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TIME-DELAYED MODELS OF INFECTIOUS DISEASES DYNAMICS

By

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ABSTRACT

This research work is on time-delayed models of infectious diseases dynamics. The dynamics of infectious diseases are studied in the presence of time delays representing temporary immunity or latency. We have designed and analysed time-delayed models with various parameters to simulate disease dynamics, in a view to gaining insight into the behaviour of a population in the presence of infectious diseases, and the reaction of the population to changes in the management procedure of such infections.

Declaration

I hereby declare that this thesis has not been and will not be, submitted in whole or in part to another University for the award of any other degree.

Signature:.....

Ime Udo Okonna

Dedication

This thesis is dedicated to my late father, in whose tutelage I acquired my academic foundation, and my mother who unfortunately could not see it completed.

Acknowledgements

I would like to extend my profound gratitude to the many people, who stood by me and helped me accomplish the work presented in this thesis.

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My PhD has been an amazing experience and I thank you all wholeheartedly. God bless you.

Contents

Definitions and Notations

$\mathbb{R}^m$	m-dimensional vector-space
ρ	Spectral radius
τ	Time delay
$\in$	Belong to
$\forall$	For all
$\mathcal{R}_0$	Basic reproduction number.
inf	Infimum
sup	Supremum
Susceptible	Population at risk of contracting the disease.
Infective	Population infected and capable of transmitting the disease.
Recovered	Population recovered from the infection.
Latency period	The period between exposure to a disease causing organism and development of a consequent disease.
Incubation period	The period between exposure to an infection and the appearance of the first symptoms.
Temporary immunity	Short term immunity to disease acquired after recovery from the disease.
Cross immunity	A form of immunity in which immunity to one disease is effective in protecting the individual against similar but different disease.

Chapter 1

Introduction

1.1 General Introduction

Time-delayed models of infectious diseases are used to understand the disease dynamics with an aim of gaining insight into the behaviour of a population in the presence of any such diseases. The reaction of the population to changes in the management procedures of such infections are represented by corresponding parameters in the model, and allow one to develop methods to control the disease by, for example, introducing vaccinations, quarantine and so forth. Mathematical models describing the development of infectious diseases in a population help to understand and prevent a possible onset of an epidemic.

The modelling of infectious diseases based on the susceptible, infective and recovered structure have witnessed an increasing interest in mathematical epi-

demiology since the pioneering work by Kermack and McKendrick in the 1930s [1, 2, 3]. They used differential equations with time (t) as an independent variable and the populations, as functions of time, subdivided into classes as follows:

$S = S(t)$ — number of susceptible individuals;

$I = I(t)$ — number of infected individuals;

$R = R(t)$ — number of recovered individuals.

Numerous authors have made improvements and modifications of the classical SIR model with the intent of better understanding of the disease dynamics by including different other factors into consideration (See [6, 7, 9, 10, 14]).

While the models mentioned above help us to understand the dynamical behaviour of some infectious diseases, factors such as incubation periods of disease causing pathogens, temporary immunity and latency periods of infections are often neglected in the models. The introduction of time delays into models helps to address these omissions and provides a more realistic scenario for modelling a wider class of infections like malaria, HIV etc (See [11, 12, 14, 15, 16, 17, 19, 20, 21] and references therein). The main aim of this thesis is mathematical modelling of the disease dynamics using time delays to capture the incubation periods or temporary immunity of disease causing pathogens and latency periods of infections.

1.2 Thesis Structure

This thesis is composed of five chapters. Chapter 1 is devoted to the general introduction into the field of time-delayed systems and literature review.

In Chapter 2, we have studied the effects of temporary immunity on the dynamics of malaria. This analysis is focused on the existence and stability of the disease-free and endemic equilibria of the model with time delay of the form $I(t-\tau)e^{-\mu_h \tau}$, where τ is the length of the period of latency of the malaria drug administered and μ_h is the death rate for humans. Numerical analysis is used to verify and confirm analytical findings. The time delay is used to investigate the effects of the temporary immunity on the dynamics of malaria infection. This work has demonstrated that even in the presence of temporary immunity, dynamics of a human mosquito model for malaria is mostly affected by the basic reproduction number. In particular, our results suggest that the treatment of malaria using long-lasting malaria drugs could significantly reduce the population infected with malaria.

Chapter 3 deals with a two-disease epidemic model with time delay (without the possibility of a co-infection). Analysis done has shown the rich dynamical behaviour of the system and established stability criteria for the steady states in terms of the threshold parameter R_0. Numerical simulations are done using TRACE-DDE suite in Matlab, a program for computing the characteristic roots and stability boundaries for delay differential equations with discrete and dis-

tributed delays.

Chapter 4 is devoted to the analysis of the dynamics of an SIR model with latency based on the logistic growth of the population in the absence of disease, with a saturated incidence rate. Here the time delay is used to represent latency.

We summarise the work in Chapter 5 with suggestions on future work on two-disease epidemic model with time delay, including the possibility for co-infection.

1.3 Literature Review

In this chapter, we review some related literature and results obtained from previous studies of similar models. Mathematical modelling of infections with time-delayed models is a fast growing research area, and has been playing an important role in analysing the behaviour of a population in the presence of infectious diseases, and the reaction of populations to changes in management protocols of such infections. Models are developed based on some various assumptions, which are made depending on the type of disease studied, the causative agent of the disease and most importantly, the interaction of the disease with the population. Here, we review some of these models that are related to the models we will derive and analyse in this thesis.

1.3.1 Malaria Models

Modelling the dynamical interaction of malaria in a population began with the work of Ronald Ross [22]. He proposed a deterministic two-dimensional model with one variable representing human and the other representing mosquito populations, where it was shown that a reduction of mosquito population below a certain threshold was sufficient to eradicate malaria. This pioneering work ignited interest in the research area, making malaria models a useful tool in the study of the dynamics of malaria infection in populations. In 1927, Kermack and McKendrick [1] published their paper based on the Ross model and proposed a threshold condition for the spread of a disease, and provided a way of predicting the ultimate size of an epidemic. Numerous authors have made an extension to the model by Ross. Macdonald [23], for instance, considered the latency period of the parasite in mosquitos and introduced the exposed class in the mosquito compartment thus modifying the original Ross model. The Macdonald model was more realistic, since malaria parasite spends approximately 10 days inside a mosquito during its life cycle [24]. Further work on the Ross and Macdonald models was undertaken by Anderson and May [25] with the introduction of an exposed class in the human compartment to account for the 21 day latency period of the parasite in humans. Most authors have used time delays in their models as a way of effectively incorporating these latency periods, see for instance [26], and most

others have extended the models to incorporate various aspects related to malaria transmission dynamics and control, such as the use of preventative and therapeutic strategies, climate change and repeated exposures to parasite bearing mosquitos (see [27, 30, 31, 32, 33, 34] and references therein).

Although these classical models have, over the decades, been used to model malaria infection, the nature of the interaction of mosquito parasites between the human and mosquito hosts demanded more inputs to the models. Yang, Wei, and Li [35] considered a 5-dimensional system of equations for the spread of malaria in the human and mosquito populations with an SIR-type model for the human population and an SI-type model for the mosquito population. The dynamics of the human population in their model is governed by the following system

$$\begin{aligned} \frac{dS(t)}{dt} &= b_1 - \lambda_1 S(t)V(t) - \mu_1 S(t), \\ \frac{dI(t)}{dt} &= \lambda_1 S(t)V(t) - \gamma I(t) - \mu_1 I(t), \\ \frac{dR(t)}{dt} &= \gamma I(t) - \mu_1 R(t), \end{aligned} \tag{1.1}$$

and that of the vectors is represented by

$$\begin{aligned} \frac{dM(t)}{dt} &= b_2 - \lambda_2 M(t)I(t) - \mu_2 M(t), \\ \frac{dV(t)}{dt} &= \lambda_2 M(t)I(t) - \mu_2 V(t), \end{aligned} \tag{1.2}$$

where b_1 and b_2 are the rates of recruitment in the human and mosquito populations, λ_1 and λ_2 are the rates of the transmission of the disease, μ_1 and μ_2 are the

death rates, and γ is the recovery rate. The authors showed that the global dynamics of the system is completely determined by the basic reproduction number R_0. If $R_0 \leq 1$, the disease-free equilibrium is globally stable, and the disease dies out. When a disease-free steady state becomes unstable for $R_0 > 1$, the model admits a biologically relevant stable endemic equilibrium. They analysed how changes in the rates of recruitment b_1 and b_2 in both host and the vector populations affect the rates of transmission of the disease λ_1 and λ_2. They have shown that the basic reproduction number R_0 grows if parameters in the model are increased.

We have extended this model with modifications for the development of the model studied in Chapter 2. In deriving our model, we have taken into account the fact that individuals infected by the mosquito parasite recover to become susceptible again after a period of temporary immunity (here representing the period within which the malaria drugs administered are still active). This period is captured by the introduction of the delay term $I(t-\tau)e^{-\mu_h \tau}$, based on the idea from Kyrychko and Blyuss [11], where τ is the length of the period of the temporary immunity.

1.3.2 Two-Infection Mathematical Model with Time Delay

Several theoretical studies have proposed two-infection models for the study of the dynamics of two diseases and their interaction within a single host (see for

example, [36, 37, 38, 39, 40, 41]). There are two cases considered in the literature, namely, the co-infection models, where a patient infected by a chronic disease may also be infected by other acute diseases and the cases without the possibility of a co-infection. Here, we will concentrate on the dynamics of a two-infection disease without the possibility of a co-infection.

A model which can allow one to describe the general features of a two-disease epidemic in a population was proposed by Kyrychko and Blyuss [38]. The authors consider a two-disease model on the assumption that each individual can be infected with one or both diseases without immunity or cross-immunity. They established the regions when the uninfected equilibrium is stable and when it is unstable, and showed the existence of endemic equilibria including the co-infected state. The interesting and motivational factor in the extension of this model to our studies is the versatility of the model in the study of various two-strain diseases, such as influenza, tuberculosis etc.

In chapter 3, a modified version of this system is presented with two time delays, which represent a temporary immunity from one or both diseases. We have assumed that there is no incidence of a co-infection, i.e. an individual can either be infected with disease one or disease two but not both. The presence of two time delays have highlighted the rich dynamical behaviour of the system.

1.3.3 Latency Model with Saturated Incidence Rate

The incidence rate plays an important role in the study of infectious diseases. The bilinear incidence rate frequently used by authors is based on the law of mass action, βSI, where β is the infection rate, S and I are the susceptibles and infected individuals respectively, (See [1, 42, 43, 44]). This may pose a challenge of correctly capturing the disease incidence in a very large population, as could be inferred from the definition that, if the number of susceptibles increases, the number of individuals who become infected per unit of time increases, which is not realistic. Several authors have over the years formulated different types of nonlinear incidence rates to incorporate the effect of crowding of infectives or behavioral changes of susceptible individuals [45, 46, 47, 48, 49]. In 1978, May and Anderson in [50] suggested the saturated incidence rate $\frac{\beta SI}{1+\beta S}$ with β as the saturation factor. Further modifications to the incidence rate have seen time delays being introduced into the saturation (see [21] and references therein). For example, Yoichi et al [20] studied the SIR model with a saturation incidence rate with time delay of the form $\frac{S(t)I(t-\tau)}{1+\alpha I(t-\tau)}$. Their model suggest that if the basic reproductive number $R_0 < 1$, the disease free equilibrium is globally asymptotically stable while the endemic equilibrium of system is shown to be globally asymptotically stable if $R_0 > 1$.

Motivated by those works, in chapter 4, we have extended the model by Xu and Ma by including a delay term for the susceptible population, giving a delayed

SIR epidemic model with saturated incidence rate of the form $\frac{S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)}$, where α is the saturation factor.

1.4 Introduction to Delay Differential Equations

1.4.1 Introduction

Time delays are ubiquitous in nature, and study of systems with time delays has attracted a lot of attention. Arising from natural or technological control problems, such systems play an important role in mathematical modelling of the various real-life phenomena. These range from models in population biology, epidemiology, economics, physiology and neural networks, as well as in control problems for engineering systems (see [4]). In a delay differential equation, rate of change of the state variable depends not only on the present values of state variables but also on its history. There are different types of delay differential equations. Here, we will focus on the delay differential equations with discrete time delays, which can be written in the form

$$\dot{x} = f(x(t), x(t-\tau_1), x(t-\tau_2), \ldots, x(t-\tau_n)), \tag{1.3}$$

where the τ_i are positive constants. Other commonly encountered types are those with state dependent delays, where the time delay is non-constant, i.e., $\tau_i = \tau_i(x)$ or distributed delay types - the right-hand side of the differential equation is a

weighted integral over past states (see [5] for examples). The initial conditions for delay differential equations, unlike the case for ordinary differential equations, are history functions.

1.4.2 Definition and Examples of Delay Differential Equations

A general delay differential equation can be written in the following form

$$\dot{x}(t) = f(t, x(t-\tau_1), ..., x(t-\tau_n); \mu), \qquad t > 0,$$

where $\tau_i \geq 0$, $i = 1, ..., n$ are the time delays, and $\mu \in \mathbb{R}^m$ is a vector of parameters. The initial condition depends on the history, and has the form

$$x(s) = \phi(s), \qquad -\tau \leq s \leq 0, \qquad \tau = \max\{\tau_1, ..., \tau_n\}.$$

In the above example, the time delay appears in the the form $x(t-\tau_i)$ and is called a discrete time delay. The simplest delay differential equation can be written as

$$\dot{x}(t) = -x(t-1), \qquad x(s) = 1, \qquad -1 \leq s \leq 0. \tag{1.4}$$

In order to solve this equation, we can use the method of steps, namely, look first at the interval $[0, 1]$. On this interval, the DDE (1.4) is reduced to the following ODE

$$\dot{x}(t) = -1, \qquad x(0) = 1,$$

which has a solution

$$x(t) = 1 - t, \qquad 0 \leq t \leq 1.$$

Now consider the next interval $[1, 2]$. the DDE (1.4) has the form

$$\dot{x}(t) = -1 + (t - 1), \qquad x(1) = 0,$$

which has the solution

$$x(t) = -(t - 1) + \frac{1}{2}(t - 1)^2, \qquad 1 \leq t \leq 2.$$

This process can be continued and the full solution can be calculated as

$$x(t) = 1 + \sum_{m=1}^{k} (-1)^m \frac{(t - (m - 1))^m}{m!}, \qquad k - 1 \leq t \leq k, \qquad k \geq 1.$$

If the time delay is non-constant and is taken from a certain distribution, then the delayed term has the form

$$\int_0^\infty g(s)x(t - s)ds,$$

where $g(\cdot) \geq 0$ is a distribution kernel and is usually normalised to unity, i.e.

$$\int_0^\infty g(s)ds = 1.$$

If the distribution kernel is taken in the form of the Dirac delta function, that is $g(s) = \delta(s)$, the DDE becomes an ODE, and if $g(s) = \delta(s - \tau)$, then distributed time delay becomes discrete. In this thesis we will concentrate on models involving discrete time delays to describe various biological phenomena.

Chapter 2

Effects of Temporary Immunity on the Dynamics of Malaria

2.1 Introduction

Malaria caused by a vector borne protozoan parasite is an infectious disease characterized by high fever, chills, flu-like symptoms and in many cases leads to death. Approximately 3.2 billion people in 97 countries and territories are at risk of malaria infection of which 1.2 billion are at high risk. According to the World Health Organisation (WHO), approximately $584,000$ people died from malaria in 2013 globally with a whopping 90% of that figure in the African region with children under 5 years accounting for 78% of all deaths. There were an estimated 198 million cases of malaria infection in 2013 worldwide [51].

The burden of malaria as reflected in the paragraph above indicates that in spite of huge resources committed and the promising results in control policies, malaria still remains one of the largest public health problems. This accounts for the growing interest devoted to the understanding of malaria transmission dynamics. Mathematical models give an important insight and useful information, especially in terms of prediction, through simulations of disease dynamics in a population. This makes it imperative for vigorous development of models targeted at the understanding of the dynamics of the epidemic and possible elimination or reduction in the infection rate among the affected population.

After the development of the mathematical model by Ross [22], we have witnessed the development of several mathematical models incorporating more realistic epidemiological features [28, 29, 30]. Recently, there have been advancements in understanding of the different scenarios for disease transmission and generally the dynamics of epidemics. Several authors have made contributions to the development of models that include a human population demographic dynamics and age-structure. Mpolya et al (2014) [52] developed a star-network of connections between a central city and peripheral villages to analyse the dynamics of a vector-borne disease as influenced by daily commuters. They concluded that understanding the demographic dynamics of villages in terms of its hosts and vectors is important for planning disease control. A deterministic model for assessing the

role of age-structure on the transmission dynamics of malaria in a community was studied in [54]. They showed that equivalent model with no age structure exhibits the same qualitative dynamics as the age-structured model.

The vector transmission process involves time delay both in human and in mosquitoes due to incubation periods of parasites [18]. This has led to the inclusion of time delays into the mathematical models as a way of capturing this incubation periods as well as the disease latency or immunity in the population [11, 12, 14, 15, 19]. In [15], a two delay system was formulated to capture temperature dependent incubation periods in human and mosquito populations, and it was shown that with increasing temperatures, the incubation period becomes shorter, showing that global warming will exacerbate the transmission of malaria. The model analysed in this paper includes a time delay to capture the period of latency of the therapeutics administered to infected individuals in the population. A similar model was extensively analysed by Kyrychko & Blyuss [11], where the delay term $I_h(t-\tau)e^{-\mu_h\tau}$ was used to reflect the fact that an individual has survived from natural death in a recovery pool before becoming susceptible again [11].

In this chapter, we have shown that if $R_0 < 1$, then the disease free equilibrium is locally and globally asymptotically stable, and when $R_0 > 1$, then the endemic equilibrium is locally asymptotically stable for $\tau = 0$ and that there is no stability

switches as τ varies. Numerical simulations support our analytical calculations and also show that we have global asymptotic stability of the endemic equilibrium for $R_0 > 1$. The chapter is organised as follows: the model is derived in Section 2.2. Section 2.3 deals with the positivity of solutions, and the results on the asymptotic stabilities of the disease free and endemic equilibria are given in Sections 2.4, 2.6, 2.7 and 2.8. We present our numerical simulations in 2.9, and conclude the work in section 2.10.

2.2 Derivation of the model

The aim of this study is to derive a mathematical model describing the spread of malaria in the human and mosquito populations. We consider the SIR-type modelling approach, and divide the human and mosquito populations into a compartment (S) for the susceptible and (I) for the infected individuals, and a compartment (R) for the recovered human population only, since mosquitos do not recover from the parasite during its short life span. In developing this model, we have considered the fact that individuals infected by the mosquito parasite recover to become susceptible again after the period within which the malaria drugs administered are still active. This period is captured by the introduction of the delayed term $I(t-\tau)e^{-\mu_h \tau}$, where τ is the length of the period. The flow chart of the model is shown in the diagrammatic sketch Fig.2.1.

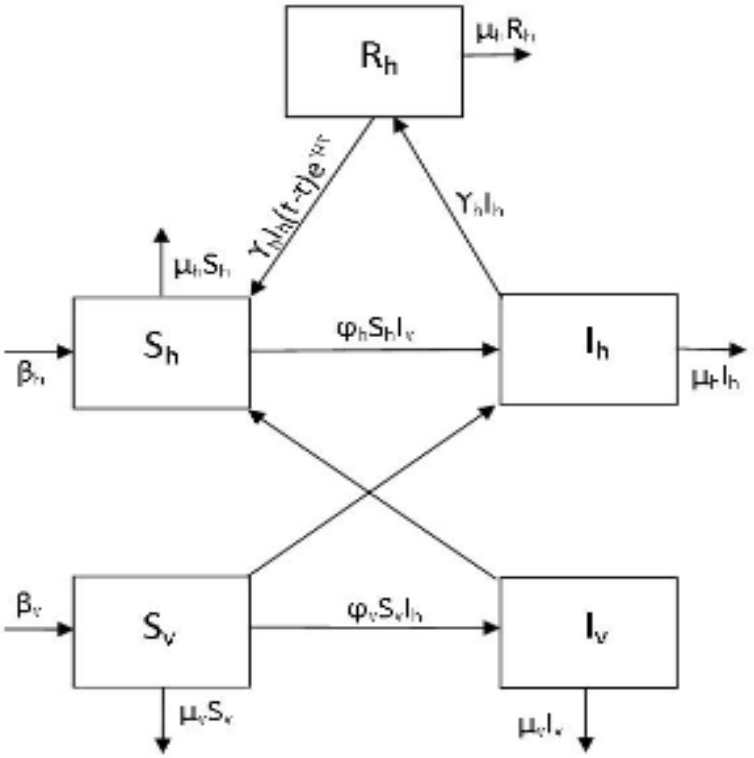


Figure 2.1: Flow chart of the model.

As seen in the flow chart Fig. 2.1, the total human population is divided into three classes based on epidemiological status and are classified as either susceptible, infected or recovered. These groups are represented by S_h, I_h and R_h respectively. All recruitment is into the susceptible class, and occurs at a constant rate β. A susceptible individual has an average $\varphi_h I_v$ contacts that would be sufficient to transmit the disease. Thus, the rate at which susceptibles in the population are infected is $\varphi_h S_h I_v$. Thus,

$$\frac{dS_h}{dt} = \beta_h - \mu_h S_h - \varphi_h S_h I_v + \gamma_h I_h(t-\tau)e^{-\mu_h \tau}.$$

While in the infective class, we assume that a number of infectives will die at the rate of μ_h and that the initiation of therapeutics immediately removes individuals from the active status of the infective class I_h, and places them into the recovered class R_h at the rate of γ_h. We have the following to complete the system of equations for the human population dynamics:

$$\begin{aligned}
\frac{dI_h}{dt} &= \varphi_h S_h I_v - (\mu_h + \gamma_h) I_h, \\
\frac{dR_h}{dt} &= \gamma_h I_h - \gamma_h I_h(t-\tau)e^{-\mu_h \tau} - \mu_h R_h.
\end{aligned}$$

The mosquito population dynamics follows a simple system of equations as follows:

$$\begin{aligned}
\frac{dS_v}{dt} &= \beta_v - \mu_v S_v - \varphi_v S_v I_h, \\
\frac{dI_v}{dt} &= \varphi_v S_v I_h - \mu_v I_v.
\end{aligned}$$

This gives us the following system of equations.

$$\begin{aligned}
\frac{dS_h}{dt} &= \beta_h - \mu_h S_h - \varphi_h S_h I_v + \gamma_h I_h(t-\tau)e^{-\mu_h \tau}, \\
\frac{dI_h}{dt} &= \varphi_h S_h I_v - (\mu_h + \gamma_h) I_h, \\
\frac{dR_h}{dt} &= \gamma_h I_h - \gamma_h I_h(t-\tau)e^{-\mu_h \tau} - \mu_h R_h, \\
\frac{dS_v}{dt} &= \beta_v - \mu_v S_v - \varphi_v S_v I_h, \\
\frac{dI_v}{dt} &= \varphi_v S_v I_h - \mu_v I_v.
\end{aligned} \tag{2.1}$$

The variables and parameters used in the model are given in Tables 2.1 and 2.2.

Table 2.1: State variables of the model.

Variable	Description
S_h	Population of susceptible humans, [biomass]
I_h	Population of infected humans, [biomass]
R_h	Population of recovered humans, [biomass]
S_v	Population of susceptible mosquitoes, [biomass]
I_v	Population of infected mosquitoes, [biomass]

Table 2.2: Parameters used in the model.

Parameter	Description
β_h	Birth rate for humans, [biomass/time]
μ_h	Death rate for humans, [1/time]
φ_h	Rate of infection (humans), $[1/(time \cdot time)]$
γ_h	Recovery rate (humans), $[1/time]$
β_v	Birth rate for mosquito, [biomass/time]
μ_v	Death rate for mosquito,[1/time]
φ_v	Rate of infection (mosquito), $[1/(time \cdot time)]$

In developing the model, we have taken into consideration the period of drug latency represented by the term $I_h(t-\tau)e^{-\mu_h\tau}$, where τ is the period within which

anti-malaria drugs administered to an infected human are still active.

The total human and mosquito populations are given by

$$N_h = S_h + I_h + R_h \tag{2.2}$$

and

$$N_v = S_v + I_v, \tag{2.3}$$

and are governed respectively by

$$\frac{dN_h}{dt} = \beta_h - \mu_h N_h, \tag{2.4}$$

$$\frac{dN_v}{dt} = \beta_v - \mu_v N_v. \tag{2.5}$$

We can easily see from (2.4) that for the human population

$$N_h \to \frac{\beta_h}{\mu_h} \text{ as } t \to \infty, \tag{2.6}$$

and, similarly, for the mosquito population, we have that

$$N_v \to \frac{\beta_v}{\mu_v} \text{ as } t \to \infty. \tag{2.7}$$

In order to analyse the system (2.1), we reduce it to a four dimensional system. The first and second equations in the system (2.1) do not depend on the third equation, and hence we omit the third equation and rewrite system (2.1) as follows,

$$
\begin{aligned}
\frac{dS_h}{dt} &= \beta_h - \mu_h S_h - \varphi_h S_h I_v + \gamma_h I_h(t-\tau)e^{-\mu_h \tau}, \\
\frac{dI_h}{dt} &= \varphi_h S_h I_v - (\mu_h + \gamma_h) I_h, \\
\frac{dS_v}{dt} &= \beta_v - \mu_v S_v - \varphi_v S_v I_h, \\
\frac{dI_v}{dt} &= \varphi_v S_v I_h - \mu_v I_v.
\end{aligned} \tag{2.8}
$$

System (2.8) has the following initial conditions: $S_h(0) = S_{h0} > 0, I_h(s) = I_{h0}(s) \geq 0$ for all $s \in [-\tau; 0)$ with $I_{h0}(0) > 0$, $S_v(0) = S_{v0} > 0$, and $I_v(0) = I_{v0} \geq 0$. Since the model (2.8) is for human and mosquito populations, it is assumed that all parameters are positive.

