\tau)=\pi(0)e^{-\int_0^{\tau}(\gamma(s)+\mu)ds}$$

We assume, at the initial time of infection, probability that an infectious individual surviving is one. That is, $\pi(0)=1$. Then,

$$\pi(\tau)=e^{-\int_0^{\tau}(\gamma(s)+\mu)ds}$$

In chemistry, the law of mass action is the proposition that the rate of a chemical reaction is directly proportional to the product of the activities or concentrations of the reactants [36, 37]. Analogous to it, in diseases modeling, the rate of disease also called as incidence is proportional to the product of I and S in the non constant population. The incidence is called as mass action incidence and is given by βSI where β is transmission rate. Similar to mass action incidence, there is another incidence called as standard incidence, normalized by the total population size and is given by $\beta \frac{SI}{N}$. Standard incidence is used to model the disease where the contact rate doesn't increase as the population size increases like in the case of sexually transmitted disease [36].

Our objective in this chapter is to formulate the model featuring vector transmission with the inclusion of direct transmission. Thus, we have used standard incidence in our model [36, 37, 38]. Newly infected individual produced by vector transmission is given by standard incidence term $\frac{\beta_v SI_v}{N}$ where β_v is transmission rate of infection by the bite of infected mosquito to susceptible individual and $\frac{S}{N}$ is the susceptible fraction of the population. Also the infectious individuals who are infectious for τ unit of times will infect $\frac{\beta_d(\tau)S}{N}$ individuals via direct transmission where $\beta_d(\tau)$ denotes the host direct transmission rate and is assumed to depend on the time since infection. As there are $i(\tau, t)\Delta\tau$ number of infectious individual in the interval $(\tau, \tau + \Delta\tau)$, total number of infectious individuals produced by such infected individuals in the interval $(\tau, \tau + \Delta\tau)$ will be $\frac{\beta_d(\tau)S}{N} i(\tau, t)\Delta\tau$. Summing up all newly infected individual, we get total number of newly infected individuals by the standard incidence term $\frac{S}{N}\int_0^\infty \beta_d(\tau)i(\tau, t)d\tau$. Adding total number of newly infected individuals generated by vector transmission and direct transmission gives the total number of newly infected individuals at time since infection τ equal to zero and is given as

$$i(0.t) = \frac{\beta_v SI_v}{N} + \frac{S}{N}\int_0^\infty \beta_d(\tau)i(\tau, t)d\tau \tag{3.6}$$

Equation (3.6) gives the boundary condition for PDE (3.4).

Next, we see how susceptible compartment of host changes over time. Let Λ be the recruitment rate via birth of susceptible population and this increases the number of susceptible individual. Susceptible individuals gets in contact with the infectious individuals, becomes infected and moves to the infected class. Thus, $\frac{\beta_v S I_v}{N}$ and $\frac{S}{N}\int_0^\infty \beta_d(\tau) i(\tau,t)d\tau$ number of individuals moves out of susceptible compartment to the infected compartment by vector transmission and direct transmission respectively. Moreover, susceptible individuals also leave the compartment by natural factor (death). Let μ be the host natural death rate. Thus, dynamics in the susceptible compartment is given by following differential equation

$$S' = \Lambda - \frac{\beta_v S I_v}{N} - \frac{S}{N}\int_0^\infty \beta_d(\tau) i(\tau,t)d\tau - \mu S \tag{3.7}$$

Now we look at the dynamics in recovered compartment of the host population. Recovered individuals are individuals who are immune to the infection and do not contribute to the transmission dynamics of the disease. Let $\gamma(\tau)$ be the recovery rate of infected host population. Then total number of infected individuals who have recovered from the disease at time since infection τ is given by $\int_0^\infty \gamma(\tau) i(\tau,t)d\tau$ and these individuals are added to the recovered compartment. Individuals exit the compartment only through natural death. Thus, the dynamics in the recovered compartment is given by

$$R' = \int_0^\infty \gamma(\tau) i(\tau,t)d\tau - \mu R \tag{3.8}$$

Next, we see the dynamics of vector population. Susceptible vector population are recruited at the recruiting rate Λ_v and leave the compartment by natural death rate of vector population given by μ_v. The process of infection of susceptible vector population is given by term $\frac{S_v}{N}\int_0^\infty \beta(\tau) i(\tau,t)d\tau$ where $\beta(\tau)$ is transmission rate of infection from an infected host to susceptible vector class and this is the number of vectors moving out of the susceptible compartment after they get infected. Then the

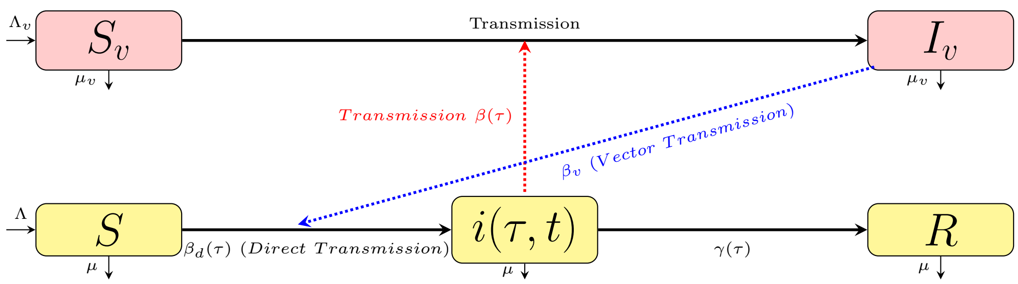

Figure 3.1: **Schematic diagram of the vector borne disease transmission dynamic**. The bold pointed solid lines represent transfer of vectors/hosts to another compartment due to infection. Red dotted line is the transmission rate of infection from an infected host to susceptible vector class. Blue dotted line is the transmission rate of infection from an infected vector to susceptible host. The shorter pointed solid lines represent recruitment, deaths (natural and disease related) of vectors/hosts.

dynamics of susceptible vector compartment is given by

$$S_v' = \Lambda_v - \frac{S_v}{N}\int_0^\infty \beta\left(\tau\right) i\left(\tau,t\right) d\tau - \mu_v S_v \tag{3.9}$$

Susceptible vector after infection moves to the infected compartment and thus the inflow of number of infected vector in the compartment is given by $\frac{S_v}{N}\int_0^\infty \beta(\tau)i(\tau,t)d\tau$. Thus the dynamics of infected compartment is given by

$$I_v' = \frac{S_v}{N}\int_0^\infty \beta(\tau)i(\tau,t)d\tau - \mu_v I_v \tag{3.10}$$

Vectors do not get ill from the infection and they remain infected and they transmit the disease thorough their life span[36, 51]. This is the reason behind not including the recovered class for the vector case.

Based on the above formation, writing together (3.4), (3.6),(3.7), (3.8), (3.9) and (3.10) gives the following time since structured model for the transmission dynamics of vector-borne disease with direct transmission.

$$
\begin{aligned}
S_v' &= \Lambda_v - \frac{S_v}{N}\int_0^\infty \beta\left(\tau\right) i\left(\tau, t\right) d\tau - \mu_v S_v, \\
I_v' &= \frac{S_v}{N}\int_0^\infty \beta(\tau) i(\tau, t) d\tau - \mu_v I_v, \\
S' &= \Lambda - \frac{\beta_v S I_v}{N} - \frac{S}{N}\int_0^\infty \beta_d(\tau) i(\tau, t) d\tau - \mu S, \\
\frac{\partial i}{\partial t} + \frac{\partial i}{\partial \tau} &= -\left(\gamma\left(\tau\right) + \mu\right) i\left(\tau, t\right), \\
i(0, t) &= \frac{\beta_v S I_v}{N} + \frac{S}{N}\int_0^\infty \beta_d(\tau) i(\tau, t) d\tau, \\
R' &= \int_0^\infty \gamma(\tau) i(\tau, t) d\tau - \mu R.
\end{aligned}
\tag{3.11}
$$

with initials conditions $S_v(0) = S_{v0}, I_v(0) = I_{v0}, S(0) = S_0, i(\tau, 0) = i_0(\tau)$ and $R(0) = R_0$. We make following assumptions for all parameters in the model and use it through out the thesis.

- Parameters $\mu, \mu_v, \Lambda, \Lambda_v, \beta_v$ are constants and $\mu, \mu_v, \Lambda, \Lambda_v, \beta_v > 0$
- Parameters $\beta(\tau), \beta_d(\tau), \gamma(\tau) \geq 0$ for all $\tau \geq 0$.
- $\beta(\tau), \beta_d(\tau), \gamma(\tau) \in L^1_+(0, \infty)$ for all $\tau \geq 0$
- $\beta(\tau) \leq \bar{\beta}, \gamma(\tau) \leq \bar{\gamma}$ and $\beta_d(\tau) \leq \bar{\beta}_d$

  where $\bar{\beta} = \sup_{\tau\in[0,\infty)} \beta(\tau), \bar{\gamma} = \sup_{\tau\in[0,\infty)} \gamma(\tau)$ and $\bar{\beta}_d = \sup_{\tau\in[0,\infty)} \beta_d(\tau)$

Model will be analyzed in a biologically-feasible region. Define the feasible region

$$
\mathrm{X}_+ = \mathbb{R}_+ \times \mathbb{R}_+ \times \mathbb{R}_+ \times L^1_+(0, \infty) \times \mathbb{R}_+
$$

where $L^1_+(0, \infty) = \{f : (0, \infty) \to \mathbb{R}_+$ such that $\int_0^\infty |f(x)| dx < \infty\}$. Note that X_+ is the non negative cone of the Banach space $\mathrm{X} = \mathbb{R} \times \mathbb{R} \times \mathbb{R} \times L^1(0, \infty) \times \mathbb{R}$ and its corresponding norm is given as $\|x\| = |x_1| + |x_2| + |x_3| + \int_0^\infty |x_4(\tau)| d\tau + |x_5|$ for all $\mathrm{x} \in \mathrm{X}_+$. Furthermore, adding first and second equations of model, we have

$$
\frac{d}{dt}\left(S_v\left(t\right) + I_v\left(t\right)\right) = \Lambda_v - \mu_v\big(S_v(t) + I_v(t)\big) \tag{3.12}
$$

And this gives,

$$\lim_{t\to\infty}\left(S_v\left(t\right)+I_v\left(t\right)\right)=\frac{\Lambda_v}{\mu_v}$$

Using integrating factor method, we solve equation (3.12) and we get

$$N_v(t)=N_v(0)e^{-\mu_v t}+\frac{\Lambda_v}{\mu_v}(1-e^{-\mu_v t}) \tag{3.13}$$

Integrating with respect to τ the PDE in system, we obtain

$$i(\tau,t)\Big|_0^\infty+I'=-\int_0^\infty\gamma(\tau)i(\tau,t)d\tau-\mu I(t)$$

we assume $\lim_{\tau\to\infty}i(\tau,t)=0$. That is infected individuals recover ultimately. Then the above equality leads to

$$I'(t)=i(0,t)-\int_0^\infty\gamma(\tau)i(\tau,t)d\tau-\mu I(t)$$

Adding 3^{rd}, 5^{th} equations of (3.11) with above equation, we get

$$\frac{d}{dt}\left(S(t)+\int_0^\infty i(\tau,t)d\tau+R(t)\right)=\Lambda-\mu\left(S(t)+\int_0^\infty i(\tau,t)d\tau+R(t)\right) \tag{3.14}$$

And this gives us,

$$\lim_{t\to\infty}\left(S(t)+\int_0^\infty i(\tau,t)d\tau+R(t)\right)=\frac{\Lambda}{\mu}$$

Using integrating factor method, we solve equation (3.14) and we get

$$N(t)=N(0)e^{-\mu t}+\frac{\Lambda}{\mu}(1-e^{-\mu t}) \tag{3.15}$$

Therefore, following set Ω is positively invariant for the model (3.11),

$$\Omega=\left\{(S_v(t),I_v(t),S(t),i(\tau,t),R(t))\in \mathrm{X}_+ : S_v(t)+I_v(t)\le\frac{\Lambda_v}{\mu_v}, S(t)+\int_0^\infty i(\tau,t)d\tau+R(t)\le\frac{\Lambda}{\mu}\right\}$$

In (4.4), we observe that $N(t)\le\dfrac{\Lambda}{\mu}$ for all t whenever $N(0)\le\dfrac{\Lambda}{\mu}$ and in (3.13), we see that $N_v(t)\le\dfrac{\Lambda_v}{\mu_v}$ for all t whenever $N_v(0)\le\dfrac{\Lambda_v}{\mu_v}$

We proved all solutions $(S_v(t),I_v(t),S(t),i(\tau,t),R(t))$ of the model having value of state variable initially in Ω will remain in $\Omega\ \forall\ t\ge 0$ and thus Ω is the positive invariant set for the model. This enables us to have a following theorem

Theorem 3. *The set*

$$\Omega = \left\{ (S_v(t), I_v(t), S(t), i(\tau,t), R(t)) \in X_+ : S_v(t) + I_v(t) \le \frac{\Lambda_v}{\mu_v}, S(t) + \int_0^\infty i(\tau,t)d\tau + R(t) \le \frac{\Lambda}{\mu} \right\}$$

is the positive invariant set for the model (3.11).

Table 3.1: Definition of the variables in the model (3.11)

Variable	Meaning
$S_v(t)$	The number of susceptible vectors at time t
$I_v(t)$	The number of infected vectors at time t
$S(t)$	The number of susceptible individuals at time t
$i(\tau,t)$	Density of the infected individuals with infection age τ at time t
$R(t)$	The number of recovered individuals at time t

Table 3.2: Definition of the parameters in the model (3.11)

Parameter	Meaning
Λ_v	Susceptible vector recruitment rate
μ_v	Vector natural death rate
Λ	Host recruitment rate
μ	Host natural death rate
$\beta(\tau)$	Transmission rate of infection from an infected host to susceptible vector class
β_v	Transmission rate of infection from an infected mosquito to susceptible host
$\beta_d(\tau)$	Direct transmission rate of infection from an infected host to a susceptible host
$\gamma(\tau)$	Recovery rate of infected host population

First we solve the PDE in (3.11) using methods of characteristics. Characteristics equation is given by $\dfrac{dt}{ds} = 1$ and $\dfrac{d\tau}{ds} = 1$ which gives $\dfrac{dt}{d\tau} = 1$. Solving $\dfrac{dt}{d\tau} = 1$ gives

$t = \tau + C$ where C is an arbitrary constant. This implies that the characteristics are lines of slope 1, called characteristic lines of the PDE. The practical significance of the characteristic lines is the value of $i(\tau, t)$ along the characteristic lines models one cohort of individuals and the value of $i(\tau, t)$ is determined by previous values of $i(\tau, t)$ along the characteristics.

Consider (τ_0, t_0) be a fixed point in the first quadrant. Then $u(s) = i(\tau_0 + s, t_0 + s)$ gives the value of i along the characteristics lines, then the derivative along the characteristic lines is given by

$$\frac{du}{ds} = \frac{\partial i}{\partial \tau} + \frac{\partial i}{\partial t}$$

Let $\hat{\mu}(s) = \gamma(\tau_0 + s) + \mu$. The PDE in the model can be written as a following ODE along the characteristic lines.

$$\frac{du}{ds} = -\hat{\mu}(s)u(s)$$

Solving the ODE above gives

$$u(s) = u(0)e^{-\int_0^{\infty} \hat{\mu}(\sigma)d\sigma} \tag{3.16}$$

Next, we write this solution in terms of i and two time variables τ and t under following two cases:

- When $\tau_0 \geq t_0$ Then solution (3.16) in the original variable is

$$i(\tau_0 + s, t_0 + s) = i(\tau_0, t_0)e^{-\int_0^{s} \big(\gamma(\tau_0 + \sigma) + \mu\big)d\sigma} \tag{3.17}$$

  Since $\tau_0 \geq t_0$, we must take $t_0 = 0$.

  This implies $s = t$ and $\tau_0 = \tau - s = \tau - t$. The choice of s, τ_0 and t is made such a way that $\tau_0 + s = \tau$ and $t_0 + s = t$.

Then we obtain solution in the case $\tau_0 \geq t_0$ i.e. when $\tau \geq t$ as

$$\begin{aligned} i(\tau,t) &= i(\tau-t,0)e^{-\int_0^t (\gamma(\sigma)+\mu)d\sigma} \\ &= i(\tau-t,0)e^{-\int_{\tau-t}^{\tau} (\gamma(\sigma)+\mu)d\sigma} \\ &= i_0(\tau-t)\frac{\pi(\tau)}{\pi(\tau-t)} \end{aligned}$$

Thus, $i(\tau,t) = i_0(\tau-t)\dfrac{\pi(\tau)}{\pi(\tau-t)} \qquad \tau \geq t$

- When $\tau_0 < t_0$

  Now we set $\tau_0 = 0$, then $s = \tau$ and $t_0 = t - \tau$. Substituting $\tau_0 < t_0$, we get $\tau < t$. Substituting in (3.17), we get

$$i(\tau,t) = i(0,t-\tau)e^{-\int_0^\tau (\gamma(\sigma)+\mu)d\sigma}$$

$$i(\tau,t) = i(0,t-\tau)\pi(\tau) \qquad \text{for} \tau < t \tag{3.18}$$

Thus, the solution of PDE is

$$i(\tau,t) = \begin{cases} i(0,t-\tau)\pi(\tau) & t > \tau \\ i(\tau-t,0)\dfrac{\pi(\tau)}{\pi(\tau-t)} & t < \tau \end{cases} \tag{3.19}$$

3.3 WELL POSEDNESS OF THE MODEL

Here, we show well-posedness of the solution for the system. In other words, we show existence of unique non-negative solution of the system for every non-negative initial conditions.

We shall prove the existence and uniqueness of the solution for the model using the technique in [56]. In this method, with the help of iterative method we create a sequence and later show the sequence converges to a limit of the sequence proving the existence of the solution.

$$
\begin{aligned}
S_v' + \alpha S_v &= \Lambda_v - \frac{S_v}{N}\int_0^\infty \beta\left(\tau\right) i\left(\tau,t\right) d\tau + \alpha S_v - \mu_v S_v,\\
I_v' + \alpha I_v &= \frac{S_v}{N}\int_0^\infty \beta(\tau) i(\tau,t) d\tau + \alpha I_v - \mu_v I_v,\\
S' + \alpha S &= \Lambda - \frac{\beta_v S I_v}{N} - \frac{S}{N}\int_0^\infty \beta_d(\tau) i(\tau,t) d\tau + \alpha S - \mu S,\\
\frac{\partial i}{\partial t} + \frac{\partial i}{\partial \tau} + \alpha i(\tau,t) &= -\left(\gamma\left(\tau\right)+\mu\right) i\left(\tau,t\right) + \alpha i(\tau,t),\\
i(0,t) &= \frac{\beta_v S I_v}{N} + \frac{S}{N}\int_0^\infty \beta_d(\tau) i(\tau,t) d\tau,\\
R' + \alpha R &= \int_0^\infty \gamma(\tau) i(\tau,t) d\tau + \alpha R - \mu R.
\end{aligned}
\tag{3.20}
$$

(3.20) is the equivalent representation of (3.11) where α is to be determined. Solving differential equations above, we get the following,

$$
\begin{aligned}
S_v(t) &= S_v(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\Lambda_v + \big(\alpha - \mu_v - \frac{1}{N}\int_0^\infty \beta(\tau) i(\tau,\zeta) d\tau\big) S_v\big) d\zeta\\
I_v(t) &= I_v(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\frac{S_v}{N}\int_0^\infty \beta(\tau) i(\tau,\zeta) d\tau + (\alpha-\mu_v) I_v\big) d\zeta\\
S(t) &= S(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\Lambda + \big(\alpha - \mu - \frac{\beta_v I_v}{N} - \frac{1}{N}\int_0^\infty \beta_d(\tau) i(\tau,\zeta) d\tau\big) S\big) d\zeta\\
i(\tau,t) &= \begin{cases} i(0,t-\tau)\pi(\tau) & t > \tau \\ i(\tau-t,0)\dfrac{\pi(\tau)}{\pi(\tau-t)} & t < \tau \end{cases}\\
R(t) &= R(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\int_0^\infty \gamma(\tau) i(\tau,\zeta) d\tau + (\alpha-\mu) R\big) d\zeta
\end{aligned}
\tag{3.21}
$$

Let $x = (S_v(t), I_v(t), S(t), i(\tau,t), R(t)) \in X_+$ where $X_+ = \mathbb{R}^3_+ \times L^1_+(0,\infty) \times \mathbb{R}_+$. To prove the existence and uniqueness of solution, we define our state solution space as $\Omega_1 = \big\{x \in X_+ | N(t) \geq \epsilon_1 > 0, N(t) \leq \dfrac{\Lambda}{\mu}, N_v \leq \dfrac{\Lambda_v}{\mu_v}\big\}$. Now we define a mapping $\mathcal{F} : \Omega_1 \to \Omega_1$ as $\mathcal{F}(x) = \big(\mathcal{F}_1(x), \mathcal{F}_2(x), \mathcal{F}_3(x), \mathcal{F}_4(x), \mathcal{F}_5(x)\big)$.

First we show $\mathcal{F}$ maps Ω_1 into Ω_1.

