LYAPUNOV FUNCTIONS IN EPIDEMIOLOGICAL MODELING

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Abstract

In this mini thesis, we study the application of Lyapunov functions in epidemiological modeling. The aim is to give an extensive discussion of Lyapunov functions, and use some specific classes of epidemiological models to demonstrate the construction of Lyapunov functions. The study begins with a review of Lyapunov functions in general, and their usage in global stability analysis. *Lyapunov's "direct method"* is used to analyse the stability of the disease-free equilibrium. Moreover, a matrix-theoretic method is critically examined for its capability and overall functionality in the construction and development of an appropriate Lyapunov function for the stability analysis of the nonlinear dynamical systems. This method additionally demonstrates the construction of the basic reproduction number for the SEIR model, and it is shown that the disease-free equilibrium is locally asymptotically stable if $\mathscr{R}_0 < 1$, but unstable if $\mathscr{R}_0 > 1$. Furthermore, a Lyapunov function is constructed for the Vector-Host model to study the global stability of the disease-free equilibrium. The results indicate that the disease-free equilibrium is globally asymptotically stable when $\mathscr{R}_0 \leq 1$ (i.e. every solution trajectory of the Vector-Host model converges to the largest compact invariant set $M = \{(S_{ho}, I_h, S_{vo}, I_v)\})$ and unstable when $\mathscr{R}_0 > 1$.

Keywords: Lyapunov function, Next-Generation matrix, Basic reproduction number, Global stability.

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LIST OF ABBREVIATIONS

SI	Susceptible Infectious
GAS	Globally Asymptotically Stable
DFE	Disease Free Equililibrium
ODEs	Ordinary Differential Equations
PDEs	Partial Differential Equations
SEIR	Susceptible Exposed Infectious Recovered

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This work is dedicated to my two best friends Rose and Hero for their support throughout the way and for their unconditional love.

DECLARATION

I, Elise Ndapwoshisho Lazarus, hereby declare that this study, **Lyapunov functions in epidemiological modeling**, is my own work and is a true reflection of my research, and that this work, or any part thereof has not been submitted for a degree at any other institution.

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Chapter 1

Introduction

1.1 Background of the study

The concept of dynamical systems originated from physics in 1600s in the area of Newtonian mechanics, when Newton invented differential equations. Since then, many researchers have contributed to this work, see [1, 15, 18]. In the late 1800s, Poincaré introduced a viewpoint of qualitative questions rather than quantitative. He developed a powerful geometric approach to the analysis of the equilibrium points of dynamical systems. During the years 1892-1899, Poincaré published a paper called "New methods of Celestial mechanics", where he successfully applied his results to the problem of the motion of the three-bodies, and carefully studied the stability and asymptotic properties of stability [27]. In the papers [27, 29], Poincaré outlined his recurrence theorem, which states clearly that certain systems will, after a sufficiently long but finite time, return to a state very close to the initial state. In 1913, the Poincaré's "last geometric theorem", was proven by George David Birkhoff, as a special case of the three-body problem. Moreover, in 1927 George David Birkhoff published his book on "Dynamical systems", and in 1931, he discovered what is now known as the ergodic theorem [4].

Ergodic theory is a branch of mathematics that studies dynamical systems. The focus here is not on finding the solutions to the equations, but rather on the behaviour of dynamical systems around the initial solutions with respect to time. In other words, we study these systems to understand the stability of equilibrium points. There exist different types of stability. The most significant one is the stability of solutions near an equilibrium point [21], which may be studied through the theory of Lyapunov.

Historically, Lyapunov stability is named after a Russian mathematician Aleksandr Lyapunov, who published his book entitled ”The General Problem of Stability of Motion” in 1892, in which he considered necessary conditions for the linearisation of the nonlinear dynamical systems for the classification of equilibrium points. Lyapunov, in his work, proposed two methods for the stability analysis. The first method developed the solutions in a series and the second method known as the Lyapunov stability criterion made use of functions called Lyapunov functions [21]. Lyapunov stability theory is one of the standard tools in the analysis of dynamical systems. In simple terms, if all the solutions of a dynamical system that start near an equilibrium point, say $\mathbf{x}^*$, stay near $\mathbf{x}^*$, then $\mathbf{x}^*$ is said to be Lyapunov stable. Moreover, if the equilibrium point $\mathbf{x}^*$ is Lyapunov stable and all solutions that start near $\mathbf{x}^*$ converge toward $\mathbf{x}^*$, then $\mathbf{x}^*$ is said to be asymptotically stable.

Lyapunov theory is used to establish global stability for epidemiological classes. There exists a long history of mathematical modeling in epidemiology since the 18th century when Daniel Bernoulli published a seminar paper which was revisited by D. Klaus and T. Heesterbeek in 2002. The paper determines the age-specification equilibrium prevalence of immune individual of an endemic potentially lethal infectious diseases [14]. However it was not until the 20th century when the dynamical systems were applied in epidemiology.

In 1927, W.O Kermack and A.W McKendrick developed a simple mathematical epidemic model for the transmission dynamics of viral and bacteria infectious agents within the population of hosts [18]. In their paper, the focus was centred on the notion of a threshold density of susceptible hosts to trigger an epidemic , and an extension of the idea was made in the definition of a basic reproduction number, which tells us how many secondary cases one infected individual will produce in an entirely susceptible population during his or her infective period. In 1985, John Jacquez wrote a major book on compartmental analysis. He successfully applied this tool in infectious diseases (especially in HIV) together with his co-workers Jim Koopman, Carl Simon and Ian Longini [11].

Stability analysis in epidemiology is studied to understand different infectious diseases as well as predicting their transmission. Diseases caused by viruses or bacteria are modeled compartmentally through the number of infected individuals. One of the crucial aspects of mathematical biology is the threshold condition that determines whether the disease will spread or die out in the population. Here the threshold is called the basic reproduction number $\mathscr{R}_0$ which is mainly determined by the eigenvalues of the Jacobian matrix, or through the Routh-Hurwitz stability criterion [19]. The classification of the basic reproduction number $\mathscr{R}_0$ is: when $\mathscr{R}_0 < 1$, the infection will die out in the long run, but if $\mathscr{R}_0 > 1$ the infection will be able to spread in a population.

The basic reproduction number is used in the construction of the Lyapunov function, which is used to study the stability of the equilibrium points for certain models [5]. The method of Lyapunov functions is commonly used to establish global stability of an equilibrium point of a mathematical model, see [20]. P. Driessche and Z. Shuai (2013) established two systematic methods of construction of Lyapunov functions to investigate stability of disease free equilibria [8], however the construction of Lyapunov functions remains a challenge since there is no general method available to use. This thesis discusses the global stability of dynamical system from the Lyapunov functions point of view and applies these methods to some epidemiological models.

1.2 Statement of the problem

This mini thesis is on the application of Lyapunov functions in epidemiological modeling, in the general area of mathematical modeling. Epidemiological modeling is a subject that deals with developing and analysing mathematical models that describe infectious diseases and their spread in populations. Mathematical models belong to a class called Dynamical systems. These are systems that evolve with respect to time. For example, the following system of differential equation is a dynamical system

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

where $\mathbf{x}(t) = (x_1(t), \ldots, x_n(t))^\top$, $\dot{\mathbf{x}} = (\frac{dx_1}{dt}, \ldots, \frac{dx_n}{dt})^\top$ and $\mathbf{f} = (f_1, \ldots, f_n)^\top$. The focus of this thesis is on the mathematical analysis part of this process.

