ANALYSIS OF THRESHOLD DYNAMICS OF EPIDEMIC MODELS IN A PERIODIC ENVIRONMENT

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ABSTRACT

ANALYSIS OF THRESHOLD DYNAMICS OF EPIDEMIC MODELS IN A PERIODIC ENVIRONMENT

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Threshold dynamics used to control the spread of the disease in infectious disease phenomena has an overwhelming importance and interest in mathematical epidemiology. One of the famous threshold quantity is known to be the basic reproduction ratio. Its formulation as well as computation is the main concern of infectious diseases.

The aim of this thesis is to analyze the basic reproduction ratio in both autonomous and periodic systems via defining R_0 as the spectral radius of the next generation operator.

This thesis presents the vector host model for the diseases Dengue fever and avian influenza. As emerging of the diseases shows periodicity, systems of periodic ordinary differential equations are considered for both types of diseases. Simple implementation of the time-averaged systems gives rise to the comparison of these with the periodic systems. Thus, we investigate the occurence of the existence of underestimation or overestimation of the basic reproduction ratio in time-averaged systems.

Keywords: Threshold dynamics, basic reproduction ratio, periodicity, compartmental models, time averaged systems

ÖZ

EPİDEMİK MODELLERİN EŞİK DEĞER DİNAMİĞİNİN PERİODİK ÇEVREDE ANALİZİ

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Bulaşıcı hastalıklarda hastalığın yayılmasını kontrol etmek için kullanılan eşik değer dinamiği matematiksel epidemiolojide büyük bir öneme ve ilgiye sahiptir. En bilinen eşik değerlerinden biri, esas çoğalma oranıdır. Onun hesaplanmasının yanı sıra formüllenmesi de bulaşıcı hastalıkların temel sorunudur.

Bu tezin amacı, R_0'yı yeni nesil operatörün spektral yarıçapı olarak tanımlayarak hem zamandan bağımsız hem de periodik zamanlı sistemlerde esas çoğalma oranını analiz etmektir.

Bu tez dang humması ve kuş gribi gibi hastalıklar için vektör-konak modelini sunmaktadır. Bulaşıcı hastalıkların ortaya çıkışı periyodiklik gösterdiğinden, bu iki hastalık için de periyodik adi diferansiyel denklemler gözönüne alındı. Zaman ortalamalı sistemlerin uygulama kolaylığı onları periyodik sistemlerle karşılaştırmaya yöneltti. Bu yüzden, esas çoğalma oranının zaman ortalamalı sistemlerde az tahmininin ya da aşırı tahmininin varlığının oluşumunu sorguladık.

Anahtar Kelimeler: eşik değer dinamiği, esas çoğalma oranı, periodiklik, kompartmansal modeller, zaman ortalamalı sistemler

To My Family

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INTRODUCTION

Mathematical epidemiology provides a way to understand the foundational structures that effect the spread of diseases and control strategies to prevent the spread of diseases. This branch differs from the most branches of epidemiology as it does not require experimental validation of the models investigated. Moreover, because of the unethical reasons, experiments become impossible to implement and compare strategies for anticipated epidemic, and it is almost inapplicable to deal with a disease outbreak in real time within an experimental setting. Thus, mathematical epidemiology gains great importance as a possible tool for dealing with diseases, specially with the infectious ones.

The first known development of mathematical epidemiology to infectious diseases is introduced by Daniel Bernuolli in [6] in 1760 as a defense of the study of vaccination against smallpox. After a long break, the first contribution in this branch seems to be made by P. D. En'ko between the years 1873 and 1894 by (see [13], for instance). Sir Ross by [24], Hamer by [16], McKendrick and Kermack by [1, 2, 3] establish the fundamentals of epidemiology constructed on compartmental models between 1900 and 1935. Compartmental models is one for which the individuals in a population are classified into compartments depending on their status with regard to the infection under study [11]. The basic and advanced material for the study of compartmental models can be found in [4, 8, 17, 23, 25].

The greatest concern for mathematical epidemiology is the threshold phenomena. The computation of nondimensional quantities which determine the nature of the disease dynamics have a long tradition in epidemiology [10]. Among all quantities, the basic reproduction ratio R_0 is arguably the most important quantity in infectious disease epidemiology [12]. This quantity can be defined as the expected number of secondary cases produced, in a completely susceptible population, by a typical infected individual during its entire period of infectiousness [11]. The famous threshold criterion then claims that the disease can invade if $R_0 > 1$, whereas it cannot if $R_0 < 1$.