As (3.20) is the equivalent representation of (3.11) so solution to (3.21) is the solution to (3.11). This implies condition $N(t) \leq \dfrac{\Lambda}{\mu}$ and $N_v \leq \dfrac{\Lambda_v}{\mu_v}$ is true. Hence, it is enough to show the condition $N(t) \geq \epsilon_1 > 0$.

$$
\begin{aligned}
N(t) &= \mathcal{F}_3(x) + \mathcal{F}_4(x) + \mathcal{F}_5(x) \\
&\geq S(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)} \big[\Lambda + \big(\alpha - \mu - \frac{\beta_v I_v}{N} - \frac{1}{N}\int_0^\infty \beta_d(\tau) i(\tau,\zeta) d\tau\big) S\big] d\zeta \\
&\geq S(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)} \Lambda d\zeta \\
&= S(0)e^{-\alpha t} + \Lambda \frac{1}{\alpha}\big(1 - e^{-\alpha t}\big) \\
&> \min\big(S(0), \frac{\Lambda}{\alpha}\big) \\
&\geq \epsilon_1 \\
&> 0
\end{aligned}
$$

Hence, $\mathcal{F}$ maps Ω_1 into Ω_1.

We required to have following for the positive solution.

$\alpha > \mu_v + \bar{\beta}$

since

$$
\begin{aligned}
\alpha - \mu_v - \frac{1}{N}\int_0^\infty \beta(\tau) i(\tau,\zeta) d\tau &> \alpha - \mu_v - \frac{\bar{\beta}}{N}\int_0^\infty i(\tau,\zeta) d\tau \\
&> \alpha - \mu_v - \bar{\beta} \qquad \Big(\text{since } \frac{\int_0^\infty i(\tau,\zeta)d\tau}{N} \leq 1\Big)
\end{aligned}
$$

and $\alpha > \mu + \beta_v \dfrac{\Lambda_v}{\mu_v}\dfrac{1}{\epsilon_1} + \bar{\beta}_d$

since

$$
\begin{aligned}
\alpha - \mu - \frac{\beta_v I_v}{N} - \frac{1}{N}\int_0^\infty \beta_d(\tau) i(\tau,\zeta) d\tau &\geq \alpha - \mu - \frac{\beta_v I_v}{N} - \bar{\beta}_d \frac{1}{N}\int_0^\infty i(\tau,\zeta) d\tau \\
&\geq \alpha - \mu - \beta_v \frac{1}{N}\frac{\Lambda_v}{\mu_v} - \bar{\beta}_d \qquad \Big(\text{since } I_v \leq \frac{\Lambda_v}{\mu_v}\Big) \\
&\geq \alpha - \mu - \beta_v \frac{\Lambda_v}{\mu_v}\frac{1}{\epsilon_1} - \bar{\beta}_d
\end{aligned}
$$

Now we choose $\alpha \geq \max\{\mu_v + \bar{\beta}, \mu + \beta_v \dfrac{\Lambda_v}{\mu_v}\dfrac{1}{\epsilon_1} + \bar{\beta}_d\}$.

Next, we show existence of unique fixed point for $\mathcal{F}$. We develop a Cauchy Sequence and for this we develop a iterative sequence using a iterative method [32, 56, 59]. In this method, we choose an arbitrary $x^{(0)}$ in a given set Ω_1, and obtain iteratively a sequence with the help of relation below

$$x^{(n+1)} = \mathcal{F}(x^{(n)}) = \big(\mathcal{F}_1(x^{(n)}), \mathcal{F}_2(x^{(n)}), \mathcal{F}_3(x^{(n)}), \mathcal{F}_4(x^{(n)}), \mathcal{F}_5(x^{(n)})\big)$$

where $x^{n+1} = \big(S_v^{n+1}(t), I_v^{n+1}(t), S^{n+1}(t), i^{n+1}(\tau,t), R^{n+1}(t)\big)$ and

$$\begin{aligned}
S_v^{(n+1)}(t) &= S_v(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\Lambda_v + \big(\alpha - \mu_v - \frac{1}{N^{(n)}}\int_0^\infty \beta(\tau) i^{(n)}(\tau,\zeta)d\tau\big)S_v^{(n)}\big)d\zeta \\
I_v^{(n+1)}(t) &= I_v(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau) i^{(n)}(\tau,\zeta)d\tau + (\alpha-\mu_v)I_v^{(n)}\big)d\zeta \\
S^{(n+1)}(t) &= S(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\Lambda + \big(\alpha - \mu - \frac{\beta_v I_v^{(n)}}{N^{(n)}} - \frac{1}{N^n}\int_0^\infty \beta_d(\tau) i^{(n)}(\tau,\zeta)d\tau\big)S^{(n)}\big)d\zeta \\
i^{(n+1)}(\tau,t) &= \begin{cases} i^{(n)}(0, t-\tau)\pi(\tau) & t > \tau \\ i(\tau - t, 0)\dfrac{\pi(\tau)}{\pi(\tau - t)} & t < \tau \end{cases} \\
R^{(n+1)}(t) &= R(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\int_0^\infty \gamma(\tau) i^{(n)}(\tau,\zeta)d\tau + (\alpha-\mu)R^{(n)}\big)d\zeta
\end{aligned} \tag{3.22}$$

Define

$$\begin{aligned}
\mathcal{H}_1^{(n)} &= \big|S_v^{(n+1)} - S_v^{(n)}\big| \\
\mathcal{H}_2^{(n)} &= \big|I_v^{(n+1)} - I_v^{(n)}\big| \\
\mathcal{H}_3^{(n)} &= \big|S^{(n+1)} - S^{(n)}\big| \\
\mathcal{H}_4^{(n)} &= \int_0^\infty \big|i^{(n+1)}(\tau,t) - i^{(n)}(\tau,t)\big|d\tau \\
\mathcal{H}_5^{(n)} &= \big|R^{(n+1)} - R^{(n)}\big|
\end{aligned} \tag{3.23}$$

Call $\mathcal{H}^{(n)}(t) = \mathcal{H}_1^{(n)}(t) + \mathcal{H}_2^{(n)}(t) + \mathcal{H}_3^{(n)}(t) + \mathcal{H}_4^{(n)}(t) + \mathcal{H}_5^{(n)}(t)$

In order to develop the sequence $\{x^{(n)}\}$, we set $x^{(0)} \in \Omega_1$ such that $x^{(0)} = 0$.

That is $x^0 = \big(S_v^{(0)}, I_v^{(0)}, S^{(0)}, i^{(0)}(\tau,t)\ R^{(0)}\big) = (0,0,0,0,0)$. Then for $n = 1$ gives,

$$S_v^{(1)} = S_v(0)e^{-\alpha t} + \frac{\Lambda_v}{\alpha}(1 - e^{-\alpha t})$$

$$I_v^{(1)} = I_v(0)e^{-\alpha t}$$

$$S^{(1)} = S(0)e^{-\alpha t} + \frac{\Lambda}{\alpha}(1 - e^{-\alpha t})$$

$$i^{(1)}(\tau, t) = \begin{cases} 0 & t > \tau \\ i(\tau - t, 0)\dfrac{\pi(\tau)}{\pi(\tau - t)} & t < \tau \end{cases}$$

$$R^{(1)} = R(0)e^{-\alpha t}$$

First we compute each of $\mathcal{H}_i^n$, $i = 1, 2, 3, 4, 5$ for $\underline{n = 0}$

$$\mathcal{H}_1^{(0)} = \left|S_v^{(1)} - S_v^{(0)}\right| = \left|S_v(0)e^{-\alpha t} + \frac{\Lambda_v}{\alpha}(1 - e^{-\alpha t})\right| = S_v(0)e^{-\alpha t} + \frac{\Lambda_v}{\alpha}(1 - e^{-\alpha t}) \leq \max(S_v(0), \frac{\Lambda_v}{\alpha})$$

$$\mathcal{H}_2^{(0)} = \left|I_v^{(1)} - I_v^{(0)}\right| = I_v^{(1)} = I_v(0)e^{-\alpha t} \leq I_v(0)$$

$$\mathcal{H}_3^{(0)} = \left|S^{(1)} - S^{(0)}\right| = S(0)e^{-\alpha t} + \frac{\Lambda}{\alpha}(1 - e^{-\alpha t}) \leq \max(S(0), \frac{\Lambda}{\alpha})$$

$$\begin{aligned}
\mathcal{H}_4^{(0)} &= \int_0^\infty \left|i^{(1)}(\tau, t) - i^{(0)}(\tau, t)\right| d\tau \\
&= \int_t^\infty \frac{\pi(\tau)}{\pi(\tau - t)} i(\tau - t, 0) d\tau \\
&\leq \int_t^\infty i(\tau - t, 0) d\tau \quad \text{since} \quad \frac{\pi(\tau)}{\pi(\tau - t)} < 1 \\
&\leq \int_0^\infty i(\tau, 0) d\tau
\end{aligned}$$

$$\mathcal{H}_5^{(0)} = \left|R^{(1)} - R^{(0)}\right| = R^{(1)}(t) = R(0)e^{-\alpha t} \leq R(0)$$

Then,

$$H^{(0)}(t) \leq \max(S_v(0), \frac{\Lambda_v}{\alpha}) + I_v(0) + \max(S(0), \frac{\Lambda}{\alpha}) + \int_0^\infty i(\tau, 0) d\tau + R(0)$$

Thus, we have $H^{(0)}(t) \leq K$
where $K = \max(S_v(0), \frac{\Lambda_v}{\alpha}) + I_v(0) + \max(S(0), \frac{\Lambda}{\alpha}) + \int_0^\infty i(\tau, 0) d\tau + R(0)$

Now, we compute each of $\mathcal{H}_i^n$, $i = 1, 2, 3, 4, 5$ for $n = 1$

$$
\begin{aligned}
\mathcal{H}_1^{(1)}(t) &= \left|S_v^{(2)} - S_v^{(1)}\right| \\
&= \Big|S_v(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\Lambda_v + \big(\alpha - \mu_v - \frac{1}{N^{(1)}}\int_0^\infty \beta(\tau) i^{(1)}(\tau,\zeta)d\tau\big)S_v^{(1)}\big)d\zeta \\
&\quad - S_v(0)e^{-\alpha t} - \frac{\Lambda_v}{\alpha}(1-e^{-\alpha t})\Big| \\
&= \Big|\int_0^t e^{-\alpha(t-\zeta)}\big(\big(\alpha - \mu_v - \frac{1}{N^{(1)}}\int_0^\infty \beta(\tau) i^{(1)}(\tau,\zeta)d\tau\big)S_v^{(1)}\big)d\zeta\Big| \\
&\leq \alpha\int_0^t e^{-\alpha(t-\zeta)}S_v^{(1)}d\zeta \quad \text{since } \alpha - \mu_v - \frac{1}{N}\int_0^\infty \beta(\tau)i(\tau,\zeta)d\tau \geq 0 \\
&\leq \max(S_v(0), \frac{\Lambda_v}{\alpha})\alpha\int_0^t e^{-\alpha(t-\zeta)}d\zeta, \quad \Big(\text{since } S_v^{(1)} \leq \max(S_v(0), \frac{\Lambda_v}{\alpha})\Big) \\
&= \max(S_v(0), \frac{\Lambda_v}{\alpha})\alpha\frac{1}{\alpha}\big(1-e^{-\alpha t}\big) \\
&\leq \max(S_v(0), \frac{\Lambda_v}{\alpha})
\end{aligned}
$$

$$
\begin{aligned}
\mathcal{H}_2^{(1)}(t) &= \left|I_v^{(2)} - I_v^{(1)}\right| \\
&= \Big|I_v(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big(\frac{S_v^{(1)}}{N^{(1)}}\int_0^\infty \beta(\tau)i^{(1)}(\tau,\zeta)d\tau + (\alpha-\mu_v)I_v^{(1)}\big)d\zeta - I_v(0)e^{-\alpha t}\Big| \\
&= \Big|\int_0^t e^{-\alpha(t-\zeta)}\big(\frac{S_v^{(1)}}{N^{(1)}}\int_0^\infty \beta(\tau)i^{(1)}(\tau,\zeta)d\tau + (\alpha-\mu_v)I_v^{(1)}\big)d\zeta\Big| \\
&\leq \Big|\int_0^t e^{-\alpha(t-\zeta)}\big(\frac{S_v^{(1)}}{N^{(1)}}\int_0^\infty \beta(\tau)i^{(1)}(\tau,\zeta)d\tau + \alpha I_v^{(1)}\big)d\zeta\Big|, \quad (\text{since } \alpha > \mu_v) \\
&\leq \bar{\beta}\int_0^t e^{-\alpha(t-\zeta)}S_v^{(1)}d\zeta + \alpha\int_0^t e^{-\alpha(t-\zeta)}I_v^{(1)}d\zeta, \qquad \Big(\text{since } \frac{\int_0^\infty i^{(1)}(\tau,\zeta)d\tau}{N^{(1)}} \leq 1\Big) \\
&\leq \bar{\beta}\max(S_v(0), \frac{\Lambda_v}{\alpha})\int_0^t e^{-\alpha(t-\zeta)}d\zeta + \alpha I_v(0)\int_0^t e^{-\alpha(t-\zeta)}d\zeta, \quad \Big(\text{since } S_v^{(1)} \leq \max(S_v(0), \frac{\Lambda_v}{\alpha})\Big) \\
&\leq \bar{\beta}\max(S_v(0), \frac{\Lambda_v}{\alpha})\frac{1}{\alpha}\big(1-e^{-\alpha t}\big) + \alpha I_v(0)\frac{1}{\alpha}\big(1-e^{-\alpha t}\big) \\
&\leq \frac{\bar{\beta}}{\alpha}\max(S_v(0), \frac{\Lambda_v}{\alpha}) + I_v(0)
\end{aligned}
$$

$$
\begin{aligned}
\mathcal{H}_3^{(1)}(t) &= \big|S^{(2)} - S^{(1)}\big| \\
&= \Big|S(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\Big(\Lambda + \big(\alpha - \mu - \frac{\beta_v I_v^{(1)}}{N^{(1)}} - \frac{1}{N^{(1)}}\int_0^\infty \beta_d(\tau) i^{(1)}(\tau,\zeta)d\tau\big)S^{(1)}\Big)d\zeta \\
&\quad - S(0)e^{-\alpha t} - \frac{\Lambda}{\alpha}(1-e^{-\alpha t})\Big| \\
&= \Big|\int_0^t e^{-\alpha(t-\zeta)}\Big(\Lambda + \big(\alpha - \mu - \frac{\beta_v I_v^{(1)}}{N^{(1)}} - \frac{1}{N^{(1)}}\int_0^\infty \beta_d(\tau) i^{(1)}(\tau,\zeta)d\tau\big)S^{(1)}\Big)d\zeta - \frac{\Lambda}{\alpha}(1-e^{-\alpha t})\Big| \\
&= \Big|\frac{\Lambda}{\alpha}(1-e^{-\alpha t}) + \int_0^t e^{-\alpha(t-\zeta)}\big(\alpha - \mu - \frac{\beta_v I_v^{(1)}}{N^{(1)}} - \frac{1}{N^{(1)}}\int_0^\infty \beta_d(\tau) i^{(1)}(\tau,\zeta)d\tau\big)S^{(1)}d\zeta \\
&\quad - \frac{\Lambda}{\alpha}(1-e^{-\alpha t})\Big| \\
&= \Big|\int_0^t e^{-\alpha(t-\zeta)}\big(\alpha - \mu - \frac{\beta_v I_v^{(1)}}{N^{(1)}} - \frac{1}{N^{(1)}}\int_0^\infty \beta_d(\tau) i^{(1)}(\tau,\zeta)d\tau\big)S^{(1)}d\zeta\Big| \\
&\leq \alpha\int_0^t e^{-\alpha(t-\zeta)}S^{(1)}d\zeta \quad \text{since } \alpha - \mu - \frac{\beta_v I_v}{N} - \frac{1}{N}\int_0^\infty \beta_d(\tau) i(\tau,\zeta)d\tau \geq 0 \\
&\leq \max(S(0),\frac{\Lambda}{\alpha})\alpha\int_0^t e^{-\alpha(t-\zeta)}d\zeta \qquad \Big(\text{since } S^{(1)} \leq \max(S(0),\frac{\Lambda}{\alpha})\Big) \\
&= \max(S(0),\frac{\Lambda}{\alpha})\alpha\frac{1}{\alpha}\big(1-e^{-\alpha t}\big) \\
&= \max(S(0),\frac{\Lambda}{\alpha}) \\
\mathcal{H}_4^{(1)}(t) &= \int_0^\infty \big|i^{(2)}(\tau,t) - i^{(1)}(\tau,t)\big|d\tau \\
&= \Big|\int_0^t \pi(\tau)i^{(1)}(0,t-\tau)d\tau + \int_t^\infty \frac{\pi(\tau)}{\pi(\tau-t)}i(\tau-t,0)d\tau - \int_t^\infty \frac{\pi(\tau)}{\pi(\tau-t)}i(\tau-t,0)d\tau\Big| \\
&= \Big|\int_0^t \pi(\tau)i^{(1)}(0,t-\tau)d\tau\Big| \\
&= \int_0^t \pi(\zeta)\frac{\beta_v S^{(1)}(t-\zeta)I_v^{(1)}(t-\zeta)}{N^{(1)}(t-\zeta)}d\zeta + \int_0^t \pi(\zeta)\frac{S^{(1)}(t-\zeta)}{N^{(1)}(t-\zeta)}\int_0^\infty \beta_d(\tau)i^{(1)}(\tau,t-\zeta)d\tau d\zeta \\
&\quad \Big(\text{since } \frac{S^{(1)}(t-\zeta)}{N^{(1)}(t-\zeta)} \leq 1 \text{ and } e^{-\mu\zeta} > \pi(\zeta)\Big) \\
&\leq \beta_v\int_0^t e^{-\mu\zeta}I_v^{(1)}(t-\zeta)d\zeta + \bar{\beta}_d\int_0^t e^{-\mu\zeta}\big(\int_0^\infty i^{(1)}(\tau,t-\zeta)d\tau\big)d\zeta \\
&\leq \beta_v I_v(0)\int_0^t e^{-\mu\zeta}d\zeta + \bar{\beta}_d\int_0^t e^{-\mu\zeta}d\zeta\int_0^\infty i(\tau,0)d\tau \\
&\leq \frac{\beta_v I_v(0)}{\mu} + \frac{\bar{\beta}_d}{\mu}\int_0^\infty i(\tau,0)d\tau
\end{aligned}
$$

$$
\begin{aligned}
\mathcal{H}_5^{(1)}(t) &= \left|R^{(2)} - R^{(1)}\right| \\
&= \Big|R(0)e^{(-\alpha t)} + \int_0^t e^{-\alpha(t-\zeta)}\Big(\int_0^\infty \gamma(\tau)i^{(1)}(\tau,\zeta)d\tau + \alpha R^{(1)}\Big)d\zeta - R(0)e^{(-\alpha t)}\Big| \\
&= \Big|\int_0^t e^{-\alpha(t-\zeta)}\Big(\int_0^\infty \gamma(\tau)i^{(1)}(\tau,\zeta)d\tau + \alpha R^{(1)}\Big)d\zeta\Big| \\
&\le \bar{\gamma}\int_0^t e^{-\alpha(t-\zeta)}\big(\int_0^\infty i^{(1)}(\tau,\zeta)d\tau\big)d\zeta + \int_0^t e^{-\alpha(t-\zeta)}\alpha R^{(1)}d\zeta \\
&\le \bar{\gamma}\int_0^t e^{-\alpha(t-\zeta)}\big(\int_\zeta^\infty i(\tau-\zeta,0)d\tau\big)d\zeta + R(0)\alpha\frac{1}{\alpha}\big(1-e^{-\alpha t}\big) \quad \text{since } R^{(1)} \le R(0) \\
&\le \bar{\gamma}\int_0^t e^{-\alpha(t-\zeta)}\big(\int_0^\infty i(\tau-\zeta,0)d\tau\big)d\zeta + R(0)\alpha\frac{1}{\alpha}\big(1-e^{-\alpha t}\big) \\
&\quad \text{(By translation property of integral [35])} \\
&\le \bar{\gamma}\int_0^t e^{-\alpha(t-\zeta)}d\zeta\int_0^\infty i(\tau,0)d\tau + R(0)\alpha\frac{1}{\alpha}\big(1-e^{-\alpha t}\big) \\
&\le \bar{\gamma}\frac{1}{\alpha}\big(1-e^{-\alpha t}\big)\int_0^\infty i(\tau,0)d\tau + R(0) \\
&\le \bar{\gamma}\frac{1}{\alpha}\int_0^\infty i(\tau,0)d\tau + R(0)
\end{aligned}
$$