2.3 Positivity of Solutions

Since the system (2.8) models the dynamics of human and mosquito populations, it is important to prove that all quantities (S_h, I_h, S_v and I_v) will stay positive for all times and given initial conditions.

Theorem 2.3.1. *Let the initial data be $S_h(0) = S_{h0} > 0, I_h(s) = I_{h0}(s) \geq 0$ for all $s \in [-\tau; 0)$ with $I_{h0}(0) > 0$, $S_v(0) = S_{v0} > 0$, and $I_v(0) = I_{v0} \geq 0$. Then solutions $S_h(t), I_h(t), S_v(t)$ and $I_v(t)$ of the system (2.8) are positive for all $t > 0$.*

Proof. We prove non-negativity of solutions of (2.8) by contradiction. Assume that $t = t_1$ is the first moment of time when $S_h(t_1)S_v(t_1)I_h(t_1)I_v(t_1) = 0$. Suppose

$S_h = 0$ at $t = t_1$ and $S_v(t_1)I_h(t_1)I_v(t_1) \geq 0$. In order for $S_h(t)$ to become negative, we require that $\frac{dS_h}{dt}\big|_{t=t_1} < 0$. However, from the first equation of system (2.8), we have

$$\frac{dS_h}{dt}\Big|_{t=t_1} = \overbrace{\beta_h}^{>0} - \overbrace{\mu_h S_h(t_1)}^{=0} - \overbrace{\varphi_h S_h(t_1) I_v(t_1)}^{=0} + \overbrace{\gamma_h I_h(t_1 - \tau)e^{-\mu_h \tau}}^{\geq 0} > 0$$

$$\Rightarrow \frac{dS_h}{dt}\Big|_{t=t_1} > 0$$

which is a contradiction. Hence $S_h(t)$ is positive.

Similarly, let us assume that $t_2 > 0$ is the first moment of time when $I_h = 0$ and $S_v I_v \geq 0$. Assume that $I_h(t_2) = 0$. For $I_h(t)$ to be negative, one has to have that $\frac{dI_h}{dt}\big|_{t=t_2} < 0$, but according to the second equation of the system (2.8), at this time we have

$$\frac{dI_h}{dt}\Big|_{t=t_2} = \overbrace{\varphi_h S_h(t_2) I_v(t_2)}^{\geq 0} - \overbrace{(\mu_h + \gamma_h) I_h(t_2)}^{=0} \geq 0$$

$$\Rightarrow \frac{dI_h}{dt}\Big|_{t=t_2} \geq 0.$$

Hence $I_h(t)$ can never become negative.

We now show the positivity of $S_v(t)$. Suppose that $t = t_3$ is the first time when $S_v = 0$ and $I_v \geq 0$. From the third equation of the system (2.8), we have

$$\frac{dS_v}{dt} > 0,$$

which means that $S_v > 0$ for all t. Lastly we consider $t_4 > 0$ as the first moment of time when $I_v(t) = 0$ and also proceed as before to prove by contradiction the

positivity of $I_v(t)$. For $I_v(t)$ to be negative, we would have that $\frac{dI_v}{dt}\big|_{t=t_4} < 0$ but according to the last equation of system (2.8), we have

$$\frac{dI_v}{dt}\Big|_{t=t_4} = \overbrace{\varphi_v S_v(t_4) I_h(t_4)}^{\geq 0} - \overbrace{\mu_v I_v(t_4)}^{=0} \geq 0$$

$$\Rightarrow \frac{dI_v}{dt}\Big|_{t=t_4} \geq 0$$

Hence $I_v(t)$ can never be negative, which implies $I_v(t)$ remains positive for all times. □

2.4 Disease Free Equilibrium

The stability of the disease-free equilibrium state can be obtained from studying the eigenvalues of the Jacobian matrix evaluated at the equilibrium point. If all the eigenvalues have negative real parts, then the equilibrium point is stable. In order to find all equilibria of the system (2.8), we have to solve the following system of equations

$$\begin{aligned} \beta_h - \mu_h S_h - \varphi_h S_h I_v + \gamma_h I_h e^{-\mu_h \tau} &= 0, \\ \varphi_h S_h I_v - (\mu_h + \gamma_h) I_h &= 0, \\ \beta_v - \mu_v S_v - \varphi_v S_v I_h &= 0, \\ \varphi_v S_v I_h - \mu_v I_v &= 0. \end{aligned} \tag{2.9}$$

For the disease free equilibrium, we have $I_h = I_v = 0$, and

$$\beta_h - \mu_h S_h = 0 \implies S_h = \frac{\beta_h}{\mu_h}, \tag{2.10}$$

$$\beta_v - \mu_v S_v = 0 \implies S_v = \frac{\beta_v}{\mu_v}. \tag{2.11}$$

Hence a disease free equilibrium given by

$$\begin{aligned} E_0 &= (S_h^0, I_h^0, S_v^0, I_v^0) \\ &= \left(\frac{\beta_h}{\mu_h}, 0, \frac{\beta_v}{\mu_v}, 0\right). \end{aligned} \tag{2.12}$$

2.5 Basic Reproduction Number

The basic reproduction number (R_0) is the average number of secondary infections created when a single infected host is placed in an entirely susceptible population. This intuitively suggests that if $R_0 < 1$, then the infection will not be able to grow in the population, and if $R_0 > 1$, then we expect an epidemic. We will show that our intuition is correct by studying the local stability of the equilibria of the system (2.8). The aim is to show that whenever $R_0 < 1$, the system will approach a disease-free equilibrium, and whenever $R_0 > 1$, there exists an endemic equilibrium, which, if stable, implies that the disease remains in the population. We now use the next generation matrix approach, that was introduced by Diekmann *et al.* [53] for autonomous models, and further developed for ordinary differential equations models with compartmental structure by Van den

Driessche and Watmough [56] in order to define R_0.

The next generation matrix comprises of two parts $\mathbf{F}$ and $\mathbf{V}^{-1}$, where

$$\mathbf{F} = \Big[\frac{\partial \mathcal{F}_i(E_0)}{\partial x_j}\Big] \quad \text{and} \quad \mathbf{V} = \Big[\frac{\partial \mathcal{V}_i(E_0)}{\partial x_j}\Big].$$

The $\mathcal{F}_i$ are the new infections, while the $\mathcal{V}_i$ are transfers from one compartment to another. E_0 is the disease-free equilibrium point. We have from System (2.8),

$$\mathcal{F} = \begin{pmatrix} 0 \\ \varphi_h S_h I_v \\ 0 \\ \varphi_v S_v I_h \end{pmatrix} \quad \text{and} \quad \mathcal{V} = \begin{pmatrix} \mu_h S_h - \beta_h - \gamma_h I_h(t-\tau)e^{-\mu_h \tau} \\ (\mu_h + \gamma_h) I_h \\ \mu_v S_v - \beta_v \\ \mu_v I_v \end{pmatrix}.$$

Evaluating the derivatives of $\mathcal{F}$ and $\mathcal{V}$ at the disease-free equilibrium point E_0 gives $\mathbf{F}$ and $\mathbf{V}$ as follows,

$$\mathbf{F} = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\varphi_h \beta_h}{\mu_h} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\varphi_v \beta_v}{\mu_v} & 0 & 0 \end{pmatrix} \quad \text{and} \quad \mathbf{V} = \begin{pmatrix} \mu_h & -\gamma_h e^{-\mu_h \tau} & 0 & 0 \\ 0 & \mu_h + \gamma_h & 0 & 0 \\ 0 & 0 & \mu_v & 0 \\ 0 & 0 & 0 & \mu_v \end{pmatrix}.$$

Now,

$$\mathbf{V}^{-1} = \begin{pmatrix} (\mu_h)^{-1} & \frac{\gamma_h e^{-\mu_h \tau}}{\mu_h(\mu_h + \gamma_h e^{-\mu_h \tau}} & 0 & 0 \\ 0 & (\mu_h + \gamma_h)^{-1} & 0 & 0 \\ 0 & 0 & (\mu_v)^{-1} & 0 \\ 0 & 0 & 0 & (\mu_v)^{-1} \end{pmatrix}$$

and

$$\mathbf{FV}^{-1} = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\varphi_h \beta_h}{\mu_h \mu_v} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\varphi_v \beta_v}{\mu_v(\mu_h+\gamma_h)} & 0 & 0 \end{pmatrix}.$$

The basic reproduction number is the spectral radius of the product $\mathbf{FV}^{-1}$, and can be found as $R_0 = \rho(\mathbf{FV}^{-1})$. Hence we have

$$R_0 = \sqrt{\frac{\varphi_h \beta_h \varphi_v \beta_v}{\mu_h \mu_v^2 (\mu_h + \gamma_h)}}. \tag{2.13}$$

2.6 Local Stability of the Disease Free Equilibrium

We now linearise the system (2.8) about the equilibrium points, and obtain

$$\begin{aligned} \dot{\tilde{S}}_h &= -\mu_h \tilde{S}_h - \varphi_h \tilde{S}_h I_v^* + \gamma_h \tilde{I}_h(t-\tau) e^{-\mu_h \tau} - \varphi_h S_h^* \tilde{I}_v, \\ \dot{\tilde{I}}_h &= \varphi_h \tilde{S}_h I_v^* - (\mu_h + \gamma_h)\tilde{I}_h + \varphi_h S_h^* \tilde{I}_v, \\ \dot{\tilde{S}}_v &= -\varphi_v S_v^* \tilde{I}_h - \mu_v \tilde{S}_v - \varphi_v \tilde{S}_v I_h^*, \\ \dot{\tilde{I}}_v &= \varphi_v S_v^* \tilde{I}_h + \varphi_v \tilde{S}_v I_h^* - \mu_v \tilde{I}_v. \end{aligned} \tag{2.14}$$

At the disease free equilibrium E_0, we have

$$\begin{aligned}
\dot{\tilde{S}}_h &= -\mu_h \tilde{S}_h + \gamma_h \tilde{I}_h(t-\tau)e^{-\mu_h \tau} - \frac{\varphi_h \beta_h}{\mu_h}\tilde{I}_v, \\
\dot{\tilde{I}}_h &= -(\mu_h + \gamma_h)\tilde{I}_h + \frac{\varphi_h \beta_h}{\mu_h}\tilde{I}_v, \\
\dot{\tilde{S}}_v &= -\frac{\varphi_v \beta_v}{\mu_v}\tilde{I}_h - \mu_v \tilde{S}_v, \\
\dot{\tilde{I}}_v &= \frac{\varphi_v \beta_v}{\mu_v}\tilde{I}_h - \mu_v \tilde{I}_v.
\end{aligned} \tag{2.15}$$

Looking for solutions of the system (2.15) in the form

$$\tilde{S}_h = C_1 e^{\lambda t},\ \tilde{I}_h = C_2 e^{\lambda t},\ \tilde{S}_v = C_3 e^{\lambda t} \text{ and } \tilde{I}_v = C_4 e^{\lambda t}$$

yields

$$\begin{aligned}
(-\mu_h - \lambda)C_1 + \gamma_h C_2 e^{-(\lambda+\mu_h)\tau} - \frac{\varphi_h \beta_h}{\mu_h}C_4 &= 0, \\
(-\mu_h - \gamma_h - \lambda)C_2 + \frac{\varphi_h \beta_h}{\mu_h}C_4 &= 0, \\
-\frac{\varphi_v \beta_v}{\mu_v}C_2 - (\mu_v + \lambda)C_3 &= 0, \\
\frac{\varphi_v \beta_v}{\mu_v}C_2 - (\mu_v + \lambda)C_4 &= 0.
\end{aligned} \tag{2.16}$$

System (2.16) can be rewritten in a matrix form as follows

$$\begin{pmatrix}
-\mu_h - \lambda & \gamma_h e^{-(\lambda+\mu_h)\tau} & 0 & \frac{-\varphi_h \beta_h}{\mu_h} \\
0 & (-\mu_h - \gamma_h - \lambda) & 0 & \frac{\varphi_h \beta_h}{\mu_h} \\
0 & \frac{-\varphi_v \beta_v}{\mu_v} & -\mu_v - \lambda & 0 \\
0 & \frac{\varphi_v \beta_v}{\mu_v} & 0 & -\mu_v - \lambda
\end{pmatrix}
\begin{pmatrix} C_1 \\ C_2 \\ C_3 \\ C_4 \end{pmatrix} =
\begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}.$$

Since we are looking for a non-zero solution of the linearised system, we assume that C_1, C_2, C_3 and C_4 are all not equal to zero, which means that

$$\begin{vmatrix} -\mu_h - \lambda & \gamma_h e^{-(\lambda+\mu_h)\tau} & 0 & \frac{-\varphi_h \beta_h}{\mu_h} \\ 0 & (-\mu_h - \gamma_h - \lambda) & 0 & \frac{\varphi_h \beta_h}{\mu_h} \\ 0 & \frac{-\varphi_v \beta_v}{\mu_v} & -\mu_v - \lambda & 0 \\ 0 & \frac{\varphi_v \beta_v}{\mu_v} & 0 & -\mu_v - \lambda \end{vmatrix} = 0,$$

and the characteristic equation, obtained from computing the above determinant in Maple, has the form

$$(-\mu_h - \lambda)\{(\mu_v + \lambda)[(\lambda + \mu_v)(\lambda + \mu_h + \gamma_h) - \frac{\varphi_h \varphi_v \beta_h \beta_v}{\mu_h \mu_v}]\} = 0. \tag{2.17}$$

From the characteristic equation it immediately follows that there are two negative eigenvalues, namely, $\lambda_1 = -\mu_h$, $\lambda_2 = -\mu_v$, and all others satisfy the quadratic equation

$$\lambda^2 + (\mu_h + \mu_v + \gamma_h)\lambda + (\mu_h \mu_v + \gamma_h \mu_v) - \frac{\varphi_h \varphi_v \beta_h \beta_v}{\mu_h \mu_v} = 0. \tag{2.18}$$

The roots of this equation will have negative real parts whenever the following condition holds

$$(\mu_h \mu_v + \gamma_h \mu_v) > \frac{\varphi_h \varphi_v \beta_h \beta_v}{\mu_h \mu_v}. \tag{2.19}$$

Let

$$\tilde{R}_0 = \frac{\varphi_h \varphi_v \beta_h \beta_v}{\mu_h \mu_v (\mu_h \mu_v + \gamma_h \mu_v)},$$

where $\tilde{R}_0 = R_0^2$.

Theorem 2.6.1. *The disease-free equilibrium is locally asymptotically stable when* $\tilde{R}_0 < 1$*, and unstable otherwise.*

Proof. We can see from (2.18) that for $\tilde{R}_0 < 1$, all eigenvalues of the linearised system have negative real parts, and this implies that the disease free equilibrium is stable whenever the condition $\tilde{R}_0 < 1$ is satisfied. □

2.7 Global Stability of the Disease Free Equilibrium

From the last section, we have seen that the disease free equilibrium point $E_0 = (\frac{\beta_h}{\mu_h}, 0, \frac{\beta_v}{\mu_v}, 0)$ is locally asymptotically stable when $\tilde{R}_0 < 1$, and unstable when $\tilde{R}_0 > 1$. In this section, we will prove global stability of the disease-free equilibrium.

Theorem 2.7.1. *If* $\tilde{R}_0 < 1$*, then the disease-free equilibrium point* E_0 *is globally asymptotically stable.*

Proof. Shifting the equilibrium point of (2.8), with the following transformation

$$\hat{S}_h = \frac{\beta_h}{\mu_h} - S_h,\ \hat{I}_h = I_h,\ \hat{S}_v = \frac{\beta_v}{\mu_v} - S_v, \text{ and } \hat{I}_v = I_v$$

gives

$$\frac{d\hat{S}_h}{dt} = -\mu_h \hat{S}_h + \varphi_h \left(\frac{\beta_h}{\mu_h} - \hat{S}_h\right) \hat{I}_v - \gamma_h \hat{I}_h(t-\tau) e^{-\mu_h \tau}, \tag{2.20}$$

$$\frac{d\hat{I}_h}{dt} = \varphi_h \left(\frac{\beta_h}{\mu_h} - \hat{S}_h \right) \hat{I}_v - (\mu_h + \gamma_h)\hat{I}_h, \tag{2.21}$$

$$\frac{d\hat{S}_v}{dt} = -\beta_v + \mu_v \left(\frac{\beta_v}{\mu_v} - \hat{S}_v \right) + \varphi_v \left(\frac{\beta_v}{\mu_v} - \hat{S}_v \right) \hat{I}_h, \tag{2.22}$$

$$\frac{d\hat{I}_v}{dt} = \varphi_v \left(\frac{\beta_v}{\mu_v} - \hat{S}_v \right) \hat{I}_h - \mu_v \hat{I}_v. \tag{2.23}$$

Now, from equation (2.21), we have

$$\frac{d\hat{I}_h}{dt} = \varphi_h \left(\frac{\beta_h}{\mu_h} - \hat{S}_h \right) \hat{I}_v - (\mu_h + \gamma_h)\hat{I}_h$$

$$\implies \quad \frac{d\hat{I}_h}{dt} \leq \frac{\varphi_h \beta_h}{\mu_h} \hat{I}_v - (\mu_h + \gamma_h)\hat{I}_h, \tag{2.24}$$

and from equation (2.23), it follows that

$$\frac{d\hat{I}_v}{dt} = \varphi_v \left(\frac{\beta_v}{\mu_v} - \hat{S}_v \right) \hat{I}_h - \mu_v \hat{I}_v$$

$$\implies \quad \frac{d\hat{I}_v}{dt} \leq \frac{\varphi_v \beta_v}{\mu_v} \hat{I}_h - \mu_v \hat{I}_v. \tag{2.25}$$

Furthermore, equations (2.24) and (2.25) can be written in the form

$$\frac{d}{dt} \begin{pmatrix} \hat{I}_h \\ \\ \hat{I}_v \end{pmatrix} \leq \mathbf{A} \begin{pmatrix} \hat{I}_h \\ \\ \hat{I}_v \end{pmatrix}, \tag{2.26}$$

where

$$\mathbf{A} = \begin{pmatrix} -(\mu_h + \gamma_h) & \frac{\varphi_h \beta_h}{\mu_h} \\ \\ \frac{\varphi_v \beta_v}{\mu_v} & -\mu_v \end{pmatrix}.$$

If the trace of $\mathbf{A}$ is negative and the determinant is positive, then the eigenvalues will be negative.

$$Trace(\mathbf{A}) = -(\mu_h + \gamma_h) - \mu_v < 0$$

$$Determinant(\mathbf{A}) = (\mu_h + \gamma_h)\mu_v - \frac{\varphi_h \varphi_v \beta_h \beta_v}{\mu_h \mu_v}$$

This determinant will be positive if

$$(\mu_h + \gamma_h)\mu_v > \frac{\varphi_h \varphi_v \beta_h \beta_v}{\mu_h \mu_v},$$

or if $\tilde{R}_0 < 1$.

The solution to (2.26) is of the form

$$\hat{\mathbf{I}} \leq \mathbf{C}e^{\lambda t},$$

where

$$\hat{\mathbf{I}} = \begin{pmatrix} \hat{I}_h(t) \\ \\ \hat{I}_v(t) \end{pmatrix} \text{ and } \mathbf{C} = \begin{pmatrix} C_1 \\ \\ C_2 \end{pmatrix}.$$

If $\tilde{R}_0 < 1$, the eigenvalues of $\mathbf{A}$ are negative as shown above, hence, as $t \to \infty$, $\hat{\mathbf{I}} \to \mathbf{0}$, which implies that $\hat{I}_h \to 0$ and $\hat{I}_v \to 0$.

We now show that

$$\hat{S}_h \to \frac{\beta_h}{\mu_h} \text{ and } \hat{S}_v \to \frac{\beta_v}{\mu_v} \text{ as } t \to \infty.$$

In the system (2.1), let $R_h = \hat{R}_h$, giving

$$\frac{d\hat{R}_h}{dt} = \gamma_h \hat{I}_h - \gamma_h \hat{I}_h(t-\tau)e^{-\mu_h \tau} - \mu_h \hat{R}_h.$$

From our earlier results, $\hat{I}_h \to 0$, which means

$$\frac{d\hat{R}_h}{dt} = -\mu_h \hat{R}_h,$$

and, hence, $\hat{R}_h = Ke^{-\mu_h t}$ (where K is an arbitrary constant). Therefore, as $t \to \infty$, $\hat{R}_h \to 0$.

From (2.2), we have

$$N_h = \hat{S}_h + \hat{I}_h + \hat{R}_h$$

It was earlier established that $N_h \to \frac{\beta_h}{\mu_h}$, and that $\hat{I}_h \to 0$, and $\hat{R}_h \to 0$ as $t \to \infty$, which yields that

$$\hat{S}_h \to \frac{\beta_h}{\mu_h} \text{ as } t \to \infty.$$

Similarly, since

$$N_v = \hat{S}_v + \hat{I}_v,$$

and we have showed earlier that $N_v \to \frac{\beta_v}{\mu_v}$ and $\hat{I}_v \to 0$ as $t \to \infty$, therefore,

$$\hat{S}_v \to \frac{\beta_v}{\mu_v} \text{ as } t \to \infty.$$

This concludes the proof, and shows that whenever the disease free equilibrium is locally asymptotically stable, it is also globally asymptotically stable. □

2.8 Local Stability of the Endemic Equilibrium

We now analyse the local stability of the endemic equilibrium point (E^*) of system (2.1). From Maple, $E^* = (S_h^*, I_h^*, S_v^*, I_v^*, R_h^*)$, where

$$
\begin{aligned}
S_h^* &= \frac{\mu_v(\mu_h+\gamma_h)(\gamma_h\mu_v e^{\mu_h\tau} + \mu_h\mu_v e^{\mu_h\tau} - \gamma_h\mu_v + \beta_h\varphi_v e^{\mu_h\tau})}{\varphi_v(\varphi_h\beta_v\mu_h e^{\mu_h\tau} + \varphi_h\beta_v\gamma_h e^{\mu_h\tau} - \varphi_h\beta_v\gamma_h + \mu_h^2\mu_v e^{\mu_h\tau} + \mu_h\mu_v\gamma_h e^{\mu_h\tau})},\\
I_h^* &= -\frac{\{\tilde{R}_0 - 1\}(\mu_h^2\mu_v^2 + \mu_h\mu_v^2\gamma_h)}{(-\mu_h\varphi_h\beta_v - \varphi_h\beta_v\gamma_h + \varphi_h\beta_v\gamma_h e^{-\mu_h\tau} - \mu_h^2\mu_v - \mu_h\mu_v\gamma_h)\varphi_v},\\
S_v^* &= \frac{\varphi_h\beta_v\mu_h e^{\mu_h\tau} + \varphi_h\beta_v\gamma_h e^{\mu_h\tau} - \varphi_h\beta_v\gamma_h + \mu_h^2\mu_v e^{\mu_h\tau} + \mu_h\mu_v\gamma_h e^{\mu_h\tau}}{\varphi_h(\gamma_h\mu_v e^{\mu_h\tau} + \mu_h\mu_v e^{\mu_h\tau} - \gamma_h\mu_v + \beta_h\varphi_v e^{\mu_h\tau})},\\
I_v^* &= -\frac{\{\tilde{R}_0 - 1\}(\mu_h^2\mu_v^2 + \mu_h\mu_v^2\gamma_h)}{\varphi_h\mu_v(-\mu_v\gamma_h - \mu_h\mu_v + \gamma_h\mu_v e^{-\mu_h\tau} - \beta_h\varphi_v)}\\
R_h^* &= -\frac{\gamma_h(\beta_h\beta_v\varphi_h\varphi_v - \gamma_h\mu_h\mu_v^2 - \mu_h^2\mu_v^2)(1 - e^{-\mu_h\tau})}{(-\mu_h\varphi_h\beta_v - \varphi_h\beta_v\gamma_h + \varphi_h\beta_v\gamma_h e^{-\mu_h\tau} - \mu_h^2\mu_v - \mu_h\mu_v\gamma_h)\varphi_v\mu_h}.
\end{aligned}
$$