The definition of R_0 is given by a next generation matrix (or operator) in [11]. Diekmann et al. [11] states that one can define a matrix, denoted by K, that relates the number of newly infected individuals in the various categories in consecutive generations. In the context, such a matrix is called the next generation

matrix and R_0 is defined to be the dominant eigenvalue of this matrix. Defining and computing of R_0 is studied by many researchers, as in [7, 9, 26, 14].

Another important concern in infectious disease epidemiology is periodicity: oscilatory behavior of the disease dynamics. This dynamics of infectious diseases can occur because of some factors such as seasonal weather changes, periodic gathering of people, or vaccination. Specificially, due to weather changes, contact rates for influenza may vary seasonally. Therefore, periodicity becomes an important issue for mathematical epidemiology. As a result, periodic models for infectious diseases are considered in many works as in [18] and [28].

This thesis brings together comparisons of basic reproduction ratios of time-averaged and periodic systems conducted by the articles [26] and [27]. In this thesis, we make use of these articles while using the notations and results related to basic reproduction ratios of time-averaged and periodic systems as well.

As a first contribution of this thesis, pest control strategy is applied to the autonomous model of Dengue fever with a vector-host model and differences between basic reproduction ratios of two systems is analyzed. Second, avian influenza is modeled by a nonautonomous vector-host model considering periodicity. Moreover, threshold dynamics of time-averaged and periodic system is analyzed and overestimation and underestimation cases of R_0 is examined.

This study is organized as follows: In Chapter 2, we review the foundations of dynamical systems. As we will be studying ordinary differential equations as a particular case of dynamical systems, we review the fundamental theory about flows and properties of ODEs. Lastly, we introduce the stability theory for ODEs.

Chapter 3 focuses on the periodicity in continuous dynamical systems. We review the Floquet theory and introduce the periodic solutions in linear systems.

In Chapter 4, we introduce the study of compartmental epidemic models described by autonomous systems. In addition to the vector-host model in [26], we introduce a pest control strategy as an eradication policy and examine its effectiveness on the basic reproduction ratio R_0.

After having reviewed the study in [27], Chapter 5 introduces the avian influenza as an epidemic model and adapts it to vector-host model. We compute R_0 of both time-averaged and periodic systems. Then we observe the overestimations and underestimations of R_0 in the time-averaged system.

As a conclusion in Chapter 6, we give a short summary of the overall study in this thesis and possible future work that can be carried out in the compartmental epidemic models of mathematical epidemiology.

CHAPTER 2

DYNAMICAL SYSTEMS

2.1 Introduction

This chapter reviews the dynamical systems in detail as discrete and continuous dynamical systems inspired by Martelli [20] and Meiss [21]. Besides, we give a revision of the fundamental theory of differential equations and flows as explained thoroughly in Liu [19] and Miller [22]. This revision includes the existence of solutions, linearization and stability of differential equations.

A *dynamical system* is defined as an evolution rule with respect to time on a state space or phase space. In this sense, a *state space* is the set of all possible states of a dynamical system and any abstract set could be a state space. It is often called as a phase space when the state space is finite.

Since the fundamentals of a dynamical system are its evolution rule, phase space and the set of times, it can be categorized accordingly: an evolution rule of a dynamical system could be deterministic or stochastic. Thus, a dynamical system is called deterministic if its evolution rule is a function which takes a given state to a unique state, otherwise it is nondeterministic. Dynamical systems that are nondeterministic are said to be stochastic. Considering phase space, a dynamical system could have a continuous phase space M, which is typically $\mathbb{R}^n$ or a discrete phase space which can illustrated in the heads-tail model of a coin toss.

Another classification type is the set of times. If the set of times is discrete, such as a subset of integers, then the system is called *discrete dynamical system* or *cascade*. If the set of times is continuous, such as $\mathbb{R}$, then the system is called *continuous dynamical system* or, sometimes, *flow*.