Then,

$$
\begin{aligned}
H^{(1)}(t) &= \mathcal{H}_1^{(1)}(t) + \mathcal{H}_2^{(1)}(t) + \mathcal{H}_3^{(1)}(t) + \mathcal{H}_4^{(1)}(t) + \mathcal{H}_5^{(1)}(t) \\
&\le \max(S_v(0), \frac{\Lambda_v}{\alpha}) + \frac{\bar{\beta}}{\alpha}\max(S_v(0), \frac{\Lambda_v}{\alpha}) + I_v(0) + \max(S(0), \frac{\Lambda}{\alpha}) + \frac{\beta_v I_v(0)}{\gamma(\tau)+\mu} \\
&+ \frac{\bar{\beta}_d}{\gamma(\tau)+\mu}\max(S(0), \frac{\Lambda}{\mu}) + \bar{\gamma}\frac{1}{\alpha}\int_0^\infty i(\tau,0)d\tau + R(0) \\
&\le \hat{L}\Big(\max(S_v(0), \frac{\Lambda_v}{\alpha}) + I_v(0) + \max(S(0), \frac{\Lambda}{\alpha}) + \int_0^\infty i(\tau,0)d\tau + R(0)\Big) \\
&= \hat{\mathcal{L}}K
\end{aligned}
$$

Now we compute each of $\mathcal{H}_i^n$, $i = 1,2,3,4,5$ for n

$$\begin{aligned}
\mathcal{H}_1^{(n)}(\zeta) &= \big|S_v^{(n+1)} - S_v^{(n)}\big| \\
&= \Big|\int_0^t e^{-\alpha(t-\zeta)}\big(\alpha - \mu_v - \frac{1}{N^{(n)}}\int_0^\infty \beta(\tau) i^{(n)}(\tau,\zeta)d\tau\big)S_v^{(n)}d\zeta \\
&\quad - \int_0^t e^{-\alpha(t-\zeta)}\big(\alpha - \mu_v - \frac{1}{N^{(n-1)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau\big)S_v^{(n-1)}d\zeta\Big| \\
&\le \int_0^t e^{-\alpha(t-\zeta)}\Bigg((\alpha-\mu_v)\big|S_v^{(n)} - S_v^{(n-1)}\big| \\
&\quad + \Big|\frac{S_v^{(n-1)}}{N^{(n-1)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau - \frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau) i^{(n)}(\tau,\zeta)d\tau\Big|\Bigg)d\zeta \\
&\le \int_0^t \Bigg((\alpha-\mu_v)\big|S_v^{(n)} - S_v^{(n-1)}\big| \\
&+ \underbrace{\Big|\frac{S_v^{(n-1)}}{N^{(n-1)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau - \frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau) i^{(n)}(\tau,\zeta)d\tau\Big|}_{A}\Bigg)d\zeta
\end{aligned}$$

Note that,

$$\begin{aligned}
A &= \Big|\frac{S_v^{(n-1)}}{N^{(n-1)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau - \frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau) i^{(n)}(\tau,\zeta)d\tau\Big| \\
&= \Big|\frac{S_v^{(n-1)}}{N^{(n-1)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau \quad - \frac{S_v^{(n)}}{N^{(n-1)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau \\
&\quad + \frac{S_v^{(n)}}{N^{(n-1)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau - \frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau \\
&\quad + \frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau - \frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau) i^{(n)}(\tau,\zeta)d\tau\Big| \\
&\le \Big|\frac{\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau}{N^{(n-1)}}\Big||S_v^{(n-1)} - S_v^{(n)}| + |S_v^{(n)}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau||\frac{1}{N^{(n-1)}} - \frac{1}{N^{(n)}}| \\
&+ |\frac{S_v^{(n)}}{N^{(n)}}|\int_0^\infty \beta(\tau)|i^{(n-1)}(\tau,\zeta) - i^{(n)}(\tau,\zeta)|d\tau \\
&\le \bar{\beta}\big|S_v^{(n)} - S_v^{(n-1)}\big| + \Big|\frac{S_v^{(n)}}{N^{(n)}N^{(n-1)}}\int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta)d\tau\Big|\big|N^{(n)} - N^{(n-1)}\big| \\
&\quad + |\bar{\beta}\frac{S_v^{(n)}}{N^{(n)}}|\int_0^\infty |i^{(n-1)}(\tau,\zeta) - i^{(n)}(\tau,\zeta)|d\tau
\end{aligned}$$

$$\leq \bar{\beta}\big|S_v^{(n)} - S_v^{(n-1)}\big| + \bar{\beta}\frac{\Lambda_v}{\mu_v}\frac{1}{\epsilon_1}\big|N^{(n)} - N^{(n-1)}\big| + \bar{\beta}\frac{\Lambda_v}{\mu_v}\frac{1}{\epsilon_1}\int_0^\infty |i^{(n-1)}(\tau,\zeta) - i^{(n)}(\tau,\zeta)|d\tau$$

$$\text{since} \quad (N > \epsilon_1)$$

$$\leq \hat{\kappa}_1\Big(|S_v^{(n)} - S_v^{(n-1)}| + |S^{(n)} - S^{(n-1)}| + \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1`)}(\tau,\zeta)|d\tau + |R^{(n)} - R^{(n-1)}|\Big)$$

Now we plug value of A into the equation of $\mathcal{H}_1^{(n)}(\zeta)$, we get

$$\mathcal{H}_1^{(n)}(t) \leq \int_0^t \Bigg((\alpha - \mu_v)\big|S_v^{(n)} - S_v^{(n-1)}\big| + \underbrace{\Big|\frac{S_v^{(n-1)}}{N^{(n-1)}}\int_0^\infty \beta(\tau)i^{(n-1)}(\tau,\zeta)d\tau - \frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau)i^{(n)}(\tau,\zeta)d\tau\Big|}_{A}\Bigg)d\zeta$$

$$\leq \int_0^t \Bigg((\alpha - \mu_v)\big|S_v^{(n)} - S_v^{(n-1)}\big| + \hat{\kappa}_1\Big(|S_v^{(n)} - S_v^{(n-1)}| + |S^{(n)} - S^{(n-1)}| + \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau + |R^{(n)} - R^{(n-1)}|\Big)\Bigg)d\zeta$$

$$\text{since } (\alpha - \mu_v \geq 0)$$

$$\leq \kappa_1 \int_0^t \Big(|S_v^{(n)} - S_v^{(n-1)}| + |S^{(n)} - S^{(n-1)}| + \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau| + |R^{(n)} - R^{(n-1)}\Big)d\zeta$$

$$\begin{aligned}
\mathcal{H}_2^{(n)}(t) &= \big|I_v^{(n+1)} - I_v^{(n)}\big| \\
&= \Big|I_v(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\Big(\frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau)i^{(n)}(\tau,\zeta)d\tau + (\alpha - \mu_v)I_v^{(n)}\Big)d\zeta \\
&\quad - I_v(0)e^{-\alpha t} - \int_0^t e^{-\alpha(t-\zeta)}\Big(\frac{S_v^{(n-1)}}{N^{(n-1)}}\int_0^\infty \beta(\tau)i^{(n-1)}(\tau,\zeta)d\tau + (\alpha - \mu_v)I_v^{(n-1)}\Big)d\zeta\Big| \\
&= \Big|\int_0^t e^{-\alpha(t-\zeta)}\Big[\frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau)i^{(n)}(\tau,\zeta)d\tau + (\alpha - \mu_v)I_v^{(n)}\Big]d\zeta \\
&\quad - \int_0^t e^{-\alpha(t-\zeta)}\Big[\frac{S_v^{(n-1)}}{N^{(n-1)}}\int_0^\infty \beta(\tau)i^{(n-1)}(\tau,\zeta)d\tau + (\alpha - \mu_v)I_v^{(n-1)}\Big]d\zeta\Big| \\
&\leq \int_0^t e^{-\alpha(t-\zeta)}\Bigg(\underbrace{\Big|\frac{S_v^{(n)}}{N^{(n)}}\int_0^\infty \beta(\tau)i^{(n)}(\tau,\zeta)d\tau - \frac{S_v^{(n-1)}}{N^{(n-1)}}\int_0^\infty \beta(\tau)i^{(n-1)}(\tau,\zeta)d\tau\Big|}_{A} \\
&\quad + (\alpha - \mu_v)|I_v^{(n)} - I_v^{(n-1)}|\Bigg)d\zeta
\end{aligned}$$

Note that A have been computed above. Plugging A back, we get $\mathcal{H}_2^{(n)}(\zeta)$ to be

$$\mathcal{H}_2^{(n)}(t) \leq \int_0^t \Bigg(\hat{\kappa}_1\Big(|S_v^{(n)} - S_v^{(n-1)}| + |S^{(n)} - S^{(n-1)}| + |\int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau|$$

$$+ |R^{(n)} - R^{(n-1)}|\Big) + (\alpha - \mu_v)|I_v^{(n)} - I_v^{(n-1)}|\Bigg)d\zeta$$

$$(\text{since } \ \alpha - \mu_v \geq 0)$$

$$\leq \kappa_2 \int_0^t \Big(|S_v^{(n)} - S_v^{(n-1)}| + |I_v^{(n)} - I_v^{(n-1)}| + |S^{(n)} - S^{(n-1)}| + \int_0^\infty |i^{(n-1)}(\tau,\zeta) - i^{(n)}(\tau,\zeta)|d\tau$$

$$+ |R^{(n)} - R^{(n-1)}|\Big)d\zeta$$

$$\mathcal{H}_3^{(n)}(t) = \big|S^{(n+1)} - S^{(n)}\big|$$

$$= \Big|S(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\big[\Lambda + \big(\alpha - \mu - \frac{\beta_v I_v^{(n)}}{N^{(n)}} - \frac{1}{N^n}\int_0^\infty \beta_d(\tau) i^{(n)}(\tau,\zeta)d\tau\big)S^{(n)}\big]d\zeta$$

$$- S(0)e^{-\alpha t} - \int_0^t e^{-\alpha(t-\zeta)}\big[\Lambda + \big(\alpha - \mu - \frac{\beta_v I_v^{(n-1)}}{N^{(n-1)}}$$

$$- \frac{1}{N^{(n-1)}}\int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\zeta)d\tau\big)S^{(n-1)}\big]d\zeta\Big|$$

$$= \Big|\int_0^t e^{-\alpha(t-\zeta)}\Big(\big(\alpha - \mu - \frac{\beta_v I_v^{(n)}}{N^{(n)}} - \frac{1}{N^{(n)}}\int_0^\infty \beta_d(\tau) i^{(n)}(\tau,\zeta)d\tau\big)S^{(n)}\Big)d\zeta$$

$$- \int_0^t e^{-\alpha(t-\zeta)}\Big(\big(\alpha - \mu - \frac{\beta_v I_v^{(n-1)}}{N^{(n-1)}} - \frac{1}{N^{(n-1)}}\int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\zeta)d\tau\big)S^{(n-1)}\Big)d\zeta$$

$$\leq \Big|\int_0^t e^{-\alpha(t-\zeta)}\Bigg((\alpha - \mu)|S^{(n)} - S^{(n-1)}| + \underbrace{\Big|\beta_v \frac{S^{(n-1)} I_v^{(n-1)}}{N^{(n-1)}} - \beta_v \frac{S^{(n)} I_v^{(n)}}{N^{(n)}}\Big|}_{B}$$

$$+ \underbrace{\Big|\frac{S^{(n-1)}}{N^{(n-1)}}\int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\zeta)d\tau - \frac{S^{(n)}}{N^{(n)}}\int_0^\infty \beta_d(\tau) i^{(n)}(\tau,\zeta)d\tau\Big|}_{C}\Bigg)\Big|d\zeta$$

where

$$
\begin{aligned}
B &= \Big|\beta_v \frac{S^{(n-1)} I_v^{(n-1)}}{N^{(n-1)}} - \beta_v \frac{S^{(n)} I_v^{(n)}}{N^{(n)}}\Big| \\
&= \Big|\beta_v \frac{S^{(n-1)} I_v^{(n-1)}}{N^{(n-1)}} - \beta_v \frac{S^{(n-1)} I_v^{(n)}}{N^{(n-1)}} + \beta_v \frac{S^{(n-1)} I_v^{(n)}}{N^{(n-1)}} - \beta_v \frac{S^{(n-1)} I_v^{(n)}}{N^{(n)}} + \beta_v \frac{S^{(n-1)} I_v^{(n)}}{N^{(n)}} - \beta_v \frac{S^{(n)} I_v^{(n)}}{N^{(n)}}\Big| \\
&\leq \Big|\beta_v \frac{S^{(n-1)}}{N^{(n-1)}}\Big|\Big|I_v^{(n-1)} - I_v^{(n)}\Big| + \Big|\beta_v \frac{S^{(n-1)} I_v^{(n)}}{N^{(n)} N^{(n-1)}}\Big|\Big|N^{(n)} - N^{(n-1)}\Big| + \Big|\beta_v \frac{I_v^{(n)}}{N^{(n)}}\Big|\Big|S^{(n-1)} - S^{(n)}\Big| \\
&\leq \beta_v \Big|I_v^{(n)} - I_v^{(n-1)}\Big| + \beta_v \frac{1}{\epsilon_1}\frac{\Lambda_v}{\mu_v}\Big|N^{(n)} - N^{(n-1)}\Big| + \beta_v \frac{\Lambda_v}{\mu_v}\frac{1}{\epsilon_1}\Big|S^{(n)} - S^{(n-1)}\Big| \\
&\leq \hat{\kappa}_{31}\Big(\Big|I_v^{(n)} - I_v^{(n-1)}\Big| + \Big|S^{(n)} - S^{(n-1)}\Big| + \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)| d\tau + \Big|R^{(n)} - R^{(n-1)}\Big|\Big)
\end{aligned}
$$

Next we compute C as below

$$
\begin{aligned}
C &= \Big|\frac{S^{(n-1)}}{N^{(n-1)}} \int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\zeta) d\tau - \frac{S^{(n)}}{N^{(n)}} \int_0^\infty \beta_d(\tau) i^{(n)}(\tau,\zeta) d\tau\Big|\Big)\Big| d\zeta \\
&= \Big|\frac{S^{(n-1)}}{N^{(n-1)}} \int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta) d\tau \quad - \frac{S^{(n)}}{N^{(n-1)}} \int_0^\infty \beta(\tau) i^{(n-1)}(\tau,\zeta) d\tau \\
&\quad + \frac{S^{(n)}}{N^{(n-1)}} \int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\zeta) d\tau - \frac{S^{(n)}}{N^{(n)}} \int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\zeta) d\tau \\
&\quad + \frac{S^{(n)}}{N^{(n)}} \int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\zeta) d\tau - \frac{S^{(n)}}{N^{(n)}} \int_0^\infty \beta_d(\tau) i^{(n)}(\tau,\zeta) d\tau\Big| d\zeta \\
&\leq \Big|\frac{\int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\zeta) d\tau}{N^{(n-1)}}\Big||S^{(n)} - S^{(n-1)}| + |S^{(n)} \int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\zeta) d\tau|\Big|\frac{1}{N^{(n-1)}} - \frac{1}{N^{(n)}}\Big| \\
&+ \Big|\frac{S^{(n)}}{N^{(n)}}\Big| \int_0^\infty \beta_d(\tau) |i^{(n-1)}(\tau,\zeta) - i^{(n)}(\tau,\zeta)| d\tau \\
&\leq \bar{\beta}_d \Big|S^{(n-1)} - S^{(n)}\Big| + \bar{\beta}_d \Big|\frac{S^{(n)}}{N^{(n)}} \frac{\int_0^\infty i^{(n-1)}(\tau,\zeta) d\tau}{N^{(n-1)}}\Big|\Big|N^{(n)} - N^{(n-1)}\Big| \\
&\quad + |\bar{\beta}_d \frac{S^{(n)}}{N^{(n)}}| \int_0^\infty |i^{(n-1)}(\tau,\zeta) - i^{(n)}(\tau,\zeta)| d\tau \\
&\leq \bar{\beta}_d \Big|S^{(n)} - S^{(n-1)}\Big| + \bar{\beta}_d \Big|N^{(n)} - N^{(n-1)}\Big| + \bar{\beta}_d \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)| d\tau \\
&\qquad\qquad \text{since} \quad (N > \epsilon_1) \\
&\leq \hat{\kappa}_{32}\Big(|S^{(n)} - S^{(n-1)}| + |\int_0^\infty |i^{(n-1)}(\tau,\zeta) - i^{(n)}(\tau,\zeta)| d\tau| + |R^{(n)} - R^{(n-1)}|\Big)
\end{aligned}
$$

Now we plug back value of B and C into the inequality for $\mathcal{H}_3^{(n)}(\zeta)$

$$\mathcal{H}_3^{(n)}(t) \leq \Bigg| \int_0^t \Bigg((\alpha-\mu)|S^{(n)} - S^{(n-1)}| + \underbrace{\Big|\beta_v \frac{S^{(n-1)} I_v^{(n-1)}}{N^{(n-1)}} - \frac{S^{(n)} I_v^{(n)}}{N^{(n)}}\Big|}_{B}$$

$$+ \underbrace{\Big|\frac{S^{(n-1)}}{N^{(n-1)}} \int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,\tau) d\zeta - \frac{S^{(n)}}{N^{(n)}} \int_0^\infty \beta_d(\tau) i^{(n)}(\tau,\zeta) d\tau\Big|}_{C} \Bigg) \Bigg| d\zeta$$

$$\leq \int_0^t \Bigg((\alpha-\mu)\big|S^{(n)} - S^{(n-1)}\big| + \hat{\kappa}_{31}\Big(\big|I_v^{(n)} - I_v^{(n-1)}\big| + \big|S^{(n)} - S^{(n-1)}\big|$$

$$+ \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)| d\tau + \big|R^{(n)} - R^{(n-1)}\big| \Big) + \hat{\kappa}_{32}\Big(|S^{(n)} - S^{(n-1)}|$$

$$+ \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)| d\tau| + |R^{(n)} - R^{(n-1)}| \Big) \Bigg) d\zeta$$

$$(\text{since } \ \alpha - \mu \geq 0)$$

$$\leq \kappa_3 \int_0^t \Big(|I_v^{(n)} - I_v^{(n-1)}| + |S^{(n)} - S^{(n-1)}| + \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)| d\tau|$$

$$+ |R^{(n)} - R^{(n-1)}| \Big) d\zeta$$

$$\mathcal{H}_4^{(n)}(t) = \int_0^\infty \big| i^{(n+1)}(\tau,t) - i^{(n)}(\tau,t) \big| d\tau$$

$$= \int_0^t \pi(\tau) \big| i^{(n)}(0,t-\tau) - i^{(n-1)}(0,t-\tau) \big| d\tau + \int_t^\infty \frac{\pi(\tau)}{\pi(\tau-t)} \big| i(\tau-t,0) - i(\tau-t,0) \big| d\tau$$

$$\leq \int_0^t \big| i^{(n)}(0,t-\tau) - i^{(n-1)}(0,t-\tau) \big| d\tau$$

$$\leq \int_0^t \Bigg(\underbrace{\Big|\beta_v \frac{S^{(n-1)} I_v^{(n-1)}}{N^{(n-1)}} - \beta_v \frac{S^{(n)} I_v^{(n)}}{N^{(n)}}\Big|}_{B} d\zeta$$

$$+ \int_0^t \underbrace{\Big|\frac{S^{(n-1)}}{N^{(n-1)}} \int_0^\infty \beta_d(\tau) i^{(n-1)}(\tau,t-\zeta) d\tau - \frac{S^{(n)}}{N^{(n)}} \int_0^\infty \beta_d(\tau) i^{(n)}(\tau,t-\zeta) d\tau\Big|}_{C} \Bigg) \Bigg| d\zeta$$

C and D are have already been computed prior. Plugging them back in the equation for $\mathcal{H}_4^{(n)}$, expanding and rearranging gives $\mathcal{H}_4^{(n)}$ as below,

$$
\begin{aligned}
\mathcal{H}_4^{(n)}(t) \leq \int_0^t \Bigg(& \hat{\kappa}_{31}\Big(\big|I_v^{(n)} - I_v^{(n-1)}\big| + \big|S^{(n)} - S^{(n-1)}\big| \\
& + \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau + \big|R^{(n)} - R^{(n-1)}\big|\Big) + \hat{\kappa}_{32}\Big(|S^{(n)} - S^{(n-1)}| \\
& + \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau| + |R^{(n)} - R^{(n-1)}|\Big)\Bigg)d\zeta \\
& \leq \kappa_4 \int_0^t \Big(|I_v^{(n)} - I_v^{(n-1)}| + |S^{(n)} - S^{(n-1)}| + \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau \\
& + |R^{(n)} - R^{(n-1)}|\Big)d\zeta
\end{aligned}
$$

$$
\begin{aligned}
\mathcal{H}_5^{(n)}(t) &= \big|R^{(n+1)} - R^{(n)}\big| \\
&= \Big|R(0)e^{-\alpha t} + \int_0^t e^{-\alpha(t-\zeta)}\Big(\int_0^\infty \gamma(\tau)i^{(n)}(\tau,\zeta)d\tau + (\alpha-\mu)R^{(n)}\Big)d\zeta - R(0)e^{-\alpha t} \\
&\quad - \int_0^t e^{-\alpha(t-\zeta)}\Big(\int_0^\infty \gamma(\tau)i^{(n-1)}(\tau,\zeta)d\tau + (\alpha-\mu)R^{(n-1)}\Big)d\zeta\Big| \\
&= \Big|\int_0^t e^{-\alpha(t-\zeta)}\Big(\int_0^\infty \gamma(\tau)i^{(n)}(\tau,\zeta)d\tau + (\alpha-\mu)R^{(n)}\Big)d\zeta \\
&- \quad \int_0^t e^{-\alpha(t-\zeta)}\Big(\int_0^\infty \gamma(\tau)i^{(n-1)}(\tau,\zeta)d\tau + (\alpha-\mu)R^{(n-1)}\Big)d\zeta\Big| \\
&\leq \int_0^t e^{-\alpha(t-\zeta)}\Big(\int_0^\infty \gamma(\tau)|i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau + (\alpha-\mu)|R^{(n)} - R^{(n-1)}|\Big)d\zeta \\
&\leq \int_0^t \Big(\int_0^\infty \gamma(\tau)|i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau + (\alpha-\mu)|R^{(n)} - R^{(n-1)}|\Big)d\zeta \\
&\leq \bar{\gamma}\int_0^t \int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau + (\alpha-\mu)|R^{(n)} - R^{(n-1)}|d\zeta \\
&\leq \kappa_5 \int_0^t \Big(\int_0^\infty |i^{(n)}(\tau,\zeta) - i^{(n-1)}(\tau,\zeta)|d\tau + |R^{(n)} - R^{(n-1)}|\Big)d\zeta
\end{aligned}
$$

Adding up all $\mathcal{H}_1^{(n)}(t), \mathcal{H}_2^{(n)}(t), \mathcal{H}_3^{(n)}(t), \mathcal{H}_4^{(n)}(t)$ and $\mathcal{H}_5^{(n)}(t)$, we get $\mathcal{H}^{(n)}(t)$ as

$$
\begin{aligned}
\mathcal{H}^{(n)}(t) &= \mathcal{H}_1^{(n)}(t) + \mathcal{H}_2^{(n)}(t) + \mathcal{H}_3^{(n)}(t) + \mathcal{H}_4^{(n)}(t) + \mathcal{H}_5^{(n)}(t) \\
&\leq Q\int_0^t \big(\mathcal{H}_1^{(n-1)}(\zeta) + \mathcal{H}_2^{(n-1)}(\zeta) + \mathcal{H}_3^{(n-1)}(\zeta) + \mathcal{H}_4^{(n-1)}(\zeta) + \mathcal{H}_5^{(n-1)}(\zeta)\big)d\zeta \\
&\leq Q\int_0^t \mathcal{H}^{(n-1)}(\zeta)d\zeta
\end{aligned}
$$

Now we use induction method for n. We have $\mathcal{H}^{(1)}(\zeta) \leq \hat{\mathcal{L}}K$. Then

$$\mathcal{H}^{(2)}(t) \leq Q \int_0^t \mathcal{H}^{(1)}(\zeta) d\zeta \leq \hat{\mathcal{L}}KQt$$
$$\mathcal{H}^{(3)}(t) \leq Q \int_0^t \mathcal{H}^{(2)}(\zeta) d\zeta \leq \hat{\mathcal{L}}K\frac{Q^2t^2}{2}$$

Induction on n gives

$$\mathcal{H}^{(n)}(t) \leq \sup_{t\in[0,\mathcal{T}]} \mathcal{H}^{(n)}(t) \leq \hat{\mathcal{L}}K\frac{Q^{n-1}\mathcal{T}^{n-1}}{(n-1)!}$$

.