This equilibrium is positive, and hence, biologically relevant when $R_0 > 1$. The Jacobian matrix at the endemic equilibrium point $\mathbf{J}_e$ has the form

$$
\mathbf{J}_e = \begin{pmatrix}
(-\mu_h - \varphi_h I_v^* - \lambda) & \gamma_h e^{-(\lambda+\mu_h)\tau} & 0 & -\varphi_h S_h^* \\
\varphi_h I_v^* & (-\mu_h - \gamma_h - \lambda) & 0 & \varphi_h S_h^* \\
0 & -\varphi_v S_v^* & (-\mu_v - \varphi_v I_h^* - \lambda) & 0 \\
0 & \varphi_v S_v^* & \varphi_v I_h^* & (-\mu_v - \lambda)
\end{pmatrix},
$$

which gives the characteristic equation for the eigenvalues λ as

$$
\begin{aligned}
(\lambda+\mu_v)[\lambda^3 &+ (\mu_v+\gamma_h+\varphi_h I_v^*+2\mu_h+\varphi_v I_h^*)\lambda^2 + (\varphi_h\mu_v I_v^*+\varphi_h\gamma_h I_v^*+2\mu_h\mu_v+\gamma_h\varphi_v I_h^* \\
&+\gamma_h\mu_v+\mu_h^2+2\mu_h\varphi_v I_h^*+\varphi_h\varphi_v S_h^* S_v^*+\varphi_h\mu_h I_v^*+\mu_h\gamma_h+\varphi_h\varphi_v I_h^* I_v^*-\varphi_h\gamma_h I_v^* e^{-(\lambda+\mu_h)\tau})\lambda \\
&+\varphi_h\mu_h\mu_v I_v^*+\mu_h^2\mu_v+2\varphi_h^2\varphi_v S_h^* S_v^* I_v^*+\varphi_h\varphi_v\mu_h I_h^* I_v^*+\mu_h\mu_v\gamma_h e^{-(\lambda+\mu_h)\tau}+\varphi_h\varphi_v\mu_h S_h^* S_v^* \\
&+\mu_h^2\varphi_v I_h^*+\mu_h\varphi_v\gamma_h I_h^*+\varphi_h\gamma_h\mu_v I_v^*-\varphi_h\varphi_v\gamma_h I_h^* I_v^* e^{-(\lambda+\mu_h)\tau}+\varphi_h\varphi_v\gamma_h I_h^* I_v^* \\
&-\varphi_h\mu_v\gamma_h I_v^* e^{-(\lambda+\mu_h)\tau}] = 0.
\end{aligned}
$$

The eigenvalues of the Jacobian matrix are $\lambda = -\mu_v$, and all others satisfy the following transcendental equation

$$\lambda^3 + A_1(\tau)\lambda^2 + A_2(\tau)\lambda + A_3(\tau) = 0, \tag{2.27}$$

where

$$A_1(\tau) = \mu_v+\gamma_h+\varphi_h I_v^*+2\mu_h+\varphi_v I_h^*,$$

$$
\begin{aligned}
A_2(\tau) = &\varphi_h\mu_v I_v^*+\varphi_h\gamma_h I_v^*+2\mu_h\mu_v+\gamma_h\varphi_v I_h^*+\gamma_h\mu_v+\mu_h^2+2\mu_h\varphi_v I_h^*+\varphi_h\varphi_v S_h^* S_v^*+\varphi_h\mu_h I_v^* \\
&+\mu_h\gamma_h+\varphi_h\varphi_v I_h^* I_v^*-\varphi_h\gamma_h I_v^* e^{-(\lambda+\mu_h)\tau},
\end{aligned}
$$

and

$$
\begin{aligned}
A_3(\tau) = &\varphi_h\mu_h\mu_v I_v^*+\mu_h^2\mu_v+2\varphi_h^2\varphi_v S_h^* S_v^* I_v^*+\varphi_h\varphi_v\mu_h I_h^* I_v^*+\mu_h\mu_v\gamma_h e^{-(\lambda+\mu_h)\tau}+\varphi_h\varphi_v\mu_h S_h^* S_v^* \\
&+\mu_h^2\varphi_v I_h^*+\mu_h\varphi_v\gamma_h I_h^*+\varphi_h\gamma_h\mu_v I_v^*-\varphi_h\varphi_v\gamma_h I_h^* I_v^* e^{-(\lambda+\mu_h)\tau}+\varphi_h\varphi_v\gamma_h I_h^* I_v^* \\
&-\varphi_h\mu_v\gamma_h I_v^* e^{-(\lambda+\mu_h)\tau}.
\end{aligned}
$$

First, we consider the case when $\tau = 0$. Let $A_1(\tau)|_{\tau=0} = A_1$, $A_2(\tau)|_{\tau=0} = A_2$ and $A_3(\tau)|_{\tau=0} = A_3$. Hence,

$$
\begin{aligned}
A_1 &= \mu_v + \gamma_h + \varphi_h \tilde{I}_v^* + 2\mu_h + \varphi_v \tilde{I}_h^*, \\
A_2 &= \varphi_h \mu_v \tilde{I}_v^* + 2\mu_h \mu_v + \gamma_h \varphi_v \tilde{I}_h^* + \gamma_h \mu_v + \mu_h^2 + 2\mu_h \varphi_v \tilde{I}_h^* + \varphi_h \varphi_v \tilde{S}_h^* \tilde{S}_v^* + \varphi_h \mu_h \tilde{I}_v^* \\
&\quad + \mu_h \gamma_h + \varphi_h \varphi_v \tilde{I}_h^* \tilde{I}_v^*, \\
A_3 &= \varphi_h \mu_h \mu_v \tilde{I}_v^* + \mu_h^2 \mu_v + 2\varphi_h^2 \varphi_v \tilde{S}_h^* \tilde{S}_v^* \tilde{I}_v^* + \varphi_h \varphi_v \mu_h \tilde{I}_h^* \tilde{I}_v^* + \mu_h \mu_v \gamma_h + \varphi_h \varphi_v \mu_h \tilde{S}_h^* \tilde{S}_v^* \\
&\quad + \mu_h^2 \varphi_v \tilde{I}_h^* + \mu_h \varphi_v \gamma_h \tilde{I}_h^*,
\end{aligned}
$$

where

$$
\begin{aligned}
\tilde{S}_h^* &= \frac{\mu_v(\mu_h + \gamma_h)(\mu_h \mu_v + \beta_h \varphi_v)}{\varphi_v(\varphi_h \beta_v \mu_h + \mu_h^2 \mu_v + \mu_h \mu_v \gamma_h)}, \\
\tilde{I}_h^* &= \frac{\{\tilde{R}_0 - 1\}(\mu_h^2 \mu_v^2 + \mu_h \mu_v^2 \gamma_h)}{(\mu_h \varphi_h \beta_v + \mu_h^2 \mu_v + \mu_h \mu_v \gamma_h)\varphi_v}, \\
\tilde{S}_v^* &= \frac{\varphi_h \beta_v \mu_h + \mu_h^2 \mu_v + \mu_h \mu_v \gamma_h}{\varphi_h(\mu_h \mu_v + \beta_h \varphi_v)}, \\
\tilde{I}_v^* &= \frac{\{\tilde{R}_0 - 1\}(\mu_h^2 \mu_v^2 + \mu_h \mu_v^2 \gamma_h)}{\varphi_h \mu_v(\mu_h \mu_v + \beta_h \varphi_v)}.
\end{aligned}
$$

By the Routh Hurwitz criterion, all roots of the characteristic equation (2.27) have negative real parts whenever $A_1 > 0$, $A_2 > 0$, $A_3 > 0$, and the condition $A_1 A_2 > A_3$ is satisfied. Hence whenever $A_1 A_2 > A_3$, the endemic equilibrium point E^* of system (2.8) is locally asymptotically stable when it exists, i.e. for $\tilde{R}_0 > 1$. This gives rise to the following theorem.

Theorem 2.8.1. *Suppose that the condition $A_1A_2 > A_3$ holds for $\tau = 0$. The endemic equilibrium point E^* of system (2.8) is locally asymptotically stable for $\tilde{R}_0 > 1$.*

We now consider the case when $\tau > 0$. To be able to analyse the characteristic equation in this case, we make use of the following lemma [55].

Lemma 2.8.2. *[55] Consider the characteristic equation of the form $P(\lambda) + Q(\lambda)e^{-\lambda\tau} = 0$, and define $F(\omega) = |P(i\omega)|^2 - |Q(i\omega)|^2$. Suppose $P(\lambda)$ and $Q(\lambda)$ have no common imaginary zeros, $P(0) + Q(0) \neq 0$, $\overline{P(-i\omega)} = P(i\omega)$, $\overline{Q(-i\omega)} = Q(i\omega)$ for real ω and $F(\omega)$ has at most a finite number of real zeros. Then if $F(\omega)$ has no positive real root then there are no stability switches as τ increases, while stability switches are possible if $F(\omega)$ has at least one positive roots.*

From the characteristic equation (2.27), we have

$$P(\lambda) + Q(\lambda)e^{-(\lambda+\mu_h)\tau} = 0, \tag{2.28}$$

where

$$P(\lambda) = \lambda^3 + \hat{A}_1\lambda^2 + \hat{A}_2\lambda + \hat{A}_3,$$

$$Q(\lambda) = -(\kappa_1\lambda + \kappa_2),$$

with

$$\hat{A}_1 = \mu_v + \gamma_h + \varphi_h I_v^* + 2\mu_h + \varphi_v I_h^*,$$

$$\hat{A}_2 = \varphi_h\mu_v I_v^* + \varphi_h\gamma_h I_v^* + 2\mu_h\mu_v + \gamma_h\varphi_v I_h^* + \gamma_h\mu_v + \mu_h^2 + 2\mu_h\varphi_v I_h^* + \varphi_h\varphi_v S_h^* S_v^* + \varphi_h\mu_h I_v^*$$
$$+ \mu_h\gamma_h + \varphi_h\varphi_v I_h^* I_v^*,$$

$$\hat{A}_3 = \varphi_h\mu_h\mu_v I_v^* + \mu_h^2\mu_v + 2\varphi_h^2\varphi_v S_h^* S_v^* I_v^* + \varphi_h\varphi_v\mu_h I_h^* I_v^* + \varphi_h\varphi_v\mu_h S_h^* S_v^* + \mu_h^2\varphi_v I_h^* + \mu_h\varphi_v\gamma_h I_h^*$$
$$+ \varphi_h\gamma_h\mu_v I_v^* + \varphi_h\varphi_v\gamma_h I_h^* I_v^*,$$

$$\kappa_1 = \varphi_h\gamma_h I_v^*,$$

$$\kappa_2 = \varphi_h\varphi_v\gamma_h I_h^* I_v^* + \varphi_h\mu_v\gamma_h I_v^* - \mu_h\mu_v\gamma_h.$$

Let $\lambda = i\omega$ with $\omega > 0$ be the root of the characteristic equation (2.28), hence,

$$(i\omega)^3 + \hat{A}_1(i\omega)^2 + \hat{A}_2(i\omega) + \hat{A}_3 = e^{-[(i\omega)+\mu_h]\tau}(\kappa_1(i\omega) + \kappa_2).$$

Furthermore,

$$-\hat{A}_1\omega^2 + \hat{A}_3 - (\omega^3 - \hat{A}_2\omega)i = e^{-\mu_h\tau}[(\kappa_1\omega\cos(\omega\tau) - \kappa_2\sin(\omega\tau))i + \kappa_2\cos(\omega\tau) + \kappa_1\omega\sin(\omega\tau)].$$

Separating into the real and imaginary parts, we obtain

$$-\hat{A}_1\omega^2 + \hat{A}_3 = e^{-\mu_h\tau}[\kappa_2\cos(\omega\tau) + \kappa_1\omega\sin(\omega\tau)],$$
$$-(\omega^3 - \hat{A}_2\omega) = e^{-\mu_h\tau}[\kappa_1\omega\cos(\omega\tau) - \kappa_2\sin(\omega\tau)].$$

Squaring and adding the last two equations yields,

$$\omega^6 + B_1\omega^4 + B_2\omega^2 + B_3 = 0, \tag{2.29}$$

where

$$B_1 = \hat{A}_1^2 - 2\hat{A}_2,$$

$$B_2 = \hat{A}_2^2 - 2\hat{A}_1\hat{A}_3,$$

$$B_3 = \hat{A}_3^2 - e^{-2\mu_h\tau}[\kappa_2^2 + \kappa_1^2\omega^2].$$

Let $\zeta = \omega^2$, then (2.29) becomes

$$\zeta^3 + B_1\zeta^2 + B_2\zeta + B_3 = 0. \tag{2.30}$$

Clearly, if $B_1 \geq 0$, $B_2 \geq 0$ and $B_3 \geq 0$, then (2.30) has no positive real roots, and if $B_3 < 0$, then the characteristic equation (2.30) has at least one positive root $\omega > 0$, i.e. $F(\omega) = 0$.

Lemma 2.8.3. *If $B_3 < 0$ in (2.30), then the function $F(\omega)$ given by $F(\omega) = \omega^6 + B_1\omega^4 + B_2\omega^2 + B_3$ has at least one positive root.*

Proof. Since we assume that for some parameter values $B_3 < 0$, this implies that $F(0) = B_3 < 0$. As the function $F(\omega)$ is continuous, and $\lim_{\omega\to\infty} F(\omega) = \infty$, this means that there exists a positive root ω of the equation $F(\omega) = 0$. □

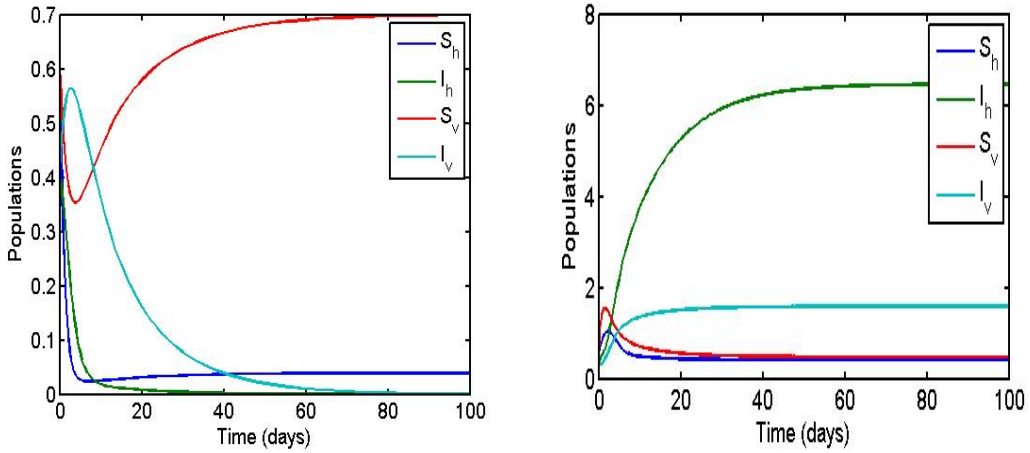
2.9 Numerical Simulations

In this section, we use DDE23 solver in MATLAB to solve the System (2.8) numerically. We show numerical simulations, which confirm theoretical results

obtained in previous sections on the stability of the disease free and endemic equilibria. The parameters used in this section are listed in Table 2.3, and taken from [57], [58] and [59], and some parameters are varied. In all simulations, the time delay is taken as $\tau = 1$, except otherwise stated in the figure.

Table 2.3: Model parameters are taken from [57], [58] and [59].

Parameter	Symbol	Value	Source
Birth rate for humans	β_h	0.55	[57]
Death rate for humans	μ_h	0.00041$\rightarrow$ 0.02	[58]
Rate of infection (Humans)	φ_h	0.8	[57]
Recovery rate	γ_h	0.02	[59]
Birth rate for mosquito	β_v	3.2	[57]
Death rate for mosquito	μ_v	0.0010$\rightarrow$0.10	[58]
Rate of infection (Mosquitos)	φ_v	0.8	[57]

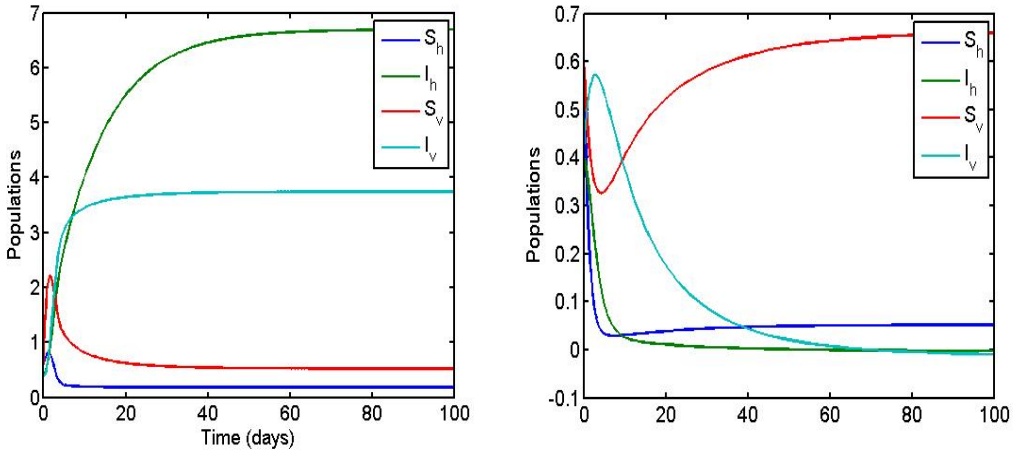


(a) $R_0 = 0.5563 < 1, \beta_h = 0.0215, \mu_h = 0.548, \beta_v = 0.07, \mu_v = 0.1$

(b) $R_0 = 7.6554 > 1, \mu_h = 0.08, \mu_v = 1.55$

Figure 2.2: Solutions of the system (2.8) converging to disease-free equilibrium for $R_0 = 0.5563 < 1$ in Figure 2.2(a), and diverging from the disease-free equilibrium to the endemic equilibrium for $R_0 = 7.6554 > 1$ in Figure 2.2(b).

Figure 2.2 shows that when the parameter values satisfy $R_0 = 0.5563 < 1$, the disease free equilibrium is stable, and the solutions of the system (2.8) tend to it, and whenever $R_0 = 7.6554 > 1$, the endemic equilibrium exists and is stable. This supports our analytical findings in Section 2.7 that the disease-free equilibrium point is globally asymptoticaly stable for $R_0 < 1$ and unstable for $R_0 > 1$.

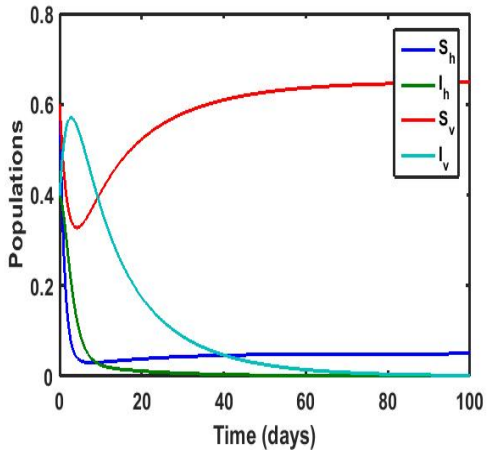


(a) $R_0 = 15.8212 > 1, \mu_h = 0.08, \mu_v = 0.75$

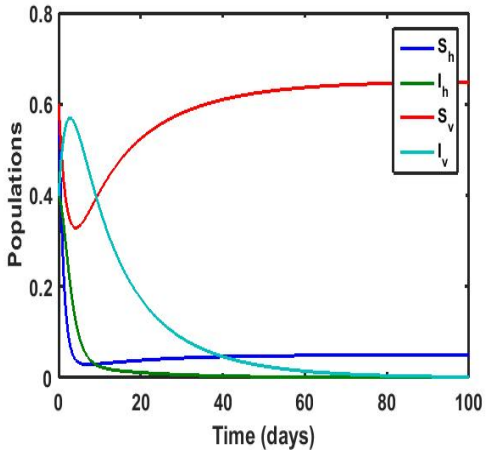
(b) $R_0 = 0.6325 < 1, \beta_h = 0.025, \mu_h = 0.5, \beta_v = 0.065, \mu_v = 0.1$

Figure 2.3: Solutions of the system (2.8) converging to endemic equilibrium for $R_0 = 15.8212 > 1$, and diverging for $R_0 = 0.6325 < 1$.

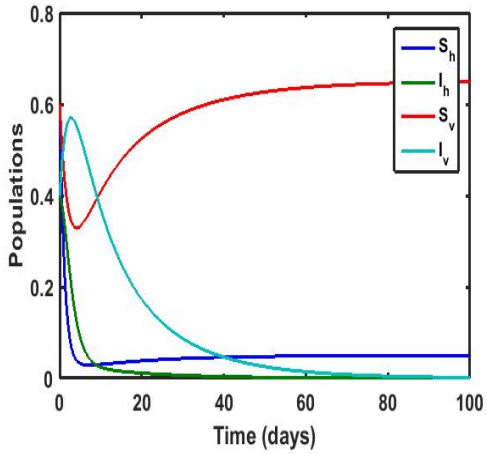
Figure 2.3 shows that when the parameters of the system (2.8) are chosen in such a way as to satisfy the condition $R_0 = 15.8212 > 1$, the solutions of the system (2.8) tend to an endemic equilibrium, and for $R_0 = 0.6325 < 1$, the solutions go to a stable disease free equilibrium.



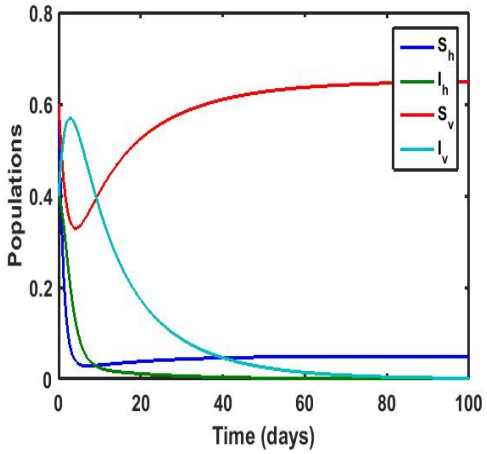
(a) $\tau = 1$



(b) $\tau = 5$



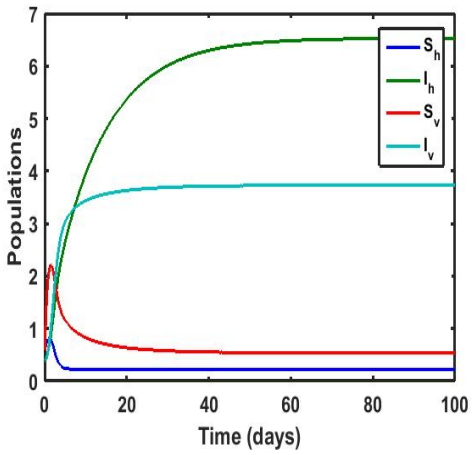
(c) $\tau = 10$



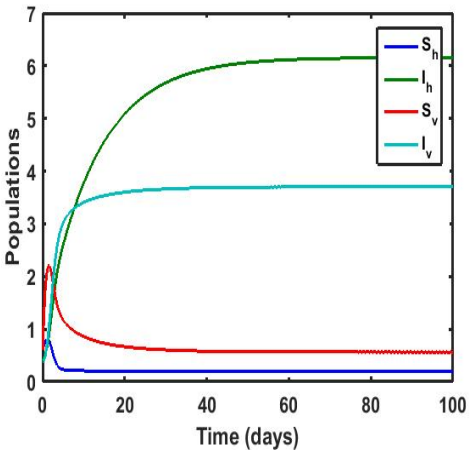
(d) $\tau = 20$

Figure 2.4: Solutions of (2.8) for different values of the time delay. Other parameters are $\beta_h = 0.025, \mu_h = 0.5, \varphi_h = 0.8, \gamma_h = 0.02, \beta_v = 0.065, \mu_v = 0.1, \varphi_v = 0.8$.

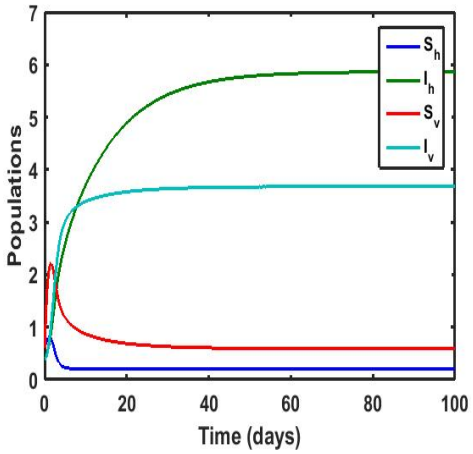
Figure 2.4 shows a stable disease free equilibrium point for all time delay (τ).