Assuming the evolution rule is deterministic, formally a dynamical system is represented as a function of time:

$$\varphi : T \times M \to M,$$

where T denotes the set of time and M denotes the phase space. In order to call

a map φ as a dynamical system, there are some properties that φ should satisfy:

$$\begin{aligned} &(i)\ \varphi(t,x) = x, \text{ for every } x \in M \text{ (identity property)},\\ &(ii)\ \varphi(s,\varphi(t,x)) = \varphi(t+s,x), \text{ for all } t,s \in T \text{ and } x \in M \text{ (group property)}. \end{aligned} \tag{2.1}$$

If a continuous dynamical system satisfies these properties for the set of time $T = \mathbb{R}$, then it is called a *complete flow*, and if it satisfies for $T = \mathbb{R}^+$ then it is called a *semi-flow*. Considering cascades, if a discrete dynamical system satisfies these properties for the set of time $T = \mathbb{Z}$ then it is called a *complete cascade*, and if it satisfies for $T = \mathbb{N}$ then it is called a *semi-cascade*. In the sequel, we call complete flows as flows and complete cascades as cascades, unless otherwise is stated.

An *orbit* or a *trajectory* of a state x is the time-ordered collection of states that follows from x using the evolution rule. It is formulated as a union of its two subsets as forward and backward orbits:

$$\Gamma(x) = \Gamma^+(x) \cup \Gamma^-(x),$$

where

$$\begin{aligned} \Gamma^+(x) &= \{\varphi(t,x) : t \geq 0\},\\ \Gamma^-(x) &= \{\varphi(t,x) : t \leq 0\}. \end{aligned}$$

If the orbit consists of only a single state x then it is called an *equilibrium*. An orbit $\Gamma_T(x)$ is called a *periodic orbit* if there is a time T such that the state returns back to itself at time T, that is

$$\varphi(T,x) = x.$$

Regarding cascades, the evolution rule of a cascade is given by a difference equation which defines recursively a sequence and mostly defined by

$$\begin{aligned} x_{n+1} &= f(x_n),\\ x_0 &= \xi. \end{aligned}$$

where f is a map such that $f : M \subset \mathbb{R}^n \to M$, and $\varphi(n,x_0) := x_n = f^n(x_0)$ for all $n \in \mathbb{Z}$. The orbit of a cascade with initial state x_0 is

$$\Gamma(x_0) = \{\ldots, x_{-1}, x_0, x_1, \ldots, x_n, \ldots\}.$$

A periodic orbit of period T consists of only T states and its given as

$$\Gamma_T(x_0) = \{x_0, x_1, \ldots, x_{T-1}\}.$$

If x^* is an equilibrium then $\Gamma(x^*) = x^*$. To illustrate these abstract definitions, we present an example for the cascades.

Example 2.1. Consider the difference equation

$$x_{n+1} = x_n^3,$$

where the map f is then $x \mapsto x^3$. The orbit of this cascade with initial state x_0 is

$$\Gamma(x_0) = \left\{\ldots, f^{-1}(x_0), x_0, f(x_0), \ldots, f^n(x_0)\right\}.$$

If we look for the equilibriums of this system, we solve the equation $f(x) = x$ as

$$\begin{aligned} x &= x^3, \\ 0 &= x(x^2 - 1). \end{aligned}$$

Then there are three equilibriums as $x = 0$, $x = -1$ and $x = 1$. Moreover, we show that $\varphi(n, x)$ satisfies the conditions (2.1):

(i) $\varphi(0, x_0) = f^0(x_0) = x_0$,

(ii) $\varphi(n, \varphi(m, x_0)) = \varphi(n + m, x_0)$ for all $n, m \in \mathbb{Z}$ is also satisfied by

$$\begin{aligned} \varphi(n, \varphi(m, x_0)) = \varphi(n, f^m(x_0)) = \varphi(n, x_0^{3m}) = f^n(x_0^{3m}) = x_0^{3mn} \\ = f^{n+m}(x_0) = \varphi(n + m, x_0). \end{aligned}$$

Considering flows, the evolution rule of a flow is given, in most cases, by an initial value problem which can be represented as

$$\begin{aligned} \dot{x} &= f(t, x), \\ x(0) &= x_0, \end{aligned}$$

where f is a function such that $f : \mathbb{R} \times M \to M$ and $x(t) = \varphi(t, x_0)$. The orbit of a flow with initial state x_0 is

$$\Gamma(x_0) = \{x(t) : \dot{x} = f(t, x), \quad x(0) = x_0, \quad t \in \mathbb{R}\}.$$

In order to find an equilibrium of a continuous dynamical system, we look for the solutions of the equation $f(t, x) = 0$ for all $t \in \mathbb{R}$. Below is a simple example to simplfy this discussion about flows.