Remainder term of the each component in the sequence $\{x^{(n)}\} = \{(S_v^{(n)}, I_v^{(n)}, S^{(n)}, i^{(n)}(\tau, t), R^{(n)})\}$ are given by

$$\begin{aligned}
\left|S_v^{(n+m)} - S_v^{(n)}\right| &\leq \sum_{k=n+1}^{n+m} |S_v^{(k)} - S_v^{(k-1)}| \\
&= \sum_{k=n+1}^{n+m} \mathcal{H}_1^{(k)} \\
&\leq \sum_{k=n+1}^{n+m} \mathcal{H}^{(k)} \\
&\leq \hat{\mathcal{L}}K \sum_{k=n+1}^{n+m} \frac{Q^{k-1}T^{k-1}}{(k-1)!} \to 0 \text{ as } n \to \infty
\end{aligned}$$

$$\begin{aligned}
\left|I_v^{(n+m)} - I_v^{(n)}\right| &\leq \sum_{k=n+1}^{n+m} |I_v^{(k)} - I_v^{(k-1)}| \\
&= \sum_{k=n+1}^{n+m} \mathcal{H}_2^{(k)} \\
&\leq \sum_{k=n+1}^{n+m} \mathcal{H}^{(k)} \\
&\leq \hat{\mathcal{L}}K \sum_{k=n+1}^{n+m} \frac{Q^{k-1}T^{k-1}}{(k-1)!} \to 0 \text{ as } n \to \infty
\end{aligned}$$

$$\begin{aligned}
\left|S^{(n+m)} - S^{(n)}\right| &\leq \sum_{k=n+1}^{n+m} |S^{(k)} - S^{(k-1)}| \\
&= \sum_{k=n+1}^{n+m} \mathcal{H}_3^{(k)} \\
&\leq \sum_{k=n+1}^{n+m} \mathcal{H}^{(k)} \\
&\leq \hat{\mathcal{L}}K \sum_{k=n+1}^{n+m} \frac{Q^{k-1}T^{k-1}}{(k-1)!} \to 0 \text{ as } n \to \infty \\
\int_0^\infty \left|i^{(n+m)}(\tau,t) - i^{(n)}(\tau,t)\right| d\tau &\leq \int_0^\infty \sum_{k=n+1}^{n+m} \left|i^{(k)}(\tau,t) - i^{(k-1)}(\tau,t)\right| d\tau \\
&= \sum_{k=n+1}^{n+m} \mathcal{H}_4^{(k)} \\
&\leq \sum_{k=n+1}^{n+m} \mathcal{H}^{(k)} \\
&\leq \hat{\mathcal{L}}K \sum_{k=n+1}^{n+m} \frac{Q^{k-1}T^{k-1}}{(k-1)!} \to 0 \text{ as } n \to \infty \\
\left|R^{(n+m)} - R^{(n)}\right| &\leq \sum_{k=n+1}^{n+m} |R^{(k)} - R^{(k-1)}| \\
&= \sum_{k=n+1}^{n+m} \mathcal{H}_5^{(k)} \\
&\leq \sum_{k=n+1}^{n+m} \mathcal{H}^{(k)} \\
&\leq \hat{\mathcal{L}}K \sum_{k=n+1}^{n+m} \frac{Q^{k-1}T^{k-1}}{(k-1)!} \to 0 \text{ as } n \to \infty
\end{aligned}$$

Here, we saw that each component of the sequence $\{x^{(n)}\}$ is a Cauchy Sequence in X_+. Since X_+ is a Complete space, each of these component converges to the limit point in X_+. That is,

$$\big(S_v, I_v, S, i(\tau,t), R\big) = x = \lim_{n\to\infty} x^{(n)} = \lim_{n\to\infty} \big(S_v^{(n)}, I_v^{(n)}, S^{(n)}, i^{(n)}(\tau,t), R^{(n)}\big)$$

Thus, the sequence $\{x^{(n)}\}$ converges to the limit point $x \in \Omega_1 \subset X_+$. Now we use the relation used to obtain the iterative sequence to see when $n \to \infty$.

$$x = \lim_{x\to\infty} x^{(n+1)} = \lim_{n\to\infty} \mathcal{F}(x^{(n)}) = \mathcal{F}\big(\lim_{n\to\infty} x^{(n)}\big) = \mathcal{F}x \tag{3.24}$$

i.e

$$\big(S_v, I_v, S, i(\tau,t), R\big) = \mathcal{F}\big(S_v, I_v, S, i(\tau,t), R\big)$$

Thus, $x = \big(S_v, I_v, S, i(\tau,t), R\big)$ is the fixed point of $\mathcal{F}$ and proves the existence of the solution for the model (3.11).

Now we prove the uniqueness of the solution for the model. Let us assume there exist two solutions $x = \big(S_v(t), I_v(t), S(t), i(\tau,t), R(t)\big)$ and $\hat{x} = \big(\hat{S}_v(t), \hat{I}_v(t), \hat{S}(t), \hat{i}(\tau,t), \hat{R}(t)\big)$ of the model. Then,

$$\mathcal{F}(x) = x \text{ and } \mathcal{F}(\hat{x}) = \hat{x}$$

We set

$$\begin{aligned}
\hat{\mathcal{H}}_1(t) &= \big|S_v(t) - \hat{S}_v(t)\big| \\
\hat{\mathcal{H}}_2(t) &= \big|I_v(t) - \hat{I}_v(t)\big| \\
\hat{\mathcal{H}}_3(t) &= \big|S(t) - \hat{S}(t)\big| \\
\hat{\mathcal{H}}_4(t) &= \int_0^\infty \big|i(\tau,t) - \hat{i}(\tau,t)\big| d\tau \\
\hat{\mathcal{H}}_5(t) &= \big|R(t) - \hat{R}(t)\big|
\end{aligned} \tag{3.25}$$

And $\hat{H}(t) = \hat{\mathcal{H}}_1(t) + \hat{\mathcal{H}}_2(t) + \hat{\mathcal{H}}_3(t) + \hat{\mathcal{H}}_4(t) + \hat{\mathcal{H}}_5(t)$. Repeating the procedure used in the process of proving existence for the set up above gives

$$\hat{H}(t) \leq \hat{Q} \int_0^t \hat{H}(\zeta) d\zeta \tag{3.26}$$

By the Gronwall's inequality in integral form in (3.26) implies $\hat{H}(t) = 0$. Thus, each of $\hat{\mathcal{H}}_i(t) = 0$ for $1 \leq i \leq 5$ proving $S_v(t) = \hat{S}_v(t), I_v(t) = \hat{I}_v(t), S(t) = \hat{S}(t), i(\tau,t) = \hat{i}(\tau,t)$, and $R(t) = \hat{R}(t)$ from (3.25). Hence, the uniqueness of the solution.

3.4 EXISTENCE OF EQUILIBRIA

A nonlinear differential equation has time-independent solutions, that is, solutions that are constant in time. Such solutions are called equilibrium points. We are interested in time-independent solution and the system for the equilibria takes the form

$$
\begin{aligned}
&\Lambda_v - \frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau - \mu_v S_v^* = 0,\\
&\frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau - \mu_v I_v^* = 0,\\
&\Lambda - \frac{\beta_v S^* I_v^*}{N^*} - \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau - \mu S^* = 0,\\
&\frac{di^*}{d\tau} = -(\gamma(\tau)+\mu)i^*(\tau),\\
&i^*(0) = \frac{\beta_v S^* I_v^*}{N^*} + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau,\\
&\int_0^\infty \gamma(\tau)i^*(\tau)d\tau - \mu R^* = 0.
\end{aligned}
\tag{3.27}
$$

System has only these equilibria: disease free equilibrium (DFE) and endemic equilibrium (EE). The disease-free equilibrium is defined as an equilibrium point at which no disease is present in the population where as endemic equilibrium is defined as an equilibrium point at which disease is prevalent in the population.

Solving the differential equation for infected individual at equilibrium in (3.27) gives $i^*(\tau) = i^*(0)\pi(\tau)$ where

$$\pi(\tau) = e^{-\int_0^\tau (\gamma(s)+\mu)ds}$$

is the probability of still being infectious τ time units after becoming infected[36]. Disease free equilibrium exist whenever $i^*(0) = 0$ and endemic equilibrium exist whenever $i^*(0) \neq 0$. In the next page, we interpret reproduction number $\mathcal{R}_0$.

3.4.1 Interpretation of Reproduction Number

Epidemiologically, the reproduction number gives the number of secondary cases one infectious individual will produce in a population consisting only of susceptible individuals during its infectious period. We notice that reproduction number is

$$\mathcal{R}_0 = \frac{\beta_v \Lambda_v \mu}{\Lambda \mu_v^2} \int_0^\infty \beta(\tau)\pi(\tau)d\tau + \int_0^\infty \beta_d(\tau)\pi(\tau)d\tau \tag{3.28}$$

where $\int_0^\infty \beta_d(\tau)\pi(\tau)d\tau$ the number of secondary case produced by one infectious human in a population consisting only of susceptible human during its infectious time by direct transmission.

Notice that there are two kind of transmission cycle in vector transmission: one from human to vector and the other being from vector to human. In human to vector transmission, let us assume one infectious human is placed in the susceptible vector population.

Human-to-vector transmission occurs when the susceptible vector bite an infectious human. In this transmission, we observe that the force of infection of susceptible vectors is given by the integral over all time since infection given by term $\frac{S_v}{N}\int_0^\infty \beta(\tau)i(\tau,t)d\tau$ and thus, one infected human in a totally susceptible vector and human population, will produce $\frac{\Lambda_v \mu}{\mu_v \Lambda}\int_0^\infty \beta(\tau)\pi(\tau)d\tau$ number of secondary vector cases during its life time as infectious. Now in the vector-to-human transmission, infectious vector transmit the disease to susceptible human. When one infectious vector is placed in the susceptible human population, secondary infected cases produced is given by $\frac{\beta_v}{\mu_v}$. To understand this term, let us take a incidence term for vector-to-human transmission given by $\frac{\beta_v S I_v}{N}$. Then one infected vector will produce $\frac{\beta_v S}{N}$ number of secondary infected human. As human population consist of only susceptible humans i.e. $S = N$, then β_v numbers of newly infected humans are produced. One infected vector will spent $\frac{1}{\mu_v}$ average time as infective, thus we see that one infected vector will produce $\beta_v.\dfrac{1}{\mu_v} = \dfrac{\beta_v}{\mu_v}$ number of secondary infected human in the susceptible human population. We obtain the total secondary infections by multiplying human-to-vector cases and vector-to-human cases resulting in $\dfrac{\beta_v \Lambda_v \mu}{\Lambda \mu_v^2}\int_0^\infty \beta(\tau)\pi(\tau)d\tau$. The threshold value $\mathcal{R}_0$ in (3.28) is then obtained by adding the secondary cases due to the direct transmission to $\dfrac{\beta_v \Lambda_v \mu}{\Lambda \mu_v^2}\int_0^\infty \beta(\tau)\pi(\tau)d\tau$.

Let $B = \int_0^\infty \beta(\tau)\pi(\tau)d\tau$ and $B_d = \int_0^\infty \beta_d(\tau)\pi(\tau)d\tau$

Theorem 4. *Let $\mathcal{R}_0 = \beta_v \dfrac{\Lambda_v \mu}{\Lambda \mu_v^2} B + B_d$, the the following statement are true.*

i. $E_0 = \big(\dfrac{\Lambda_v}{\mu_v}, 0, \dfrac{\Lambda}{\mu}, 0, 0\big) \in X_+$ is a disease free equilibrium of (3.27).

ii. When $\mathcal{R}_0 > 1$, then there exist a unique endemic equilibrium given by $E^* = \big(S_v^*, I_v^*, S^*, i^*(\tau), R^*\big)$ where

$$S_v^* = \frac{\Lambda_v}{\dfrac{i^*(0)B}{N^*} + \mu_v} \qquad I_v^* = \frac{N_v^* i^*(0)B}{i^*(0)B + N^*\mu_v}$$

$$S^* = \frac{N^*}{\beta_v \dfrac{N_v^* B}{i^*(0)B + N^*\mu_v} + B_d} \qquad R^* = \frac{i^*(0)\int_0^\infty \gamma(\tau)\pi(\tau)d\tau}{\mu}$$

and $i^*(0)$ is unique positive solution of

$$\frac{B_d B}{\Lambda} i^{*^2}(0) + \frac{\mu_v}{\mu}\big(\mathcal{R}_0 + B\frac{\mu}{\mu_v} - B_d B\frac{\mu}{\mu_v}\big) i^*(0) + N^*\mu_v(1 - \mathcal{R}_0) = 0$$

Proof. The system for the equilibria is given by (3.27).

Solving differential equation in (3.27) gives $i^*(\tau) = i^*(0)\pi(\tau)$.

If $i^*(0) = 0$, then we obtain disease free equilibrium $E^0 = \big(\dfrac{\Lambda_v}{\mu_v}, 0, \dfrac{\Lambda}{\mu}, 0, 0, 0\big)$.

Let $i^*(0) \neq 0$ and we know $N_v^* = S_v^* + I_v^*$, then from 2^{nd} equation in (3.27) we obtain

$$\frac{N_v^* - I_v^*}{N^*} i^*(0)\int_0^\infty \beta(\tau)\pi(\tau)d\tau - \mu_v I_v^* = 0$$

Solving for I_v^*, we get,

$$I_v^* = \frac{N_v^* i^*(0)B}{i^*(0)B + N^*\mu_v},$$

Solving first equation of (3.27) for S_v^* gives,

$$S_v^* = \frac{\Lambda_v}{\dfrac{i^*(0)B}{N^*} + \mu_v}$$

. Plugging I_v^* in 5^{th} equation of (3.27) and solving for S^* , we get

$$\begin{aligned}
i^*(0) &= \beta_v \frac{S^*}{N^*} \frac{N_v^* i^*(0)B}{i^*(0)B + N^*\mu_v} + \frac{S^*}{N^*} i^*(0) B_d \\
1 &= \beta_v \frac{S^*}{N^*} \frac{N_v^* B}{i^*(0)B + N^*\mu_v} + \frac{S^*}{N^*} B_d \\
1 &= \frac{S^*}{N^*} \Big(\beta_v \frac{N_v^* B}{i^*(0)B + N^*\mu_v} + B_d \Big)
\end{aligned}$$

This give S^* to be

$$S^* = \frac{N^*}{\beta_v \dfrac{N_v^* B}{i^*(0)B + N^*\mu_v} + B_d}$$

Equation (3.14) can be written as $\dfrac{dN(t)}{dt} = \Lambda - \mu N(t)$.

At equilibrium point, we have $0 = \Lambda - \mu N^*$. Thus, we get $N^* = \dfrac{\Lambda}{\mu}$.

Next, we write (3.12) as $\dfrac{dN_v(t)}{dt} = \Lambda_v - \mu_v N_v(t)$.

At equilibrium point, we have $0 = \Lambda_v - \mu_v N_v^*$. Thus, we get $N_v^* = \dfrac{\Lambda_v}{\mu_v}$.

Since $\Lambda - i^*(0) - \mu S^* = 0$, substituting S^* and rearranging , we obtain

$$i^*(0) = \Lambda - \frac{\Lambda}{\beta_v \dfrac{N_v^* B}{i^*(0)B + \mu_v N^*} + B_d}$$

.

$$i^*(0) = \Lambda - \frac{\Lambda \Big(i^*(0)B + \mu_v N^* \Big)}{\beta_v N_v^* B + B_d \Big(i^*(0)B + \mu_v N^* \Big)}$$

Next we expand this as below substituting $N_v^* = \dfrac{\Lambda_v}{\mu_v}$.

$$i^*(0)\beta_v \frac{\Lambda_v}{\mu_v} B + B B_d i^{*2}(0) + B_d \mu_v N^* i^*(0) = \beta_v \Lambda \frac{\Lambda_v}{\mu_v} B + \Lambda B B_d i^*(0) + \Lambda \mu_v B_d N^* - \Lambda B i^*(0) - \Lambda \mu_v N^*$$

Rearranging above equation we can rewrite it as below

$$\frac{BB_d}{\Lambda}i^{*2} + \frac{\mu_v}{\mu}\Big(\underbrace{\beta_v\frac{\Lambda_v\mu}{\Lambda\mu_v^2}B + B_d}_{\mathcal{R}_0} + B\frac{\mu}{\mu_v} - \frac{BB_d\mu}{\mu_v}\Big) + \frac{\Lambda}{\mu}\mu_v\Big(1 \underbrace{- B_d - \beta_v\frac{\Lambda_v\mu}{\Lambda\mu_v^2}B}_{-\mathcal{R}_0}\Big) = 0$$

$$\frac{BB_d}{\Lambda}i^{*2} + \frac{\mu_v}{\mu}\Big(\mathcal{R}_0 + B\frac{\mu}{\mu_v} - \frac{BB_d\mu}{\mu_v}\Big) + \frac{\Lambda}{\mu}\mu_v\Big(1 - \mathcal{R}_0\Big) = 0$$

$$\frac{BB_d}{\Lambda}i^{*2} + \frac{\mu_v}{\mu}\Big(\mathcal{R}_0 + B\frac{\mu}{\mu_v} - \frac{BB_d\mu}{\mu_v}\Big) + N^*\mu_v\Big(1 - \mathcal{R}_0\Big) = 0$$

which can be written as quadratic equation

$$a_2 {i^*}^2(0) + a_1 i^*(0) + a_0 = 0$$

where

$$a_2 = \frac{B_d B}{\Lambda},$$

$$a_1 = \frac{\mu_v}{\mu}\big(\mathcal{R}_0 + B\frac{\mu}{\mu_v} - B_d B\frac{\mu}{\mu_v}\big),$$

$$a_0 = N^*\mu_v(1 - \mathcal{R}_0).$$

and solutions of quadratic equation is given by $i^*(0) = \dfrac{-a_1 \mp \sqrt{a_1^2 - 4a_2a_0}}{2a_2}$.

Clearly, $a_2 > 0$.

When $\mathcal{R}_0 > 1$, $a_0 = N^*\mu_v(1 - \mathcal{R}_0) < 0$. Thus, there exists a unique positive $i^*(0)$. when $\mathcal{R}_0 > 1$.