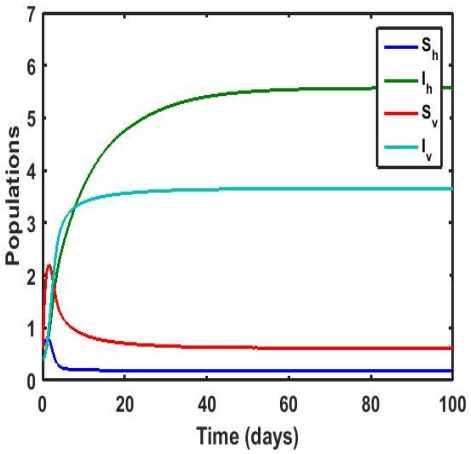
(a) $\tau = 1$



(b) $\tau = 5$



(c) $\tau = 10$

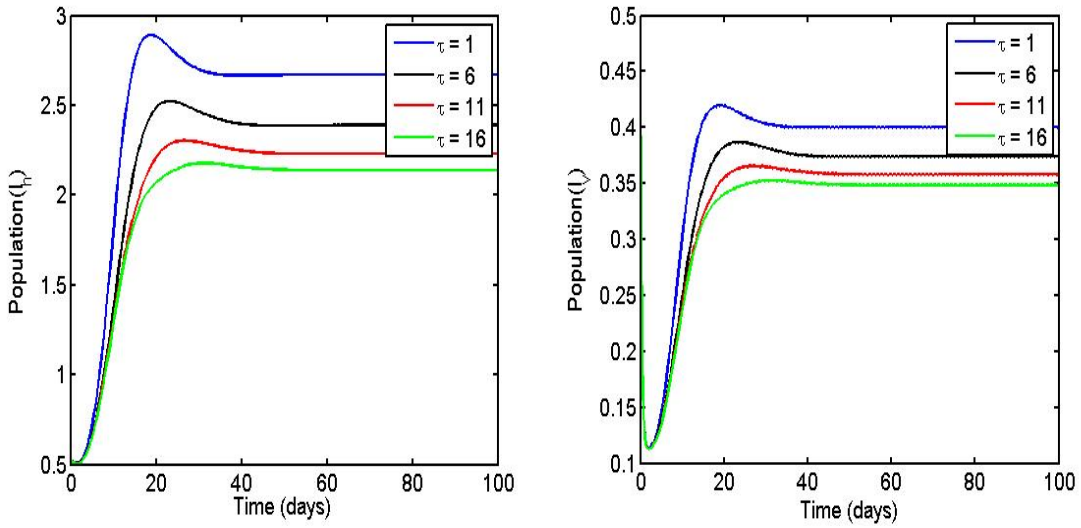


(d) $\tau = 20$

Figure 2.5: Solutions of (2.8) for different values of the time delay. Other parameters are $\beta_h = 0.55, \mu_h = 0.08, \varphi_h = 0.8, \gamma_h = 0.02, \beta_v = 3.2, \mu_v = 0.75, \varphi_v = 0.8$.

Figure 2.5 shows the solutions of the system (2.8) as the time delay is varied,

and the endemic equilibrium is stable for any of the chosen values of the time delay τ.



(a) Number of infected humans in the population for different values of time delay τ.

(b) Number of infected mosquitoes in the population for different values of time delay τ.

Figure 2.6: Solution trajectories of the number of infected humans (I_h) in Figure 2.6(a) and number of infected mosquitos (I_v) in Figure 2.6(b) as time delay τ was varied. $\mu_h = 0.1, \gamma_h = 0.1, \mu_v = 3.2$.

We can see from Figure 2.6 that there is a significant reduction in the number of infected humans in the population as we increase the time delay (τ) from 1 through 16. Moreover, we observe a reduction in the number of infected mosquito population, as shown in Figure 2.6 as the time delay (τ) is increased.

2.10 Conclusions

In this chapter, we have developed an SIR-type mathematical model to describe the spread of Malaria. We have incorporated into the model a time delay to account for the effect of malaria drugs even after they have been stopped to be administered. We have proved the positivity of solutions of the model in section 2.3, and calculated the basic reproduction number R_0. We have also analysed the existence of the disease-free and endemic equilibria, and found that if $R_0 < 1$, then the disease-free equilibrium exists and is both locally and globally asymptotically stable. If $R_0 > 1$, then the endemic equilibrium exists and is asymptotically stable. It is worth mentioning that in Chapter 2.8, it was impossible to prove analytically the global stability of the endemic equilibrium. However, our numerical simulations (see Fig 2.5) suggest that the endemic equilibrium of the system 2.8 is globally asymptotically stable for all chosen values of the time delay as long as the basic reproduction number R_0 is greater than one, and unstable otherwise.

This study has shown that the treatment of malaria using long-lasting malaria drugs could significantly reduce the population infected with malaria (see Fig 2.6), and this in turn reduces the number of infected mosquito vectors due to the reduction in the population of the infected human host (Fig 2.6). This suggest a potential way to effectively address the problem of the spread of malaria in the population.

Chapter 3

Two-Infection Mathematical Model with Time Delay

3.1 The model

In this chapter we consider a model, where the total population $N = N(t)$ is subdivided into the following classes: susceptible $S = S(t)$, those infected with disease one $I_D(t)$, population infected with disease two $I_d(t)$, recovered from disease one $R_D(t)$ and the population that have recovered from disease two $R_d(t)$. This gives the total population as $N = S + I_D + I_d + R_D + R_d$. Recruitment is at a constant rate β and apart from the natural death rate μ, we have death rate as a result of the disease one μ_D, and a death rate as a result of disease two μ_d. The flow chart of the model is shown in Fig. 3.1.

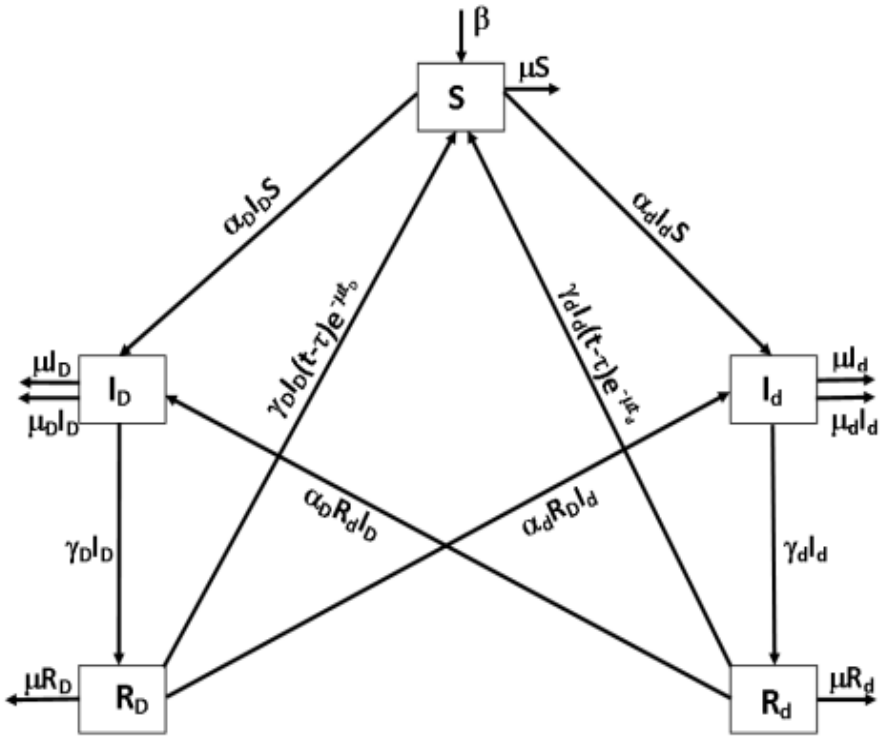


Figure 3.1: Flow chart of the model.

This model does not include the possibility of a co-infection, hence, the absence of the compartment for disease one and two. The model includes two temporary immunities: a temporary immunity from diseases one (τ_D) and a temporary immunity from disease two (τ_d). This means that each individual after recovery from disease one or two goes into a disease one or two recovery pool respectively. The temporary immunity becomes active once in the recovery compartment against the disease the individual recovered from, but the individual could still be infected with another disease type. This gives us the following system of equations

$$
\begin{aligned}
\frac{dS}{dt} &= \beta - \mu S - \alpha_D I_D S - \alpha_d I_d S + \gamma_D I_D(t-\tau_D)e^{-\mu\tau_D} + \gamma_d I_d(t-\tau_d)e^{-\mu\tau_d},\\
\frac{dI_D}{dt} &= \alpha_D I_D S - (\mu+\mu_D)I_D + \alpha_D R_d I_D - \gamma_D I_D,\\
\frac{dI_d}{dt} &= \alpha_d I_d S - (\mu+\mu_d)I_d + \alpha_d R_D I_d - \gamma_d I_d,\\
\frac{dR_D}{dt} &= \gamma_D I_D - \gamma_D I_D(t-\tau_D)e^{-\mu\tau_D} - \alpha_d R_D I_d - \mu R_D,\\
\frac{dR_d}{dt} &= \gamma_d I_d - \gamma_d I_d(t-\tau_d)e^{-\mu\tau_d} - \alpha_D R_d I_D - \mu R_d.
\end{aligned}
\tag{3.1}
$$

The variables and parameters used in the model (3.1) are summarised in Tables 3.1 and 3.2 respectively.

Table 3.1: State variables of the model

Variable	Description
S	Population of susceptibles, [biomass]
I_D	Infected with disease one, [biomass]
I_d	Infected with disease two, [biomass]
R_D	Recovered from disease one, [biomass]
R_d	Recovered from disease two, [biomass]

Table 3.2: Parameters used in the model

Parameter	Description
β	Natural birth rate, [biomass/time]
μ	Natural death rate, [1/time]
μ_D	Disease one induced death rate, [1/time]
μ_d	Disease two induced death rate, [1/time]
α_D	Disease one transmission rate, $[1/(time \cdot time)]$
α_d	Disease two transmission rate, $[1/(time \cdot time)]$
τ_D	Temporary immunity from disease one, [time]
τ_d	Temporary immunity from disease two, [time]
γ_D	Disease one recovery rate, $[1/time]$
γ_d	Disease two recovery rate, $[1/time]$

System (3.1) has the following initial conditions

$$S(0) > 0, I_D(s) = I_{D0}(s) \geq 0, I_d(s) = I_{d0}(s) \geq 0, R_D(0) \geq 0, R_d(0) \geq 0, \quad (3.2)$$

$s \in [-\tau, 0]$, where $\tau = \max\{\tau_D, \tau_d\}$.

Adding all equations in system (3.1), the total variable population size is governed by the differential equation

$$N'(t) = \beta - \mu S - (\mu + \mu_D + \gamma_D)I_D - (\mu + \mu_d + \gamma_d)I_d + \gamma_D I_D - \mu R_D + \gamma_d I_d - \mu R_d,$$

which gives

$$N'(t) = \beta - \mu S - (\mu + \mu_D)I_D - (\mu + \mu_d)I_d - \mu R_D - \mu R_d.$$

We have that

$$N'(t) \leq \beta - hN(t),$$

where $h = \min\{\mu, \mu_D, \mu_d\}$.

This gives

$$\limsup_{t\to\infty} N(t) \leq \frac{\beta}{h}. \tag{3.3}$$

It follows that, evolution of the total population $N(t)$ is bounded above by β/h.

3.2 Positivity of Solutions

Since system (3.1) models the dynamics of the human population, it is important to prove that all quantities S, I_D, I_d, R_D and R_d will remain positive for all time.

Theorem 3.2.1. *Let the initial data be* $S(0) = S_0 > 0$, $I_D(s) = I_{D0}(s) \geq 0$, $I_d(s) = I_{d0}(s) \geq 0$, $R_D(0) = R_{D0} \geq 0$ *and* $R_d(0) = R_{d0} \geq 0$, $\forall\ s \in [-\tau; 0)$ *with* $\tau = \max\{\tau_D, \tau_d\}$. *Then solutions* $S(t)$, $I_D(t)$, $I_d(t)$, $R_D(t)$ *and* $R_d(t)$ *of the system* (3.1) *are positive for all* $t > 0$.

Proof. We prove non-negativity of solutions of the system (3.1) by contradiction. Assume that $t_1 > 0$ is the first moment of time when $S(t)I_D I_d R_D R_d = 0$. Assume

that $S(t) = 0$ and $I_D I_d R_D R_d \geq 0$. In order for $S(t)$ to become negative, we would need to have that $\frac{dS}{dt}\big|_{t=t_1} < 0$. However, from the first equation of system (3.1), we have

$$\frac{dS}{dt}\Big|_{t=t_1} = \overbrace{\beta}^{>0} - \overbrace{\mu S(t_1)}^{=0} - \overbrace{\alpha_D I_D(t_1) S(t_1)}^{=0} - \overbrace{\alpha_d I_d(t_1) S(t_1)}^{=0}$$
$$+ \overbrace{\gamma_D I_D(t_1 - \tau_D) e^{-\mu \tau_D}}^{\geq 0} + \overbrace{\gamma_d I_d(t_1 - \tau_d) e^{-\mu \tau_d}}^{\geq 0}$$

This implies that $\frac{dS}{dt}\big|_{t=t_1} \geq 0$, which is a contradiction. Hence $S(t)$ is positive. Similarly, let us assume that $t_2 > 0$ is the first instant of time when $I_D(t_2) = 0$ and $S(t) \geq 0$. For $I_D(t)$ to be negative, one has to have that $\frac{dI_D}{dt}\big|_{t=t_2} < 0$. Let us define

$$B = \min_{0 \leq t \leq t_2} \{\alpha_D S - (\mu + \mu_D) + \alpha_D R_d - \gamma_D\}.$$

Therefore, for $t \in [0, t_2]$, $dI_D/dt \geq B I_D(t)$, and hence, $I_D(t_2) \geq I_{D0}(0) e^{B t_2} > 0$, which implies contradiction. Thus, $I_D(t)$ can never become negative. A similar argument holds for proving positivity of $I_d(t)$.

We now show the positivity of $R_D(t)$. From the fourth equation of system (3.1), we have that $\{\gamma_D I_D - \gamma_D I_D(t - \tau_D) e^{-\mu \tau_D}\} \geq 0$ since $I_D(t)$ was proved to be positive. Let us define

$$A = \min_{t \geq 0} \{\alpha_d I_d(t) + \mu\}.$$

Then, for $t > 0$,

$$\frac{dR_D(t)}{dt} \geq -A R_D(t),$$

and, therefore, $R_D(t) \geq R_D(0)e^{-At} \geq 0$. Thus $R_D(t) \geq 0$, $\forall\ t > 0$. The same can be used to show positivity of $R_d(t)$. This concludes the proof. □

3.3 Steady States

The steady states of the system (3.1) can be found as solutions of the following system of algebraic equations

$$\begin{aligned}
\beta - \mu S - \alpha_D I_D S - \alpha_d I_d S + \gamma_D I_D e^{-\mu\tau_D} + \gamma_d I_d e^{-\mu\tau_d} &= 0,\\
\alpha_D I_D S - (\mu + \mu_D) I_D + \alpha_D R_d I_D - \gamma_D I_D &= 0,\\
\alpha_d I_d S - (\mu + \mu_d) I_d + \alpha_d R_D I_d - \gamma_d I_d &= 0,\\
\gamma_D I_D - \gamma_D I_D e^{-\mu\tau_D} - \alpha_d R_D I_d - \mu R_D &= 0,\\
\gamma_d I_d - \gamma_d I_d e^{-\mu\tau_d} - \alpha_D R_d I_D - \mu R_d &= 0.
\end{aligned} \tag{3.4}$$

This gives four real steady states. *Disease free steady state ($I_D = I_d = 0$)*

$$\begin{aligned}
E^0 &= (S^0, I_D^0, I_d^0, R_D^0, R_d^0)\\
&= \left(\frac{\beta}{\mu}, 0, 0, 0, 0\right).
\end{aligned} \tag{3.5}$$

Disease two only (Disease one free) steady state ($I_D = 0$)

$$E_d^* = (S_d^*, 0, I_d^*, 0, R_d^*),$$

where

$$S_d^* = \frac{\mu_d + \mu + \gamma_d}{\alpha_d},$$
$$I_d^* = \frac{\beta\alpha_d - \mu^2 - \mu\mu_d - \mu\gamma_d}{\alpha_d(\mu + \mu_d + \gamma_d - e^{-\mu\tau_d}\gamma_d)},$$
$$R_d^* = \frac{\gamma_d(1 - e^{-\mu\tau_d})[\beta\alpha_d - \mu^2 - \mu\mu_d - \mu\gamma_d]}{\mu\alpha_d(\mu + \mu_d + \gamma_d - e^{-\mu\tau_d}\gamma_d)}.$$

This steady state is biologically relevant when $\beta\alpha_d > \mu^2 + \mu\mu_d + \mu\gamma_d$.

Disease one only (Disease two free) steady state ($I_d = 0$):

$$E_D^* = (S_D^*, I_D^*, 0, R_D^*, 0),$$

where

$$S_D^* = \frac{\mu_D + \mu + \gamma_D}{\alpha_D},$$
$$I_D^* = \frac{\beta\alpha_D - \mu^2 - \mu\mu_D - \mu\gamma_D}{\alpha_D(\mu + \mu_D + \gamma_D - e^{-\mu\tau_D}\gamma_D)},$$
$$R_D^* = \frac{\gamma_D(1 - e^{-\mu\tau_D})[\beta\alpha_D - \mu^2 - \mu\mu_D - \mu\gamma_D]}{\mu\alpha_D(\mu + \mu_D + \gamma_D - e^{-\mu\tau_D}\gamma_D)},$$

and it is biologically relevant when $\beta\alpha_D > \mu^2 + \mu\mu_D + \mu\gamma_D$.

We also have an endemic steady state $E_e^* = (S_e^*, I_{De}^*, I_{de}^*, R_{De}^*, R_{de}^*)$, where S_e^* is the root of the following cubic equation

$$a_1 S_e^{*3} + a_2 S_e^{*2} + a_3 S_e^* + a_4 = 0 \tag{3.6}$$

with

$$
\begin{aligned}
a_1 =&\alpha_D^2\alpha_d^2\mu,\\
a_2 =&\alpha_D^2\alpha_d^2\beta - \alpha_D\mu_D\alpha_d^2\mu - \mu^2\alpha_D^2\alpha_d - 2\alpha_D\alpha_d^2\gamma_D\mu - 2\alpha_D^2\gamma_d\mu\alpha_d - \mu_d\alpha_D^2\mu\alpha_d - \alpha_D\mu^2\alpha_d^2,\\
a_3 =&-\alpha_D^2\gamma_d\beta\alpha_d + \alpha_D\mu^2\mu_d\alpha_d + \mu\mu_D\gamma_D\alpha_d^2 + \alpha_D\mu^2\gamma_D\alpha_d + \alpha_D\mu^2\mu_D\alpha_d - \alpha_D\mu_D\alpha_d^2\beta\\
&+\alpha_D\mu^2\gamma_d\alpha_d - \alpha_D^2\mu_d\beta\alpha_d - \alpha_D\mu\alpha_d^2\beta - \mu\alpha_D^2\beta\alpha_d - \alpha_D\alpha_d^2\gamma_D\beta + \mu_d\alpha_D^2\mu\gamma_d + \mu\gamma_D^2\alpha_d^2\\
&+\alpha_D^2\mu\gamma_d^2 + \mu^2\gamma_D\alpha_d^2 + \alpha_D\mu^3\alpha_d + \mu^2\alpha_D^2\gamma_d + \alpha_D\mu_D\mu_d\mu\alpha_d - \alpha_D\gamma_d e^{-\mu(\tau_d+\tau_D)}\gamma_D\mu\alpha_d\\
&+\alpha_D\mu_D\mu\alpha_d\gamma_d e^{-\mu\tau_d} + \alpha_D\mu\alpha_d e^{-\mu\tau_D}\gamma_D\mu_d + \alpha_D\mu^2\alpha_d e^{-\mu\tau_D}\gamma_D + \alpha_D\gamma_d e^{-\mu\tau_d}\gamma_D\mu\alpha_d\\
&+\alpha_D\mu^2\alpha_d\gamma_d e^{-\mu\tau_d} + \alpha_D\gamma_D\mu_d\mu\alpha_d + \alpha_D\mu_D\gamma_d\mu\alpha_d + \alpha_D e^{-\mu\tau_D}\gamma_D\gamma_d\mu\alpha_d + 2\mu\gamma_D\alpha_d\alpha_D\gamma_d,\\
a_4 =&\alpha_D\mu^2\beta\alpha_d - \mu^2\gamma_D^2\alpha_d e^{-\mu\tau_D} - \mu^3\gamma_D\alpha_d e^{-\mu\tau_D} - \alpha_D\gamma_d^2\mu^2 e^{-\mu\tau_d} - \alpha_D\mu^3\gamma_d e^{-\mu\tau_d}\\
&+\mu\mu_D\gamma_D\alpha_d\gamma_d e^{-\mu(\tau_d+\tau_D)} - \alpha_D\gamma_D\mu\gamma_d^2 e^{-\mu\tau_D} + \alpha_D\mu_D\gamma_d\beta\alpha_d - \alpha_D\gamma_D\mu\mu_d\gamma_d e^{-\mu\tau_d}\\
&+\alpha_D\mu\gamma_d\beta\alpha_d + \alpha_D\gamma_d^2 e^{-\mu(\tau_d+\tau_D)}\gamma_D\mu + \alpha_D\mu_D\mu_d\beta\alpha_d + \alpha_D\mu\mu_d\beta\alpha_d - \alpha_D\mu_D\mu\gamma_d^2 e^{-\mu\tau_d}\\
&-\alpha_D\gamma_D\mu^2\gamma_d e^{-\mu\tau_d} - \mu^2\gamma_D\alpha_d e^{-\mu\tau_D}\gamma_d + \alpha_D\mu\mu_D\beta\alpha_d - \mu\gamma_D^2\alpha_d\gamma_d e^{-\mu\tau_d} + \alpha_D\gamma_d e^{-\mu(\tau_d+\tau_D)}\gamma_D\mu^2\\
&+\alpha_D\gamma_D\mu_d\beta\alpha_d - \alpha_D\mu_D\mu\mu_d\gamma_d e^{-\mu\tau_d} - \mu\mu_D\gamma_D\alpha_d\gamma_d e^{-\mu\tau_d} + \alpha_D\mu\gamma_D\beta\alpha_d\\
&-\alpha_D\gamma_d e^{-\mu(\tau_d+\tau_D)}\gamma_D\beta\alpha_d + \alpha_D\gamma_d e^{-\mu(\tau_d+\tau_D)}\gamma_D\mu\mu_d - \alpha_D\gamma_D\mu\gamma_d^2 e^{-\mu\tau_d} - \mu^2\gamma_D\alpha_d\gamma_d e^{-\mu\tau_d}\\
&+\mu^2\gamma_D\alpha_d e^{-\mu(\tau_d+\tau_D)}\gamma_d + \mu\gamma_D^2\alpha_d\gamma_d e^{-\mu(\tau_d+\tau_D)} - \alpha_D\mu^2\mu_d\gamma_d e^{-\mu\tau_d} + \alpha_D\gamma_d e^{-\mu\tau_d}\gamma_D\beta\alpha_d\\
&-\alpha_D\mu_D\mu^2\gamma_d e^{-\mu\tau_d} - \mu^2\gamma_D\alpha_d e^{-\mu\tau_D}\mu_d + \alpha_D e^{-\mu\tau_D}\gamma_D\gamma_d\beta\alpha_d - \alpha_D\gamma_D\mu_d e^{-\mu\tau_D}\mu\gamma_d\\
&-\alpha_D\mu^2\gamma_D e^{-\mu\tau_D}\gamma_d - \mu^2\mu_D\gamma_D\alpha_d e^{-\mu\tau_D} - \mu\mu_D\gamma_D\alpha_d e^{-\mu\tau_D}\mu_d - \mu\mu_D\gamma_D\alpha_d e^{-\mu\tau_D}\gamma_d\\
&-\mu\gamma_D^2\alpha_d e^{-\mu\tau_D}\mu_d - \mu\gamma_D^2\alpha_d e^{-\mu\tau_D}\gamma_d,
\end{aligned}
$$

and I^*_{De}, I^*_{de}, R^*_{De} and R^*_{de} are given bellow in terms of S^*_e as follows

$$
\begin{aligned}
I^*_{De} &= \frac{\mu R^*_{De}\kappa_1}{\alpha_D\psi},\\
I^*_{de} &= \frac{\mu R^*_{de}\kappa_2}{\alpha_d\psi},\\
R^*_{De} &= \frac{-\alpha_d S^*_e + (\mu+\mu_d+\gamma_d)}{\alpha_d},\\
R^*_{de} &= \frac{-\alpha_D S^*_e + (\mu+\mu_D+\gamma_D)}{\alpha_D},
\end{aligned}
$$

where

$$
\begin{aligned}
\kappa_1 &= e^{\mu(\tau_D+\tau_d)}\alpha_d S^*_e\alpha_D - e^{\mu(\tau_D+\tau_d)}\gamma_D\alpha_d - e^{\mu(\tau_D+\tau_d)}\alpha_d\mu - e^{\mu(\tau_D+\tau_d)}\alpha_d\mu_D,\\
&\quad + e^{\mu\tau_D}\alpha_D\gamma_d - e^{\mu(\tau_D+\tau_d)}\gamma_d\alpha_D\\
\kappa_2 &= e^{\mu(\tau_D+\tau_d)}\alpha_d S^*_e\alpha_D - e^{\mu(\tau_D+\tau_d)}\mu\alpha_D - e^{\mu(\tau_D+\tau_d)}\alpha_D\mu_d - e^{\mu(\tau_D+\tau_d)}\gamma_d\alpha_D\\
&\quad + e^{\mu\tau_d}\gamma_D\alpha_d - e^{\mu(\tau_D+\tau_d)}\gamma_D\alpha_d,\\
\psi &= \mu\mu_D e^{\mu(\tau_D+\tau_d)} - \mu_D\alpha_d S^*_e e^{\mu(\tau_D+\tau_d)} + \alpha_D S^{*2}_e\alpha_d e^{\mu(\tau_D+\tau_d)} + \mu^2 e^{\mu(\tau_D+\tau_d)}\\
&\quad + \gamma_D\gamma_d e^{\mu\tau_d} - \gamma_D\gamma_d - \mu\alpha_D S^*_e e^{\mu(\tau_D+\tau_d)} - \alpha_D S^*_e\mu_d e^{\mu(\tau_D+\tau_d)} - \alpha_D S^*_e\gamma_d e^{\mu(\tau_D+\tau_d)}\\
&\quad - \mu\alpha_d S^*_e e^{\mu(\tau_D+\tau_d)} + \mu\mu_d e^{\mu(\tau_D+\tau_d)} + \gamma_d\mu e^{\mu(\tau_D+\tau_d)} + \mu_d\mu_D e^{\mu(\tau_D+\tau_d)}\\
&\quad + \mu_D\gamma_d e^{\mu(\tau_D+\tau_d)} - \gamma_D\alpha_d S^*_e e^{\mu(\tau_D+\tau_d)} + \gamma_D\mu e^{\mu(\tau_D+\tau_d)} + \gamma_D\mu_d e^{\mu(\tau_D+\tau_d)} + \gamma_D\gamma_d e^{\mu\tau_D}.
\end{aligned}
$$