A crucial part of analysing mathematical models is the interrogation of the equilibrium points of these models, defined as the points $\mathbf{x}^*$ such that $\mathbf{f}(\mathbf{x}^*) = \mathbf{0}$. Dynamical systems can have multiple equilibrium points, but the area of Interest for thesis is on the stability of the disease-free equilibrium point. In epidemiological models, this information helps in determining conditions under which the disease would be contained. There are several tools for analysing the stability of equilibrium points of a dynamical system. This thesis will use a method called *Lyapunov's "direct method"*. The idea behind *Lyapunov's "direct method"* is to establish properties of the equilibrium point by studying how certain carefully selected scalar functions of the state evolve as the system state evolves. These scalar functions are called Lyapunov functions.

The thesis aims to give an extensive discussion of the Lyapunov functions, highlighting some problems pertaining to Lypunov functions in Epidemiological modeling. Moreover, this thesis will also include a discussion of some specific classes of epidemiological models in the Lyapunov stability context.

1.3 Literature review

The stability theory of dynamical systems has been studied to understand how systems evolve with respect to time. A lot of research have been conducted since 1892, when the first stability theory of the analysis of arbitrary differential equations was developed by a Russian mathematician, Aleksandr Mikhailovich Lyapunov. In 1892, Lyapunov presented two methods for stability analysis in his PHD thesis entitled The General Problem of Motion stability (Lyapunov (English translation), 1992) [21]. These were: the linearization method and the direct method. The linearization method draws conclusions about the local stability of a nonlinear system in a close vicinity of its steady states from the stability properties of its linear approximation. Since then, many researchers took interest in the stability of non-linear dynamical systems. In 1960, V.V. Nemytskii and V.V. Stepanov wrote a book on the qualitative theory of differential equations, in which they discussed the behaviour of the trajectories in the neighbourhood of a closed trajectory [25]. A similar study was done by J.P LaSalle in 1962, when he initiated the study of the asymptotic stability of an automatic control system. The objective of his paper was to show that if $xf(x) > 0$ for $x \neq 0$, and the first derivative of the scalar energy-like function is negative definite, then the control system is completely stable [14].

According to Zubov [33], as cited in [9], the stability theorems of Lyapunov are applicable to dynamical systems. As a result, this plays a significant role in the study of stability analysis. The paper by J.K Hale and E.F Infante [9] extended the results of limiting sets of trajectories in a compact subset, that allowed the derivative of a Lyapunov function to vanish, as well as extending other stability results .

J.P. LaSalle demonstrated quite an interest in the theory of stability of dynamical systems, see literature [12, 13, 14]. In [12], the focus was on stability and instability of a system. The purpose of the study was to communicate some mathematical theorems that present methods for estimating regions of asymptotic stability. He stated that an equilibrium state of a system may be asymptotically stable in a mathematical sense but be unstable from a practical point of view, and, conversely, it may be mathematically unstable but practically stable [12]. In [13], the study was on “An invariance principle in the theory of stability”. The purpose of the paper was to give a unified presentation of Lyapunov’s theory of stability; the classical Lyapunov theorems on stability and instability, as well as their extensions. He presented a fundamental theorem which is a modified version of Yoshizawa's theorem of stability in literature [9]. In spite of the fact that the results of this paper [13] were improved, Miller [24] as cited in [13] obtained a similar stability theorem for almost periodic stability.

Moreover, an extension of LaSalle's invariance principle was further addressed by Hespanha in 2004 [10]. The purpose of the study was to provide a collection of results that could be viewed as an extension of Lasalle's invariance principle. A conclusion was made that asymptotic stability can be deduced using multiple Lyapunov functions whose Lie derivatives are only negative semi-definite. Furthermore, [14] addressed the idea of the size of the perturbation the system can undergo and still return to the equilibrium state. This idea was demonstrated by means of non-linear system approximation. In addition, the theorems and methods for determining the regions of asymptotic stability were underlined [10].

Lyapunov's direct method, also known as Lyapunov's second method, determines the stability properties of a nonlinear system by constructing a scalar energy-like function known as a Lyapunov function. A large number of publications appeared after the introduction of the Lyapunov's direct method in 1892, see, for instance [31, 32]. In [31], the stability of fractional-order nonlinear dynamical systems is studied using Lyapunov's direct method. The study focused on the Mittag-Leffler stability notions. As a result, the fractional Lyapunov's direct method of non-autonomous system was proven. Furthermore, the class-κ functions to the fractional Lyapunov's direct method was introduced, and the fractional comparison principle was provided. Moreover, [22, 28], as cited in [31], relate strongly to the stability problems of fractional systems. A similar study in 2002 by Zhihua and Jian-Xin addressed the Model-based learning control and their comparisons using Lyapunov's direct method [32]. The main idea was to study two types of algorithms used in learning the unknown time functions. However, the drawback of the direct method is that finding such a function is usually a non-trivial task.

1.4 Thesis organisation

This thesis is partitioned in five major chapters. This being the very first chapter. The second chapter presents preliminaries on dynamical systems, in which notations and terminologies are defined. The third chapter gives an outline on the stability of equilibria and the *Lyapunov's "direct method"*. The fourth chapter discusses the next-generation matrix and assumptions necessary to determine the basic reproduction number. The fifth chapter studies the global stability of the disease-free equilibrium (DFE). A Lyapunov function is constructed to determine the global stability of the disease-free equilibrium, and under necessary conditions the DFE is said to be globally asymptotically stable if $\mathscr{R}_0 < 1$.

Chapter 2

Preliminaries on Dynamical systems

In this chapter we discuss some concepts on dynamical systems. Readers unfamiliar with dynamical systems are advised to go through this chapter to be able to understand the content of this thesis.

2.1 Dynamical systems

A dynamical system is defined to be a system which evolves with time. There are two types of dynamical systems: Differential equations and difference equations. Differential equations describe the evolution of systems in continuous time while difference equations arise in problems where time is discrete [30]. This thesis focuses on differential equations. There are two types of differential equations: ordinary differential equations (ODEs) and partial differential equations (PDEs). We will deal exclusively with ODEs. Generally, we have the following form;

$$\begin{aligned}
\dot{x}_1 &= f_1(x_1, \ldots\ldots., x_n) \\
\dot{x}_2 &= f_2(x_1, \ldots\ldots., x_n) \\
. & \\
. & \\
\dot{x}_2 &= f_n(x_1, \ldots\ldots., x_n),
\end{aligned} \tag{2.1}$$

where $\dot{x}_i = \frac{dx_i}{dt}$ and the functions $f_1, \ldots., f_n$ are determined by the problem at hand. If all the x_i on the right-hand side are all to the power of one, then the system is said to be linear. Otherwise the system is nonlinear. For example,

$$\begin{aligned} \dot{x}_1 &= 5x_1 + 2x_2 \\ \dot{x}_2 &= x_1 + x_2 \end{aligned} \tag{2.2}$$

is a linear equation in $2-$dimensions and

$$\begin{aligned} \dot{x}_1 &= x_2 \\ \dot{x}_2 &= -\tfrac{g}{L}\sin x \end{aligned} \tag{2.3}$$

is a nonlinear system [30].

Consider system (2.1). For $n = 1$, we get a single equation of the form $\dot{x} = f(x)$. This type of equation is called a one-dimensional or first-order dynamical system. The system is called autonomous if it does not depend explicitly on time t. Time-dependent systems are called nonautonomous dynamical systems and they are complicated to deal with, as one needs two pieces of information, x and t, to predict the state of the system [23]. Therefore this project focuses on nonlinear autonomous dynamical systems.