When $\mathcal{R}_0 < 1$ then $a_0 > 0$ and $B_d < 1$. This implies

$$a_1 = \frac{\mu_v}{\mu}\big(\mathcal{R}_0 + B\frac{\mu}{\mu_v} - B_d B\frac{\mu}{\mu_v}\big) = \frac{\mu_v}{\mu}\mathcal{R}_0 + B(1 - B_d) > 0,$$

Thus, in this case no positive endemic equilibrium is present.

Hence, the endemic equilibrium only exists when $\mathcal{R}_0 > 1$. □

3.5 STABILITY OF EQUILIBRIA

In this section we discuss local and global stability of disease free equilibrium and endemic equilibrium. An equilibrium is said to be locally stable if solution that start close to the equilibrium converges to equilibrium as $t \to \infty$. An equilibrium is called globally stable if it is stable for almost all initial conditions, not just those that are close to it. Stability of non linear system is concluded from the stability of corresponding linear system obtain from the non linear system by the process of linearization. First we discuss the stability of disease free equilibrium.

To investigate the local stability of the equilibria, we linearize the system. Let $S(t) = S^* + x(t), i(\tau, t) = i^*(\tau) + y(\tau, t), R(t) = R^* + z(t), S_v(t) = S_v^*(t) + x_v(t), I_v(t) = I_v^*(t) + y_v(t), N(t) = N^* + n(t)$ where $x(t), y(\tau, t), z(t), x_v(t), y_v(t), n(t)$ are the perturbations. Substituting $S_v(t), I_v(t), S(t), i(\tau, t), R(t)$, in (3.11) and using (3.27) we get

$$
\begin{aligned}
x_v'(t) &= -\frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)y(\tau,t)d\tau - \frac{x_v(t)}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau + \frac{S_v^* n(t)}{N^{*2}}\int_0^\infty \beta(\tau)i^*(\tau)d\tau \\
&\quad - \mu_v x_v(t) \\
y_v'(t) &= \frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)y(\tau,t)d\tau + \frac{x_v(t)}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau - \frac{S_v^* n(t)}{N^{*2}}\int_0^\infty \beta(\tau)i^*(\tau)d\tau \\
&\quad - \mu_v y_v(t) \\
x'(t) &= -\frac{\beta_v S^* y_v(t)}{N^*} - \frac{\beta_v I_v^* x(t)}{N^*} + \frac{\beta_v S^* I_v^*}{N^{*2}}n(t) - \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)y(\tau,t)d\tau - \frac{x(t)}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau \\
&\quad + \frac{S^* n(t)}{N^{*2}}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau - \mu x(t), \\
\frac{\partial y(\tau,t)}{\partial t} &+ \frac{\partial y(\tau,t)}{\partial \tau} = -(\gamma(\tau)+\mu)y(\tau,t), \\
y(0,t) &= \frac{\beta_v S^* y_v(t)}{N^*} + \frac{\beta_v I_v^* x(t)}{N^*} - \frac{\beta_v S^* I_v^*}{N^{*2}}n(t) + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)y(\tau,t)d\tau + \frac{x(t)}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau \\
&\quad - \frac{S^* n(t)}{N^{*2}}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau, \\
z'(t) &= \int_0^\infty \gamma(\tau)y(\tau,t)d\tau - \mu z(t).
\end{aligned}
\tag{3.29}
$$

System (3.29) is a linear system for $x(t), y(\tau, t), z(t), x_v(t), y_v(t)$. Let $x(t) = \bar{x}e^{\lambda t}, y(\tau, t) = \bar{y}(\tau)e^{\lambda t}, z(t) = \bar{z}e^{\lambda t}, x_v(t) = \bar{x}_v e^{\lambda t}, y_v(t) = \bar{y}_v e^{\lambda t}, n(t) = \bar{n}e^{\lambda t}$ be the solution of the system (3.29) where $\bar{x}, \bar{y}(\tau), \bar{z}, \bar{x}_v, \bar{y}_v, \lambda$ are not all zero. Substituting the constitutive form of the solutions in the system (3.29), we obtain following eigenvalue problem (the bars have been omitted)

$$\begin{aligned}
\lambda x_v &= -\frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)y(\tau)d\tau - \frac{x_v}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau + \frac{S_v^*}{N^{*2}}n\int_0^\infty \beta(\tau)i^*(\tau)d\tau \\
&\quad - \mu_v x_v \\
\lambda y_v &= \frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)y(\tau)d\tau + \frac{x_v}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau - \frac{S_v^*}{N^{*2}}n\int_0^\infty \beta(\tau)i^*(\tau)d\tau \\
&\quad - \mu_v y_v \\
\lambda x &= -\frac{\beta_v S^* y_v}{N^*} - \frac{\beta_v I_v^* x}{N^*} + \frac{\beta_v S^* I_v^*}{N^{*2}}n - \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)y(\tau)d\tau - \frac{x}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau \\
&\quad + \frac{S^*}{N^{*2}}n\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau - \mu x, \\
\lambda y + \frac{\partial y}{\partial \tau} &= -(\gamma(\tau)+\mu)y(\tau), \\
y(0) &= \frac{\beta_v S^* y_v}{N^*} + \frac{\beta_v I_v^* x}{N^*} - \frac{\beta_v S^* I_v^*}{N^{*2}}n + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)y(\tau)d\tau + \frac{x}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau \\
&\quad - \frac{S^*}{N^{*2}}n\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau, \\
\lambda z &= \int_0^\infty \gamma(\tau)y(\tau)d\tau - \mu z.
\end{aligned} \tag{3.30}$$

Solutions of system (3.30) gives the eigenvalues λ. Next we obtain the characteristics equation for each equilibria.

3.5.1 Local Stability of Disease Free Equilibrium

Here we show the local stability of disease free equilibrium. That is, given the conditions on parameters, if the initial condition are close enough to equilibrium then the solution will converge to the equilibrium. At disease free equilibrium $E_0 =$

$(S_v^0, 0, S^0, 0, 0) = (\dfrac{\Lambda_v}{\mu_v}, 0, \dfrac{\Lambda}{\mu}, 0, 0)$, system (3.30) reduces to

$$\begin{aligned}
\lambda x_v &= -\frac{S_v^0}{N^0}\int_0^\infty \beta(\tau)y(\tau)d\tau - \mu_v x_v \\
\lambda y_v &= \frac{S_v^0}{N^0}\int_0^\infty \beta(\tau)y(\tau)d\tau - \mu_v y_v \\
\lambda x &= -\frac{\beta_v S^0 y_v}{N^0} - \frac{S^0}{N^0}\int_0^\infty \beta_d(\tau)y(\tau)d\tau - \mu x, \\
\lambda y + \frac{\partial y}{\partial \tau} &= -(\gamma(\tau)+\mu)y(\tau), \\
y(0) &= \frac{\beta_v S^0 y_v}{N^0} + \frac{S^0}{N^0}\int_0^\infty \beta_d(\tau)y(\tau)d\tau, \\
\lambda z &= \int_0^\infty \gamma(\tau)y(\tau)d\tau - \mu z.
\end{aligned} \tag{3.31}$$

Using value of y_v from 2^{nd} equation of model (3.31) in 5^{th} equation, we get,

$$y(0) = \frac{S^0}{N^0}\left(\frac{\beta_v S_v^0}{N^0(\lambda+\mu_v)}\int_0^\infty \beta(\tau)y(\tau)d\tau) + \int_0^\infty \beta_d(\tau)y(\tau)d\tau\right) \tag{3.32}$$

It is easy to see that the differential equation involving $y(\tau)$ is independent of x, z, x_v and y_v. Solving the differential equation of the model (3.31), we obtain,

$$y(\tau) = y(0)e^{-\lambda\tau}\pi(\tau)$$

substituting $y(\tau)$ in the boundary condition (3.32) and cancelling $y(0)$ and using $S^0 = N^0$, we obtain following characteristic equation,

$$\frac{\beta_v S_v^0}{N^0(\lambda+\mu_v)}\int_0^\infty \beta(\tau)e^{-\lambda\tau}\pi(\tau)d\tau) + \int_0^\infty \beta_d(\tau)e^{-\lambda\tau}\pi(\tau)d\tau = 1, \tag{3.33}$$

Equation (3.33) may have many solutions. For stability of disease free equilibrium, we need to show that all solutions λ of the equation (3.33) have negative real part. If there is a solution λ with positive real part, then disease free equilibrium is unstable. To investigate this, we define

$$f(\lambda) = \frac{\beta_v S_v^0}{N^0(\lambda+\mu_v)}\int_0^\infty \beta(\tau)e^{-\lambda\tau}\pi(\tau)d\tau) + \int_0^\infty \beta_d(\tau)e^{-\lambda\tau}\pi(\tau)d\tau, \tag{3.34}$$

We define reproduction number by setting $\lambda = 0$ in $f(\lambda)$ and thus reproduction number for the model is given by $\mathcal{R}_0 = \frac{\beta_v \Lambda_v \mu}{\Lambda \mu_v^2} \int_0^\infty \beta(\tau)\pi(\tau)d\tau + \int_0^\infty \beta_d(\tau)\pi(\tau)d\tau$

We have two cases:

case 1 If $\mathcal{R}_0 > 1$. Assuming $\beta(\tau)$ and $\beta_d(\tau)$ are strictly positive and λ is real and $\lambda > -\mu_v$, then clearly $f(\lambda)$ is decreasing function on λ. Here, $f(0) = \mathcal{R}_0 > 1$ and $\lim_{\lambda \to \infty} f(\lambda) = 0$, then there exist $\lambda^* > 0$ such that $f(\lambda^*) = 1$. Thus disease free equilibrium is unstable if $\mathcal{R}_0 > 1$

case 2 If $\mathcal{R}_0 < 1$. Assuming $\beta(\tau)$ and $\beta_d(\tau)$ are strictly positive and λ is real, then clearly $f(\lambda)$ is decreasing function on λ. Since $f(0) = \mathcal{R}_0 < 1$ and $\lim_{\lambda \to \infty} f(\lambda) = 0$, then there exist $\lambda^* < 0$ such that $f(\lambda^*) = 1$. Next we take $\lambda = c + id$ where $c, d \in \mathbb{R}$ and assume $c \geq 0$. Then we have,

$$|f(\lambda)| \leq \frac{\beta_v S_v^0}{N^0 \mu_v} \int_0^\infty \beta(\tau)|e^{-\lambda\tau}|\pi(\tau)d\tau + \int_0^\infty \beta_d(\tau)|e^{-\lambda\tau}|\pi(\tau)d\tau$$

$$\leq \frac{\beta_v S_v^0}{N^0 \mu_v} \int_0^\infty \beta(\tau)|e^{-c\tau}|\pi(\tau)d\tau + \int_0^\infty \beta_d(\tau)|e^{-c\tau}|\pi(\tau)d\tau$$

$$\leq \frac{\beta_v S_v^0}{N^0 \mu_v} \int_0^\infty \beta(\tau)\pi(\tau)d\tau + \int_0^\infty \beta_d(\tau)\pi(\tau)d\tau = \mathcal{R}_0 < 1$$

Thus we see that those λ whose real part is non negative cannot satisfy the equation $f(\lambda) = 1$. Therefore, the disease free equilibrium is locally asymptotically stable in this case. This allows us to have a following theorem:

Theorem 5. *If $\mathcal{R}_0 < 1$, the disease-free equilibrium is locally asymptotically stable. If $\mathcal{R}_0 > 1$, the disease-free equilibrium is unstable.*

3.5.2 Local Stability of Endemic Equilibria

Here we discuss the local stability of endemic equilibrium.

Theorem 6. *Endemic equilibrium* $E^* = (S_v^*, I_v^*, S^*, I^*, R^*)$ *is locally asymptotically stable whenever it exists.*

Proof. Lets us define $B(\lambda) = \int_0^\infty \beta(\tau)e^{-\lambda\tau}\pi(\tau)d\tau$, $B_d(\lambda) = \int_0^\infty \beta_d(\tau)e^{-\lambda\tau}\pi(\tau)d\tau$, $B_d^* = \dfrac{\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau}{N^*}$, and $B^* = \dfrac{\int_0^\infty \beta(\tau)i^*(\tau)d\tau}{N^*}$

Adding 3^{rd} and 5^{th} equation of (3.30), we get

$$x = \frac{-y(0)}{\lambda + \mu} \tag{3.35}$$

Adding 1^{st} and 2^{nd} equations of (3.30), we get $\lambda(x_v + y_v) = -\mu_v(x_v + y_v)$. If you take $\lambda = -\mu_v$, it gives the first eigenvalue. In order to determine other eigenvalues, we take $x_v = -y_v$.

Using $x_v = -y_v$ in 2^{nd} equation of (3.30) and rearranging, we get,

$$\Big(\lambda + \mu_v + B^*\Big)y_v - \frac{S_v^*}{N^*}B(\lambda)y(0) = -\frac{S_v^*}{N^*}B^* n \tag{3.36}$$

Substituting x from (3.35) in 5^{th} equation of (3.30) and rearranging gives

$$-\frac{\beta_v S^*}{N^*}y_v + \left(1 + \frac{\beta_v I_v^*}{N^*(\lambda+\mu)} - \frac{S^* B_d(\lambda)}{N^*} + \frac{B_d^*}{\lambda+\mu}\right)y(0) = -\Big(\frac{\beta_v S_v^* I_v^*}{N^{*2}}n + \frac{S^*}{N^*}nB_d^*\Big) \tag{3.37}$$

Since $N = S + \int_0^\infty i(\tau,t)d\tau + R$, total perturbation in the population is

$$n = x + \int_0^\infty y(\tau)d\tau + z$$

Substituting z from (3.30) gives

$$\begin{aligned}
n &= x + \int_0^\infty y(\tau)d\tau + \frac{1}{\lambda+\mu}\int_0^\infty \gamma(\tau)y(\tau)d\tau \\
&= x + y(0)\int_0^\infty \Big(1 + \frac{\gamma(\tau)}{\lambda+\mu}\Big)e^{-\lambda\tau}\pi(\tau)d\tau \\
&= x + y(0)\frac{1}{\lambda+\mu}\int_0^\infty \Big(\lambda+\mu+\gamma(\tau)\Big)e^{-\int_0^\tau \Big(\lambda+\mu+\gamma(s)\Big)ds} d\tau \\
&= x + y(0)\frac{1}{\lambda+\mu}
\end{aligned}$$

Substituting values of x from (3.35) results $n = 0$.

Thus, (3.36) and (3.37) reduces

$$
\begin{aligned}
(\lambda + \mu_v + B^*)\, y_v - \frac{S_v^*}{N^*} B(\lambda) y(0) = 0 \\
-\frac{\beta_v S^*}{N^*} y_v + \left(1 + \frac{\beta_v I_v^*}{N^*(\lambda+\mu)} - \frac{S^* B_d(\lambda)}{N^*} + \frac{B_d^*}{\lambda+\mu}\right) y(0) = 0
\end{aligned}
$$

Above equations and combined gives the system of characteristics equation for the model. Both $x \neq 0$ and $y_v \neq 0$, we set determinant to zero.

$$
\begin{vmatrix}
(\lambda + \mu_v + B^*) & -\dfrac{S_v^*}{N^*} B(\lambda) \\
-\dfrac{\beta_v S^*}{N^*} & \left(1 + \dfrac{\beta_v I_v^*}{N^*(\lambda+\mu)} - \dfrac{S^* B_d(\lambda)}{N^*} + \dfrac{B_d^*}{\lambda+\mu}\right)
\end{vmatrix} = 0
$$

gives the characteristic equation as $F(\lambda) = G(\lambda)$ where

$$
\begin{aligned}
F(\lambda) &= 1 + \frac{\beta_v I_v^*}{N^*(\lambda+\mu)} + \frac{B_d^*}{\lambda+\mu} \\
G(\lambda) &= \frac{S^*}{N^*}\left(\frac{\beta_v S_v^* B(\lambda)}{N^*(\lambda+\mu_v+B^*)} + B_d(\lambda)\right)
\end{aligned}
$$

Let $\lambda = a + ib$ with $a > 0$. Clearly $|F(\lambda)| > 1$ and

$$
|G(\lambda)| \leq \frac{S^*}{N^*}\left(\frac{\beta_v S_v^* B(a)}{N^*\sqrt{(a+\mu_v+B^*)^2 + b^2}} + B_d(a)\right) \leq \frac{S^*}{N^*}\left(\frac{\beta_v S_v^* B}{N^* \mu_v} + B_d\right) = 1
$$

Since $\frac{S_v^*}{N^*}\int_0^\infty \beta(\tau) i^*(\tau) d\tau - \mu_v I_v^* = 0$ gives $I_v^* = \frac{S_v^* i^*(0) B}{N^* \mu_v}$, and substituting it into

$$
i^*(0) = \frac{\beta_v S^* I_v^*}{N^*} + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau) i^*(\tau) d\tau \quad \text{yields} \quad \frac{S^*}{N^*}\left(\frac{\beta_v S_v^* B}{N^* \mu_v} + B_d\right) = 1
$$

Here, we observed that for λ with non-negative real part, left hand side remains strictly greater than 1 whereas right hand side is less than or equal to 1. Thus, characteristic equation above can only have solution with negative real which proves that endemic equilibrium is locally asymptotically stable whenever it exists. □

3.6 SUMMARY OF THE CHAPTER

In this chapter, we have presented a mathematical model of ZIKV incorporating both vector and direct transmission. In order to simulate the transmission of the disease, two compartmental models were combined: SIR (Susceptible-Infected-Recovered) model for the human population and SI (Susceptible-Infected) model for the vector population. Transmission and recovery varies during the infectious period and infectivity for infectious individuals varies with the time since infection, we structure the infected class by time and time since infection parameter τ. The novelty of our model is that we have introduced a model infected individuals are structured by time-since infection and vector transmission and direct transmission are both modeled as standard incidences.

Infection age plays a vital role in the transmission of ZIKV. In this study, we formulate a hyperbolic PDE model of Zika virus infections, which includes both vector and direct transmissions and where the new infections are modeled as standard incidence. Qualitative analysis of the model showed that there exists a domain where the model is epidemiologically and mathematically well-posed. We obtain the explicit representation of the reproduction number, $\mathcal{R}_0$. We showed that the disease-free-equilibria is locally stable when $\mathcal{R}_0 < 1$. We also showed endemic equilibrium is locally stable when $\mathcal{R}_0 > 1$. Persistence of endemic equilibrium is established when $\mathcal{R}_0 > 1$, however global stability of endemic equilibrium for $\mathcal{R}_0 > 1$ is still an open question.

CHAPTER 4

TIME SINCE INFECTION STRUCTURED VECTOR-BORNE MODEL WITH DIRECT TRANSMISSION INCLUDING DISEASE INDUCED DEATH RATE.

4.1 INTRODUCTION

As detailed in the introduction, fatality of human cases because of Zika is uncommon [45]. The New England Journal of Medicine have reported nine human deaths from ZIKV infection that was unconnected to Guillain-Barré syndrome [50]. NBC reported that in Puerto Rico, a man in his $70s$ died by ZIKV infection and is believed to be first U.S. death from the virus [47]. As per the report [48] on September $28, 2016$, an unidentified man died who was ZIKV patient, contracted during his travel to Mexico died in July in Salt Lake City. Medical team who was taking care of the patient at University of Utah Health Care believed and made clear the man died by ZIKV infection.

The completion of the first project lead to the next question: does the inclusion of disease induced death rate in the previous model changes the dynamics of the disease? The aim of this chapter is to design a new time since infection structured PDE model for the transmission dynamics of vector borne disease with direct transmission including disease induced death rate, in a community. The model to be designed here is an extension work of [6] where the researcher have analyzed ODE Zika model with vector borne and direct transmission. Here, we formulate a mathematical PDE vector borne disease model with direct transmission with the inclusion of disease induced death rate $\alpha(\tau)$.