3.4 Basic Reproduction Number

The basic reproduction number (R_0) is the average number of secondary infections created when a single infected host is placed in an entirely susceptible population. We now use the next generation matrix approach introduced by Diekmann et al [53] and analysed in [60]. We have the new infection terms as

$$\mathcal{F} = \begin{pmatrix} 0 \\ \alpha_D I_D S \\ \alpha_d I_d S \\ 0 \\ 0 \end{pmatrix},$$

and all other terms are

$$\mathcal{V} = \begin{pmatrix} \mu S - \beta - \gamma_D I_D(t-\tau_D)e^{-\mu\tau_D} - \gamma_d I_d(t-\tau_d)e^{-\mu\tau_d} \\ (\mu + \mu_D + \gamma_D)I_D - \alpha_D R_d I_D \\ (\mu + \mu_d + \gamma_d)I_d - \alpha_d R_D I_d \\ \alpha_d R_D I_d + \mu R_D - \gamma_D I_D + \gamma_D I_D(t-\tau_D)e^{-\mu\tau_D} \\ \alpha_D R_d I_D + \mu R_d - \gamma_d I_d + \gamma_d I_d(t-\tau_d)e^{-\mu\tau_d} \end{pmatrix}.$$

The derivatives of $\mathcal{F}$ and $\mathcal{V}$ at the disease-free equilibrium point E_0 gives $\mathbf{F}$ and $\mathbf{V}$ respectively, where

$$\mathbf{F} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\alpha_D\beta}{\mu} & 0 & 0 & 0 \\ 0 & 0 & \frac{\alpha_d\beta}{\mu} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad \mathbf{V} = \begin{pmatrix} \mu & -\gamma_D e^{-\mu\tau_D} & -\gamma_d e^{-\mu\tau_d} & 0 & 0 \\ 0 & (\mu+\mu_D+\gamma_D) & 0 & 0 & 0 \\ 0 & 0 & (\mu+\mu_d+\gamma_d) & 0 & 0 \\ 0 & -\gamma_D+\gamma_D e^{-\mu\tau_D} & 0 & \mu & 0 \\ 0 & 0 & -\gamma_d+\gamma_d e^{-\mu\tau_d} & 0 & \mu \end{pmatrix}$$

$$\mathbf{V}^{-1} = \begin{pmatrix} (\mu)^{-1} & \frac{\gamma_D e^{-\mu\tau_D}}{\mu(\mu+\mu_D+\gamma_D)} & \frac{\gamma_d e^{-\mu\tau_d}}{\mu(\mu+\mu_d+\gamma_d)} & 0 & 0 \\ 0 & (\mu+\mu_D+\gamma_D)^{-1} & 0 & 0 & 0 \\ 0 & 0 & (\mu+\mu_d+\gamma_d)^{-1} & 0 & 0 \\ 0 & -\frac{(e^{-\mu\tau_D}-1)\gamma_D}{\mu(\mu+\mu_D+\gamma_D)} & 0 & (\mu)^{-1} & 0 \\ 0 & 0 & -\frac{(e^{-\mu\tau_d}-1)\gamma_d}{\mu(\mu+\mu_d+\gamma_d)} & 0 & (\mu)^{-1} \end{pmatrix}$$

$$\mathbf{FV}^{-1} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\alpha_D\beta}{\mu(\mu+\mu_D+\gamma_D)}0 & 0 & 0 & \\ 0 & 0 & \frac{\alpha_d\beta}{\mu(\mu+\mu_d+\gamma_d)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

with eigenvalues

$$\lambda_{1,2,3} = 0, \qquad \lambda_4 = \frac{\alpha_D\beta}{\mu(\mu+\mu_D+\gamma_D)} \text{ and } \lambda_5 = \frac{\alpha_d\beta}{\mu(\mu+\mu_d+\gamma_d)}.$$

Consequently, the basic reproduction number associated with the disease one and two are given respectively as

$$R_1 = \frac{\alpha_D \beta}{\mu(\mu + \mu_D + \gamma_D)} \tag{3.7}$$

and

$$R_2 = \frac{\alpha_d \beta}{\mu(\mu + \mu_d + \gamma_d)}. \tag{3.8}$$

This gives the basic reproduction number of the system (3.1) as

$$R_0 = \max\{R_1, R_2\}. \tag{3.9}$$

Both disease one and two will die out if $R_0 < 1$, while either or both diseases may become endemic if $R_0 > 1$.

3.5 Local Stability of Disease Free Equilibrium

In this section, we analyse the disease-free equilibrium of the system (3.1) and its stability. The disease-free steady state occur when both disease one and two are absent from the population, i.e. $E^0 = \left(\frac{\beta}{\mu}, 0, 0, 0, 0\right)$.

Theorem 3.5.1. *The disease-free equilibrium E^0 is locally asymptotically stable if $R_i < 1, \quad i = 1, 2$ and unstable if either of $R_i > 1$.*

Proof. Linearising the system (3.1) about the steady states gives

$$\begin{aligned}
\dot{\tilde{S}} &= -\mu\tilde{S} - \alpha_D I_D^*\tilde{S} - \alpha_D\tilde{I}_D S^* - \alpha_d I_d^*\tilde{S} - \alpha_d\tilde{I}_d S^* + \gamma_D\tilde{I}_D(t-\tau_D)e^{-\mu\tau_D} \\
&\quad + \gamma_d\tilde{I}_d(t-\tau_d)e^{-\mu\tau_d}, \\
\dot{\tilde{I}}_D &= \alpha_D\tilde{I_D}S^* + \alpha_D I_D^*\tilde{S} - (\mu+\mu_D)\tilde{I}_D + \alpha_D\tilde{R}_d I_D^* + \alpha_D R_d^*\tilde{I}_D - \gamma_D\tilde{I}_D, \\
\dot{\tilde{I}}_d &= \alpha_d\tilde{I}_d S^* + \alpha_d I_d^*\tilde{S} - (\mu+\mu_d)\tilde{I}_d + \alpha_d\tilde{R}_D I_d^* + \alpha_d R_D^*\tilde{I}_d - \gamma_d\tilde{I}_d, \\
\dot{\tilde{R}}_D &= \gamma_D\tilde{I}_D - \gamma_D\tilde{I}_D(t-\tau_D)e^{-\mu\tau_D} - \alpha_d\tilde{R}_D I_d^* - \alpha_d R_D^*\tilde{I}_d - \mu\tilde{R}_D, \\
\dot{\tilde{R}}_d &= \gamma_d\tilde{I}_d - \gamma_d\tilde{I}_d(t-\tau_d)e^{-\mu\tau_d} - \alpha_D\tilde{R}_d I_D^* - \alpha_D R_d^*\tilde{I}_D - \mu\tilde{R}_d.
\end{aligned} \tag{3.10}$$

At the equilibrium E^0, we have

$$\begin{aligned}
\dot{\tilde{S}} &= -\mu\tilde{S} - \frac{\alpha_D\beta}{\mu}\tilde{I}_D - \frac{\alpha_D\beta}{\mu}\tilde{I}_d + \gamma_D\tilde{I}_D(t-\tau_D)e^{-\mu\tau_D} + \gamma_d\tilde{I}_d(t-\tau_d)e^{-\mu\tau_d}, \\
\dot{\tilde{I}}_D &= \frac{\alpha_D\beta}{\mu}\tilde{I_D} - (\mu+\mu_D)\tilde{I}_D - \gamma_D\tilde{I}_D, \\
\dot{\tilde{I}}_d &= \frac{\alpha_d\beta}{\mu}\tilde{I}_d - (\mu+\mu_d)\tilde{I}_d - \gamma_d\tilde{I}_d, \\
\dot{\tilde{R}}_D &= \gamma_D\tilde{I}_D - \gamma_D\tilde{I}_D(t-\tau_D)e^{-\mu\tau_D} - \mu\tilde{R}_D, \\
\dot{\tilde{R}}_d &= \gamma_d\tilde{I}_d - \gamma_d\tilde{I}_d(t-\tau_d)e^{-\mu\tau_d} - \mu\tilde{R}_d.
\end{aligned} \tag{3.11}$$

Looking for solutions of the linearised system in the form

$$\tilde{S} = C_1e^{\lambda t},\ \tilde{I}_D = C_2e^{\lambda t},\ \tilde{I}_d = C_3e^{\lambda t},\ \tilde{R}_D = C_4e^{\lambda t} \text{ and } \tilde{R}_d = C_5e^{\lambda t}$$

gives

$$(\lambda+\mu)C_1+(\frac{\alpha_D\beta}{\mu}-\gamma_De^{-(\lambda+\mu)\tau_D})C_2+(\frac{\alpha_d\beta}{\mu}-\gamma_de^{-(\lambda+\mu)\tau_d})C_3=0,$$

$$(\lambda-\frac{\alpha_D\beta}{\mu}+\mu+\mu_D+\gamma_D)C_2=0,$$

$$(\lambda-\frac{\alpha_d\beta}{\mu}+\mu+\mu_d+\gamma_d)C_3=0,$$

$$(\lambda+\mu)C_4+(\gamma_De^{-(\lambda+\mu)\tau_D}-\gamma_D)C_2=0,$$

$$(\lambda+\mu)C_5+(\gamma_de^{-(\lambda+\mu)\tau_d}-\gamma_d)C_3=0.$$

Since $C_1,\ C_2,\ C_3,\ C_4$ and C_5 are not all zero, we have that

$$\begin{vmatrix}
(\lambda+\mu) & (\frac{\alpha_D\beta}{\mu}-\gamma_De^{-(\lambda+\mu)\tau_D}) & (\frac{\alpha_d\beta}{\mu}-\gamma_de^{-(\lambda+\mu)\tau_d}) & 0 & 0 \\
0 & (\lambda-\frac{\alpha_D\beta}{\mu}+\mu+\mu_D+\gamma_D) & 0 & 0 & 0 \\
0 & 0 & (\lambda-\frac{\alpha_d\beta}{\mu}+\mu+\mu_d+\gamma_d) & 0 & 0 \\
0 & (\gamma_De^{-(\lambda+\mu)\tau_D}-\gamma_D) & 0 & (\lambda+\mu) & 0 \\
0 & 0 & (\gamma_de^{-(\lambda+\mu)\tau_d}-\gamma_d) & 0 & (\lambda+\mu)
\end{vmatrix}=0.$$

This yields the characteristic equation in the form

$$(\lambda+\mu)[(\lambda+\mu)\{(\lambda+\mu)(\lambda-\frac{\alpha_D\beta}{\mu}+\mu+\mu_D+\gamma_D)(\lambda-\frac{\alpha_d\beta}{\mu}+\mu+\mu_d+\gamma_d)\}]=0,$$

and, hence, we have

$$\lambda_i=-\mu\quad(i=1,2,3),$$

$$\lambda_4=\frac{\alpha_D\beta}{\mu}-(\mu+\mu_D+\gamma_D)=\{\mu+\mu_D+\gamma_D\}(R_1-1),$$

$$\lambda_5=\frac{\alpha_d\beta}{\mu}-(\mu+\mu_d+\gamma_d)=\{\mu+\mu_d+\gamma_d\}(R_2-1).$$

We obtain that E^0 is locally asymptotically stable if $R_i < 1,\ i = 1, 2$ and unstable otherwise. This completes the proof. □

3.6 Local Stability of the Endemic Equilibrium

We analyse the local stability of the endemic equilibrium of the system (3.1) in this section. Here we consider three endemic scenarios: Disease one, disease two and when both diseases are endemic.

The Jacobian matrix of the system $(\mathbf{J}_e) =$

$$\begin{pmatrix} (\lambda+\mu+\alpha_D I_D^*+\alpha_d I_d^*) & (\alpha_D S^*-\gamma_D e^{-(\lambda+\mu)\tau_D}) & (\alpha_d S^*-\gamma_d e^{-(\lambda+\mu)\tau_d}) & 0 & 0 \\ -\alpha_D I_D^* & (\lambda+\kappa_D-\alpha_D R_d^*-\alpha_D S^*) & 0 & 0 & -\alpha_D I_D^* \\ -\alpha_d I_d^* & 0 & (\lambda-\alpha_d S^*+\kappa_d-\alpha_d R_D^*) & -\alpha_d I_d^* & 0 \\ 0 & (\gamma_D e^{-(\lambda+\mu)\tau_D}-\gamma_D) & \alpha_d R_D^* & (\lambda+\mu+\alpha_d I_d^*) & 0 \\ 0 & \alpha_D R_d^* & (\gamma_d e^{-(\lambda+\mu)\tau_d}-\gamma_d) & 0 & (\lambda+\mu+\alpha_D I_D^*) \end{pmatrix},$$

with the constants $\kappa_d = \mu + \mu_d + \gamma_d$ and $\kappa_D = \mu + \mu_D + \gamma_D$ used for typographical convenience.

We first consider the case when disease one only is endemic. From $\mathbf{J}_e$ above, we have the Jacobian matrix $(\mathbf{J}_D)$, when disease one only is endemic as

$$\mathbf{J}_D = \begin{pmatrix} (\lambda+\mu+\alpha_D I_D^*) & (\alpha_D S^*-\gamma_D e^{-(\lambda+\mu)\tau_D}) & (\alpha_d S^*-\gamma_d e^{-(\lambda+\mu)\tau_d}) & 0 & 0 \\ -\alpha_D I_D^* & (\lambda+\kappa_D-\alpha_D R_d^*-\alpha_D S^*) & 0 & 0 & -\alpha_D I_D^* \\ 0 & 0 & (\lambda-\alpha_d S^*+\kappa_d-\alpha_d R_D^*) & 0 & 0 \\ 0 & (\gamma_D e^{-(\lambda+\mu)\tau_D}-\gamma_D) & \alpha_d R_D^* & (\lambda+\mu) & 0 \\ 0 & \alpha_D R_d^* & (\gamma_d e^{-(\lambda+\mu)\tau_d}-\gamma_d) & 0 & (\lambda+\mu+\alpha_D I_D^*) \end{pmatrix}.$$

This gives the following characteristic equation

$$(\lambda+\mu)(\lambda+\mu+\alpha_D I_D^*)(-\lambda-\kappa_d+\alpha_d R_D^*+\alpha_d S^*)(S^*\alpha_D\mu+\alpha_D S^*\lambda+\mu\alpha_D R_d^*-\mu\kappa_D$$
$$-\lambda\mu+\alpha_D I_D^*\gamma_D e^{-(\lambda+\mu)\tau_D}+\alpha_D R_d^*\lambda-\kappa_D\lambda-\kappa_D\alpha_D I_D^*-\lambda^2-\lambda\alpha_D I_D^*)=0. \tag{3.12}$$

The eigenvalues from (3.12) are

$$\begin{aligned}\lambda_1&=-\mu,\\ \lambda_2&=-\mu-\alpha_D I_D^*,\\ \lambda_3&=-\mu-\mu_d-\gamma_d+\alpha_d R_D^*+\alpha_d S^*,\end{aligned} \tag{3.13}$$

and the solution to the following transcendental equation

$$-\lambda^2+(\alpha_D S^*-\alpha_D I_D^*+\alpha_D R_d^*-2\mu-\mu_D-\gamma_D)\lambda+\mu\alpha_D S^*+\mu\alpha_D R_d^*$$
$$-\mu(\mu+\mu_D+\gamma_D)-\alpha_D I_D^*(\mu+\mu_D+\gamma_D)+\alpha_D I_D^*\gamma_D e^{-(\lambda+\mu)\tau_D}=0. \tag{3.14}$$

After simplification, we have

$$\lambda^2+(\mu+\alpha_D I_D^*)\lambda+\alpha_D I_D^*(\mu+\mu_D+\gamma_D)-\alpha_D I_D^*\gamma_D e^{-(\lambda+\mu)\tau_D}=0. \tag{3.15}$$

Consider the case $\tau_D=0$. When $\tau_D=0$, we have that

$$\begin{aligned}\lambda_1&=-\mu,\\ \lambda_2&=-\mu-\left\{\frac{\mu(\mu+\mu_D+\gamma_D)[R_1-1]}{(\mu+\mu_D)}\right\},\\ \lambda_3&=\frac{\alpha_d}{\alpha_D}[\mu+\mu_D+\gamma_D]-[\mu+\mu_d+\gamma_d],\end{aligned}$$

and the solution to the following equation

$$\lambda^2 + (\mu + \alpha_D I_D^*)\lambda + \alpha_D I_D^*(\mu + \mu_D) = 0. \tag{3.16}$$

We have that λ_1 is negative, λ_2 is negative provided that $R_1 > 1$. λ_3 is negative whenever

$$\frac{\alpha_d}{\alpha_D}[\mu + \mu_D + \gamma_D] < [\mu + \mu_d + \gamma_d],$$

or

$$\frac{\alpha_d[\mu + \mu_D + \gamma_D]}{\alpha_D[\mu + \mu_d + \gamma_d]} < 1,$$

i.e when $R_2 < R_1$. And from (3.16), it is easily seen from (I_D^*) that the coefficients and constant term are positive if $R_1 > 1$. This implies that (3.1) is stable. We can formulate this result as the following theorem.

Theorem 3.6.1. *The endemic equilibrium point, when disease one only is endemic of the system* (3.1) *at* $\tau_D = 0$ *is locally asymptotically stable for* $R_1 > 1$ *whenever* $R_2 < R_1$.

Consider now the case where $\tau_D > 0$. From (3.13), λ_2 will be negative if $R_1 > 1$. λ_3 is negative provided that the following condition holds

$$f_D(\tau_D) = \frac{\alpha_d(\gamma_D - e^{-\mu\tau_D}\gamma_D)\{\mu(\mu + \mu_D + \gamma_D)\}[R_1 - 1]}{\alpha_D\mu(\mu + \mu_d + \gamma_d)[\mu + \mu_D + \gamma_D - e^{-\mu\tau_D}\gamma_D]} + \frac{R_2}{R_1} < 1. \tag{3.17}$$

We know that $f_D(\tau_D)$ is a monotonically increasing function, so that

$$f_D(\tau_D) \leq f_D(\infty), \quad \forall \tau_D \geq 0.$$

Hence,

$$f_D(\infty) < 1 \Rightarrow f_D(\tau_D) \leq f_D(\infty) < 1.$$

This implies that (3.17) holds for all $\tau_D \geq 0$.

From (3.15)

$$P_1(\lambda) + Q_1 e^{(\lambda+\mu)\tau_D} = 0, \tag{3.18}$$

where

$$P_1(\lambda) = \lambda^2 + (\mu + \alpha_D I_D^*)\lambda + \alpha_D I_D^*(\mu + \mu_D + \gamma_D),$$

$$Q_1 = -\alpha_D I_D^* \gamma_D.$$

Let $\lambda = i\omega$ with $\omega > 0$ be the root of (3.18). This yields,

$$-\omega^2+(\mu+\alpha_D I_D^*)(i\omega)+\alpha_D I_D^*(\mu+\mu_D+\gamma_D) = e^{-\mu\tau_D}\alpha_D I_D^*\gamma_D\{\cos(\omega\tau_D)-i\sin(\omega\tau_D)\}.$$

Separating the last equation into the real and imaginary parts gives

$$-\omega^2 + \alpha_D I_D^*(\mu + \mu_D + \gamma_D) = e^{-\mu\tau_D}\alpha_D I_D^*\gamma_D \cos(\omega\tau_D), \tag{3.19}$$

$$-(\mu + \alpha_D I_D^*)\omega = e^{-\mu\tau_D}\alpha_D I_D^*\gamma_D \sin(\omega\tau_D). \tag{3.20}$$

Squaring (3.19) and (3.20) and adding them gives

$$\omega^4+\{(\mu+\alpha_D I_D^*)^2-2\alpha_D I_D^*(\mu+\mu_D+\gamma_D)\}\omega^2+\alpha_D^2 {I_D^*}^2(\mu+\mu_D+\gamma_D)^2-\alpha_D^2 {I_D^*}^2\gamma_D^2 e^{-2\mu\tau_D} = 0. \tag{3.21}$$

Let $\zeta = \omega^2$, then (3.21) becomes

$$\zeta^2+\{(\mu+\alpha_D I_D^*)^2-2\alpha_D I_D^*(\mu+\mu_D+\gamma_D)\}\zeta+\alpha_D^2 {I_D^*}^2(\mu+\mu_D+\gamma_D)^2-\alpha_D^2 {I_D^*}^2\gamma_D^2 e^{-2\mu\tau_D} = 0. \tag{3.22}$$

Clearly (3.22) has no positive real roots if

$$(\mu + \alpha_D I_D^*)^2 > 2\alpha_D I_D^*(\mu + \mu_D + \gamma_D),$$

i.e if the following condition holds:

$$g_D(\tau_D) = \mu^2 + \Big[\frac{\mu(\mu + \mu_D + \gamma_D)(R_1 - 1)}{\mu + \mu_D + \gamma_D - e^{-\mu\tau_D}\gamma_D}\Big]^2 - 2\Big[\frac{(R_1 - 1)\mu(\mu + \mu_D + \gamma_D)(\mu_D + \gamma_D)}{\mu + \mu_D + \gamma_D - e^{-\mu\tau_D}\gamma_D}\Big] > 0. \tag{3.23}$$

We have from (3.23) that

$$g_D(\tau_D) \geq g_D(0), \quad \forall \tau_D \geq 0.$$

This implies that

$$g_D(\tau_D) \geq g_D(0) > 0, \quad \forall \tau_D \geq 0.$$

Hence (3.23) always holds for all $\tau_D \geq 0$. Therefore, (3.18) does not have any purely imaginary roots for all $\tau_D > 0$, so that all roots of the characteristics equation (3.12) have negative real parts if $R_1 > 1$. It is clear from (3.17) that if $R_2 \geq R_1$, f_D becomes greater than 1 and the condition fails, hence the condition (3.17) holds only if $R_2 < R_1$. With these conditions fulfilled, the endemic equilibrium of (3.1) is asymptotically stable. We summarise these findings in the theorem below.

Theorem 3.6.2. *The endemic equilibrium point of the system* (3.1)*, when disease one only is endemic, is locally asymptotically stable for all* $\tau_D > 0$ *whenever* $R_2 < R_1$ *and conditions* (3.17) *and* (3.23) *hold with* $R_1 > 1$.