2.2 Notations

Throughout this thesis, $\mathbf{x}^*$, denote an equilibrium point/steady state/fixed point of a dynamical system and $\|\cdot\|$ will denote an euclidean norm.

2.3 Definitions

The following definitions are presented in order to develop lemmas and theorems intoduced in subsequent chapters [3, 23]. By a nonnegative matrix we mean a matrix whose entries are nonnegative real numbers. By positive matrix we mean a matrix all of whose entries are strictly positive real numbers.

Definition 1. *An **equilibrium point/a steady state/a fixed point** of the system* $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$, *is a point,* $\mathbf{x}^*$, *such that* $\mathbf{f}(\mathbf{x}^*) = \mathbf{0}$ *(i.e* $\mathbf{x}^*$ *is a point where the rate of change of* $\mathbf{x}$ *is zero).*

Definition 2. *Let V be a vector space over $\mathbb{R}$. A **norm** on V is a function* $\|\cdot\|: V \to \mathbb{R}$ *such that for all* $u, v \in V$,
$N1)$ $\| u \| \geq 0$, $\forall u \in V$, *and* $\| u \| = 0 \Leftrightarrow u = 0$.

N2) $\| \lambda u \| = |\lambda| \| u \|$, $\forall u \in V$ *and* $\lambda \in \mathbb{R}$ *(Compatibility with constant multiplication).*
N3) $\| u + v \| \leq \| u \| + \| v \|$, $\forall u, v \in V$ *(Triangular inequality).*

If $\| \cdot \|$ is a norm on V, then the pair $(V, \| \cdot \|)$ is called a normed vector space [6].

Definition 3. *A function $f(x)$ from $D \subset \mathbb{R}^n$ to $\mathbb{R}^m$ is **Lipschitz continuous** at $x \in D$ if there is a constant L such that $\| f(y) - f(x) \| \leq L \| y - x \|$ for all $y \in D$ sufficiently near x.*

Definition 4. *Let A be a square matrix. Then the **spectral radius** of A is*
$\rho(A) = \max\{| \lambda | : \lambda$ *is an eigenvalue of* $A\}$

Definition 5. *A matrix A is said to be **reducible** if there exist a permutation matrix P such that*

$$P^T A P = \begin{bmatrix} A_{11} & 0 \\ A_{12} & A_{22} \end{bmatrix}$$

where A_{11} and A_{22} are square matrices. A square matrix that is not reducible is said to be irreducible.

Definition 6. *A non-negative square matrix A is said to be **primitive** if there is a $k \in \mathbb{Z}$ such that $A^k > 0$.*
A sufficient condition for a matrix to be a primitive matrix is for the matrix to be a nonnegative, irreducible matrix with a positive element on the main diagonal.

Definition 7. *A matrix A is called an $M-$**matrix** if it can be expressed in the form $A = sI - B$, where $B = (b_{ij})$ with $b_{ij} \geq 0$ for all $1 \leq i, j \leq n$, s is greater than the spectral radius of B and I is the identity matrix.*

Definition 8. *A **sign pattern matrix** (or sign pattern for short) is a matrix having entries in $\{$+,-,0$\}$.*

Definition 9. *A square sign pattern matrix A is a $Z-$**sign pattern matrix** if $a_{ij} \neq +$ for all $i \neq j$.*

Definition 10. *A **feasible region** Γ of a system is the set of all points in the plane which satisfy the system of inequalities.*

Definition 11. *In dynamical systems, a **trajectory** is the set of points in state space that are the future states resulting from a given initial state.*

Definition 12. *Let* $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$ *be a nonlinear autonomous dynamical system. A set* $M \subset \Gamma$ *is said to be an* ***invariant set*** *if for every trajectory* $x(0) \in M$, $x(\tau) \in M$ *for all* $\tau \in \mathbb{R}$.

Definition 13. *Let* $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$ *be a nonlinear autonomous dynamical system. A set* $M \subset \Gamma$ *is said to be a* ***positively invariant set*** *if for every trajectory* $x(0) \in M$, $x(\tau) \in M$ *for all* $\tau \geq 0$.

Chapter 3

Stability and Lyapunov functions

Consider a nonlinear autonomous dynamical system

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}), \tag{3.1}$$

with an equilibrium point $\mathbf{x}^*$. The characterization of the stability of the equilibrium point answers certain questions. The major question is whether the trajectories $\mathbf{x}(t)$ for system (3.1) with initial condition $\mathbf{x}_0$ will converge to $\mathbf{x}^*$ as t goes to infinity or will diverge away from the equilibrium point $\mathbf{x}^*$. The stability analysis of equilibrium points of equation (3.1) is difficult in general. This is due to the fact that it had been a major task to write a simple formula relating the trajectory to the initial state. The main area of concern is to establish properties of the equilibrium points by studying how scalar functions of the state evolve as the system state evolve. In this chapter, we give a brief review of the stability of equilibria. Firstly, in Section 3.1 we will discuss the concept of stability. Then, in Section 3.2 we present a number of definitions of stability. Lastly, in Section 3.3 we will introduce the Lyapunov's direct method and its proof.

3.1 The stability of equilibrium points

Stability theory is developed to examine dynamical systems under small disturbance as time approaches infinity. This idea of stability is considered in a qualitative context, in which the behaviour of equilibrium points can be investigated locally and extended globally. The qualitative method of stability is the simplest method to summarize and manipulate non-linear systems as trajectories oscillate in the neighbourhood of the equilibrium point. The idea above is illustrated by the figures below [16].

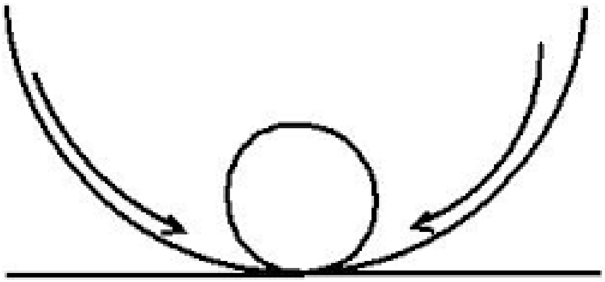

Figure 3.1: Stable equilibrium point

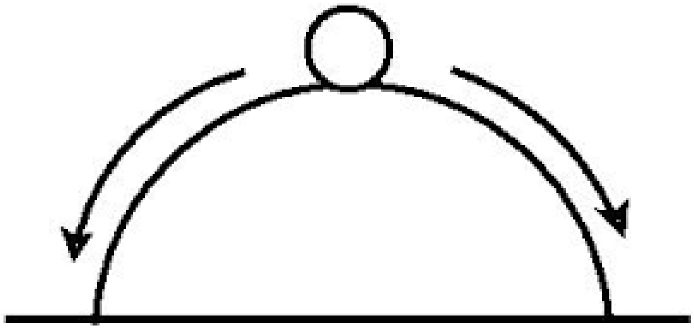

Figure 3.2: Unstable equilibrium point

That is, if a marble ball is placed near an equilibrium point of the system in Figure 3.1, then the ball will settle down at that equilibrium point, illustrating the concept of stability or, more precisely, asymptotic stability. Similarly, if a marble ball is placed near an equilibrium point of the system in Figure 3.2, then the ball will move away from the point, illustrating the concept of instability due to high acceleration.