Example 2.2. Consider the ordinary differential equation

$$\dot{x} = ax, \qquad a \in \mathbb{R},$$

with the initial condition $x(0) = x_0 \in \mathbb{R}^n$. The solution of the differential equation is $x(t) = x_0 e^{at} = \varphi(t, x_0)$. It is easy to see that $\dot{x} = 0$ if and only if $x = 0$, that is an equilibrium of this system is $x = 0$. Moreover, we can show that $\varphi(t, x)$ satisfies the conditions (2.1):

(i) $\varphi(0, x_0) = x_0 e^{a.0} = x_0$,

(ii) $\varphi(t, \varphi(s, x_0)) = \varphi(t + s, x_0)$ is also justified by

$$\varphi(t, \varphi(s, x_0)) = \varphi(t, x_0 e^{as}) = x_0 e^{a(s+t)} = \varphi(t + s, x_0).$$

Throughout this work we will be interested in mostly the deterministic continuous dynamical systems, therefore, we recall more detailed information about flows and ordinary differential equations in the following section.

2.2 Flows and Differential Equations

In the previous section, we see that a flow is defined by an ordinary differential equation. However, every ordinary differential equation does not define a dynamical system since its solution may not be defined for all $t \in \mathbb{R}$ or may not be unique. Therefore, we will make use of theorems in [19] to be able to qualify an ODE in terms of a dynamical system. We start with basic definitions which are necessary to understand the theorems better. The definitions and properties of these concepts can be found in [19]. Consider an IVP as

$$\begin{aligned} \dot{x} &= f(t,x), \\ x(t_0) &= x_0, \end{aligned} \tag{2.2}$$

where $f : D \subset \mathbb{R} \times \mathbb{R}^n \to \mathbb{R}^n$ and $(x_0, t_0) \in D$.

A function $f(t,x)$ on a domain $D \subset \mathbb{R} \times \mathbb{R}^n$ is said to satisfy a *Lipschitz condition* with respect to x on D if there exists a constant $k > 0$ (called a *Lipschitz constant*) such that

$$\|f(t,x) - f(t,y)\| \leq k \|x - y\| \quad \text{for} \quad (t,x),(t,y) \in D.$$

A weaker version of the condition is the Weak Lipschitz condition: a function $f(t,x)$ on a domain $D \subset \mathbb{R} \times \mathbb{R}^n$ is said to satify a *weak Lipschitz condition* with respect to x on D if there exists a nonnegative continuous fucntion $k(t)$ such that

$$\|f(t,x) - f(t,y)\| \leq k(t) \|x - y\| \quad \text{for} \quad (t,x),(t,y) \in D.$$

Accordingly, one can also define the Lipschitz condition locally. Specifically, a function $f(t,x)$ on a domain $D \subset \mathbb{R} \times \mathbb{R}^n$ is said to satify a *local Lipschitz condition* with respect to x on D if for any $(t_1, x_1) \in D$, there exists a domain D_1 such that $(t_1, x_1) \in D_1 \subset D$ and that $f(t,x)$ satisfies a Lipschitz condition with respect to x on D_1. That is, there exists a positive constant k_1 such that

$$\|f(t,x) - f(t,y)\| \leq k_1 \|x - y\| \quad \text{for all} \quad (t,x),(t,y) \in D_1.$$

Using these definitions, local existence and uniqueness of a solution of a differential equation (2.2) could be examined by the following theorem with the Lipschitz condition on f.

Theorem 2.1 (Local Existence and Uniqueness)**.** *Assume that $f(t,x)$ is continuous on a domain $D \subset \mathbb{R} \times \mathbb{R}^n$ and satisfies a Lipschitz condition with respect to x on D. Let $(t_0, x_0) \in D$. Then there exist positive constants a and b such that the region*

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

is in D. Moreover, if we define

$$r = \min\left\{a, \frac{b}{M}\right\}, \quad \textit{where} \quad M = \max_{(t,x)\in\mathbb{R}} \|f(t,x)\|,$$

then $r > 0$ is finite and in the interval $I = (t_0 - r, t_0 + r)$, (2.2) has a unique solution, denoted by $x(t, t_0, x_0)$, passing through (t_0, x_0).

Considering the existence and uniqueness of a solution, by Theorem 2.1, the maximal interval on which the solution is defined and unique is important, especially in dynamical systems theory.