4.2 MODEL FORMULATION

$$\begin{cases} S_v' = \Lambda_v - \dfrac{S_v}{N}\displaystyle\int_0^\infty \beta\left(\tau\right) i\left(\tau,t\right) d\tau - \mu_v S_v, \\ I_v' = \dfrac{S_v}{N}\displaystyle\int_0^\infty \beta(\tau) i(\tau,t) d\tau - \mu_v I_v, \\ S' = \Lambda - \dfrac{\beta_v S I_v}{N} - \dfrac{S}{N}\displaystyle\int_0^\infty \beta_d(\tau) i(\tau,t) d\tau - \mu S, \\ \dfrac{\partial i}{\partial t} + \dfrac{\partial i}{\partial \tau} = -\left(\gamma\left(\tau\right) + \alpha\left(\tau\right) + \mu\right) i\left(\tau,t\right), \\ i(0,t) = \dfrac{\beta_v S I_v}{N} + \dfrac{S}{N}\displaystyle\int_0^\infty \beta_d(\tau) i(\tau,t) d\tau, \\ R' = \displaystyle\int_0^\infty \gamma(\tau) i(\tau,t) d\tau - \mu R. \end{cases} \tag{4.1}$$

$N(t) = S(t) + I(t) + R(t)$ for any time $t \geq 0$ and with initial conditions $S_v(0) = S_{v_0}, S_v(0) = S_{v_0}, S(0) = S_0, i(\tau,0) = i(0)$ and $R(0) = R_0$. Models of vector-borne diseases with direct transmission is not new and have been considered before as ODE models for homogeneous population [6]. Assumptions made for all parameters in the chapter 3 is used model parameters in this model. In addition to those assumptions, we assume disease induced death rate $\alpha(\tau) \in L^1_+(0,\infty)$ and $\alpha(\tau) > 0$ for all $\tau \geq 0$. Model will be analyzed in a biologically-feasible region. Define the feasible region

$$\mathrm{X}_+ = \mathbb{R}_+ \times \mathbb{R}_+ \times \mathbb{R}_+ \times L^1_+(0,\infty) \times \mathbb{R}_+$$

and its corresponding norm is given as $\|x\| = |x_1| + |x_2| + |x_3| + \displaystyle\int_0^\infty |x_4(\tau)| d\tau + |x_5|$ for all x $\in \mathrm{X}_+$. Furthermore, adding first and second equations of model, we have

$$\frac{d}{dt}\left(S_v\left(t\right) + I_v\left(t\right)\right) = \Lambda_v - \mu_v \big(S_v(t) + I_v(t)\big) \tag{4.2}$$

Using integrating factor method, solution $N_v(t)$ is $N_v(t) = N_v(0)e^{-\mu_v t} + \frac{\Lambda_v}{\mu_v}(1 - e^{-\mu_v t})$

And thus we get,

$$\lim_t \left(S_v\left(t\right) + I_v\left(t\right)\right) = \frac{\Lambda_v}{\mu_v}$$

Integrating with respect to τ the PDE in system (4.1), we obtain

$$i(\tau,t)\big|_0^\infty + I' = -\int_0^\infty \alpha(\tau)i(\tau,t)dt - \int_0^\infty \gamma(\tau)i(\tau,t)d\tau - \mu I(t)$$

If we assume $\lim_{\tau\to\infty} i(\tau,t) = 0$, the above equality leads to

$$I'(t) = i(0,t) - \int_0^\infty \alpha(\tau)i(\tau,t)dt - \int_0^\infty \gamma(\tau)i(\tau,t)d\tau - \mu I(t)$$

Adding 3^{rd},5^{th} equations of with above equation, we get

$$\frac{d}{dt}\left(S(t) + \int_0^\infty i(\tau,t)dt + R(t)\right) = \Lambda - \int_0^\infty \alpha(\tau)i(\tau,t)dt - \mu\left(S(t) + \int_0^\infty i(\tau,t)dt + R(t)\right) \tag{4.3}$$

Using integrating factor method, we solve equation (4.3) and we get

$$N(t) \le N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t}) \tag{4.4}$$

And this gives us,

$$\lim_t \left(S(t) + \int_0^\infty i(\tau,t)dt + R(t)\right) \le \frac{\Lambda}{\mu}$$

Therefore, using the same argument as used for model in chapter 3, following set Ω is positively invariant for the system,

$$\Omega = \left\{(S_v, I_v, S, I, R) \in \mathrm{X}_+ : S_v(t) + I_v(t) \le \frac{\Lambda_v}{\mu_v}, S(t) + \int_0^\infty i(\tau,t)dt + R(t) \le \frac{\Lambda}{\mu}\right\}$$

Table 4.1: Definition of the variables in the Between host model

Variable	Meaning
$S_v(t)$	The number of susceptible vectors at time t
$I_v(t)$	The number of infected vectors at time t
$S(t)$	The number of susceptible individuals at time t
$i(\tau,t)$	Density of the infected host with infection age τ at time t
$R(t)$	The number of recovered individuals at time t

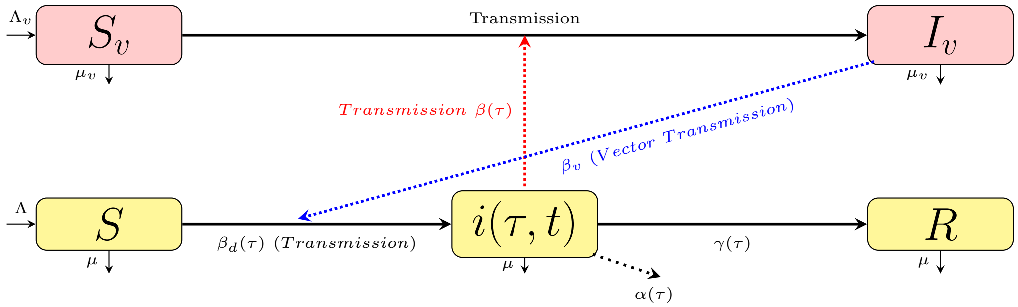

Figure 4.1: **Schematic diagram of the vector borne disease transmission dynamic**. The bold pointed solid lines represent transfer of vectors/hosts to another compartment due to infection. Red dotted line is the transmission rate of infection from an infected host to susceptible vector class. Blue dotted line is the transmission rate of infection from an infected vector to susceptible host. The shorter pointed solid lines represent recruitment, deaths (natural and disease related) of vectors/hosts.

Table 4.2: Definition of the parameters in the between host model

Parameter	Meaning
Λ_v	Susceptible vector recruitment rate
μ_v	Vector natural death rate
Λ	Host recruitment rate
μ	Host natural death rate
$\alpha(\tau)$	Host disease induced death rate
$\beta(\tau)$	Transmission rate of infection from an infected host to susceptible vector class
β_v	Transmission rate of infection from an infected mosquito to susceptible host
$\beta_d(\tau)$	Direct transmission rate of infection from an infected host to a susceptible host
$\gamma(\tau)$	Recovery rate of infected host population

4.3 EXISTENCE OF STEADY STATES AND LOCAL STABILITY OF DISEASE FREE EQUILIBRIUM

The steady state solutions of an epidemiological model at which the population remains in the absence of disease is called disease-free equilibrium point. To find the steady states, we look for time-independent solution that satisfy the system with the time derivatives equal to zero. The system for the equilibria takes the form

$$\begin{aligned}
&\Lambda_v - \frac{S_v^*}{N^*}\int_0^\infty \beta(\tau) i^*(\tau) d\tau - \mu_v S_v^* = 0,\\
&\frac{S_v^*}{N^*}\int_0^\infty \beta(\tau) i^*(\tau) d\tau - \mu_v I_v^* = 0,\\
&\Lambda - \frac{\beta_v S^* I_v^*}{N^*} - \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau) i^*(\tau) d\tau - \mu S^* = 0,\\
&\frac{di^*}{d\tau} = -\left(\gamma(\tau) + \alpha(\tau) + \mu\right) i^*(\tau),\\
&i^*(0) = \frac{\beta_v S^* I_v^*}{N^*} + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau) i^*(\tau) d\tau,\\
&\int_0^\infty \gamma(\tau) i^*(\tau) d\tau - \mu R^* = 0.
\end{aligned} \tag{4.5}$$

Note $\pi_1(\tau) = e^{-\int_0^\tau (\gamma(s)+\alpha(s)+\mu) ds}$ and $i^*(\tau) = i^*(0)\pi_1(\tau)$

If $i^*(0) = 0$, then we obtain disease free equilibrium $E^0 = \left(\frac{\Lambda_v}{\mu_v}, 0, \frac{\Lambda}{\mu}, 0, 0\right)$

4.3.1 Stability of Disease Free Equilibrium

To investigate the local stability of the equilibria, we linearize the system. Let $S(t) = S^* + x(t), i(\tau, t) = i^*(\tau) + y(\tau, t), R(t) = R^* + z(t), S_v(t) = S_v^*(t) + x_v(t), I_v(t) = I_v^*(t) + y_v(t), N(t) = N^* + n(t)$ where $x(t), y(\tau, t), z(t), x_v(t), y_v(t), n(t)$ are the perturbations.

Substituting $S_v(t), I_v(t), S(t), i(\tau,t), R(t)$, in M_2 and using (4.8) we get

$$\begin{aligned}
x_v'(t) &= -\frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)y(\tau,t)d\tau - \frac{x_v(t)}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau + \frac{S_v^* n(t)}{N^{*2}}\int_0^\infty \beta(\tau)i^*(\tau)d\tau \\
&\quad - \mu_v x_v(t) \\
y_v'(t) &= \frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)y(\tau,t)d\tau + \frac{x_v(t)}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau - \frac{S_v^* n(t)}{N^{*2}}\int_0^\infty \beta(\tau)i^*(\tau)d\tau \\
&\quad - \mu_v y_v(t) \\
x'(t) &= -\frac{\beta_v S^* y_v(t)}{N^*} - \frac{\beta_v I_v^* x(t)}{N^*} + \frac{\beta_v S^* I_v^*}{N^{*2}}n(t) - \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)y(\tau,t)d\tau \\
&\quad - \frac{x(t)}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau + \frac{S^* n(t)}{N^{*2}}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau - \mu x(t), \\
\frac{\partial y(\tau,t)}{\partial t} &+ \frac{\partial y(\tau,t)}{\partial \tau} = -(\gamma(\tau)+\alpha(\tau)+\mu)y(\tau,t), \\
y(0,t) &= \frac{\beta_v S^* y_v(t)}{N^*} + \frac{\beta_v I_v^* x(t)}{N^*} - \frac{\beta_v S^* I_v^*}{N^{*2}}n(t) + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)y(\tau,t)d\tau \\
&\quad + \frac{x(t)}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau - \frac{S^* n(t)}{N^{*2}}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau, \\
z'(t) &= \int_0^\infty \gamma(\tau)y(\tau,t)d\tau - \mu z(t).
\end{aligned} \tag{4.6}$$

System (4.6) is a linear system for $x(t), y(\tau,t), z(t), x_v(t), y_v(t)$. Let $x(t) = \bar{x}e^{\lambda t}, y(\tau,t) = \bar{y}(\tau)e^{\lambda t}, z(t) = \bar{z}e^{\lambda t}, x_v(t) = \bar{x}_v e^{\lambda t}, y_v(t) = \bar{y}_v e^{\lambda t}, n(t) = \bar{n}e^{\lambda t}$ be the solution of the system (4.6) where $\bar{x}, \bar{y}(\tau), \bar{z}, \bar{x}_v, \bar{y}_v, \lambda$ are not all zero. Substituting the constitutive form of the solutions in the system (4.6), we obtain following eigenvalue problem (the bars have been omitted)

$$
\begin{aligned}
\lambda x_v &= -\frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)y(\tau)d\tau - \frac{x_v}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau + \frac{S_v^*}{N^{*2}}n\int_0^\infty \beta(\tau)i^*(\tau)d\tau \\
&- \mu_v x_v \\
\lambda y_v &= \frac{S_v^*}{N^*}\int_0^\infty \beta(\tau)y(\tau)d\tau + \frac{x_v}{N^*}\int_0^\infty \beta(\tau)i^*(\tau)d\tau - \frac{S_v^*}{N^{*2}}n\int_0^\infty \beta(\tau)i^*(\tau)d\tau - \mu_v y_v \\
\lambda x &= -\frac{\beta_v S^* y_v}{N^*} - \frac{\beta_v I_v^* x}{N^*} + \frac{\beta_v S^* I_v^*}{N^{*2}}n - \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)y(\tau)d\tau - \frac{x}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau \\
&+ \frac{S^*}{N^{*2}}n\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau - \mu x, \\
\lambda y + \frac{dy}{d\tau} &= -(\gamma(\tau)+\alpha(\tau)+\mu)y(\tau), \\
y(0) &= \frac{\beta_v S^* y_v}{N^*} + \frac{\beta_v I_v^* x}{N^*} - \frac{\beta_v S^* I_v^*}{N^{*2}}n + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau)y(\tau)d\tau + \frac{x}{N^*}\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau \\
&- \frac{S^*}{N^{*2}}n\int_0^\infty \beta_d(\tau)i^*(\tau)d\tau, \\
\lambda z &= \int_0^\infty \gamma(\tau)y(\tau)d\tau - \mu z.
\end{aligned}
\tag{4.7}
$$

Solutions of system (4.7) gives the eigenvalues λ. Next we obtain the characteristics equation. At disease free equilibrium $E^0 = (S_v^0, I_v^0, S^0, I^0, R^0) = (\frac{\Lambda_v}{\mu_v}, 0, \frac{\Lambda}{\mu}, 0, 0)$, system (4.7) reduces to

$$
\begin{aligned}
\lambda x_v &= -\frac{S_v^0}{N^0}\int_0^\infty \beta(\tau)y(\tau)d\tau - \mu_v x_v \\
\lambda y_v &= \frac{S_v^0}{N^0}\int_0^\infty \beta(\tau)y(\tau)d\tau - \mu_v y_v \\
\lambda x &= -\frac{\beta_v S^0 y_v}{N^0} - \frac{S^0}{N^0}\int_0^\infty \beta_d(\tau)y(\tau)d\tau - \mu x, \\
\lambda y + \frac{dy}{d\tau} &= -(\gamma(\tau)+\alpha(\tau)+\mu)y(\tau), \\
y(0) &= \frac{\beta_v S^0 y_v}{N^0} + \frac{S^0}{N^0}\int_0^\infty \beta_d(\tau)y(\tau)d\tau, \\
\lambda z &= \int_0^\infty \gamma(\tau)y(\tau)d\tau - \mu z.
\end{aligned}
\tag{4.8}
$$

Using value of y_v from 2^{nd} equation of model (4.8) in 5^{th} equation, we get,

$$
y(0) = \frac{S^0}{N^0}\left(\frac{\beta_v S_v^0}{N^0(\lambda+\mu_v)}\int_0^\infty \beta(\tau)y(\tau)d\tau) + \int_0^\infty \beta_d(\tau)y(\tau)d\tau\right), \tag{4.9}
$$

Differential equation in (4.8) is independent of of x, z, x_v and y_v and solving it, we obtain,

$$y(\tau) = y(0)e^{-\lambda\tau}\pi_1(\tau)$$

where

$$\pi_1(\tau) = e^{-\int_0^\tau (\gamma(s) + \alpha(\tau) + \mu)ds}$$

Notice here the probability of survival an infectious individual survives to the time since infection τ after being infected depends on disease induced death rate.

Using $S^0 = N^0$ and substituting $y(\tau)$ in (4.9), we obtain following characteristic equation,

$$\frac{\beta_v S_v^0}{N^0(\lambda + \mu_v)} \int_0^\infty \beta(\tau)e^{-\lambda\tau}\pi_1(\tau)d\tau) + \int_0^\infty \beta_d(\tau)e^{-\lambda\tau}\pi_1(\tau)d\tau = 1, \tag{4.10}$$

We use same strategy used in proving the stability for disease free equilibrium in Chapter 3. We will show that all solutions λ of the equation (4.10) have negative real part.

We denote left hand side of (4.10) by function $g(\lambda)$.

$$g(\lambda) = \frac{\beta_v S_v^0}{N^0(\lambda + \mu_v)} \int_0^\infty \beta(\tau)e^{-\lambda\tau}\pi_1(\tau)d\tau) + \int_0^\infty \beta_d(\tau)e^{-\lambda\tau}\pi_1(\tau)d\tau, \tag{4.11}$$

We obtain the reproduction number by setting $\lambda = 0$ and denote the the reprodcution number for this model by $\mathcal{R}_{02}$. Then,

$$\mathcal{R}_{02} = g(0) = \frac{\beta_v \Lambda_v \mu}{\Lambda \mu_v^2} \int_0^\infty \beta(\tau)\pi_1(\tau)d\tau + \int_0^\infty \beta_d(\tau)\pi_1(\tau)d\tau$$

Now we analysis two different cases below:

<u>case 1</u> If $\mathcal{R}_{02} > 1$. Assuming $\beta(\tau)$ and $\beta_d(\tau)$ are strictly positive and $\lambda > -\mu_v$, then clearly $g(\lambda)$ is decreasing function on λ. Here, $g(0) = \mathcal{R}_{02} > 1$ and

$$\lim_{\lambda\to\infty} g(\lambda) = 0$$

Then there exist $\lambda^* > 0$ such that $g(\lambda^*) = 1$. Thus disease free equilibrium is unstable if $\mathcal{R}_{02} > 1$

case 2 If $\mathcal{R}_{02} < 1$. For all $\lambda = c + id$ where $c, d \in \mathbb{R}$ and assume $c \geq 0$. Then we have,

$$
\begin{aligned}
|g(\lambda)| &\leq \frac{\beta_v S_v^0}{N^0 \mu_v} \int_0^\infty \beta(\tau)|e^{-\lambda\tau}|\pi_1(\tau)d\tau + \int_0^\infty \beta_d(\tau)|e^{-\lambda\tau}|\pi_1(\tau)d\tau \\
&\leq \frac{\beta_v S_v^0}{N^0 \mu_v} \int_0^\infty \beta(\tau)|e^{-c\tau}|\pi_1(\tau)d\tau + \int_0^\infty \beta_d(\tau)|e^{-c\tau}|\pi_1(\tau)d\tau \\
&\leq \frac{\beta_v S_v^0}{N^0 \mu_v} \int_0^\infty \beta(\tau)\pi_1(\tau)d\tau + \int_0^\infty \beta_d(\tau)\pi_1(\tau)d\tau \\
&= \mathcal{R}_{02} \\
&< 1
\end{aligned}
$$

Thus we see that those λ whose real part is non negative cannot satisfy the equation $g(\lambda) = 1$. Therefore, the disease free equilibrium is locally asymptotically stable in this case. This allows us to have a following theorem:

Theorem 7. *If $\mathcal{R}_{02} < 1$, the disease-free equilibrium is locally asymptotically stable. If $\mathcal{R}_{02} > 1$, the disease-free equilibrium is unstable.*

4.3.2 Existence of Endemic Equilibrium

Disease regularly found among particular people or within a given geographic area is called endemic. The endemic equilibrium state is the state where the disease cannot be totally eradicated but remains in the population. In order to find positive solution, we take $i^*(0) \neq 0$. We denote endemic equilibrium of the above model by $E^* = (S_v^*, I_v^*, S^*, i^*(\tau), R^*)$. Let $B_1 = \int_0^\infty \beta(\tau)\pi_1(\tau)d\tau$ and $B_{1d} = \int_0^\infty \beta_d(\tau)\pi_1(\tau)d\tau$ Adding 1^{st} and 2^{nd} equations of (4.5) we get, $N_v^* = \dfrac{\Lambda_v}{\mu_v}$ and adding 3^{rd}, 4^{th} and 6^{th} of (4.5), we get

$$
N^* = \frac{\Lambda}{\mu} - \frac{i^*(0)D}{\mu} \quad \text{where } D = \int_0^\infty \alpha(\tau)\pi_1(\tau)d\tau \tag{4.12}
$$

Next, we show $\int_0^\infty (\alpha(\tau)+\gamma(\tau)+\mu)\pi_1(\tau)d\tau = 1$ which implies that $D < 1$.
Let

$$u = \int_0^\tau (\alpha(s)+\gamma(s)+\mu)\, ds$$

Using Fundamental theorem of calculus, we get $du = (\alpha(\tau)+\gamma(\tau)+\mu)\, d\tau$, thus

$$\begin{aligned}\int_0^\infty (\alpha(\tau)+\gamma(\tau)+\mu)\pi_1(\tau)d\tau &= \int_0^\infty (\alpha(\tau)+\gamma(\tau)+\mu)e^{-\int_0^\tau (\alpha(s)+\gamma(s)+\mu)} d\tau \\ &= \int_0^\infty e^{-u} du \\ &= 1\end{aligned}$$

Solving 1^{st} equation for S_v^* and 2^{nd} equation for I_v^* in (4.5), we get,

$$S_v^* = \frac{N^*\Lambda_v}{i^*(0)B_1 + N^*\mu_v} \tag{4.13}$$

$$I_v^* = \frac{S_v i^*(0)B_1}{N^*\mu_v} \tag{4.14}$$

We can rewrite the boundary condition in (4.5) as

$$i^*(0) = S\left(\frac{\beta_v I_v^*}{N^*} + \frac{i^*(0)B_{1d}}{N^*}\right) = S^*X \text{ where } X = \left(\frac{\beta_v I_v^*}{N^*} + \frac{i^*(0)B_{1d}}{N^*}\right) \text{ is a function of } i^*(0).$$

Solving 3^{rd} equation for S^* gives $S^* = \dfrac{\Lambda}{X+\mu}$. We can rewrite (4.12) after substituting $i^*(0)$ as $N^* = \dfrac{\Lambda}{\mu}\left(1 - \dfrac{DX}{X+\mu}\right)$. Plugging N^* in (4.13), we get

$$\frac{S_v^*}{N^*} = \frac{\Lambda_v\mu(X+\mu)}{\Lambda\mu B_1 X + \mu_v\Lambda(X+\mu-DX)}$$

Next we use I_v^* in boundary condition in (4.5) to get

$$N^* = \frac{\beta_v B_1}{\mu_v}\frac{S^*S_v^*}{N} + S^*B_{1d} \tag{4.15}$$

Substituting S^*, $\dfrac{S_v^*}{N^*}$, and N^* in (4.15), and expanding and rearranging, we obtain

$$b_1X^2 + b_2X + b_3 = 0 \tag{4.16}$$

Where,

$$b_1 = \Lambda\mu_v(1-D)\left(\mu_v(1-D)+\mu B_1\right)$$

$$b_2 = \Lambda\mu\mu_v\Big[\mu_v(1-R_0)+\mu_v(1-D)+\mu B_1(1-B_{1d})-\mu_v D(1-B_{1d})\Big]$$

$$b_3 = \Lambda\left(\mu\mu_v\right)^2\left(1-\mathcal{R}_{02}\right)$$

and

$$\mathcal{R}_{02} = \frac{\beta_v\Lambda_v\mu}{\mu_v^2\Lambda}B_1 + B_{1d} \quad \text{is the reproduction number.}$$

Let $K(X) = b_1X^2 + b_2X + b_3$. Next, we explore the existence of the positive root in $K(X) = 0$. Roots of (4.16) is given as

$$X_{12} = \frac{-b_2 \pm \sqrt{b_2^2 - 4b_1b_3}}{2b_1} \tag{4.17}$$

Where $X_1 = \dfrac{-b_2 + \sqrt{b_2^2 - 4b_1b_3}}{2b_1}$ and $X_2 = \dfrac{-b_2 - \sqrt{b_2^2 - 4b_1b_3}}{2b_1}$

First, we note following:

- b_1 is always positive since $D < 1$,
- if $\mathcal{R}_{02} < 1$, $b_3 > 0$,
- if $\mathcal{R}_{02} = 1$, $b_3 = 0$,
- if $\mathcal{R}_{02} > 1$, $b_3 < 0$

Note that, if $\theta = b_2^2 - 4b_1b_3 = 0$, the two roots coincide and there exists a unique positive root of multiplicity 2 only if $\dfrac{b_2}{b_1} < 0$. We take $\theta \neq 0$ to explore the existence of the positive roots of (4.16) which proves the existence of positive endemic equilibrium under following different cases:

case 1. $\mathcal{R}_{02} > 1$. We have following different sub-cases

a. When $b_2 > 0$

In this case, $\sqrt{b_2^2 - 4b_1b_3} > |b_2|$. Roots of (4.16) are $X_1 > 0$ and $X_2 < 0$. Thus, unique positive endemic equilibrium *b*. <u>When $b_2 < 0$</u>

In this case, $\sqrt{b_2^2 - 4b_1b_3} > |b_2|$. Roots of (4.16) are $X_1 > 0$ and $X_2 < 0$. Thus, unique positive endemic equilibrium

<u>case 2.</u> $\mathcal{R}_{02} = 1$. In this case, we see that $\sqrt{b_2^2 - 4b_1b_3} = b_2$ and so there exists a unique positive root provided that $b_2 < 0$.