3.2 Some definitions of stability

Consider the nonlinear autonomous dynamical system (3.1), where $\mathbf{x} \in D \subseteq \mathbb{R}^n$ and $\mathbf{f} : D \longrightarrow \mathbb{R}^n$ a locally Lipschitz continuous function from an open domain $D \subseteq \mathbb{R}^n$ to $\mathbb{R}^n$. For the system (3.1), an equilibrium point $\mathbf{x}^*$ can be classified as stable or unstable. Without loss of generality, it can be assumed that $\mathbf{x}^*$ is at the origin, i.e $\mathbf{x}^* = \mathbf{0}$. This is because any equilibrium point can be shifted to the origin by means of simple coordinate transformation (change of variables). If $\zeta = \mathbf{x} - \mathbf{x}^*$, then the derivative of ζ is given by $\dot{\zeta} = \mathbf{f}(\zeta + \mathbf{x}^*) = \mathbf{g}(\zeta)$. Thus, with the new variable ζ, the stability of the system can be studied with respect to an equilibrium point at the origin.

The following definitions are presented to understand different types of stability of equilibrium points [21, 15, 30].

Definition 14. [***Stability in the sense of Lyapunov***]
An equilibrium point $\mathbf{x}^*$ of the system (3.1) is said to be stable (in the sense of Lyapunov) if for any given $\varepsilon > 0$, there is $\delta > 0$ such that for any $t \geq 0$, we have that $\| \mathbf{x}(0) - \mathbf{x}^* \| < \delta$ implies $\| \mathbf{x}(t) - \mathbf{x}^* \| < \varepsilon$, where $\mathbf{x}(t)$ is the solution trajectory subject to the initial condition $\mathbf{x}(0)$.

In other words, stability in the sense of Lyapunov means that solution trajectories starting within the δ-neighbourhood of the equilibrium point $\mathbf{x}^*$ remain forever in some ε-neighbourhood. Asymptotic stability on the other hand means that solution trajectories that start close enough to equilibrium points not only stay close enough but eventually converge to it. More precisely, we have the following definition:

Definition 15. [***Asymptotic stability***]
An equilibrium point $\mathbf{x}^*$ of the system (3.1) is called an asymptotically stable equilibrium point if
(i) Definition 14. holds, and if
(ii) there exist $\delta_1 > 0$ such that $\| \mathbf{x}(t) - \mathbf{x}^* \| < \delta_1$, then

$$\lim_{t \to \infty} \| \mathbf{x}(t) - \mathbf{x}^* \| = 0, \tag{3.2}$$

i.e $\mathbf{x}(t)$ converges to $\mathbf{x}^*$ as $t \to \infty$.
In this case, $\mathbf{x}^* = 0$ is said to be locally attractive.

Definition 16. [***Global asymptotic stability***]
An equilibrium point $\mathbf{x}^*$ of the system (3.1) is called a globally asymptotically stable equilibrium point iff
(i) Definition 14. holds for all $x(0) \in \mathbb{R}^n$, and
(ii) Definition 16. holds for all $x(0) \in \mathbb{R}^n$.

Local stability can be extended to a stability in a global sense.

Definition 17. [***Global stability***]
An equilibrium point $\mathbf{x}^* = 0$ is globally stable if it is stable for all initial conditions $\mathbf{x}_0 \in \mathbb{R}^n$.

Finally, one can refer to an equilibrium point as being unstable, if it is not stable.

Definition 18. [***Instability***]
An equilibrium point $\mathbf{x}^*$ *of the system (3.1) is said to be unstable if there is* $\varepsilon > 0$, *such that for all* $\delta \geq 0$ *there is* $t > 0$ *such that* $\| x(0) - \mathbf{x}^* \| < \delta \wedge \| x(t) - \mathbf{x}^* \| \geq \varepsilon$.

Particularly, in the local concept, if at least one trajectory exits outside the neighbourhood of the equilibrium point, then instability occurs.

The stability definitions 14. and 16. above describe the behaviour of a system near an equilibrium point, and Definition 17 extends the stability in a global sense. Figures $3.3 - 3.5$ sum up this section.

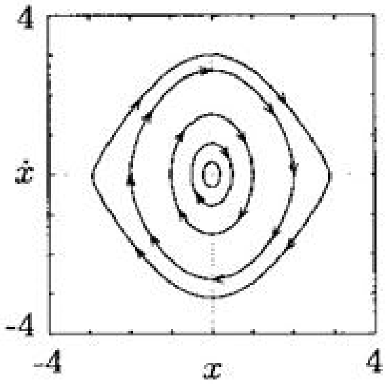

Figure 3.3: Stability in the sense of Lyapunov

Figure 3.3, illustrates stability in the sense of Lyapunov [15]. Figure 3.4 and Figure 3.5 illustrate asymptotic stability and an unstable spiral respectively [15].

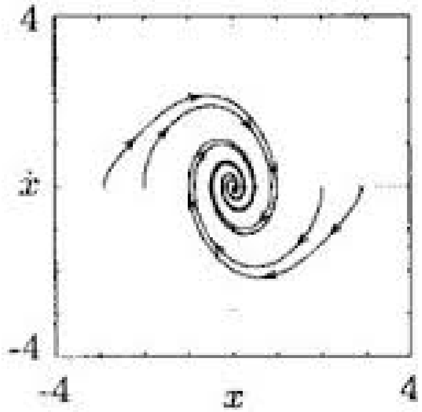

Figure 3.4: Asymptotic stability

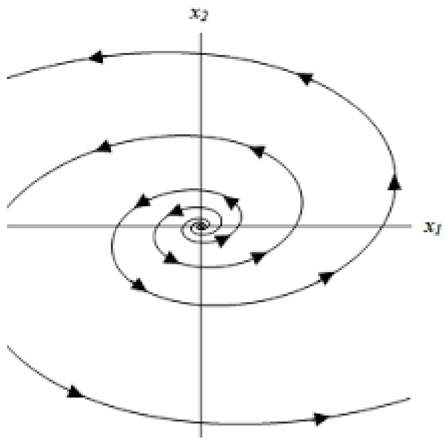

Figure 3.5: Unstable (Spiral)

3.3 Lyapunov's Direct Method

Lyapunov's direct method (also known as Lyapunov second method) provides a way of analysing the stability of nonlinear systems without actually solving the differential equations. The idea behind Lyapunov's direct method is that the system is stable if there exists some Lyapunov function in the neighbourhood of the equilibrium point. Thus it can be shown that Lyapunov's direct method is a sufficient condition for the stability of nonlinear system.

Consider system 3.1 and let $V : D \longrightarrow \mathbb{R}$ be a continuously differentiable function, defined on the domain $D \subset \mathbb{R}^n$ containing a fixed point $\mathbf{x}^*$. The derivative of the function $V(\mathbf{x})$ along the trajectories of (3.1) is defined as:

$$\begin{aligned} \dot{V}(\mathbf{x}) = \frac{dV(\mathbf{x})}{dt} &= \left[\frac{\partial V(\mathbf{x})}{\partial x_1}, \frac{\partial V(\mathbf{x})}{\partial x_2}, \ldots\ldots, \frac{\partial V(\mathbf{x})}{\partial x_n}\right]^T \dot{\mathbf{x}} \\ &= \nabla V(\mathbf{x}) \cdot \mathbf{f}(\mathbf{x}) \end{aligned} \tag{3.3}$$

where $\nabla V(\mathbf{x})$ is the gradient vector or Jacobian of V with respect to $\mathbf{x}$ [25]. The necessary condition of the Lyapunov stability theory is that all the trajectories of the system decrease along the graph of $V(\mathbf{x})$ toward $\mathbf{x}^*$, i.e $\dot{V}(\mathbf{x}) < 0$, $\forall x$.

To develop Lyapunov's direct method, we will need the following definitions [2].