We now consider the case when disease two only is endemic. The Jacobian matrix ($\mathbf{J}_d$) when disease two only is endemic has the form

$$\mathbf{J}_d = \begin{pmatrix} (\lambda+\mu+\alpha_d I_d^*) & (\alpha_D S^* - \gamma_D e^{-(\lambda+\mu)\tau_D}) & (\alpha_d S^* - \gamma_d e^{-(\lambda+\mu)\tau_d}) & 0 & 0 \\ 0 & (\lambda+\kappa_D - \alpha_D R_d^* - \alpha_D S^*) & 0 & 0 & 0 \\ -\alpha_d I_d^* & 0 & (\lambda - \alpha_d S^* + \kappa_d - \alpha_d R_D^*) & -\alpha_d I_d^* & 0 \\ 0 & (\gamma_D e^{-(\lambda+\mu)\tau_D} - \gamma_D) & \alpha_d R_D^* & (\lambda+\mu+\alpha_d I_d^*) & 0 \\ 0 & \alpha_D R_d^* & (\gamma_d e^{-(\lambda+\mu)\tau_d} - \gamma_d) & 0 & (\lambda+\mu) \end{pmatrix}.$$

The characteristic equation is thus

$$(\lambda+\mu)(\lambda+\mu+\alpha_d I_d^*)(\alpha_D S^* - \lambda - \kappa_D + \alpha_D R_d^*)(\alpha_d S^* \mu + \alpha_d S^* \lambda + \alpha_d R_D^* \mu - \lambda\mu - \kappa_d \mu$$
$$+ \alpha_d I_d^* \gamma_d e^{-(\lambda+\mu)\tau_d} + \alpha_d R_D^* \lambda - \lambda^2 - \kappa_d \lambda - \lambda \alpha_d I_d^* - \kappa_d \alpha_d I_d^*) = 0. \tag{3.24}$$

The eigenvalues of the Jacobian matrix ($\mathbf{J}_d$) are: $\lambda_1 = -\mu$, $\lambda_2 = -\mu - \alpha_d I_d^*$, $\lambda_3 = -\mu - \mu_D - \gamma_D + \alpha_D S^* + \alpha_D R_d^*$, and the solution to the following transcendental equation

$$-\lambda^2 + (\alpha_d S^* - \alpha_d I_d^* + \alpha_d R_D^* - 2\mu - \mu_d - \gamma_d)\lambda + \mu\alpha_d S^* + \mu\alpha_d R_D^*$$
$$- \mu(\mu + \mu_d + \gamma_d) - \alpha_d I_d^*(\mu + \mu_d + \gamma_d) + \alpha_d I_d^* \gamma_d e^{-(\lambda+\mu)\tau_d} = 0. \tag{3.25}$$

This simplifies to

$$\lambda^2 + (\mu + \alpha_d I_d^*)\lambda + \alpha_d I_d^*(\mu + \mu_d + \gamma_d) - \alpha_d I_d^* \gamma_d e^{-(\lambda+\mu)\tau_d} = 0. \tag{3.26}$$

First, consider the case when $\tau_d = 0$. At $\tau_d = 0$, we have that $\lambda_1 = -\mu$, $\lambda_2 = -\mu - \frac{\mu(\mu+\mu_d+\gamma_d)[R_2-1]}{(\mu+\mu_d)}$, $\lambda_3 = -\mu - \mu_D - \gamma_D + \frac{\alpha_D}{\alpha_d}(\mu + \mu_d + \gamma_d)$ and the solution to

the following equation

$$\lambda^2 + (\mu + \alpha_d I_d^*)\lambda + \alpha_d I_d^*(\mu + \mu_d) = 0. \tag{3.27}$$

We have that λ_1 is negative, λ_2 is negative if $R_2 > 1$ and λ_3 is negative if

$$\frac{\alpha_D}{\alpha_d}[\mu + \mu_d + \gamma_d] - [\mu + \mu_D + \gamma_D] < 0$$

i.e if $R_1 < R_2$. This proves the following theorem.

Theorem 3.6.3. *The endemic equilibrium point, when disease two only is endemic, of the system* (3.1) *at* $\tau_d = 0$ *is locally asymptotically stable for* $R_2 > 1$ *whenever* $R_1 < R_2$.

We now take the case where $\tau_d > 0$. From the eigenvalues of (3.24), λ_2 will be negative if $R_2 > 1$. λ_3 is negative provided that the following condition holds

$$f_d(\tau_d) = \frac{\alpha_D(\gamma_d - e^{-\mu\tau_d}\gamma_d)\{\mu(\mu + \mu_d + \gamma_d)\}[R_2 - 1]}{\alpha_d\mu(\mu + \mu_D + \gamma_D)[\mu + \mu_d + \gamma_d - e^{-\mu\tau_d}\gamma_d]} + \frac{R_1}{R_2} < 1. \tag{3.28}$$

We know that $f_d(\tau_d)$ is a monotonically increasing function, so that

$$f_d(\tau_d) \leq f_d(\infty), \quad \forall \tau_d \geq 0.$$

Hence

$$f_d(\infty) < 1 \Rightarrow f_d(\tau_d) \leq f_d(\infty) < 1.$$

This implies that (3.28) holds for all $\tau_d \geq 0$.

From (3.26)

$$P_2(\lambda) + Q_2 e^{(\lambda+\mu)\tau_d} = 0, \tag{3.29}$$

where

$$P_2(\lambda) = \lambda^2 + (\mu + \alpha_d I_d^*)\lambda + \alpha_d I_d^*(\mu + \mu_d + \gamma_d)$$

$$Q_2 = -\alpha_d I_d^* \gamma_d.$$

Let $\lambda = i\psi$ with $\psi > 0$ be the root of (3.29). We have

$$-\psi^2 + (\mu + \alpha_d I_d^*)(i\psi) + \alpha_d I_d^*(\mu + \mu_d + \gamma_d) = e^{-\mu\tau_d}\alpha_d I_d^* \gamma_d\{\cos(\psi\tau_d) - i\sin(\psi\tau_d)\}.$$

Separating the real and imaginary parts yields,

$$-\psi^2 + \alpha_d I_d^*(\mu + \mu_d + \gamma_d) = e^{-\mu\tau_d}\alpha_d I_d^* \gamma_d \cos(\psi\tau_d), \tag{3.30}$$

$$-(\mu + \alpha_d I_d^*)\psi = e^{-\mu\tau_d}\alpha_d I_d^* \gamma_d \sin(\psi\tau_d). \tag{3.31}$$

We now square and add both sides of (3.30) and (3.31) to have an equation for the Hopf frequency ψ as

$$\psi^4 + \{(\mu+\alpha_d I_d^*)^2 - 2\alpha_d I_d^*(\mu+\mu_d+\gamma_d)\}\psi^2 + \alpha_d^2 I_d^{*2}(\mu+\mu_d+\gamma_d)^2 - \alpha_d^2 I_d^{*2}\gamma_d^2 e^{-2\mu\tau_d} = 0. \tag{3.32}$$

Let $\nu = \psi^2$, then (3.32) becomes

$$\nu^2 + \{(\mu+\alpha_d I_d^*)^2 - 2\alpha_d I_d^*(\mu+\mu_d+\gamma_d)\}\nu + \alpha_d^2 I_d^{*2}(\mu+\mu_d+\gamma_d)^2 - \alpha_d^2 I_d^{*2}\gamma_d^2 e^{-2\mu\tau_d} = 0. \tag{3.33}$$

Clearly (3.33) has no positive real roots if $(\mu + \alpha_d I_d^*)^2 > 2\alpha_d I_d^*(\mu + \mu_d + \gamma_d)$ i.e if the following condition holds

$$g_d(\tau_d) = \mu^2 + \Big[\frac{\mu(\mu + \mu_d + \gamma_d)(R_2 - 1)}{\mu + \mu_d + \gamma_d - e^{-\mu\tau_d}\gamma_d}\Big]^2 - 2\Big[\frac{(R_2 - 1)\mu(\mu + \mu_d + \gamma_d)(\mu_d + \gamma_d)}{\mu + \mu_d + \gamma_d - e^{-\mu\tau_d}\gamma_d}\Big] > 0. \tag{3.34}$$

We have from (3.34) that

$$g_d(\tau_d) \geq g_d(0), \quad \forall \tau_d \geq 0.$$

This implies that

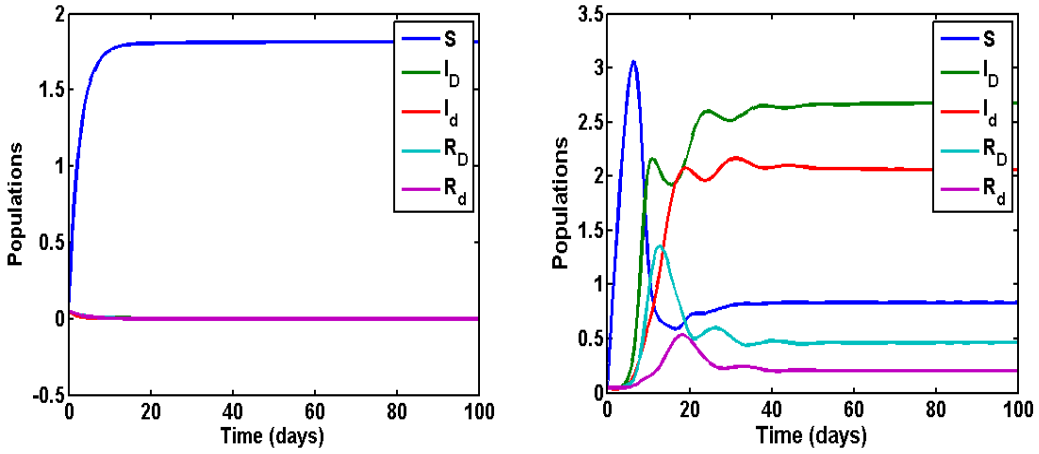
$$g_d(\tau_d) \geq g_d(0) > 0, \quad \forall \tau_d \geq 0.$$

Hence (3.34) always holds for all $\tau_d \geq 0$. Therefore, (3.29) does not have any purely imaginary roots for all $\tau_d > 0$, so that all roots of the characteristics equation (3.26) have negative real parts if $R_2 > 1$. It is clear from (3.28) that if $R_1 \geq R_2$, f_d becomes greater than 1 and the condition fails, hence the condition (3.28) holds only if $R_1 < R_2$. With these conditions fulfilled, the endemic equilibrium of the system (3.1) is asymptotically stable. We summarise these findings in the theorem below.

Theorem 3.6.4. *The endemic equilibrium point of the system* (3.1)*, when disease two only is endemic, is locally asymptotically stable for all* $\tau_d > 0$ *whenever* $R_1 < R_2$ *and the conditions* (3.28) *and* (3.34) *hold with* $R_2 > 1$.

3.7 Numerical Simulations

In this section, we carry out numerical simulations to illustrate the theoretical results obtained in the previous sections. We start by investigating the dynamical behaviour of the system (3.1) by computing solutions using the DDE23 suite in Matlab. Parameters used in the simulations are chosen for illustration purposes, and do not reflect actual data. In all simulations, the time delays $\tau_D = \tau_d = 10$, except otherwise stated in the figure.

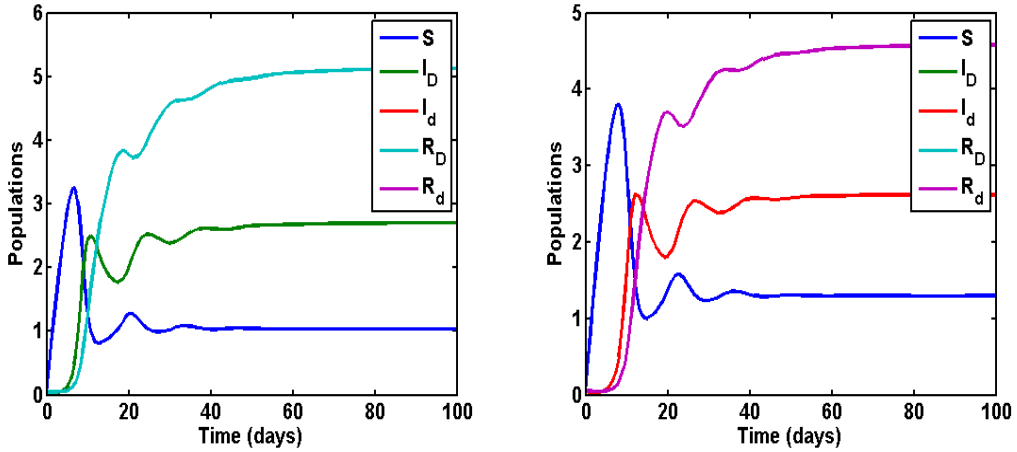


(a) $R_1 = 0.941 < 1$, $R_2 = 0.742 < 1$, $\mu = 0.38$

(b) $R_1 = 11.482 > 1$, $R_2 = 9.176 > 1$, $\mu = 0.058$

Figure 3.2: Solutions of the system (3.1) for $R_1 = 0.941 < 1$ and $R_2 = 0.742 < 1$ in figure 3.2(a) and for $R_1 = 11.482 > 1$ and $R_2 = 9.176 > 1$ in figure 3.2(b). Parameters are: $\beta = 0.69$; $\mu_D = 0.065$; $\mu_d = 0.075$; $\alpha_D = 0.36$; $\alpha_d = 0.28$; $\gamma_D = 0.25$; $\gamma_d = 0.23$.

Figures 3.2(a) and 3.2(b) show the the solutions of the system (3.1) converging to disease-free steady states for $R_1 = 0.941 < 1$, $R_2 = 0.742 < 1$, and diverging for $R_1 = 11.482 > 1$, $R_2 = 9.176 > 1$ respectively, supporting the analytical calculations in Section 3.5.



(a) $R_2 = 9.176 < R_1 = 11.482$, $R_1 > 1$, $\alpha_D = 0.36$

(b) $R_1 = 5.103 < R_2 = 9.176$, $R_2 > 1$, $\alpha_D = 0.16$

Figure 3.3: Solutions of the system (3.1) when disease one is endemic in figure 3.3(a) and when disease two is endemic figure 3.3(b). Other parameters are: $\beta = 0.69$; $\mu = 0.058$; $\mu_D = 0.065$; $\mu_d = 0.075$; $\alpha_d = 0.28$; $\gamma_D = 0.25$; $\gamma_d = 0.23$

Straightforward calculations show that in Figure 3.3(a), $R_2 = 9.176 < R_1 = 11.482$, $f_D = 0.7569 < 1$ and $g_D = 101.1056 > 0$, which is in agreement with Theorem 3.6.2 in Section 3.6. Also, in Figure 3.3(b), $R_1 = 5.103 < R_2 = 9.176$, $f_d = 0.5872 < 1$ and $g_d = 11.2752 > 0$ supporting Theorem 3.6.4.

Next, we investigate the stability properties of the system (3.1) varying different parameters of the model. The numerical simulations are done with TRACE-DDE toolbox in Matlab, which is used for computing the characteristic roots for delay differential equations with discrete and distributed delays. Note that the colour in the figures corresponds to the real part of the leading eigenvalues of the characteristic polynomial ($\mathbf{J}_e$) in Section 3.6. Areas shaded grey are the areas, where the steady states are negative and, hence, are not biologically feasible.

We start by investigating how the stability of the endemic steady state changes in the τ_D, α_D parameter plane as disease one recovery rate γ_D varies. We observe from the stability chart that for sufficiently small values of α_D, the steady state is stable for any time delay, but for α_D which exceeds some critical value corresponding to R_1, it is stable for small time delay then it looses stability for larger time delay. We also observe from Figure 3.4(a) that for sufficiently small γ_D, there is initially a range of values where even with no time delay the system may be stable for small α_D, and unstable for large α_D. But actually, here, it is interesting that as τ_D increases, the system can gain stability, but this region itself also becomes smaller and smaller with increasing γ_D.

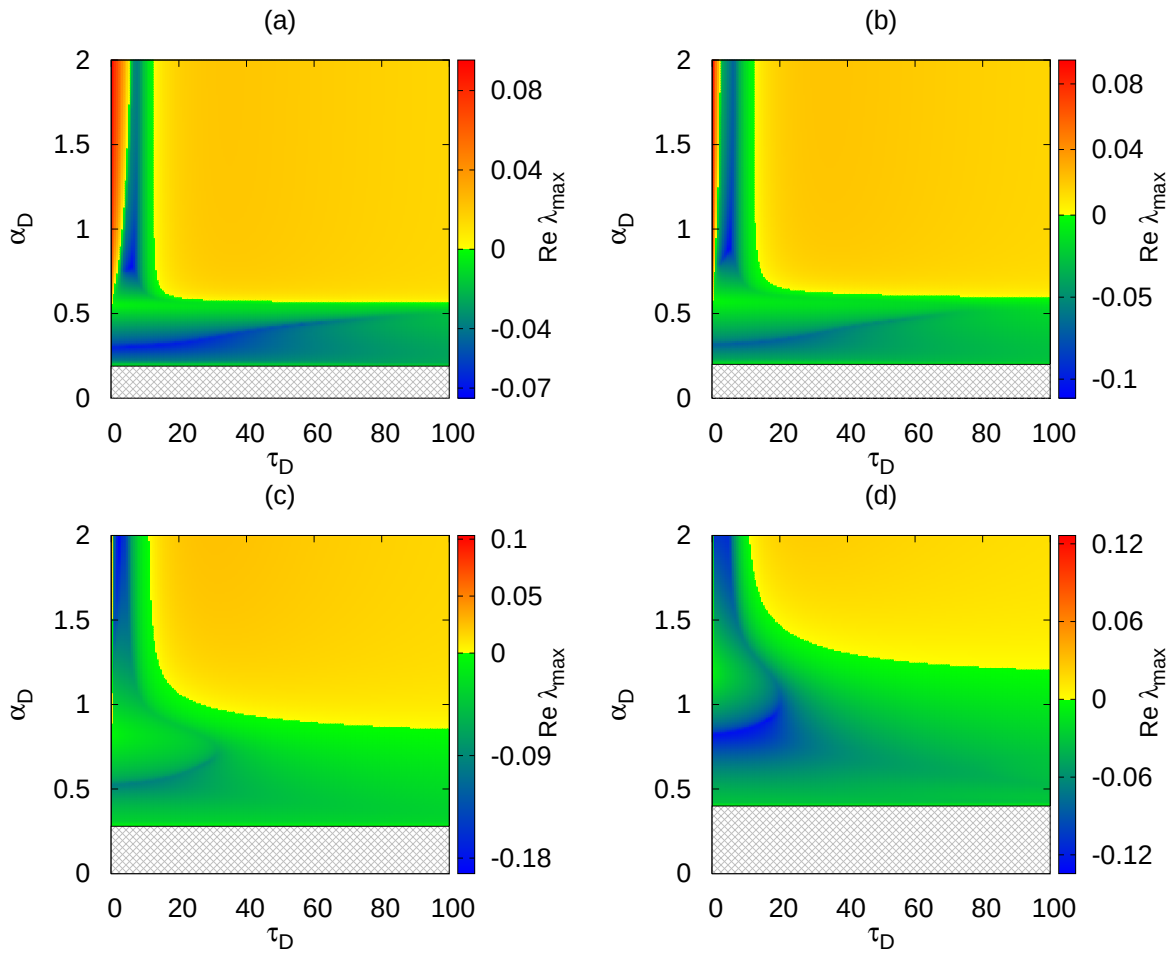


Figure 3.4: Stability boundary in $\tau_D - \alpha_D$ plane: (a) $\gamma_D = 0.0045$, (b) $\gamma_D = 0.0095$, (c) $\gamma_D = 0.068$, (d) $\gamma_D = 0.15$, other parameters are: $\beta = 0.95$, $\mu = 0.058$, $\mu_D = 0.065$, $\mu_d = 0.085$, $\alpha_d = 0.95$, $\gamma_d = 0.075$ and $\tau_d = 1$. Areas shaded grey are biologically not feasible.

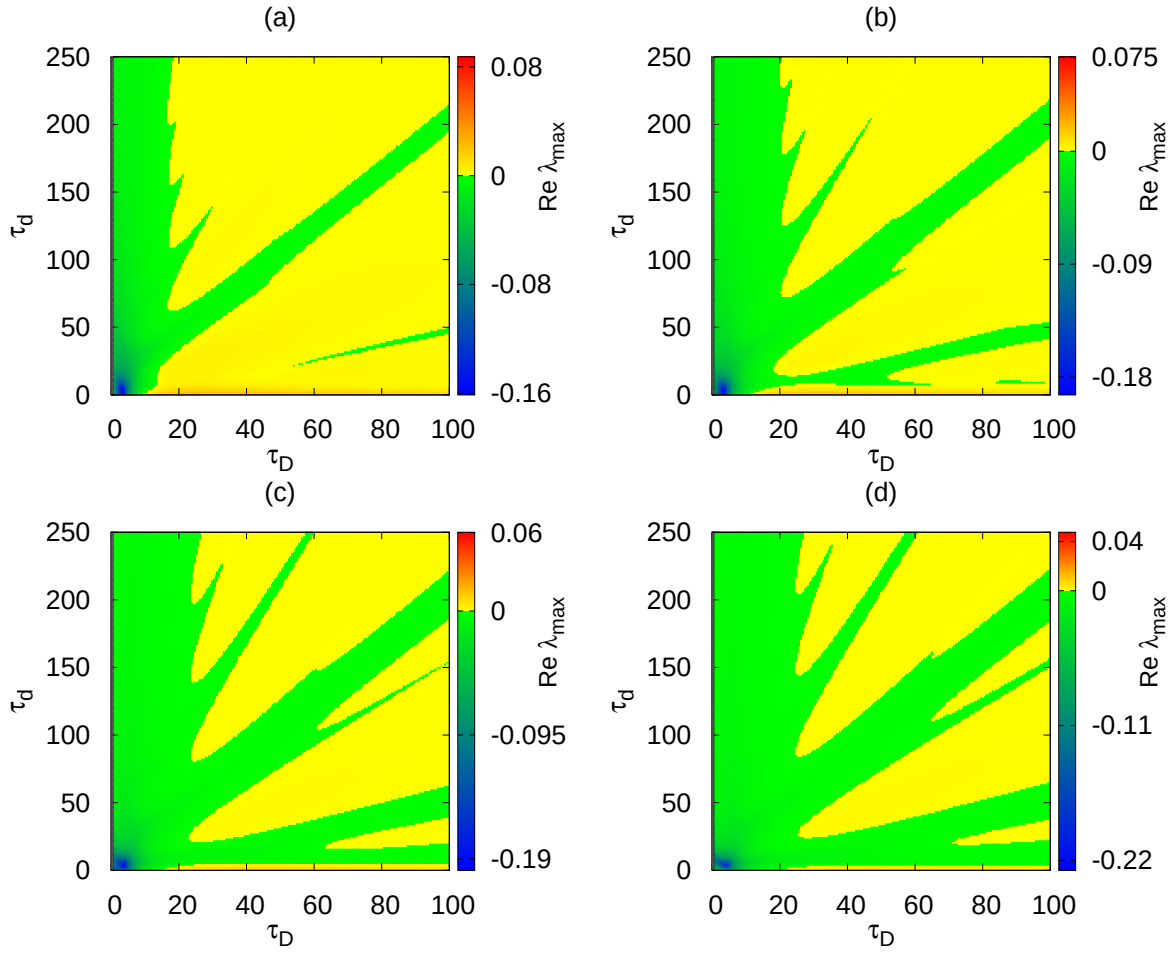


Figure 3.5: Stability boundary in the $\tau_D - \tau_d$ plane: (a) $\alpha_d = 0.22$, (b) $\alpha_d = 0.25$, (c) $\alpha_d = 0.28$, (d) $\alpha_d = 0.30$. Other parameters are: $\beta = 0.69$, $\mu = 0.058$, $\mu_D = 0.065$, $\mu_d = 0.075$, $\alpha_D = 0.36$, $\gamma_D = 0.28$, $\gamma_d = 0.25$.

We now investigate how the stability of the endemic steady state changes in the τ_D, τ_d parameter plane as the disease two infection rate α_d varies.

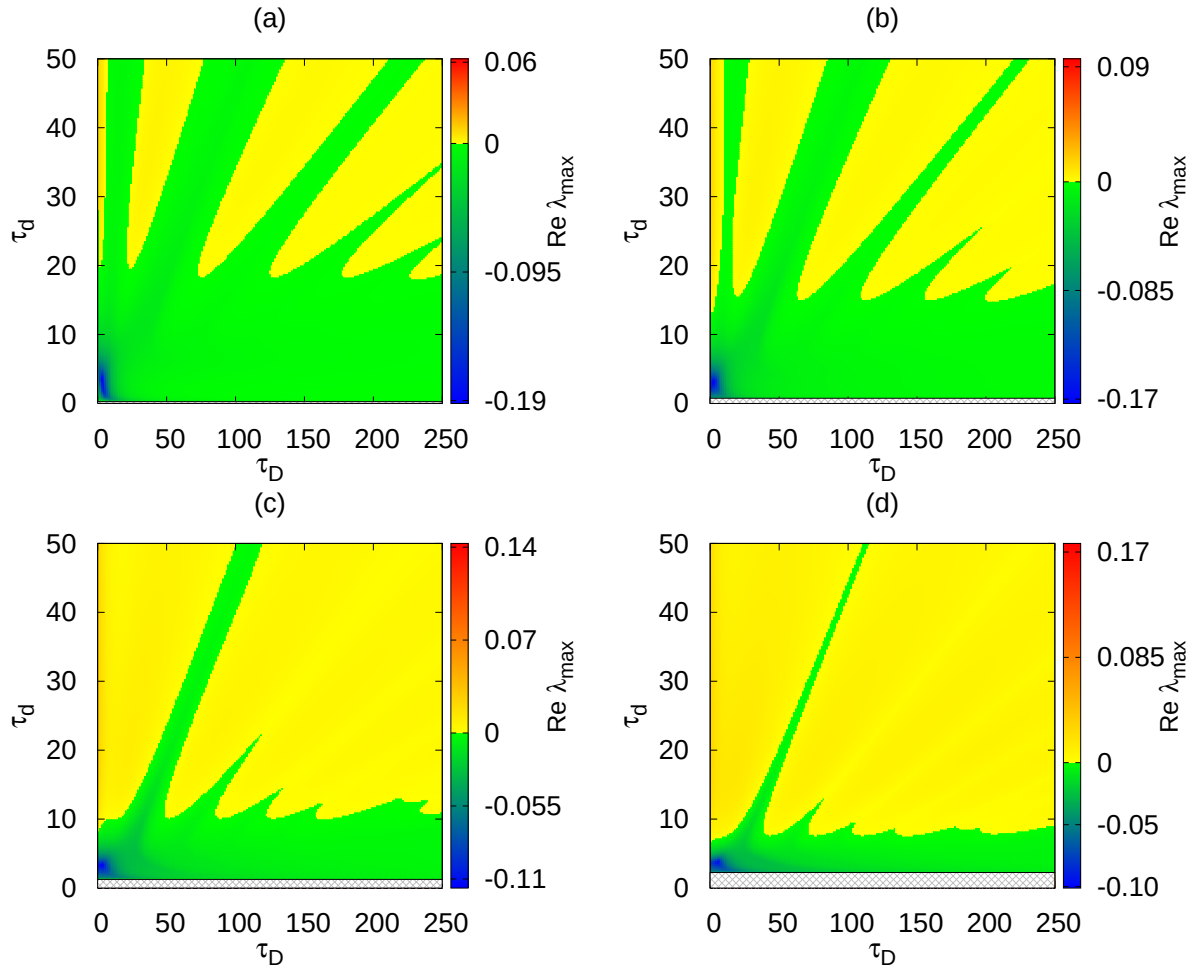


Figure 3.6: Stability boundary in the $\tau_D - \tau_d$ plane: (a) $\gamma_D = 0.36$, (b) $\gamma_D = 0.42$, (c) $\gamma_D = 0.55$, (d) $\gamma_D = 0.68$. Other parameters are: $\beta = 0.82$, $\mu = 0.088$, $\mu_D = 0.065$, $\mu_d = 0.085$, $\alpha_D = 0.36$, $\alpha_d = 0.25$, $\gamma_d = 0.15$.