<u>case 3.</u> $\mathcal{R}_{02} < 1$. We observe that $b_3 > 0$. We have following different sub-cases

a. <u>When $b_2 > 0$</u>

In this case, $\sqrt{b_2^2 - 4b_1b_3} < |b_2|$. Roots of (4.16) are $X_1 < 0$ and $X_2 < 0$. Thus, no positive endemic equilibrium.

b. <u>When $b_2 < 0$</u>

In this case, $\sqrt{b_2^2 - 4b_1b_3} < |b_2|$. Roots of (4.16) are $X_1 > 0$ and $X_2 > 0$. Thus, there exist two positive endemic equilibrium.

Based on above analysis we can formulate following theorems.

Theorem 8. *For the model* (1)

a. If $\mathcal{R}_{02} > 1$, *then there exist unique positive endemic equilibrium.*

b. If $\mathcal{R}_{02} = 1$, *there exist unique positive endemic equilibrium provided* $b_2 < 0$.

c. If $\mathcal{R}_{02} < 1$ *and* $b_2 < 0$ *,then there exists two positive endemic equilibrium.*

Theorem 10 gives the possibility of backward bifurcation at $\mathcal{R}_{02} = 1$ when $b_2 < 0$.

4.3.3 Backward Bifurcation of Endemic Steady States

Theoretically, we have proved the existence of backward bifurcation in the presence of disease induced death rate. Graphically, using fcontour in MATLAB, we were able to verify the existence of backward bifurcation when disease induced death rate is include. To plot the model, we kept all other parameters constant varying mortality rate of vector within the the range $[0.7, 0.9]$. While doing this simulation, for the value of $D \geq 1$ the plot did not show any backward bifurcation and when D was kept between $(0, 0.8)$, existence of backward bifurcation was observed.

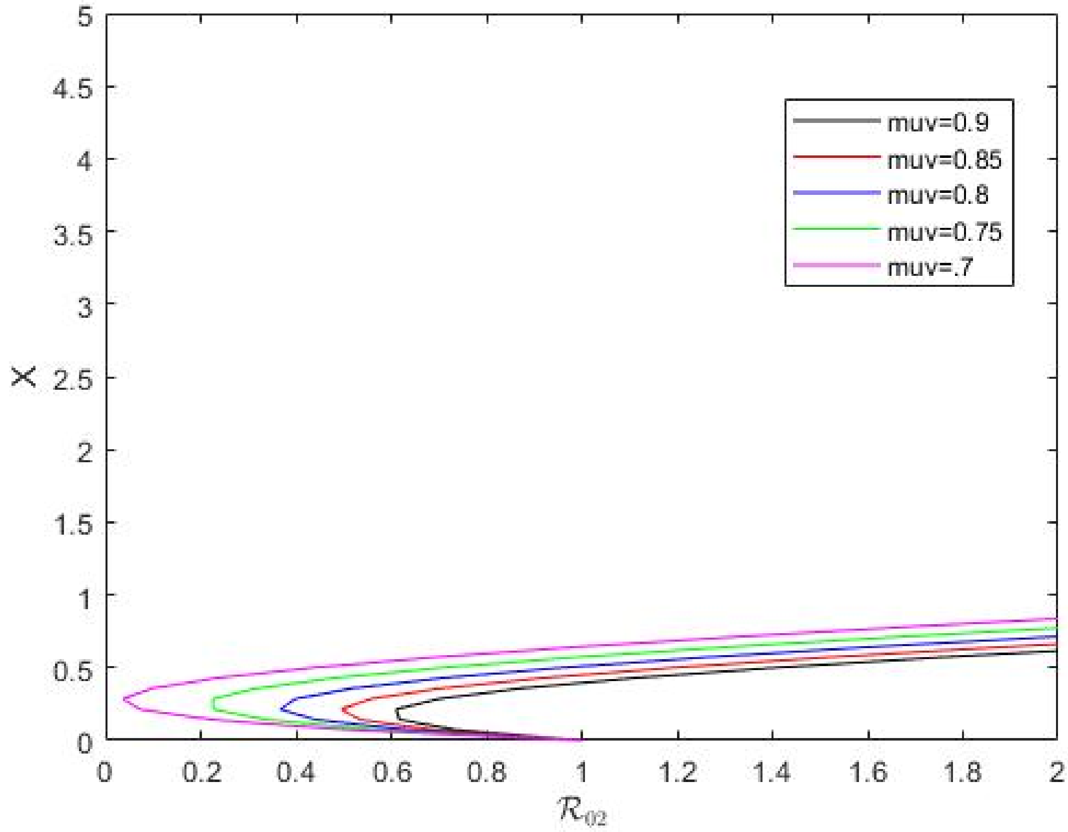

Figure 4.2: The figure of X versus $\mathcal{R}_{02}$ that shows a backward bifurcation with endemic equilibria when $\mathcal{R}_{02} < 1$, where Theorem 10 holds. The parameter μ_v is varied in the range $[0.7, 0.9]$ whereas other parameters values are: $B_1 = 0.9, \Lambda = .6, \mu = 0.3, D = 0.1, \Lambda_v = 2, \beta_v = 3$

In the figure below, we observe that there is a value say $\mathcal{R}_C$ which is the value of $\mathcal{R}_{02}$ where two non trivial endemic equilibrium collide and know as critical reproduction number.

To determine the critical reproduction number, we set discriminant Δ to zero, we get as follows

$$b_2^2 - 4b_1b_3 = 0$$

$$b_3 = \frac{b_2^2}{4b_1}$$

Substituting $b_3 = \Lambda\left(\mu\mu_v\right)^2\left(1 - \mathcal{R}_{02}\right)$ above and we solve for $\mathcal{R}_{02}$ and name this $\mathcal{R}_{02}$

as $\mathcal{R}_C$ and called as critical reproduction number.

we obtain $\mathcal{R}_C = 1 - \dfrac{b_2^2}{4b_1\phi}$ where $\phi = \Lambda(\mu\mu_v)^2$. These endemic equilibrium bifurcates backward at $\mathcal{R}_{02} = 1$ and thus we observe existence of two non trivial equilibira when $\mathcal{R}_C < \mathcal{R}_{02} < 1$.

Backward bifurcation is identified by negative slope at $\mathcal{R}_{02} = 1$. Consider X as a function of $\mathcal{R}_{02}$. Differentiating implicitly (4.16) with respect to $\mathcal{R}_{02}$.

$$\frac{\partial X}{\partial \mathcal{R}_{02}}(2Xb_1 + b_2) = \Lambda\mu\mu_v^2 X + \Lambda(\mu\mu_v)^2$$

Which can be written as

$$\frac{\partial X}{\partial \mathcal{R}_{02}} = \frac{\Lambda\mu\mu_v^2 X + \Lambda(\mu\mu_v)^2}{2b_1X + \Lambda\mu\mu_v\Big[\mu_v(1-R_0) + \mu_v(1-D) + \mu B_1(1-B_{1d}) - \mu_v D(1-B_{1d})\Big]}$$

At critical value $(\mathcal{R}_{02}, X) = (1, 0)$ gives

$$\frac{\partial X}{\partial \mathcal{R}_{02}} = \frac{\mu\mu_v}{\mu_v(1-D) + \mu B_1(1-B_{1d}) - \mu_v D(1-B_{1d})} \tag{4.18}$$

This derivative can be negative if and only if the denominator is negative.

$$\mu_v(1-D) + \mu B_1(1-B_{1d}) - \mu_v D(1-B_{1d}) < 0$$

$$\mu_v - 2\mu_v D + \mu B_1 - \mu B_1 B_{1d} + \mu_v D B_{1d} < 0$$

$$\mu_v + \mu B_1 - \mu B_1 B_{1d} + \mu_v D B_{1d} < 2\mu_v D$$

$$1 + \frac{\mu B_1}{\mu_v}\big(1 - B_{1d}\big) + D B_{1d} < 2D$$

Thus, condition for backward bifurcation is given by :

$$1 + \frac{\mu B_1}{\mu_v}\big(1 - B_{1d}\big) + D B_{1d} < 2D \tag{4.19}$$

We observe that if D which is disease induced mortality is zero i.e. disease induced death rate is zero, then, inequality (4.19) does not hold true. This is because backward bifurcation occur for $\mathcal{R}_{02} < 1$ which implies that $B_{1d} < 1$. This makes left hand side of (4.19) negative which is not true. Thus, necessary and sufficient condition for backward bifurcation is only true when $D > 0$.

This characteristics of backward bifurcation of the model can written as theorem below.

Theorem 9. *The system* (4.1) *has a backward bifurcation when* $\mathcal{R}_{02} < 1$ *and* $b_2 < 0$. *The condition for backward bifurcation is given by* $1 + \dfrac{\mu B_1}{\mu_v}\big(1 - B_{1d}\big) + DB_{1d} < 2D$ *provided that* $D > 0$.

4.4 LOCAL STABILITY OF ENDEMIC EQUILIBRIA

In this section, we see local stability of endemic equilibrium that is in backward bifurcation when $\mathcal{R}_{02} < 1$. First, we deduce some terms that will be useful later. Plugging back $i^*(0)$ from 5^{th} equation into the 3^{rd} equation in (4.5), we get

$$\Lambda - i^*(0) - \mu S^* = 0$$

Solving above equation for S^*, we get $S^* = \dfrac{\Lambda - i^*(0)}{\mu}$. We know $N^* = \dfrac{\Lambda - i^*(0)D}{\mu}$ from (4.12). Then

$$\frac{S^*}{N^*} = \frac{\Lambda - i^*(0)}{\Lambda - i^*(0)D} \tag{4.20}$$

We plug $N^* = \dfrac{\Lambda - i^*(0)D}{\mu}$ in (4.13), to write $\dfrac{S_v^*}{N^*}$ as

$$\frac{S_v^*}{N^*} = \frac{\Lambda_v}{i^*(0)B_1 + N^*\mu_v} = \frac{\Lambda_v \mu}{\mu i^*(0)B_1 + \mu_v(\Lambda - i^*(0)D)} = \frac{\Lambda_v \mu}{M} \tag{4.21}$$

where $M = \mu i^*(0)B_1 + \mu_v(\Lambda - i^*(0)D)$ and using $N^* = \dfrac{\Lambda - i^*(0)D}{\mu}$, we get,

$$\frac{\mu}{M} = \frac{1}{i^*(0)B_1 + N^*\mu_v}$$

Next we substitute $I_v^* = \dfrac{S_v i^*(0) B_1}{N^* \mu_v}$ from (4.14) into 5^{th} equation of (4.5) to get equation for endemic equilibrium as below.

$$\begin{aligned} i^*(0) &= \frac{\beta_v S^* I_v^*}{N^*} + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau) i^*(\tau) d\tau \\ i^*(0) &= \frac{\beta_v S^*}{N^*}\frac{S_v i^*(0) B_1}{N^* \mu_v} + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau) i^*(\tau) d\tau \\ \text{implies } 1 &= \frac{\beta_v S^*}{N^*}\frac{S_v B_1}{N^* \mu_v} + \frac{S^*}{N^*}\int_0^\infty \beta_d(\tau) \pi_1(\tau) d\tau \end{aligned}$$

which yields

$$0 = \beta_v \frac{S^*}{N^*}\frac{B_1}{\mu_v}\frac{S_v^*}{N^*} + \frac{S^*}{N^*} B_{1d} - 1 \tag{4.22}$$

Let us denote right hand side of endemic equilibrium equation (4.22) by

$$\mathcal{J}(i^*(0)) = \beta_v \frac{S^*}{N^*}\frac{B_1}{\mu_v}\frac{S_v^*}{N^*} + \frac{S^*}{N^*} B_{1d} - 1 \tag{4.23}$$

Substituting $\dfrac{S^*}{N^*}$ and $\dfrac{S_v^*}{N^*}$ in (4.22), we get

$$\begin{aligned} \mathcal{J}(i^*(0)) &= \beta_v \frac{S^*}{N^*}\frac{B_1}{\mu_v}\frac{S_v^*}{N^*} + \frac{S^*}{N^*} B_{1d} - 1 \\ &= \beta_v \frac{\Lambda - i^*(0)}{\Lambda - i^*(0)D}\frac{B_1}{\mu_v}\Big(\frac{\Lambda_v \mu}{\mu i^*(0) B + \mu_v(\Lambda - i^*(0)D)}\Big) + \frac{\Lambda - i^*(0)}{\Lambda - i^*(0)D} B_{1d} - 1 \end{aligned} \tag{4.24}$$

At $i^*(0) = 0$, the endemic equilibrium function $\mathcal{F}(i^*)$ is reduced to

$$\begin{aligned} \mathcal{J}(0) &= \beta_v \frac{\Lambda_v \mu}{\Lambda \mu_v^2} B_1 + B_{1d} - 1 \\ &= \mathcal{R}_{02} - 1 \\ &< 0 \quad (\text{since } \mathcal{R}_{02} < 1) \end{aligned}$$

We proved in Theorem 10, when $\mathcal{R}_{02} < 1$, there exist two endemic equilibrium. As $\mathcal{J}(0) < 1$, thus, in the XY plane with the ordered pair $(i^*(0), \mathcal{J}(i^*(0)))$, the graph of $\mathcal{J}(i^*(0))$ first moves upward to cross the X axis and is the first zeros of (4.23) giving the lower endemic equilibrium, denote it by $i_1^*(0)$. In this endemic equilibrium, the slope is positive i.e. $\mathcal{J}'(i_1^*(0)) > 0$.

Like wise the graph for $\mathcal{J}(i^*(0))$ then moves downward to cross the X axis and is the second zeros of (4.24) giving upper endemic equilibrium(second) and we denote it by $i_2^*(0)$. In this endemic equilibrium, slope is negative $\mathcal{J}'(i_2^*(0)) < 0$. The reason we named them as upper and lower endemic equilibrium is because $i_2^*(0) > i_1^*(0)$. Epidemiologically, this means number of infected individuals in upper endemic equilibrium($i_2^*(0)$) is greater than the number of infected individuals in lower endemic equilibrium($i_2^*(0)$) [58].

Next we find the derivative of $\mathcal{J}(i^*(0))$ as below.

$$\mathcal{J}'(i^*(0)) = \beta_v \big(\frac{S^*}{N^*}\big)' \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} + \beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \big(\frac{S_v^*}{N^*}\big)' + \big(\frac{S^*}{N^*}\big)' B_{1d} \tag{4.25}$$

First we compute derivative terms in (4.25) as below

$$\begin{aligned}
\big(\frac{S^*}{N^*}\big)' &= \frac{-\big(\Lambda - i^*(0)\big)D - \big(\Lambda - i^*(0)\big)(-D)\big)}{\big(\Lambda - i^*(0)D\big)^2} \\
&= \frac{\Lambda(D-1)}{\big(\Lambda - i^*(0)D\big)^2}
\end{aligned}$$

and

$$\begin{aligned}
\big(\frac{S_v^*}{N^*}\big)' &= \frac{-\Lambda_v \mu\big(\mu B_1 - \mu_v D\big)}{\big(\mu i^*(0)B_1 + \mu_v(\Lambda - i^*(0)D)\big)^2} \\
&= \frac{-\Lambda_v \mu\big(\mu B_1 - \mu_v D\big)}{M^2} \\
&= -\frac{\Lambda_v \mu}{M}\big(\frac{\mu_v B_1}{M} - \frac{\mu D}{M}\big) \\
&= \frac{S_v}{N}\big(\frac{\mu_v D}{M} - \frac{\mu B_1}{M}\big) \quad \text{using (4.21)}
\end{aligned}$$

Now we plug value of $(\frac{S^*}{N^*})'$ and $(\frac{S_v^*}{N^*})'$ in (4.25), we get

$$\begin{aligned}
\mathcal{J}'(i^*(0)) &= \beta_v \frac{\Lambda(D-1)}{\big(\Lambda - i^*(0)D\big)^2} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} + \beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} \big(\frac{\mu_v D}{M} - \frac{\mu B_1}{M}\big) + \frac{\Lambda(D-1)}{\big(\Lambda - i^*(0)D\big)^2} B_{1d} \\
&= \frac{\Lambda(D-1)}{\big(\Lambda - i^*(0)D\big)^2} \Big(\beta_v \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} + B_{1d}\Big) + \beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} \big(\frac{\mu_v D}{M} - \frac{\mu B_1}{M}\big) \\
&= \frac{\Lambda(D-1)}{\big(\Lambda - i^*(0)D\big)^2} \frac{N^*}{S^*} + \beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} \big(\frac{\mu_v D}{M} - \frac{\mu B_1}{M}\big) \\
&\quad \Big(\text{since } \beta_v \frac{B_1}{\mu_v} \frac{S_v}{N} + B_{1d} = \frac{N^*}{S^*}\Big) \\
&= \frac{\Lambda(D-1)}{\big(\Lambda - i^*(0)D\big)^2} \frac{\Lambda - i^*(0)D}{\Lambda - i^*(0)} + \beta_v \frac{S^*}{N^*} \frac{B}{\mu_v} \frac{S_v^*}{N^*} \big(\frac{\mu_v D}{M} - \frac{\mu B_1}{M}\big) \\
&\quad \Big(\text{since } \frac{S^*}{N^*} = \frac{\Lambda - i^*(0)}{\Lambda - i^*(0)D}\Big) \\
&= \frac{\Lambda(D-1)}{\big(\Lambda - i^*(0)D\big)\big(\Lambda - i^*(0)\big)} + \beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} \big(\frac{\mu_v D}{M} - \frac{\mu B_1}{M}\big)
\end{aligned} \tag{4.26}$$

Now we derive the characteristics equation for endemic equilibrium.
Lets $B_1(\lambda) = \int_0^\infty \beta(\tau) e^{-\lambda\tau} \pi_1(\tau) d\tau$, $B_{1d}(\lambda) = \int_0^\infty \beta_d(\tau) e^{-\lambda\tau} \pi_1(\tau) d\tau$,
Adding 3^{rd} and 5^{th} equation of (4.7), we get

$$x = \frac{-y(0)}{\lambda + \mu} \tag{4.27}$$

Adding 1^{st} and 2^{nd} equations of (4.7), we get $x_v = -y_v$ when $\lambda \neq -\mu_v$. Using $x_v = -y_v$ in 2^{nd} equation of (4.7) and rearranging, we get,

$$\Big(\lambda + \mu_v + \frac{i^*(0)B_1}{N^*}\Big) y_v - \frac{S_v^*}{N^*} B_1(\lambda) y(0) = -\frac{S_v^*}{N^*} \frac{i^*(0)B_1}{N^*} n \tag{4.28}$$