Definition 19. [***Locally positive semidefinite function***]
Let $V : \mathbb{R}^n \longrightarrow \mathbb{R}$ be a continuously differentiable real valued function. Then $V(\mathbf{x})$ is said to be a locally positive semi-definite function if

(a) $V(\mathbf{x}^*) = \mathbf{0}$*, and*

(b) $V(\mathbf{x}) \geq \mathbf{0}$ *for all* $\mathbf{x} \neq \mathbf{x}^*$.

More strictly, we have the following definition.

Definition 20. [***Locally positive definite function***]
Let $V : \mathbb{R}^n \longrightarrow \mathbb{R}$ *be a continuously differentiable real valued function. Then* $V(\mathbf{x})$ *is said to be a locally positive definite function if*

(a) $V(\mathbf{x}^*) = \mathbf{0}$*, and*

(b) $V(\mathbf{x}) > \mathbf{0}$ *for all* $\mathbf{x} \neq \mathbf{x}^*$.

Remark 3.1. *The function* $V(\mathbf{x})$ *is locally negative definite, if* $-V(\mathbf{x})$ *is locally positive definite. Similarly,* $V(\mathbf{x})$ *is locally negative semi-definite, if* $-V(\mathbf{x})$ *is locally positive semi-definite.*

This brings us to what is known as Lyapunov's direct method.

Theorem 3.2. [***Lyapunov's Direct Method***]
Consider system (3.1). Let D be an open subset of $\mathbb{R}^n$ *containing* $\mathbf{x}^* = 0$*, where* $\mathbf{f}(\mathbf{x}^*) = \mathbf{0}$*. Furthermore, suppose that* $V : D \longrightarrow \mathbb{R}$ *is a real valued positive-definite function. Then*

(a) if $\dot{V}(\mathbf{x}) \leq \mathbf{0}$ *for all* $\mathbf{x} \in D$*, then* $\mathbf{x}^*$ *is stable.*

(b) if $\dot{V}(\mathbf{x}) < \mathbf{0}$ *for all* $\mathbf{x} \in D - \{\mathbf{x}^*\}$*, then* $\mathbf{x}^*$ *is asymptomatically stable.*

Proof. (a) Let $\varepsilon > 0$. We want to show that there exists $\delta > 0$ such that if $\mathbf{x}(0) \in B_\delta(0)$, then we have that $\mathbf{x}(t) \in B_\varepsilon(0)$ for all $t > 0$. i.e $\forall \varepsilon > 0, \exists \delta > 0$ such that if $\| \mathbf{x}(0) \| < \delta$, then $\| \mathbf{x}(t) \| < \varepsilon$ holds for all $t > 0$. Here $\mathbf{x}(0) = \mathbf{x}_0$ is the initial condition and $\mathbf{x}(t)$ is the trajectory of the system (3.1).

Let $\varepsilon_1 > 0$ and choose $r \in (0, \varepsilon_1]$ such that $B_r = \{x \in \mathbb{R}^n | \| x \| \leq r\} \subset D$. Define

$$\alpha = \min_{\|\mathbf{x}\| = \varepsilon_1} V(\mathbf{x}). \tag{3.4}$$

Since $V(\mathbf{x})$ is continuous, α is well defined and positive. Choose $\delta \in (0, \varepsilon_1]$ such that $\| \mathbf{x} \| < \delta$ and $V(\mathbf{x}) < \alpha$. Given that α is positive and $V(\mathbf{x})$ is continuous such a δ always exists. Now, consider the initial condition $\mathbf{x}_0$ such that $\| \mathbf{x}_0 \| < \delta$, $V(\mathbf{x}_0) < \alpha$ and let $\mathbf{x}(t)$ be the resulting trajectory. Since $\dot{V}(\mathbf{x}) \leq 0$, $V(\mathbf{x}(t)) < \alpha$. Suppose now that there exists a t_1 such that $\| \mathbf{x}(t_1) \| > \varepsilon_1$. then by continuity we have that at an earlier time t_2, $\| \mathbf{x}(t_2) \| = \varepsilon_1$ and

$$\min_{\|\mathbf{x}_0\|=\varepsilon_1} \| V(\mathbf{x}) \| = \alpha > V(\mathbf{x}(t_2)) \tag{3.5}$$

which is a contradiction and thus stability in the sense of Lyapunov follows.

(b) To prove asymptotic stability, we choose $\delta > 0$ such that $\| \mathbf{x}_0 \| < \delta$ for all initial conditions $\mathbf{x}_0$. We show that $V(\mathbf{x}(t)) \to 0$ as $t \to \infty$. Suppose that $\mathbf{x}_0$ satisfies $\| \mathbf{x}_0 \| < \delta$, and $\mathbf{x}(t)$ is the resulting trajectory. Since $\dot{V}(\mathbf{x}) < 0$ and $V(\mathbf{x}(t)) \geq 0$, then if follows that $V(\mathbf{x}(t)) \to c$ for some $c \geq 0$. We want to show that c is zero.

To this end, suppose that $c > 0$ and define S as follows

$$S = \{\mathbf{x} \in \mathbb{R}^n | V(\mathbf{x}) \leq c\} \tag{3.6}$$

and let $T_\alpha \subset S$ be a ball of radius α,

$$T_\alpha = \{\mathbf{x} \in \mathbb{R}^n | \, \| \mathbf{x} \| < \alpha\} \tag{3.7}$$

Since $V(\mathbf{x}(t))$ is monotonically decreasing and bounded from below by c for all t, then $\mathbf{x}(t) \notin T_\alpha$. Introduce

$$-\gamma = \max_{\alpha \leq \|\mathbf{x}\| \leq \varepsilon} \dot{V}(\mathbf{x}). \tag{3.8}$$

Clearly $-\gamma < 0$. Since $\dot{V}(\mathbf{x})$ is locally negative definite, we observe that,

$$V(\mathbf{x}(t)) = V(\mathbf{x}(0)) + \int_0^t \dot{V}(\mathbf{x}(\tau))d\tau \leq V(\mathbf{x}(0)) - \gamma t, \tag{3.9}$$

which implies that $V(\mathbf{x}(t))$ will be negative, which is a contradiction. Thus it follows that c is zero, resulting in asymptotic stability. □

A Lyapunov function is defined as follows.

Definition 21. ***[Lyapunov function]***
A continuously differentiable real-valued function $V : D \subseteq \mathbb{R}^n \longrightarrow \mathbb{R}$ satisfying the conditions in Theorem 3.2. is called a Lyapunov function.

Chapter 4

Basic reproduction number

4.1 Introduction

In epidemiology, stability theory is used to understand different infectious diseases as well as predicting their transmission. In depicting the transmission of infectious diseases, the population is commonly divided into susceptible (S), infectious (I), exposed (E) and recovered (R) individuals, see [17]. The key concept in epidemiology is the basic reproduction number. The basic reproduction number, usually denoted by $\mathscr{R}_0$, is defined as the average number of secondary infections produced by a single individual during his or her entire infectious period, in a fully susceptible population. Mostly, the basic reproduction number plays the role of a threshold parameter that predicts whether the disease will spread or die out. If $\mathscr{R}_0 > 1$, then introducing an infected individual into a population results in an epidemic (the disease will spread throughout the population). If $\mathscr{R}_0 < 1$, then introducing a few infected individuals into a fully susceptible population will cause the disease to die out.

4.2 Next-generation matrix

The *next-generation matrix* is a general method of deriving $\mathscr{R}_0$, given by Diekmann et al. [7] and P. Driessche et al. [26]. This method is useful when the population can be divided into discrete, disjoint categories. Suppose there are $n > 0$ disease compartments and $m > 0$ non-disease compartments. Let $\mathscr{F}_i$ be the rate of new infections in the i^{th} disease compartment, and $\mathscr{V}_i$ be the transition term, normally death and recovery, in the i^{th} disease compartment.