Here, we fixed all other parameters and varied α_d as it is one of the most biologically relevant parameters, representing the rate at which new disease two

infections occur through contacts between infected and susceptible individuals. From Figure 3.5, we can see that the disease two infection rate (α_d) plays an important role in the dynamics of the system (3.1). As we increase α_d, the region of stability of the endemic steady state spread over a larger area of the ($\tau_D,\ \tau_d$) parameter plane. Biologically, the severity of an epidemic depends on the basic reproduction number R_0, and this is reflected in the figures. The basic reproduction number R_2 associated with the disease two transmission rate α_d increased from 6.834 in Figure 3.5(a) to 9.318 in Figure 3.5(d). In (a) $R_2 = 6.834$, (b) $R_2 = 7.765$, (c) $R_2 = 8.697$ and in (d) $R_2 = 9.318$. $R_1 = 10.627$ in the four figures.

We observe in Fig 3.6(a) that for some values of τ_d, the endemic steady state of the system is always stable for all $\tau_D > 0$. However for higher values of τ_d, stability switches are observed as regions of instability are formed for lower values of γ_D which gradually fades away as γ_D increases (see Fig. 3.6(d)).

3.8 Conclusions

In this chapter, we have modelled and analysed a two-disease system with two time delays but without the possibility of a co-infection. We have computed independent basic reproduction numbers for disease one (R_1) and disease two (R_2). Conditions for local stability for the disease free and endemic equilibria are obtained. It is proved that the disease free equilibrium (E^0) is locally asymptotically

stable if $R_i < 1$, $i = 1, 2$, and unstable otherwise.

We have established that system (3.1) has three different endemic equilibria. Namely, the case when disease one only is endemic; when disease two only is endemic, and when both diseases are endemic. Apart from the case when both diseases are endemic, conditions for the existence and stability of these equilibria are established in Section 3.6. Theoretical calculations and numerical simulations support that the endemic equilibrium when disease one only is endemic in the absence of time delay is locally asymptotically stable when $R_2 < R_1$ for $R_1 > 1$ with two conditions as stated in Theorem 3.6.2. Similar results were also obtained for the case when disease two only is endemic and corresponding results are summarised in Theorem 3.6.4.

We were unable to analyse theoretically the endemic steady state when the two diseases are endemic. However, we numerically calculated the real part of the leading eigenvalues of the characteristic polynomial ($\mathbf{J}_e$) in Section 3.6 to obtain the stability charts in the τ_D, α_D and τ_D, τ_d parameter planes. These charts are presented in Figs. 3.4-3.6. Observation from Figure 3.5 shows the importance the disease two infection rate (α_d) plays in the dynamics of the system (3.1). As we increased α_d, the region of stability of the endemic steady state spread over a larger area of the (τ_D, τ_d) parameter plane. This shows that as the disease two infection rate increases, more individuals in the population are infected with the disease two,

hence the larger region of stability of the endemic steady state. Similar results are expected from the disease one infection rate (α_D) since the system is symmetrical.

The model developed in this chapter can be used to study any two-disease epidemics without the possibility of a co-infection like yaws and syphilis, respiratory syncytial virus and human para influenza virus.

Chapter 4

Latency Model with Saturated Incidence Rate

4.1 Introduction

The Susceptible-Infected-Recovered (SIR) model has given us a veritable tool to gaining an insight into the dynamics of infectious diseases. A lot of developments have been made since the introduction of the famous model by Kermack-McKendrick [1], especially in the introduction of models with time delay to account for the effects of latency and temporary immunity (see, for example, [11]-[19] and the references cited therein).

In most of the literature, it is frequently assumed that the incident rate is of the bilinear form βSI, which is based on the law of mass action. However, for some

diseases, such as cholera, where in times of epidemic, the number of infections tends to a saturation point, a saturated incidence rate is better suited to be used in the model. Capasso and Serio [61] introduced a saturated incidence rate $g(I)S$ into their model, where $g(I)$ is given as $\frac{\beta I}{1+\alpha I}$. Here $g(I)$ tends to a saturation level when I gets large. The dynamics of such models have been found to be very rich and exciting (see [12], [13], [20] and [21]).

In this chapter, we develop an SIR type model with latency and nonlinear incidence rate similar to the model in [20] but with a delayed susceptible population in the nonlinear incidence rate. The equilibria of the model are found, and the relationship of the basic reproduction number with stability investigated.

4.2 Derivation of the Model

Yoichi et al [20] have considered the following model

$$\begin{aligned}
\frac{dS(t)}{dt} &= r(1-S(t))S(t) - S(t)\Big\{\frac{I(t-\tau)}{1+\alpha I(t-\tau)}\Big\},\\
\frac{dI(t)}{dt} &= S(t)\Big\{\frac{I(t-\tau)}{1+\alpha I(t-\tau)}\Big\} - (\mu_1+\gamma)I(t),\\
\frac{dR(t)}{dt} &= \gamma I(t) - \mu_2 R(t),
\end{aligned}$$

where $r > 0$ is the birthrate and $\alpha \geq 0$ determines the level at which the force of infection saturates. The model considered a population growth subject to the logistic growth in absence of disease, with a nonlinear incidence rate that had

Table 4.1: State variables of the model (4.1)

Variable	Description
S	Population of susceptible individuals, [biomass]
I	Population of infected individuals, [biomass]
R	Population of recovered individuals, [biomass]

instantaneous susceptibles but delayed infectives pool to the infectives class. In the derivation of our model, we consider the inclusion of a delay term for the susceptible also in the nonlinear incidence rate as follows

$$\begin{aligned}
\frac{dS(t)}{dt} &= \beta(1-S(t))S(t) - S(t-\tau)\Big\{\frac{I(t-\tau)}{1+\alpha I(t-\tau)}\Big\},\\
\frac{dI(t)}{dt} &= S(t-\tau)\Big\{\frac{I(t-\tau)}{1+\alpha I(t-\tau)}\Big\} - (\mu_1+\gamma)I(t),\\
\frac{dR(t)}{dt} &= \gamma I(t) - \mu_2 R(t).
\end{aligned} \tag{4.1}$$

The initial conditions for system (4.1) are

$$S(s) = \phi_1(s),\ I(s) = \phi_2(s),\ R(0) \geq 0,$$

$$\phi_i(s) \geq 0,\ \phi_i(0) > 0,\ i = \{1,2\},\ s \in [-\tau, 0].$$

The variables and parameters used in the model (4.1) are summarised in Tables 4.1 and 4.2 respectively.

Table 4.2: Parameters used in the model (4.1)

Parameter	Description
β	Birth rate, [biomass/time]
μ_1	Death rate (Infected), [1/time]
μ_2	Death rate (Recovered), [1/time]
α	Saturation parameter
γ	Disease recovery rate, $[1/time]$

4.3 Steady States

To obtain the steady states, we have, from (4.1),

$$\begin{aligned} \beta(1-S)S - S\Big\{\frac{I}{1+\alpha I}\Big\} &= 0, \\ S\Big\{\frac{I}{1+\alpha I}\Big\} - (\mu_1+\gamma)I &= 0, \\ \gamma I - \mu_2 R &= 0. \end{aligned} \tag{4.2}$$

Solutions of the system (4.2) show that the model (4.1) always has a trivial equilibrium $E^t = (0,0,0)$, a disease free equilibrium given by $E^0 = (1,0,0)$, and the endemic equilibrium given as $E^* = (S^*, I^*, R^*)$, where I^* is the root of the following quadratic equation

$$a_1 I^{*2} + a_2 I^* + a_3 = 0, \tag{4.3}$$

with

$$\begin{aligned} a_1 =& \beta\alpha^2\mu_1 + \beta\alpha^2\gamma, \\ a_2 =& -\beta\alpha + 2\beta\mu_1\alpha + 2\beta\gamma\alpha + 1, \\ a_3 =& -\beta + \beta\mu_1 + \beta\gamma, \end{aligned}$$

and S^* and R^* are given bellow in terms of I^* as

$$\begin{aligned} S^* =& \mu_1 + \mu_1\alpha I^*, \\ R^* =& \frac{\gamma I^*}{\mu_2}. \end{aligned}$$

4.4 Basic Reproduction Number

We find the basic reproduction number which is defined as the average number of secondary cases generated by a typical infectious host. Using the next generation matrix approach, from (4.1), we have

$$\mathcal{F} = \begin{pmatrix} 0 \\ \frac{S(t-\tau)I(t-\tau)}{1+\alpha I(t-\tau)} \\ 0 \end{pmatrix} \quad \text{and} \quad \mathcal{V} = \begin{pmatrix} -\beta S(1-S) \\ (\mu_1+\gamma)I \\ \mu_2 R - \gamma I \end{pmatrix}.$$

Finding the derivatives of $\mathcal{F}$ and $\mathcal{V}$ at the disease-free equilibrium point E^0 gives $\mathbf{F}$ and $\mathbf{V}$, where

$$\mathbf{F} = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad \mathbf{V} = \begin{pmatrix} \beta & 0 & 0 \\ 0 & \mu_1 + \gamma & 0 \\ 0 & -\gamma & \mu_2 \end{pmatrix},$$

$$\mathbf{V}^{-1} = \begin{pmatrix} \frac{1}{\beta} & 0 & 0 \\ 0 & \frac{1}{\mu_1+\gamma} & 0 \\ 0 & \frac{\gamma}{\mu_2(\mu_1+\gamma)} & \frac{1}{\mu_2} \end{pmatrix},$$

$$\mathbf{FV}^{-1} = \begin{pmatrix} 0 & 0 & 0 \\ 0 & \frac{1}{\mu_1+\gamma} & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

The basic reproduction number ($\mathcal{R}_0$) is the spectral radius of the product $\mathbf{FV}^{-1}$, $\mathcal{R}_0 = \rho(\mathbf{FV}^{-1})$. This gives

$$\mathcal{R}_0 = \frac{1}{\mu_1 + \gamma}. \tag{4.4}$$

4.5 Stability analysis of the Equilibria

In this section, we analyse the local stability of the trivial, disease free and endemic equilibria of (4.1). We now linearise the system (4.1) about the equilibrium

points as follows

$$\begin{aligned}
\dot{\tilde{S}} &= \beta\tilde{S} - 2\beta\tilde{S}S^* - \Big\{\frac{I^*\tilde{S}(t-\tau)}{(1+\alpha I^*)} + \frac{S^*\tilde{I}(t-\tau)}{(1+\alpha I^*)^2}\Big\}, \\
\dot{\tilde{I}} &= \Big\{\frac{I^*\tilde{S}(t-\tau)}{(1+\alpha I^*)} + \frac{S^*\tilde{I}(t-\tau)}{(1+\alpha I^*)^2}\Big\} - (\mu_1+\gamma)\tilde{I}, \\
\dot{\tilde{R}} &= \gamma\tilde{I} - \mu_2\tilde{R}.
\end{aligned} \tag{4.5}$$

Looking for solutions of the linearised system in the form

$$\tilde{S} = C_1e^{\lambda t},\ \tilde{I} = C_2e^{\lambda t},\ \text{and}\ \tilde{R} = C_3e^{\lambda t}$$

we obtain

$$\begin{aligned}
\Big[\Big(\beta - 2\beta S^* - \frac{I^*e^{-\lambda\tau}}{(1+\alpha I^*)}\Big) - \lambda\Big]C_1 - \frac{S^*e^{-\lambda\tau}}{(1+\alpha I^*)^2}C_2 = 0, \\
\frac{I^*e^{-\lambda\tau}}{(1+\alpha I^*)}C_1 + \Big[\Big(\frac{S^*e^{-\lambda\tau}}{(1+\alpha I^*)^2} - \mu_1 - \gamma\Big) - \lambda\Big]C_2 = 0, \\
\gamma C_2 - \mu_2 C_3 - \lambda C_3 = 0.
\end{aligned}$$

Since we are interested in non-trivial solutions, we assume that $C_i \neq 0$, $i = 1, 2, 3$.

The Jacobian matrix in this case has the form

$$\mathbf{J} = \begin{pmatrix}
\Big(\beta - 2\beta S^* - \frac{I^*e^{-\lambda\tau}}{(1+\alpha I^*)}\Big) - \lambda & -\frac{S^*e^{-\lambda\tau}}{(1+\alpha I^*)^2} & 0 \\
\frac{I^*e^{-\lambda\tau}}{(1+\alpha I^*)} & \Big(\frac{S^*e^{-\lambda\tau}}{(1+\alpha I^*)^2} - \mu_1 - \gamma\Big) - \lambda & 0 \\
0 & \gamma & -\mu_2 - \lambda
\end{pmatrix}$$

The characteristic matrix at the trivial equilibrium point $E^t = (0, 0, 0)$ is given

by

$$\begin{vmatrix} \beta-\lambda & 0 & 0 \\ 0 & -(\mu_1+\gamma)-\lambda & 0 \\ 0 & \gamma & -\mu_2-\lambda \end{vmatrix} = 0,$$

which gives the characteristic equation for the eigenvalues λ as

$$(\beta-\lambda)(\mu_1+\gamma+\lambda)(\mu_2+\lambda)=0. \tag{4.6}$$

The eigenvalues are

$$\lambda_1 = \beta,$$

$$\lambda_2 = -(\mu_1+\gamma),$$

$$\lambda_3 = -\mu_2.$$

Obviously, since one of the eigenvalues λ_1 is always positive, this shows that the trivial equilibrium (E^t) of the system (4.1) is always unstable.

We now consider the disease free equilibrium. The characteristic matrix corresponding to the disease free equilibrium point $E^0=(1,0,0)$ is given by

$$\begin{vmatrix} -\beta-\lambda & -e^{-\lambda\tau} & 0 \\ 0 & e^{-\lambda\tau}-(\mu_1+\gamma)-\lambda & 0 \\ 0 & \gamma & -\mu_2-\lambda \end{vmatrix} = 0,$$

or

$$(\lambda+\mu_2)[\lambda^2+(\beta+\mu_1+\gamma-e^{-\lambda\tau})\lambda+\beta\mu_1+\beta\gamma-\beta e^{-\lambda\tau}]=0. \tag{4.7}$$

The eigenvalues are $-\mu_2$ and the solution to the following transcendental equation

$$\lambda^2 + (\beta + \mu_1 + \gamma - e^{-\lambda\tau})\lambda + \beta\mu_1 + \beta\gamma - \beta e^{-\lambda\tau} = 0. \tag{4.8}$$

When $\tau = 0$, equation (4.8) becomes

$$\lambda^2 + (\beta + \mu_1 + \gamma)\lambda + \beta(\mu_1 + \gamma)[1 - \mathcal{R}_0] = 0 \tag{4.9}$$

We can infer from (4.9) that if $\mathcal{R}_0 < 1$, the disease free equilibrium of the system (4.1) is asymptotically stable, marginally stable for $\mathcal{R}_0 = 1$, and unstable for $\mathcal{R}_0 > 1$. We can summarise these conclusions as the following theorem.

Theorem 4.5.1. *The disease free equilibrium E^0 of the system* (4.1) *for $\tau = 0$ is*

(i) locally asymptotically stable if $\mathcal{R}_0 < 1$;

(ii) marginally stable if $\mathcal{R}_0 = 1$;

(iii) unstable if $\mathcal{R}_0 > 1$.

We now consider the case $\tau > 0$. From (4.8), we have

$$\lambda^2 + (\beta + \mu_1 + \gamma)\lambda + \beta\mu_1 + \beta\gamma - (\beta + \lambda)e^{-\lambda\tau} = 0. \tag{4.10}$$

Let $\lambda = i\omega$ with $\omega > 0$ be the root of (4.10), hence,

$$\beta\mu_1 + \beta\gamma - \omega^2 + (\beta\omega + \mu_1\omega + \gamma\omega)i = \beta\cos(\omega\tau) + \omega\sin(\omega\tau) + (\omega\cos(\omega\tau) - \beta\sin(\omega\tau))i.$$

Separating the real and imaginary parts yields,

$$\beta\mu_1 + \beta\gamma - \omega^2 = \beta\cos(\omega\tau) + \omega\sin(\omega\tau),$$

$$\beta\omega + \mu_1\omega + \gamma\omega = \omega\cos(\omega\tau) - \beta\sin(\omega\tau).$$

After squaring and adding the two equations above, it follows that

$$\omega^4 + p\omega^2 + q = 0, \tag{4.11}$$

where

$$p = \beta^2 + \mu_1^2 + 2\mu_1\gamma + \gamma^2 - 1,$$

$$q = \beta^2\mu_1^2 + 2\beta^2\mu_1\gamma + \beta^2\gamma^2 - \beta^2.$$

Let $\zeta = \omega^2$, then (4.11) becomes

$$\zeta^2 + p\zeta + q = 0. \tag{4.12}$$

Clearly if $p > 0$ and $q > 0$ then the equation (4.11) has no positive real roots. Consequently, from the expressions for p and q, we have

$$p = \beta^2 + 2\mu_1\gamma + (\mu_1^2 + \gamma^2)[1 - \mathcal{R}_0^2] > 0$$

and

$$q = \beta^2(2\mu_1\gamma + (\mu_1^2 + \gamma^2)[1 - \mathcal{R}_0^2]) > 0,$$

whenever $0 \leq \mathcal{R}_0 \leq 1$.

It is clear from the definition of $\mathcal{R}_0$ that $\mathcal{R}_0 \not\leq 0$. Hence if $\mathcal{R}_0 \leq 1$, the equation (4.12) has no positive root. Accordingly, if $\mathcal{R}_0 \leq 1$, the disease free equilibrium E^0 of the system (4.1) is locally stable for all $\tau > 0$. This gives us the following theorem.

Theorem 4.5.2. *The disease free equilibrium point E^0 of the system* (4.1) *for $\tau > 0$ is locally stable whenever $\mathcal{R}_0 \leq 1$.*

Next, we will study the stability of the system (4.1) at the endemic equilibrium point E^*. From (4.3), I^* is given by

$$I^* = \frac{-a_2 \pm \sqrt{a_2^2 - 4a_1a_3}}{2a_1} \tag{4.13}$$

where

$$\begin{aligned} a_2 &= -\beta\alpha + 2\beta\mu_1\alpha + 2\beta\gamma\alpha + 1 \\ &= \beta\alpha[2(\mu_1 + \gamma) - 1] + 1 \\ &= \beta\alpha(\mu_1 + \gamma)[2 - \mathcal{R}_0] + 1 \\ &= -(\mu_1 + \gamma)\{\beta\alpha(\mathcal{R}_0 - 2) - R_0\} \end{aligned}$$

and

$$\begin{aligned} 4a_1a_3 &= 4\beta^2\alpha^2(\mu_1 + \gamma)(\mu_1 + \gamma - 1) \\ &= 4\beta^2\alpha^2(\mu_1 + \gamma)^2(1 - \mathcal{R}_0). \end{aligned}$$

Therefore, we can simplify the expression for I^* as follows

$$I^* = \frac{\{\beta\alpha(\mathcal{R}_0 - 2) - R_0\} \pm \sqrt{[\beta\alpha(\mathcal{R}_0 - 2) - \mathcal{R}_0]^2 + 4\beta^2\alpha^2(\mathcal{R}_0 - 1)}}{2\beta\alpha^2}.$$

The only biologically relevant solution for $\mathcal{R}_0 > 1$ is

$$I^* = \frac{\{\beta\alpha(\mathcal{R}_0 - 2) - R_0\} + \sqrt{[\beta\alpha(\mathcal{R}_0 - 2) - \mathcal{R}_0]^2 + 4\beta^2\alpha^2(\mathcal{R}_0 - 1)}}{2\beta\alpha^2}.$$

From the Jacobian matrix above, the characteristic equation for the endemic steady state has the form

$$
\begin{aligned}
&((\mu_2+\lambda)(-2\beta\mu_1\alpha I^* + 2\beta S^*\gamma\alpha^2 I^{*2} + 4\beta S^*\gamma\alpha I^* + 2\beta S^*\lambda + 2\beta S^*\lambda\alpha^2 I^{*2} \\
&+ \lambda^2\alpha^2 I^{*2} - \beta\gamma\alpha^2 I^{*2} + I^{*2}e^{(-\lambda\tau)}\mu_1\alpha + I^{*2}e^{(-\lambda\tau)}\gamma\alpha + I^{*2}e^{(-\lambda\tau)}\lambda\alpha + 2\lambda\gamma\alpha I^* + \lambda\gamma\alpha^2 I^{*2} \\
&- 2\beta\gamma\alpha I^* - \beta\lambda + \lambda\mu_1 + \lambda^2 - \beta\lambda\alpha^2 I^{*2} + 2\beta S^*\mu_1 + \lambda\gamma - \beta\gamma + 2\lambda^2\alpha I^* + I^*e^{(-\lambda\tau)}\gamma \\
&+ I^*e^{(-\lambda\tau)}\lambda + 2\beta S^*\gamma - \lambda S^*e^{(-\lambda\tau)} - 2\beta S^{*2}e^{(-\lambda\tau)} + \beta S^*e^{(-\lambda\tau)} + I^*e^{(-\lambda\tau)}\mu_1 + 4\beta S^*\mu_1\alpha I^* \\
&+ 2\beta S^*\mu_1\alpha^2 I^{*2} + 4\beta S^*\lambda\alpha I^* + 2\lambda\mu_1\alpha I^* + \lambda\mu_1\alpha^2 I^{*2} - \beta\mu_1\alpha^2 I^{*2} - 2\beta\lambda\alpha I^* - \beta\mu_1)) = 0.
\end{aligned}
$$

The eigenvalues are $-\mu_2$ and the solution to the following transcendental equation

$$p_2\lambda^2 + p_1\lambda + p_0 = -(q_1\lambda + q_0)e^{-\lambda\tau}, \tag{4.14}$$

where

$$
\begin{aligned}
p_2 =& \alpha^2 I^{*2} + 2\alpha I^* + 1, \\
p_1 =& 2\gamma\alpha I^* + 4\beta S^*\alpha I^* + \gamma\alpha^2 I^{*2} + \mu_1 + \gamma - \beta - 2\beta\alpha I^* - \beta\alpha^2 I^{*2} + 2\mu_1\alpha I^* + \mu_1\alpha^2 I^{*2} \\
&+ 2\beta S^* + 2\beta S^*\alpha^2 I^{*2}, \\
p_0 =& -\beta\gamma\alpha^2 I^{*2} + 4\beta S^*\mu_1\alpha I^* - 2\beta\gamma\alpha I^* - \beta\mu_1 - \beta\gamma + 4\beta S^*\gamma\alpha I^* + 2\beta S^*\mu_1 + 2\beta S^*\gamma \\
&- 2\beta\mu_1\alpha I^* + 2\beta S^*\mu_1\alpha^2 I^{*2} + 2\beta S^*\gamma\alpha^2 I^{*2} - \beta\mu_1\alpha^2 I^{*2}, \\
q_1 =& I^* - S^* + I^{*2}\alpha, \\
q_0 =& I^{*2}\mu_1\alpha + I^{*2}\gamma\alpha - 2S^{*2}\beta + I^*\gamma + \beta S^* + I^*\mu_1.
\end{aligned}
$$

When $\tau = 0$, the equation (4.14) simplifies and becomes a quadratic equation in

the form

$$p_2\lambda^2 + (p_1 + q_1)\lambda + p_0 + q_0 = 0. \tag{4.15}$$

Therefore, the endemic equilibrium of the system (4.1) is locally asymptotically stable for $\tau = 0$ if the following conditions are satisfied.

$$p_1 + q_1 > 0 \text{ and } p_0 + q_0 > 0. \tag{4.16}$$

Next, we consider the case when $\tau > 0$. Suppose $\lambda = i\omega$, $\omega > 0$ is a root of (4.14). Substituting $\lambda = i\omega$ into the characteristic equation (4.14) yields an equation, which when split into its real and imaginary parts becomes

$$\begin{aligned} -p_2\omega^2 + p_0 &= -q_1\omega\sin(\omega\tau) - q_0\cos(\omega\tau), \\ p_1\omega &= -q_1\omega\cos(\omega\tau) + q_0\sin(\omega\tau). \end{aligned} \tag{4.17}$$

Squaring and adding both sides of the equations gives

$$p_2^2\omega^4 + (-q_1^2 + p_1^2 - 2p_2p_0)\omega^2 - q_0^2 + p_0^2 = 0. \tag{4.18}$$

Letting $\xi = \omega^2$, we obtain

$$p_2^2\xi^2 + (-q_1^2 + p_1^2 - 2p_2p_0)\xi - q_0^2 + p_0^2 = 0. \tag{4.19}$$

The equation (4.19) does not have real roots whenever the following conditions hold

$$p_1^2 - q_1^2 - 2p_2p_0 > 0 \text{ and } p_0^2 - q_0^2 > 0. \tag{4.20}$$

Hence, if there is no positive ξ satisfying (4.19), accordingly, the equation (4.18) has no real solutions. We summarise these results in the following theorem.