Substituting x from (4.27) in 5^{th} equation of (4.7) and rearranging gives

$$-\frac{\beta_v S^*}{N^*} y_v + \Big(1 + \frac{\beta_v I_v^*}{N^*(\lambda+\mu)} - \frac{S^* B_{1d}(\lambda)}{N^*} + \frac{i^*(0) B_{1d}}{N^*(\lambda+\mu)}\Big) y(0) = -\Big(\frac{\beta_v S^* I_v^*}{N^{*2}} n + \frac{S^*}{N^*} n \frac{i^*(0) B_{1d}}{N^*}\Big) \tag{4.29}$$

Since $N = S + \int_0^\infty i(\tau, t) d\tau + R$, total perturbation in the population is

$$n = x + \int_0^\infty y(\tau) d\tau + z$$

Substituting z from (4.7) gives

$$
\begin{aligned}
n &= x + \int_0^\infty y(\tau)d\tau + \frac{1}{\lambda+\mu}\int_0^\infty \gamma(\tau)y(\tau)d\tau \\
&= x + y(0)\int_0^\infty \Big(1+\frac{\gamma(\tau)}{\lambda+\mu}\Big)e^{-\lambda\tau}\pi_1(\tau)d\tau \\
&= x + y(0)\frac{1}{\lambda+\mu}\int_0^\infty \Big(\lambda+\mu+\gamma(\tau)\Big)e^{-\int_0^\tau \Big(\lambda+\mu+\alpha(s)+\gamma(s)\Big)ds} d\tau \\
&= x + y(0)\frac{1}{\lambda+\mu} - \frac{y(0)}{\lambda+\mu}\int_0^\infty \alpha(\tau)e^{-\lambda\tau}\pi_1(\tau)d\tau \\
&= x + y(0)\frac{1}{\lambda+\mu} - \frac{y(0)}{\lambda+\mu}D(\lambda)
\end{aligned}
$$

Substituting value of x from (4.27) results $n = -\frac{y(0)}{\lambda+\mu}D(\lambda)$

Substituting n in (4.28) and arranging, we get

$$\Big(\lambda+\mu_v+\frac{i^*(0)B_1}{N^*}\Big)y_v - \frac{S_v^*}{N^*}B_1(\lambda)y(0) = \frac{S_v^*}{N^*}\frac{i^*(0)B_1}{N^*}\frac{y(0)}{\lambda+\mu}D(\lambda)$$

implies

$$\Big(\lambda+\mu_v+\frac{i^*(0)B_1}{N^*}\Big)y_v - \Big(\frac{S_v^*}{N^*}B_1(\lambda) + \frac{S_v^*}{N^*}\frac{i^*(0)B_1}{N^*}\frac{D(\lambda)}{\lambda+\mu}\Big)y(0) = 0 \tag{4.30}$$

Substituting n in (4.29) and arranging, we get

$$
\begin{aligned}
&-\frac{\beta_v S^*}{N^*}y_v + \left(1+\frac{\beta_v I_v^*}{N^*(\lambda+\mu)} - \frac{S^* B_{1d}(\lambda)}{N^*} + \frac{i^*(0)B_{1d}}{N^*(\lambda+\mu)}\right)y(0) \\
&= \Big(\frac{\beta_v S^* I_v^*}{{N^*}^2} + \frac{S^*}{N^*}\frac{i^*(0)B_{1d}}{N^*}\Big)\frac{y(0)}{\lambda+\mu}D(\lambda)
\end{aligned}
$$

implies

$$-\frac{\beta_v S^*}{N^*}y_v + \Big(1+\frac{\beta_v I_v^*}{N^*(\lambda+\mu)} - \frac{S^* B_{1d}(\lambda)}{N^*} + \frac{i^*(0)B_{1d}}{N^*(\lambda+\mu)} - \Big(\frac{\beta_v S^* I_v^*}{{N^*}^2} + \frac{S^*}{N^*}\frac{i^*(0)B_{1d}}{N^*}\Big)\frac{D(\lambda)}{\lambda+\mu}\Big)y(0) = 0 \tag{4.31}$$

Equations (4.30) and (4.31) combined gives the system of characteristics equation for the model. Both $y(0) \neq 0$ and $y_v \neq 0$, we set determinant to zero.

$$\begin{vmatrix} (\lambda+\mu_v+\frac{i^*(0)B_1}{N^*}) & -(\frac{S_v^*}{N^*}B_1(\lambda) + \frac{S_v^*}{N^*}\frac{i^*(0)B_1}{N^*}\frac{D(\lambda)}{\lambda+\mu}) \\ -\frac{\beta_v S^*}{N^*} & (1+\frac{\beta_v I_v^*}{N^*(\lambda+\mu)} - \frac{S^* B_{1d}(\lambda)}{N^*} + \frac{i^*(0)B_{1d}}{N^*(\lambda+\mu)} - (\frac{\beta_v S^* I_v^*}{{N^*}^2} + \frac{S^*}{N^*}\frac{i^*(0)B_{1d}}{N^*})\frac{D(\lambda)}{\lambda+\mu}) \end{vmatrix} = 0$$

giving the characteristics equation as

$$(\lambda+\mu_v+\frac{i^*(0)B_1}{N^*})\Big(1+\frac{\beta_v I_v^*}{N^*(\lambda+\mu)}-\frac{S^*B_{1d}(\lambda)}{N^*}+\frac{i^*(0)B_{1d}}{N^*(\lambda+\mu)}$$
$$-(\frac{\beta_v S^* I_v^*}{N^{*2}}+\frac{S^*}{N^*}\frac{i^*(0)B_{1d}}{N^*})\frac{D(\lambda)}{\lambda+\mu}\Big)=\beta_v\frac{S^*}{N^*}\Big(\frac{S_v^*}{N^*}B_1(\lambda)+\frac{S_v^*}{N^*}\frac{i^*(0)B_1}{N^*}\frac{D(\lambda)}{\lambda+\mu}\Big)$$

gives

$$1+\frac{\beta_v I_v^*}{N^*(\lambda+\mu)}-\frac{S^*B_{1d}(\lambda)}{N^*}+\frac{i^*(0)B_{1d}}{N^*(\lambda+\mu)}-(\frac{\beta_v S^* I_v^*}{N^{*2}}+\frac{S^*}{N^*}\frac{i^*(0)B_{1d}}{N^*})\frac{D(\lambda)}{\lambda+\mu}=$$
$$\beta_v\frac{S^*}{N^*}\frac{S_v^*}{N^*}\frac{1}{(\lambda+\mu_v+\frac{i^*(0)B_1}{N^*})}\Big(B_1(\lambda)+\frac{i^*(0)B_1D(\lambda)}{N^*(\lambda+\mu)}\Big)$$

Rearranging we can rewrite the characteristics equation as

$$1=\beta_v\frac{S^*}{N^*}\frac{S_v^*}{N^*}\frac{1}{(\lambda+\mu_v+\frac{i^*(0)B_1}{N^*})}\Big(B_1(\lambda)+\frac{i^*(0)B_1D(\lambda)}{N^*(\lambda+\mu)}\Big)-\beta_v\frac{I_v^*}{(\lambda+\mu)N^*}$$
$$+\beta_v\frac{S^*}{N^*}\frac{I_v^*}{N^*}\frac{1}{(\lambda+\mu)}D(\lambda)+\frac{S^*}{N^*}B_{1d}(\lambda)-\frac{i^*(0)B_{1d}}{N^*(\lambda+\mu)}+\frac{S^*}{N^*}\frac{1}{\lambda+\mu}D(\lambda)\frac{i^*(0)B_{1d}}{N^*}$$

$$1=\beta_v\frac{S^*}{N^*}\frac{S_v^*}{N^*}\frac{1}{(\lambda+\mu_v+\frac{i^*(0)B_1}{N^*})}\Big(B_1(\lambda)+\frac{1}{N^*}\frac{D(\lambda)i^*(0)B_1}{\lambda+\mu}\Big)-\beta_v\frac{I_v^*}{(\lambda+\mu)N^*}$$
$$+\beta_v\frac{S^*}{N^*}\frac{I_v^*}{N^*}\frac{1}{(\lambda+\mu)}D(\lambda)+\frac{S^*}{N^*}B_{1d}(\lambda)-\frac{i^*(0)B_{1d}}{(\lambda+\mu)N^*}+\frac{S^*}{N^{*2}}\frac{1}{\lambda+\mu}D(\lambda)i^*(0)B_{1d} \tag{4.32}$$

We denote right hand side of characteristics equation by $\mathcal{G}(\lambda)$.

Then we have, $\mathcal{G}(\lambda)=1$ First we compute $\mathcal{G}(0)$ as below

$$\mathcal{G}(0)=\beta_v\frac{S^*}{N^*}\frac{S_v^*}{N^*}\frac{N^*B_1}{(\mu_vN^*+i^*(0)B_1)}\Big(1+\frac{i^*(0)D}{N^*\mu}\Big)-\beta_v\frac{1}{\mu N^*}I_v^*-\frac{i^*(0)B_{1d}}{\mu N^*}+\beta_v\frac{S^*}{N^*}\frac{1}{N^*}\frac{1}{\mu}DI_v^*$$
$$+\frac{S^*}{N^*}B_{1d}+\frac{S^*}{N^{*2}}\frac{1}{\mu}Di^*(0)B_{1d}\quad \text{(Note that } D(0)=D)$$

(Replacing $I_v^*=\dfrac{S_vi^*(0)B_1}{N^*\mu_v}$ to get)

$$=\beta_v\frac{S^*}{N^*}\frac{S_v^*}{N^*}\frac{N^*B_1}{(\mu_vN^*+i^*(0)B_1)}\Big(1+\frac{i^*(0)D}{N^*\mu}\Big)-\beta_v\frac{1}{\mu N^*}\frac{S_v^*i^*(0)B_1}{N^*\mu_v}-\frac{i^*(0)B_{1d}}{\mu N^*}$$
$$+\beta_v\frac{S^*}{N^*}\frac{1}{N^*}\frac{1}{\mu}D\frac{S_v^*i^*(0)B}{N^*\mu_v}+\frac{S^*}{N^*}B_{1d}+\frac{S^*}{N^{*2}}\frac{1}{\mu}Di^*(0)B_{1d}$$
$$=\beta_v\frac{S^*}{N^*}\frac{S_v^*}{N^*}\frac{N^*B_1}{(\mu_vN^*+i^*(0)B_1)}\Big(1+\frac{i^*(0)D}{N^*\mu}\Big)-\Big(\beta_v\frac{1}{\mu N^*}\frac{S_v^*i^*(0)B_1}{N^*\mu_v}+\frac{i^*(0)B_{1d}}{\mu N^*}\Big)+\frac{S^*}{N^*}B_{1d}$$
$$+\beta_v\frac{S^*}{N^*}\frac{i^*(0)B_1}{\mu_v}\frac{S_v^*}{N^*}\frac{1}{N^*}\frac{1}{\mu}D+\frac{S^*}{N^*}\frac{1}{\mu}\frac{i^*(0)DB_{1d}}{N^*}$$

we use the relation $\dfrac{\mu}{M}=\dfrac{1}{i^*(0)B_1+N^*\mu_v}$, and $N^*=\dfrac{\Lambda-i^*(0)D}{\mu}$, then,

$$= \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \frac{N^* B_1 \mu}{M} \Big(1 + \frac{i^*(0)D}{\Lambda - i^*(0)D}\Big) - \frac{i^*(0)}{N^* \mu} \underbrace{\Big(\beta_v \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} + B_{1d}\Big)}_{=\frac{N^*}{S^*}} + \frac{S^*}{N^*} B_{1d}$$

$$+ \frac{i^*(0)D}{N^* \mu} \underbrace{\Big(\beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} + \frac{S^*}{N^*} B_{1d}\Big)}_{=1}$$

$$= \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \frac{N^* B_1 \mu}{M} \frac{\Lambda}{\Lambda - i^*(0)D} - \frac{i^*(0)}{N^* \mu} \frac{N*}{S^*} + \frac{S^*}{N^*} B_{1d} + \frac{i^*(0)D}{\Lambda - i^*(0)D}$$

$$= \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \frac{B_1 \Lambda}{M} \frac{N^* \mu}{\Lambda - i^*(0)D} - \frac{i^*(0)}{\mu} \frac{1}{S^*} + \frac{S^*}{N^*} B_{1d} + \frac{i^*(0)D}{\Lambda - i^*(0)D}$$

$$= \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \frac{B_1 \Lambda}{M} \frac{N^* \mu}{\Lambda - i^*(0)D} - \frac{i^*(0)}{\mu} \frac{1}{S^*} + \frac{S^*}{N^*} B_{1d} + \frac{i^*(0)D}{\Lambda - i^*(0)D}$$

$$\text{since } N^* = \frac{\Lambda - i^*(0)D}{\mu} \text{ and } S^* = \frac{\Lambda - i^*(0)}{\mu}$$

$$= \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \frac{B_1 \Lambda}{M} + \frac{S^*}{N^*} B_{1d} - \frac{i^*(0)}{\Lambda - i^*(0)} + \frac{i^*(0)D}{\Lambda - i^*(0)D}$$

$$= \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \frac{B_1 \Lambda}{M} + \frac{S^*}{N^*} B_{1d} + \frac{i^*(0)\Lambda(D-1)}{(\Lambda - i^*(0)D)(\Lambda - i^*(0))}$$

Now we look at the stability for lower endemic equilibrium when $\mathcal{R}_{02} < 1$.

Suppose $\mathcal{J}'(i^*(0)) > 0$ as we know slope at lower endemic equilibrium is positive. Then, equation (4.26) gives

$$\frac{\Lambda(D-1)}{\big(\Lambda - i^*(0)D\big)(\Lambda - i^*(0))} > \beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} \Big(\frac{\mu B}{M} - \frac{\mu_v D}{M}\Big)$$

$$\frac{i^*(0)\Lambda(D-1)}{\big(\Lambda - i^*(0)D\big)(\Lambda - i^*(0))} > \beta_v i^*(0) \frac{S^*}{N^*} \frac{B}{\mu_v} \frac{S_v^*}{N^*} \Big(\frac{\mu B_1}{M} - \frac{\mu_v D}{M}\Big)$$

Plugging this inequality in $\mathcal{G}(0)$, we get

$$\mathcal{G}(0) > \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \frac{B_1 \Lambda}{M} + \beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} \Big(\frac{\mu B_1}{M} - \frac{\mu_v D}{M}\Big) + + \frac{S^*}{N^*} B_{1d}$$

$$= \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \Big(\frac{B_1 \Lambda}{M} + \frac{i^*(0) B_1}{\mu_v} \frac{\mu B_1}{M} - \frac{i^*(0) B_1 \mu_v D}{\mu_v M}\Big) + 1 - \beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*}$$

$$\Big(\text{since } \beta_v \frac{S^*}{N^*} \frac{B_1}{\mu_v} \frac{S_v^*}{N^*} + \frac{S^*}{N^*} B_{1d} = 1 \quad \text{from (4.22)}\Big)$$

$$= \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \Big(\frac{B_1 \Lambda \mu_v}{M \mu_v} + \frac{i^*(0) \mu B_1^2}{\mu_v M} - \frac{i^*(0) B_1 \mu_v D}{\mu_v M} - \frac{B_1 M}{\mu_v M}\Big) + 1$$

$$= \beta_v \frac{S^*}{N^*} \frac{S_v^*}{N^*} \left(\frac{B_1 \Big(\Lambda \mu_v + i^*(0) \mu B_1 - i^*(0) \mu_v D - M\Big)}{M \mu_v}\right) + 1$$

$$= \beta_v \frac{S^*}{N^*}\frac{S_v^*}{N^*}\left(\frac{B_1\Big(\overbrace{\Lambda\mu_v + i^*(0)\big(\mu B_1 - \mu_v D\big)}^{M} - M\Big)}{M\mu_v}\right) + 1$$

$$= 1$$

Here, we observe that if $\mathcal{F}'(i^*(0)) > 0$, then $\mathcal{G}(0) > 1$ and note that for $\lambda \in \mathcal{R}$,

$$\lim_{\lambda\to\infty} \mathcal{G}(\lambda) = 0$$

.

Then, there exists a positive $\lambda^* > 0$ such that $\mathcal{G}(\lambda^*) = 1$ proving the lower endemic equilibrium is unstable. We write this as a theorem below.

Theorem 10. *When $\mathcal{R}_{02} < 1$, the lower endemic equilibrium $(i_1^*(0))$ in the backward bifurcation is unstable.*

4.5 SUMMARY OF THE CHAPTER

We formed a new model by including one additional parameter disease induced death rate $\alpha(\tau)$ in the model (3.11) in the Chapter 3. Our aim is to analyze whether these two models have same or different disease dynamics. The disease dynamics in this model is different from the dynamics of the (3.11). We first computed explicit expression for the reproduction number given as $\mathcal{R}_{02} = \frac{\beta_v \Lambda_v \mu}{\Lambda \mu_v^2}\int_0^\infty \beta(\tau)\pi_1(\tau)d\tau + \int_0^\infty \beta_d(\tau)\pi_1(\tau)d\tau$ where probability that an infectious individual survives to the time since infection τ after being infected, $\pi(\tau)$ is given by $\pi_1(\tau) = e^{-\int_0^\tau (\gamma(s)+\alpha(\tau)+\mu)ds}$. We exhibited local stability of disease free equilibrium when $\mathcal{R}_{02} < 1$ and unstable when $\mathcal{R}_{02} > 1$. In order to determine the condition for the existence of endemic equilibrium, we formed the quadratic equation by letting $X = \frac{\beta_v I_V}{N} + \frac{i^*(0)B_d}{N^*}$ where X dependent on $i^*(0)$. Solutions of the quadratic gives number of endemic equilibrium. We examined that , under the case $\mathcal{R}_{02} > 1$, there exist unique positive endemic equilibrium. Under the case $\mathcal{R}_{02} = 1$, existence of positive endemic equilibrium is only possible whenever $\dfrac{b_2}{b_1} < 0$. For the last case $\mathcal{R}_{02} < 1$, no positive endemic equilibrium is existed when $b_2 > 0$ and two positive endemic equilibrium exist when $b_2 < 0$. Thus, backward bifurcation is true. Later, simulation for the model supported the backward bifurcation for $0 < D < 1$ keeping all other parameters in the reproduction number constant. We finally showed that when $\mathcal{R}_{02} < 1$, lower endemic equilibrium in backward bifurcation is locally stable.

CHAPTER 5

CONCLUSION AND FUTURE WORK

5.1 CONCLUSION

We constructed a novel nonlinear PDE model to understand the complex dynamics of ZIKV in the population where infected host population are structured with the time and time since infection. We used vector mode of transmission and direct transmission in this model in order to understand their collaborative contribution in dynamics of disease in the population. We assume infectivity for infectious individuals, transmission rate of infection from an infected host to susceptible vector class, direct transmission rate of infection from an infected host to a susceptible host, and recovery rate of infected host population varies with the time since infection.

In Chapter 3, we identified the basic reproduction number $\mathcal{R}_0$ for the model. We then analysed the existence and stability of both disease free and endemic equilibria. We have shown, as in many other disease mathematical model that when $\mathcal{R}_0 < 1$, the disease free equilibrium E_0 is locally stable and unstable whenever $\mathcal{R}_0 > 1$. The epidemiological implication of this finding is that disease will be eliminated for the short period of time.

In Chapter 4, we an analyzed a new model formed by including one additional parameter, disease induced death rate $\alpha(\tau)$. We identified reproduction number $\mathcal{R}_{02}$. Analyzing the existence of endemic equilibria, backward bifurcation is established and is supported by the simulation for the model. This shows that in order to control these disease, it is not sufficient to have reproduction number less than unity but necessary. At last, we exhibited that lower endemic equilibrium in backward bifurcation is locally stable when $\mathcal{R}_{02} < 1$.

5.2 FUTURE WORK

The study of ZIKV dynamics in the population level can be broaden in different other direction in order to understand the dynamics of this disease more.

- Global stability of an endemic equilibrium for the model in Chapter 3 is still an open question when $\mathcal{R}_0 > 1$. Proof of the global stability of endemic equilibrium imply that in long run, the disease prevails, in the population means that it becomes endemic. However, global stability of an endemic equilibrium for the model in Chapter 3 is still an open question when $\mathcal{R}_0 > 1$.

- Local stability of upper endemic equilibrium in the backward bifurcation when $\mathcal{R}_{02} < 1$ and of unique endemic equilibrium when $\mathcal{R}_{02} > 1$ is an open question in chapter 4.

- In the nearby future, I would like to further extend my dissertation work. I am interested in understanding the collaborative affect of other mode of transmission including vertical transmission and transmission structured on infected pregnant on the dynamics of disease in the population.

- In modeling quickly progressing diseases such as meningitis or plague, it is acceptable to ignore host dynamics, and we can assume infectivity of infectious individuals is constant throughout their infectious period. However, host dynamics are included in slowly progressive diseases like HIV/AIDS, Tuberculosis, and Hepatitis C. Spread of infectious disease depends on the level of pathogen in the infectious person. Pathogen is in continuous dynamic interaction with the host immune system. The pathogen's transmission or the death of the host is dependent on the interaction between pathogen level and host immune response. The characteristics of within-host disease dynamics of infectious individuals plays a significant role in understanding the spread of disease in the population level [36, 60, 24, 61]. Therefore, it would be interesting to link this between host(epidemiological processes) ZIKV model with the within-host (immunological) model in understanding the spread of disease in the population level.

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