We consider a general compartmental disease transmission model as described by P. Driessche [26] as follows;

$$x_i' = \mathscr{F}_i(x,y) - \mathscr{V}_i(x,y), \qquad i = 1, ..., n. \tag{4.1}$$

$$y_j' = g_j(x,y), \qquad j = 1, ..., m. \tag{4.2}$$

where $x = (x_1, ..., x_n)^T \in \mathbb{R}^n$ represent the population in the disease compartment and $y = (y_1, ..., y_m)^T \in \mathbb{R}^m$ represent the population in the non-disease compartment.

The following assumptions, as presented in [8, 23], are made to ensure the well-posedness of the model and the existence of the disease-free equilibrium.

$(A1)$ Assume $\mathscr{F}_i(0,y) = \mathscr{V}_i(0,y) = 0$ for all $y \geq 0$ and $i = 1, ..., n$.
No new infections into the disease compartments.

$(A2)$ Assume $\mathscr{F}_i(x,y) \geq 0$ for all nonnegative x and y and $i = 1, ..., n$.
The function $\mathscr{F}$ represents new infections and cannot be negative.

$(A3)$ Assume $\mathscr{V}_i(x,y) \leq 0$ whenever $x_i = 0$, $i = 1, ..., n$.

$(A4)$ Assume $\sum_{i=1}^{n} \mathscr{V}_i(x,y) \geq 0$ for all $x_i \geq 0$ and $y_i \geq 0$.
The sum is the net outflow from infected compartments.

$(A5)$ Assume the disease-free system $y' = g(0,y)$ has a unique equilibrium that is globally asymptotically stable. That is, all solutions with initial conditions of the form $(0,y)$ approach a point $(0,y_o)$ as $t \to \infty$. We refer to this point as the disease-free equilibrium.

Using assumptions $(A1)-(A5)$, we can define $n \times n$ matrices F and V as,

$$F = \left[\frac{\partial \mathscr{F}_i}{\partial x_j}(0,y_o)\right] \tag{4.3}$$

and

$$V = \left[\frac{\partial \mathscr{V}_i}{\partial x_j}(0,y_o)\right]. \tag{4.4}$$

The disease compartments, x, can be separated from the remaining equations and the general system can be written as

$$x' = (F - V)x. \tag{4.5}$$

If $F = 0$, that is, there are no new infections, then

$$x' = -Vx, \quad x(0) = x_0, \tag{4.6}$$

and hence

$$x = x_0 \exp(-Vt). \tag{4.7}$$

The expected number of secondary infectious produced by the index case spends in each compartment is given by the following integral [8]

$$\int_0^\infty F \exp(-Vt) x_o dt = FV^{-1} x_o. \tag{4.8}$$

Assuming that $F \geq 0$ and $V^{-1} \geq 0$, the matrix

$$\mathscr{K} = FV^{-1} \tag{4.9}$$

is called the **next-generation matrix**, and the spectral radius of $\mathscr{K}$ gives the basic reproduction number, $\mathscr{R}_o = \rho(FV^{-1})$. The next-generation matrix is nonnegative and therefore has a nonnegative eigenvalue and a corresponding nonnegative eigenvector. This follows from *Perron-Frobenius theorem* [3], stated below without a proof. Readers interested in the proof can consult [3].

Theorem 4.1. [***Perron-Frobenius theorem***]
Let $\mathscr{K}$ be a matrix whose elements are nonnegative, and such that for some positive integer l, every element of the matrix $\mathscr{K}^l$ is positive. Then $\mathscr{K}$ has a simple positive eigenvalue λ_o with a corresponding eigenvector having all positive components, and $|\lambda_j| < \lambda_o$ for every other eigenvalue λ_j.

The following SEIR with relapse model is used here to illustrate the derivation of the basic reproduction number, $\mathscr{R}_o$. The formulation of this model is presented in [26].

$$
\begin{aligned}
S^{'} &= \kappa - \beta SI - dS, \\
E^{'} &= \beta SI - (d+\varepsilon)E, \\
I^{'} &= \varepsilon E - (d+\gamma+\alpha)I + \eta R, \\
R^{'} &= \gamma I - (d+\eta)R,
\end{aligned} \tag{4.10}
$$

with nonnegative initial conditions. Equating the above ODEs to zero gives equilibrium points. The disease-free equilibrium of the model is given by $E_o = (S_o, 0, 0, 0) = (\frac{\kappa}{d}, 0, 0, 0)$. Using the next-generation matrix introduced in (4.9), we have the following

$$
F = \begin{bmatrix} 0 & \beta S_o & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},
$$

$$
V = \begin{bmatrix} d+\varepsilon & 0 & 0 \\ -\varepsilon & d+\gamma+\alpha & -\eta \\ 0 & -\gamma & d+\eta \end{bmatrix}.
$$

The inverse of V is given by

$$
V^{-1} = \frac{1}{(d+\varepsilon)((d+\alpha)(d+\eta)+d\gamma)} \begin{bmatrix} (d+\eta)(d+\gamma+\alpha)-\eta\gamma & 0 & 0 \\ \varepsilon(d+\eta) & -(d+\varepsilon)(d+\eta) & \eta(d+\varepsilon) \\ \varepsilon\gamma & -\gamma(d+\varepsilon) & (d+\varepsilon)(d+\gamma+\varepsilon) \end{bmatrix},
$$

so that the next-generation matrix is calculated as

$$
\mathscr{K} = FV^{-1} = \begin{bmatrix} \frac{\beta S_o \varepsilon(d+\eta)}{(d+\varepsilon)((d+\alpha)(d+\eta)+d\gamma)} & \frac{-\beta S_o(d+\eta)}{(d+\alpha)(d+\eta)+d\gamma} & \frac{\beta S_o \eta}{(d+\alpha)(d+\eta)+d\gamma} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}.
$$

Thus the basic reproduction number is given by the spectral radius of FV^{-1} as

$$
\mathscr{R}_o = \rho(FV^{-1}) = \frac{\beta S_o \varepsilon(d+\eta)}{(d+\varepsilon)((d+\alpha)(d+\eta)+d\gamma)}. \tag{4.11}
$$

Using the basic reproduction number in (4.11), it follows that if $\mathscr{R}_o < 1$ then disease-free equilibrium is stable, and it is unstable if $\mathscr{R}_o > 1$. This idea will be shown through the following lemmas [26].