Theorem 4.5.3. *If the conditions* (4.16) *and* (4.20) *hold, then all roots of the equation* (4.14) *have negative real parts for all* $\tau \geq 0$. *Furthermore, the endemic steady state* E^* *of the system* (4.1) *is locally asymptotically stable for* $\mathcal{R}_0 > 1$, *and all* $\tau \geq 0$.

If the conditions are not satisfied, then there is a unique positive ξ satisfying (4.19). That is, there is a single pair of purely imaginary roots $\pm i\omega_0$ to (4.14). We now obtain the $\tau_k > 0$ such that the characteristic equation (4.14) has a pair of purely imaginary roots.

$$\tau_k = \frac{1}{\omega_0}\Big\{ \arccos\Big(\frac{-p_1\omega^2 q_1 + q_0 p_2 \omega^2 - q_0 p_0}{q_1^2\omega^2 + q_0^2}\Big)\Big\} + \frac{2k\pi}{\omega_0}, \quad k = 1, 2, 3 \ldots \tag{4.21}$$

We now show that

$$\frac{d(Re\lambda)}{d\tau}\Big|_{\tau=\tau_k} > 0. \tag{4.22}$$

Differentiating the equation (4.14) with respect to τ, we obtain

$$2p_2\lambda\frac{d\lambda}{d\tau} + q_1 e^{-\lambda\tau}\frac{d\lambda}{d\tau} + (q_0 + q_1\lambda)e^{-\lambda\tau} \times \Big(-\frac{d\lambda}{d\tau}\tau - \lambda\Big) + p_1\frac{d\lambda}{d\tau} = 0,$$

and, therefore

$$\begin{aligned}
\left(\frac{d\lambda}{d\tau}\right)^{-1} &= \frac{2p_2\lambda + q_1 e^{-\lambda\tau} + p_1 - (q_0 + q_1\lambda)\tau e^{-\lambda\tau}}{(q_0 + q_1\lambda)\lambda e^{-\lambda\tau}} \\
&= \frac{p_1 + 2p_2\lambda}{(q_0 + q_1\lambda)\lambda e^{-\lambda\tau}} + \frac{q_1}{(q_0 + q_1\lambda)\lambda} - \frac{(q_0 + q_1\lambda)\tau}{(q_0 + q_1\lambda)\lambda} \\
&= \frac{p_1 + 2p_2\lambda}{(q_0 + q_1\lambda)\lambda e^{-\lambda\tau}} + \frac{q_1}{(q_0 + q_1\lambda)\lambda} - \frac{\tau}{\lambda} \\
&= \frac{p_1 + 2p_2\lambda}{-\lambda(p_2\lambda^2 + p_1\lambda + p_0)} + \frac{q_1}{(q_0 + q_1\lambda)\lambda} - \frac{\tau}{\lambda}.
\end{aligned}$$

We have that

$$sign\left\{ \frac{d(Re\lambda)}{d\tau}\bigg|_{\tau=\tau_k} \right\} = sign\left\{ Re\left(\frac{d\lambda}{d\tau}\right)^{-1}\bigg|_{\lambda=i\omega_0} \right\}.$$

This gives

$$\begin{aligned}
&sign\left\{ Re\left[\frac{p_1+2p_2\lambda}{-\lambda(p_2\lambda^2+p_1\lambda+p_0)}\right]\bigg|_{\lambda=i\omega_0} - Re\left[\frac{q_1}{(q_0+q_1\lambda)\lambda}\right]\bigg|_{\lambda=i\omega_0} \right\} \\
&= sign\left\{ Re\left[\frac{2p_2\omega_0^2 - p_1 i\omega_0}{\omega_0^2(p_2\omega_0^2 - p_1 i\omega_0 - p_0)} + \frac{q_1 i\omega_0}{\omega_0^2(q_0+q_1 i\omega_0)}\right] \right\} \\
&\quad -sign\left\{ \frac{2p_2(p_2\omega_0^2-p_0)+p_1^2}{(p_2\omega_0^2-p_0)^2+p_1^2\omega_0^2} + \frac{q_1^2}{q_1^2\omega_0^2+q_0^2} \right\} \\
&= sign\left\{ \frac{3p_2^2q_1^2\omega_0^4 + (2p_2^2q_0^2 + [2p_1^2q_1^2 - 4p_0p_2q_1^2])\omega_0^2 + [p_1^2q_0^2 - 2p_0p_2q_0^2] + p_0^2q_1^2}{(p_1^2\omega_0^2 + (p_0 - p_2\omega_0^2)^2)(q_1^2\omega_0^2+q_0^2)} \right\}.
\end{aligned} \tag{4.23}$$

We now show that the expressions in square brackets in (4.23) are positive.

$$[2p_1^2q_1^2 - 4p_0p_2q_1^2] = 2\{\beta^2(2S^*-1)^2 + \mu_1^2 + 2\mu_1\gamma + \gamma^2\}(\alpha I^* + 1)^4(\alpha I^{*2} + I^* - S^*)^2 > 0,$$

and

$$\begin{aligned}
[p_1^2q_0^2 - 2p_0p_2q_0^2] = \{\beta^2(2S^*-1)^2 + \mu_1^2 + 2\mu_1\gamma + \gamma^2\}(\alpha I^* + 1)^4(\mu_1\alpha I^{*2} + \alpha\gamma I^{*2} - 2\beta S^{*2} \\
+ \mu_1 I^* + \gamma I^* + \beta S^*)^2 > 0.
\end{aligned}$$

Hence the expression in (4.23) is positive, and we have shown that $d(Re\lambda)/d\tau|_{\tau=\tau_k} > 0$. Therefore, the transversality condition holds and the conditions for Hopf bifurcation are satisfied at $\tau = \tau_k$ for the system (4.1).

4.6 Global Stability of the Disease Free Equilibrium Point

In this section, we analyse the global stability of the disease free equilibrium E^0 of the system (4.1). We follow the idea introduced in the proof in [21]. First, we introduce the following Lemma, which will later be used in the proof. Consider the following equation

$$\dot{u}(t) = \frac{au(t-\tau)}{1+\alpha u(t-\tau)} - cu(t) \tag{4.24}$$

$$u(\theta) = \phi(\theta) \geq 0,$$

$$\theta \in [-\tau, 0),\ \phi(o) > 0$$

where a, c and α are positive constants with $\tau \geq 0$. Equation (4.24) has a trivial equilibrium $u = 0$ if $a < c$ and a unique positive equilibrium $u^* = \frac{(a-c)}{\alpha c}$ if $a > c$.

Lemma 4.6.1. *[21] If $a > c$, then the positive equilibrium $u^* = \frac{(a-c)}{\alpha c}$ of (4.24) is globally asymptotically stable; if $a < c$, then the trivial equilibrium $u = 0$ of (4.24) is globally asymptotically stable.*

Theorem 4.6.2. *The disease free equilibrium point E^0 of the system (4.1) is globally asymptotically stable whenever $\mathcal{R}_0 < 1$.*

Proof. Let $S(t)$, $I(t)$ and $R(t)$ be any positive solution of (4.1) with its associated

initial conditions. It follows from the first equation of the system (4.1) that

$$\dot{S}(t) \leq \beta(1 - S(t))S(t).$$

By comparison, we have

$$\lim_{t \to +\infty} \sup S(t) \leq 1. \tag{4.25}$$

Hence for $\epsilon > 0$, there is a $T_1 > 0$ such that if $t > T_1$, $S(t) \leq 1 + \epsilon$.

Now, for $t > T_1 + \tau$, we have from the second equation of (4.1) that

$$\dot{I}(t) \leq \left\{ \frac{(1+\epsilon)I(t-\tau)}{1 + \alpha I(t-\tau)} \right\} - (\mu_1 + \gamma)I(t).$$

Consider the following auxiliary equation

$$\dot{u}(t) = \left\{ \frac{(1+\epsilon)u(t-\tau)}{1 + \alpha u(t-\tau)} \right\} - (\mu_1 + \gamma)u(t).$$

When $(1 + \epsilon) < (\mu_1 + \gamma)$, by Lemma (4.6.1), it follows that

$$\lim_{t \to +\infty} u(t) = 0.$$

By comparison we have that

$$\lim_{t \to +\infty} \sup I(t) = 0. \tag{4.26}$$

Hence for $\epsilon > 0$, there is a $T_2 > T_1 + \tau$ such that if $t > T_2$,

$$I(t) \leq \epsilon.$$

For $\epsilon > 0$ and $t > T_2$, we have from the third equation of (4.1)

$$\dot{R}(t) \leq \gamma\epsilon - \mu_2 R(t).$$

By comparison, we have that

$$\lim_{t\to+\infty} \sup R(t) = 0. \tag{4.27}$$

We have from the first equation of the system (4.1) that for $t > T_2 + \tau$

$$\dot{S}(t) \geq \beta(1 - S(t))S(t) - \frac{\epsilon}{1+\alpha\epsilon}S(t). \tag{4.28}$$

By comparison it follows that

$$\lim_{t\to+\infty} \inf S(t) \geq \frac{\beta + \beta\alpha\epsilon - \epsilon}{\beta + \beta\alpha\epsilon}. \tag{4.29}$$

Letting $\epsilon \to 0$, we obtain

$$\lim_{t\to+\infty} \inf S(t) \geq 1. \tag{4.30}$$

From (4.25) and (4.30), we conclude that

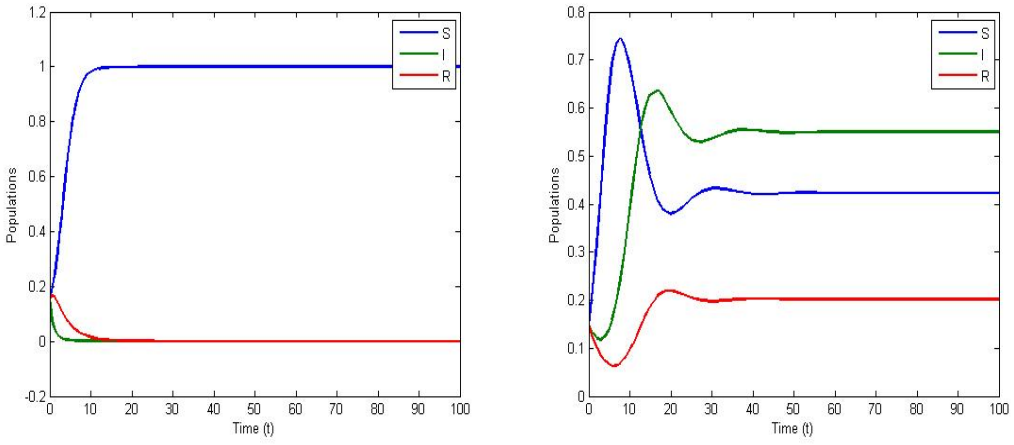
$$\lim_{t\to+\infty} S(t) = 1.$$

Since the inequalities hold true for arbitrary $\epsilon > 0$ sufficiently small, we conclude that $E^0 = (S^0, I^0, R^0) \to (1, 0, 0)$ as $t \to \infty$. We know that for $\mathcal{R}_0 < 1$ the disease-free equilibrium point was found to be locally asymptotically stable, here we conclude that E^0 is globally asymptotically stable. This completes the proof.

□

4.7 Numerical Simulations

In this section, we analyse numerically by solving the system (4.1) using MATLAB. In particular, we show solution profiles illustrating the theoretical results obtained in earlier sections concerning the existence and stability of the disease-free and endemic equilibria.The parameters used in this section are as stated in the figures.



(a) $\mathcal{R}_0 = 0.7704 < 1$, $\mu_1 = 0.548$, $\gamma = 0.75$

(b) $\mathcal{R}_0 = 3.6630 > 1$, $\mu_1 = 0.148$, $\gamma = 0.125$

Figure 4.1: Solutions of the system (4.1). $\mathcal{R}_0 = 0.7704 < 1$ in Figure 4.1(a) and $\mathcal{R}_0 = 3.6630 > 1$ in Figure 4.1(b). $\tau = 1$, $\beta = 0.615$, $\mu_2 = 0.34$, $\alpha = 1.0$.

To illustrate the theoretical results obtained in the previous sections about the existence and stability of the disease free and endemic equilibria, we first set

the parameters as follows: $\tau = 1$, $\beta = 0.615$, $\mu_1 = 0.548$, $\mu_2 = 0.34$, $\alpha = 1.0$ and $\gamma = 0.75$. Straightforward calculation shows that $\mathcal{R}_0 = 0.7704 < 1$. Then, by Theorem 4.5.2, the disease will die out of the population. For the endemic equilibrium, which stability properties are outlined in Theorem 4.5.3, we change μ_1 to 0.148 and γ to 0.125 giving $\mathcal{R}_0 = 3.6630 > 1$. With these parameter values, the endemic equilibrium becomes stable, meaning that the disease will remain in the population. This is shown in Figures 4.1(a) and 4.1(b).

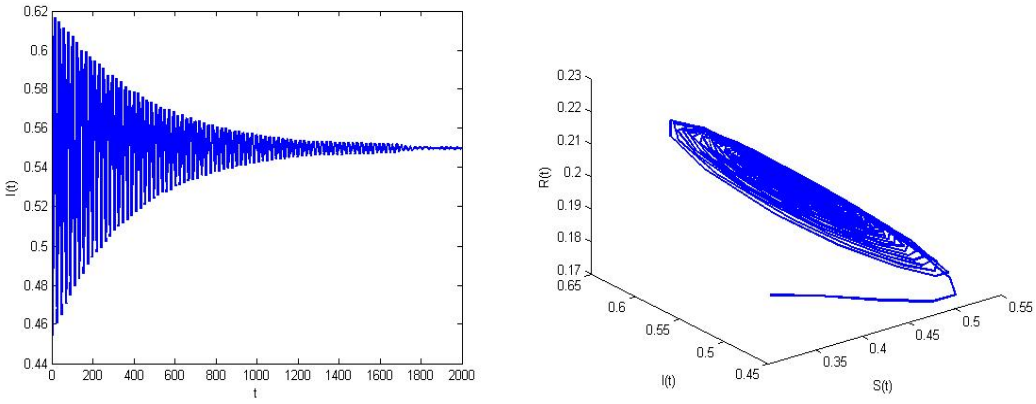


Figure 4.2: Time series plot for $I(t)$ with $\tau = 2.9$ and its corresponding phase portrait. $\mathcal{R}_0 = 3.6630$, $\beta = 0.615$, $\mu_1 = 0.148$, $\mu_2 = 0.34$, $\alpha = 1.0$, $\gamma = 0.125$.

Figure 4.2 shows the dynamics of $I(t)$ and its corresponding phase portrait for the system (4.1). As can be seen in the figure, for $\tau = 2.9$, the system tends to the endemic steady state. However, as the time delay is increased to $\tau = 2.9424$, the system undergoes a Hopf bifurcation and periodic solutions are observed in

Figure 4.3(a). As the time delay is increased further still, the equilibrium point E^* becomes unstable at $\tau = 2.95$ as shown in Figure 4.4(a).

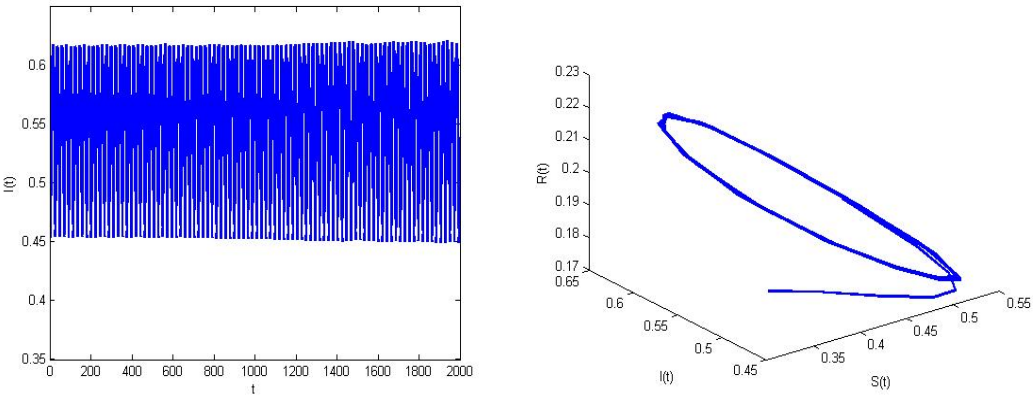


Figure 4.3: Time series plot for $I(t)$ with $\tau = 2.9424$ and its corresponding phase portrait. $\mathcal{R}_0 = 3.6630$, $\beta = 0.615$, $\mu_1 = 0.148$, $\mu_2 = 0.34$, $\alpha = 1.0$, $\gamma = 0.125$.

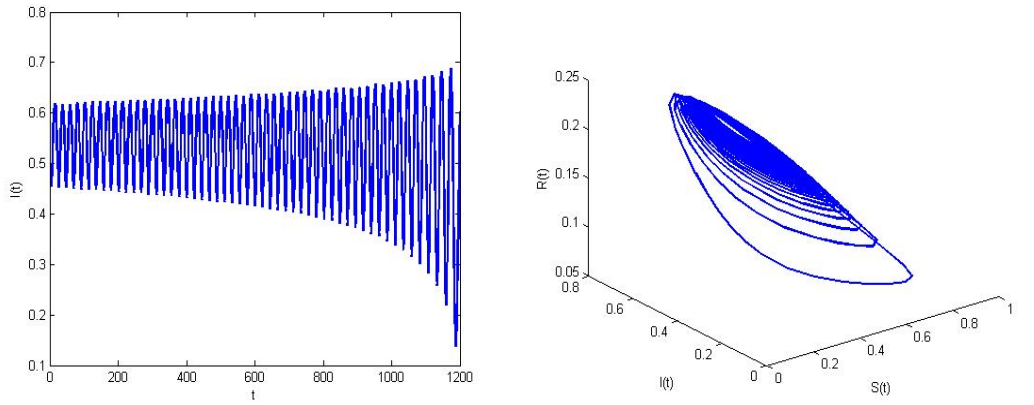


Figure 4.4: Time series plot for $I(t)$ with $\tau = 2.95$ and its corresponding phase portrait. $\mathcal{R}_0 = 3.6630$, $\beta = 0.615$, $\mu_1 = 0.148$, $\mu_2 = 0.34$, $\alpha = 1.0$, $\gamma = 0.125$.

4.8 Conclusions

In this chapter, we have modelled and analysed an SIR-type model with latency and nonlinear incidence rate. The basic reproduction number was found and its relationship with the stability of the system investigated.

System (4.1) admits three types of equilibria, namely, the trivial, the disease-free and the endemic equilibrium. The trivial equilibrium was found to always be unstable while the stability of the disease-free and endemic equilibria depends on the basic reproduction number $\mathcal{R}_0$. We found that for $\mathcal{R}_0 < 1$, the disease-free equilibrium point is locally asymptotically stable, marginally stable for $\mathcal{R}_0 = 1$ and unstable for $\mathcal{R}_0 > 1$. Comparison argument was used to prove the global asymptotic stability of the disease free steady state when $\mathcal{R}_0 < 1$. The endemic equilibrium point was found to be stable whenever $\mathcal{R}_0 > 1$, for values of $\tau \geq 0$, when the conditions summarised in Theorem (4.5.3) are fulfilled. By satisfying the transversality condition, we have shown that when the conditions stated in Theorem (4.5.3) are not fulfilled, the system (4.1) undergoes a Hopf bifurcation and this gives rise to periodic oscillations. We have also performed numerical simulations of the full nonlinear system, and have illustrated the dynamical behaviour suggested by the analytical findings, and the agreement is perfect.

Chapter 5

Conclusions

In this thesis, we have derived and studied the dynamics of infectious diseases using time-delayed mathematical models. Analytical results about the dynamical behaviour of the models analysed have been obtained with the results supported by the direct numerical simulations, and numerical analysis was employed to understand the behaviour of the systems, when analytical results were not possible to derive.

The system modelled in Chapter 2 describes the model for understanding the dynamics of human-mosquito interaction in a population. We developed an SIR malaria model with time delay for the transmission dynamics of malaria. A delay term was introduced to represent the length of the period of latency of malaria therapeutics administered to infected humans. We have proved that if the basic reproduction number $R_0 < 1$, then the disease-free equilibrium exists and is

asymptotically stable. If $R_0 > 1$, then the endemic equilibrium exists and is asymptotically stable for all time delays. Numerical simulations supported our analytical findings and further demonstrated that the endemic equilibrium of the system (2.8) is globally asymptotically stable for all delay values as long as $R_0 > 1$, and unstable otherwise. This study has shown that the treatment of malaria using long-lasting malaria drugs could significantly reduce the population infected with malaria (see Fig 2.6(a)), and this in turn reduces the number of infected mosquito vectors due to the reduction in the population of the infected human hosts (Fig 2.6(b)). This in the long run could offer an effective way for tackling malaria infection in the most endemic areas.

In Chapter 3, we have derived and analysed an SIR model to describe the dynamics of a two-disease epidemic in a population. The model was designed to exclude the possibility of co-infection in order to be able to make analytical progress. Three different endemic equilibria were calculated for this system. These are the cases when disease one only is endemic, when disease two only is endemic and when both diseases are endemic. Apart from the case when both diseases are endemic, conditions for the existence and stability of these equilibria were established. Theoretical calculations and numerical simulations support that the endemic equilibrium when the disease one only is endemic in the absence of time delay is locally asymptotically stable when $R_2 < R_1$ for $R_1 > 1$ with two conditions

as stated in Theorem 3.6.2. Similar results were also obtained for the case when the disease two only is endemic and these are summarised in Theorem 3.6.4. We have numerically calculated the real part of the leading eigenvalues of the characteristic polynomial of the system to obtain stability charts in the τ_D, α_D and τ_D, τ_d parameter planes. These charts as presented in Figs. 3.4-3.6 show the importance the disease two infection rate (α_d) plays on the dynamics of the system. As we increased α_d, the region of stability of the endemic steady state spread over a larger area of the (τ_D, τ_d) parameter plane. Similar results are expected from the disease one infection rate (α_D) since the system is symmetrical. This model is suitable for analysing any two-disease epidemics without the possibility of a co-infection, such as, for example, yaws and syphilis, respiratory syncytial virus and human para influenza virus and so forth.

Finally, in Chapter 4, we have analysed an SIR model with latency based on the logistic growth of the population in the absence of the disease, with a saturated incidence rate. We found three types of equilibria for the system; the trivial, disease-free and endemic equilibria. The trivial equilibrium was found to always be unstable while the stability of the disease-free and endemic equilibria depends on the basic reproduction number $\mathcal{R}_0$. We found that for $\mathcal{R}_0 < 1$, the disease-free equilibrium point is locally asymptotically stable, marginally stable for $\mathcal{R}_0 = 1$ and unstable for $\mathcal{R}_0 > 1$. Comparison argument was used to prove the global

asymptotic stability when $\mathcal{R}_0 < 1$. The endemic equilibrium was found to be stable whenever $\mathcal{R}_0 > 1$, for values of $\tau \geq 0$, when the conditions summarised in Theorem (4.5.3) are satisfied. Analysis has also shown that the local stability of the endemic equilibrium point E^* depends on the time delay τ. The system (4.1) changes its behaviour from stable to unstable nature when τ crosses the critical value τ_0 through a Hopf bifurcation, and periodic solutions are observed. The oscillatory behaviour exhibited by system (4.1) is called epidemic waves and shows that there maybe periodic outbreaks of epidemic in the population when τ crosses the critical value τ_0.

The epidemiological relevance of this research work is evident in the models derived and analysed. While the model in Chapter 2 is specifically targeted at how to reduce malaria infection by using long lasting Malaria drugs, the model in Chapter 3 has a stability chart that could save as a guide to the region of epidemic safety and was developed to have a wider application to any two-disease infection without the possibility of a co-infection. The knowledge of the existence of a critical value to the latent period (τ) in Chapter 4, and the expectation of periodic outbreak to an epidemic as τ gets larger than its critical value (τ_0), is of great importance to the design of intervention to the epidemic described by system (4.1). Suggested future work will be on a two-disease infection with the possibility of a co-infection.

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