Lemma 4.2. *If K has the Z-sign pattern, then $K^{-1} \geq 0$ if and only if K is a nonsingular $M-$matrix.*

Proof. By assumptions (A1) and (A2), it follows that F is nonnegative, and by assumption (A3) V has the $Z-$sign patten. That is the off-diagonal entries of V are negative or zero. In addition, assumption (A4) together with assumption (A1) ensures that the column sums of V are positive or zero. Using the fact that V has a $Z-$sign patten, we get that V is a $M-$matrix. So, by assuming that V is a nonsingular $M-$matrix, implies that $V^{-1} \geq 0$. Hence $K = FV^{-1}$ is nonnegative. □

Lemma 4.3. *If F is nonnegative and V is a nonsingular M-matrix, then* $\mathscr{R}_o = \rho(FV^{-1}) < 1$ *if and only if all eigenvalues of* $(F-V)$ *have negative real parts.*

Proof. Let F be nonnegative and V be a nonsingular $M-$matrix. Then by the lemma 4.2 $V^{-1} \geq 0$. That is, $(I - FV^{-1})$ has the $Z-$sign patten, where I denotes the identity matrix. Since $(I - FV^{-1})$ has the $Z-$sign patten, then by lemma 4.2, we have that $(I - FV^{-1})^{-1} \geq 0$ if and only if $\rho(FV^{-1}) < 1$. Let $(V-F)^{-1} = V^{-1}(I - FV^{-1})^{-1}$ and $(V-F)^{-1} = I + F(V-F)^{-1}$. Then $(V-F)^{-1} \geq 0$ if and only if $(I - FV^{-1})^{-1} \geq 0$. In addition $(V-F)^{-1} \geq 0$ if and only if $(V-F)$ is nonsingular. Since the eigenvalues of a nonsingular $M-$matrix all have positive parts, then the result follows. □

Theorem 4.4. *Consider the disease transmission model given by (4.1). The disease-free equilibrium of (4.1) is locally asymptotically stable if* $\mathscr{R}_o < 1$*, but unstable if* $\mathscr{R}_o > 1$*, where* $\mathscr{R}_o$ *is as defined in (4.11).*

Proof. Let F and V be defined as in (4.3) and (4.4), and let J_{21} and J_{22} bethe matrices of partial derivatives of g in (A5), evaluated at the disease-free equilibrium. Consider the Jacobian matrix,

$$J = \begin{bmatrix} F-V & 0 \\ J_{21} & J_{22} \end{bmatrix}.$$

Then the disease-free equilibrium is locally asymptotically stable if and only if the eigenvalues of J have negative real parts. The eigenvalues of J are those of $F-V$ and J_{22} which all have negative real parts by assumption (A5). Thus by Lemma4.3, this is only possible if and only if $\rho(FV^{-1}) < 1$. Hence the disease-free equilibrium is locally asymptotically stable if $R_o < 1$.

If $R_o \leq 1$, then $\forall \varepsilon > 0$, $((1+\varepsilon)I - FV^{-1})$ is nonsingular $M-$matrix, which implies that $((1+\varepsilon)I - FV^{-1})^{-1} \geq 0$ and all eigenvalues of $((1+\varepsilon)V - F)$ have positive real parts. Taking $\varepsilon > 0$ arbitrary, it will follow that $V-F$ have eigenvalues with nonnegative real parts. Reversely, suppose that $V-F$ have eigenvalues with nonnegative real parts, then $\forall \varepsilon > 0$, $(V + \varepsilon I - F)$ is a nonsingular $M-$matrix, and thus by Lemma 4.3 $\rho(F(V+\varepsilon I)^{-1}) < 1$. Thus $(F-V)$ has atleast one eigenvalue with a positive real part if and only if $\rho(FV^{-1}) > 1$, implying the instability of the disease-free equilibrium. $\square$

Chapter 5

Global stability of disease-free equilibrium

In this chapter, we will discuss global stability of the disease-free equilibrium by means of an example. Consider the following vector-host model [26],

$$\begin{aligned} I_h' &= \beta_h S_h I_v - (\mu_h + \gamma) I_h, \\ I_v' &= \beta_v S_v I_h - \mu_v I_v, \\ S_h' &= \Lambda_h - \mu_h S_h - \beta_h S_h I_v + \gamma I_h, \\ S_v' &= \Lambda_v - \mu_v S_v - \beta_v S_v I_h, \end{aligned} \tag{5.1}$$

This is a simplest vector-host model that couples a simple *SIS* model for the host population with an *SI* model for the vectors. Transmission happens indirectly from host to host through a vector. A susceptible host (S_h) becomes infectious host (I_h) at the rate $\beta_h S_h I_v$, and a susceptible vector (S_v) becomes infectious host (I_v) through contact with an infected host (I_h) at the rate $\beta_v S_v I_h$.

In this section a Lyapunov function is constructed to study the global stability of the disease-free equilibrium of the model (5.1). Following [8], a matrix-theoretic method is used to guide the construction. Set

$$f(x,y) = (F-V)x - \mathscr{F}(x,y) + \mathscr{V}(x,y). \tag{5.2}$$

The disease compartment can be written as

$$x' = (F-V)x - f(x,y). \tag{5.3}$$

For the vector-host model (5.1), the disease component is $x = (I_h, I_v)^T$, and the nondisease component is $y = (S_h, S_v)^T$. Given that the initial conditions of the system (5.1) are

$$S_h(0) > 0, I_h(0) \geq 0, S_v(0) > 0, I_v(0) \geq 0, \tag{5.4}$$

we can define a feasible region $\varGamma$ such that

$$\varGamma = \{(I_h, I_v, S_h, S_v) \in \mathbb{R}^4_+ : 0 \leq I_h + S_h = \frac{\Lambda_h}{\mu_h}, 0 \leq I_v + S_v = \frac{\Lambda_v}{\mu_v}\}. \tag{5.5}$$

We then have the following theorem.

Theorem 5.1. *The feasible region $\varGamma$, with the initial conditions in (5.4), is positively invariant and attracting.*

Proof. Since the right hand side of the system (5.1) is Lipschitz continuous then solutions exist and are unique.

For $i = 1$, $f_1(S_h, I_h, S_v, I_v) = \Lambda_h - \mu_h S_h - \beta_h S_h I_v + \gamma I_h$. If $S_h = 0$, then $f_1(0, I_h, S_v, I_v) = \Lambda_h + \gamma I_h$. Considering $I_h, S_v, I_v \geq 0$, $f_1(0, I_h, S_v, I_v) \geq 0$ and thus $S_h(t) \geq 0$ for all t for which it exists.

For $i = 2$, $f_2(S_h, I_h, S_v, I_v) = \beta_h S_h I_v - (\mu_h + \gamma) I_h$. If $I_h = 0$, then $f_2(S_h, 0, S_v, I_v) = \beta_h S_h I_v$. Considering $S_h, S_v, I_v \geq 0$, $f_2(S_h, 0, S_v, I_v) \geq 0$ and thus $I_h(t) \geq 0$ for all t for which it exists.

For $i = 3$, $f_3(S_h, I_h, S_v, I_v) = \Lambda_v - \mu_v S_v - \beta_v S_v I_h$. If $S_v = 0$, then $f_3(S_h, I_h, 0, I_v) = \Lambda_v$. Considering $S_h, I_h, I_v \geq 0$, $f_3(S_h, I_h, 0, I_v) \geq 0$ and thus $S_v(t) \geq 0$ for all t for which it exists.

For $i = 4$, $f_4(S_h, I_h, S_v, I_v) = \beta_v S_v I_h - \mu_v I_v$. If $I_v = 0$, then $f_4(S_h, I_h, S_v, 0) = \beta_v S_v I_h$. Considering $S_h, I_h, S_v \geq 0$, $f_4(S_h, I_h, S_v, 0) \geq 0$ and thus $I_v(t) \geq 0$ for all t for which it exists.

Therefore given the initial conditions in (5.4), the solutions $I_h(t), I_v(t), S_v(t), S_h(t)$ are positive for all t for which they exist. Adding S_h' and I_h' gives

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h, \tag{5.6}$$

and by adding S_v' and I_v' gives

$$\frac{dN_v}{dt} = \Lambda_v - \mu_v N_v. \tag{5.7}$$

Solving (5.6) and (5.7), and taking the limit as $t \to \infty$ yields

$$N_h(t) = \frac{\Lambda_h}{\mu_h} - \frac{N_h(0)e^{-\mu_h t}}{\mu_h}, \tag{5.8}$$

so that

$$\lim_{t\to\infty} N_h(t) = \frac{\Lambda_h}{\mu_h} = S_{ho}. \tag{5.9}$$

Similarly

$$N_v(t) = \frac{\Lambda_v}{\mu_v} - \frac{N_v(0)e^{-\mu_v t}}{\mu_v}, \tag{5.10}$$

so that

$$\lim_{t\to\infty} N_v(t) = \frac{\Lambda_v}{\mu_v} = S_{vo}. \tag{5.11}$$

Therefore the region Γ is positively invariant. Furthermore, if $N_h(0) > S_{ho}$ and $N_v(0) > S_{vo}$, then either the solution enter Γ in finite time, or $N_h(t)$ approaches S_{ho} and $N_v(t)$ approaches S_{vo} asymptotically. Hence, the region Γ attract all solutions in $\mathbb{R}^4_+$. $\square$

The disease-free equilibrium of the model (5.1) is $E_o = (S_{ho}, 0, S_{vo}, 0) = (\frac{\Lambda_h}{\mu_h}, 0, \frac{\Lambda_v}{\mu_v}, 0)$.

$$\mathscr{F}(x,y) = \begin{bmatrix} \beta_h S_h I_v \\ \beta_v S_v I_h \end{bmatrix},$$

and

$$\mathscr{V}(x,y) = \begin{bmatrix} (\mu_h + \gamma) I_h \\ \mu_v I_v \end{bmatrix}.$$

Using the next-generation matrix, introduced in (4.3) and (4.4), we have that

$$F = \begin{bmatrix} 0 & \beta_h S_{ho} \\ \beta_v S_{vo} & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} (\mu_h + \gamma) & 0 \\ 0 & \mu_v \end{bmatrix},$$

and

$$V^{-1} = \begin{bmatrix} \frac{1}{(\mu_h+\gamma)} & 0 \\ 0 & \frac{1}{\mu_v} \end{bmatrix}.$$

The next-generation matrix is therefore given as

$$\mathscr{K} = FV^{-1} = \begin{bmatrix} 0 & \frac{\beta_h S_{ho}}{\mu_v} \\ \frac{\beta_v S_{vo}}{(\mu_h+\gamma)} & 0 \end{bmatrix}.$$

Thus, the basic reproduction number is given by the spectral radius of FV^{-1} as

$$\mathscr{R}_o = \rho(FV^{-1}) = \sqrt{\frac{\beta_h S_{ho} \beta_v S_{vo}}{\mu_v(\mu_h+\gamma)}}. \tag{5.12}$$

The left eigenvector of the nonnegative matrix, $V^{-1}F$, is $\omega^T = (\frac{(\mu_h+\gamma)}{\beta_h S_{ho}}\mathscr{R}_o, 1)$, and

$$f(x,y) = \begin{bmatrix} \beta_h I_v (S_{ho} - S_h) \\ \beta_v I_h (S_{vo} - S_v) \end{bmatrix}.$$

Notice that $f(x,y) \geq 0$ in $\Gamma = \{(I_h, I_v, S_h, S_v) \in \mathbb{R}^4_+ : 0 \leq I_h + S_h = \frac{\Lambda_h}{\mu_h}, 0 \leq I_v + S_v = \frac{\Lambda_v}{\mu_v}\}$, if $S_h \leq S_{ho}$ and $S_v \leq S_{vo}$, and $f(0, y_o) = 0$. Since $F \geq 0$, $V^{-1} \geq 0$ and $f(x,y) \geq 0$. By Theorem 2.1 of [8], $Q = \omega^T V^{-1} x$ is the Lyapunov function, where $\omega^T = (\frac{(\mu_h+\gamma)}{\beta_h S_{ho}}\mathscr{R}_o, 1)$ is the left eigenvector of the matrix $V^{-1}F$. Straightforward calculation gives

$$Q = \frac{\mathscr{R}_0 I_h}{\beta_h S_{ho}} + \frac{I_v}{\mu_v}, \tag{5.13}$$

which is the Lyapunov function for the model (5.1). The following Theorem is needed to establish the GAS of the disease-free equilibrium.

Theorem 5.2. *The disease-free equilibrium of the model (5.1) is globally asymptotically stable in Γ if $\mathscr{R}_o \leq 1$.*

Proof. Let $Q = \frac{\mathscr{R}_0 I_h}{\beta_h S_{ho}} + \frac{I_v}{\mu_v}$ be a Lyapunov function for the model (5.1) on Γ with $\mathscr{R}_o < 1$ and $f(x,y) \geq 0$. Then by differentiating Q along solutions of (5.1), gives

$$\begin{aligned} Q' &= \omega^T V^{-1} x' \\ &= \omega^T V^{-1}(F - V)x - \omega^T V^{-1} f(x,y) \\ &= (\mathscr{R}_o - 1)\omega^T x - \omega^T V^{-1} f(x,y) \\ &= (\mathscr{R}_o - 1)(I_h + \tfrac{\mu_v I_v \mathscr{R}_o}{\beta_h S_{ho}}) - \tfrac{\beta_h I_v (S_{ho} - S_h)}{(\mu_h+\gamma)} - \tfrac{\beta_v I_h}{\beta_h I_{ho}}(S_{vo} - S_v)\mathscr{R}_o \end{aligned} \tag{5.14}$$

Thus it follows that $Q' \leq 0$ if $\mathscr{R}_o \leq 1$. If $\mathscr{R}_0 = 1$ then $Q' = 0$ if and only if
$I_h = I_v = 0$. If $\mathscr{R}_0 = 1$ then $Q' = 0$ if and only if case1: $I_h = I_v = 0$, case2: $I_h = 0$

and $S_{ho} = S_h$ and case3: $I_v = 0$ and $S_{vo} = S_v$. Therefore every solution trajectory of equations in the model (5.1) converges to the largest compact invariant set $M = \{(S_{ho}, I_h, S_{vo}, I_v)\}$, and the only point in M is the disease-free equilibrium. Then by LaSalle's invariant principle [20], E_o is globally asymptotically stable in $\mathit{\Gamma}$ if $\mathscr{R}_o \leq 1$. That is every solution trajectory of equations in the model (5.1) approaches E_o as $t \to \infty$. $\square$

Chapter 6

Conclusion and recommendations

6.1 Conclusion

In this thesis, Lyapunov's direct method has shown success in the study of global stability of nonlinear autonomous dynamical systems. The method indicate that if there is a Lyapunov function V in the neighbourhood of an equilibrium point such that $\dot{V} < 0$, then the equilibrium point $\mathbf{x}^*$ is globally asymptotically stable. Specific epidemiological models were used to demonstrate the construction of Lyapunov functions. In doing so, a matrix-theoretic method was presented to guide construction of Lyapunov functions. The method additionally demonstrated the construction of the basic reproduction number, $\mathscr{R}_0$, for the SEIR model. It was pointed out that the disease-free equilibrium (DFE) is locally asymptotically stable if $\mathscr{R}_0 < 1$, but unstable if $\mathscr{R}_0 > 1$.

A Lyapunov function was constructed for the Vector-Host model. The results indicated that the DFE is globally asymptotically stable when $\mathscr{R}_0 \leq 1$ (i.e. every solution trajectory of the Vector-Host model converges to the largest compact invariant set $M = \{(S_{ho}, I_h, S_{vo}, I_v)\}$) and unstable when $\mathscr{R}_0 > 1$.

6.2 Recommendations

Throughout this thesis, attention has been drawn to studying the global stability of the disease free equilibrium. For the Vector-Host model considered, we notice that solution trajectories converge to the largest compact invariant set. In terms of recommendations for future research, one may look at what is really happening to solution trajectories once they are in the invariant set.

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