For a differential equation, if $x = \varphi(t)(t)$ is a unique solution defined on an interval q, and if there is no interval p such that $q \subset p$, $q \neq p$, and x is also a unique solution of the same differential equation on p, then q is called the *maximal interval of existence* of x .

On the other hand, the global existence of solutions for (2.2) could be examined by having a weak Lipschitz condition on f. Specifically, if $f(t, x)$ is continuous on $\mathbb{R} \times \mathbb{R}^n$ and satisfies a weak Lipschitz condition with respect to x on $\mathbb{R} \times \mathbb{R}^n$ and $x(t) = x(t, t_0, x_0)$ be the unique solution of (2.2) on its maximal interval of existence (α, β), then $\alpha = -\infty$, and $\beta = \infty$.

Another way of showing global existence of a solution of (2.2) is to have a local Lipschitz condition on f and boundedness of f: if $f(t, x)$ is continuous on $\mathbb{R} \times \mathbb{R}^n$ and satisfies a local Lipschitz condition with respect to x on $\mathbb{R} \times \mathbb{R}^n$, and that for some constant $M > 0$, $\|f(t, x)\| \leq M$, $(t, x) \in \mathbb{R} \times \mathbb{R}^n$ and $x(t) = x(t, t_0, x_0)$ be the unique solution of (2.2) on its maximal interval of existence (α, β), then $\alpha = -\infty$, $\beta = \infty$.

Consequently, one can determine the interval of existence of solutions according to the form of the function f in (2.2). In particular, weak Lipschitz condition and local Lipschitz condition together with the boundedness of f play an important role in dynamical systems.

In the following parts of this section we introduce the linear homogeneous and nonhomogeneous systems. This piece of information can be found, for instance, in the book of Miller [22]. Consider, now, linear homogeneous and nonhomogeneous systems as

$$\dot{x} = A(t)x, \tag{2.3}$$

and

$$\dot{x} = A(t)x + g(t), \tag{2.4}$$

respectively, where $x \in \mathbb{R}^n$, $A(t) = [a_{ij}(t)]$ is $n \times n$ matrix and $g(t)$ is an n-vector valued function. These systems have unique solutions for every $(t_0, x_0) \in D$ where

$$D = \{(t, x) : t \in J = (\alpha, \beta), x \in \mathbb{R}^n\}.$$

First, we introduce the basic definitions of linear systems. Consider a set of n linearly independent solutions of (2.3) on J, $\{\phi_1, \cdots, \phi_n\}$, which is called a *fundamental set* of solutions of (2.3). The $n \times n$ matrix

$$\Phi = \begin{bmatrix} \phi_1 & \phi_2 & \cdots & \phi_n \end{bmatrix}$$

is called a *fundamental matrix* for (2.3). Furthermore, a fundamental matrix Φ for (2.3) whose columns are determined by the linearly independent solutions $\phi_1, \ldots, \phi_n$ with

$$\phi_1(t_0) = e_1, \ldots, \phi_n(t_0) = e_n, \quad \text{for} \quad t_0 \in J,$$

is called the *state transition matrix* for (2.3). Equivalently, if Ψ is any fundamental matrix for(2.3), then the matrix Φ determined by

$$\Phi(t, t_0) = \Psi(t)\Psi^{-1}(t_0) \quad \text{for all} \quad t, t_0 \in J,$$

is the (unique) *state transition matrix* for (2.3).

The characteristic properties of the state transition matrix can be summarized in the following way: Let $t_0 \in J$, let $x(t_0) = x_0$, and let $\Phi(t, t_0)$ denote the state transition matrix for (2.3) for all $t \in J$. Then:

(i) $\Phi(t, t_0)$ is the unique solution of the matrix equation

$$\frac{\partial}{\partial t}X = X' = A(t)X$$

with $X(t_0) = I$, the $n \times n$ identity matrix;

(ii) $\Phi(t, t_0)$ is nonsingular for all $t \in J$;

(iii) for any $t, s, t_0 \in J$, we have

$$\Phi(t, t_0) = \Phi(t, s)\Phi(s, t_0),$$

(iv) $[\Phi(t, t_0)]^{-1} = \Phi^{-1}(t, t_0) = \Phi(t_0, t)$ for all $t, t_0 \in J$,

(v) the unique solution $x(t, t_0, x_0)$ of (2.3), with $x(t_0, t_0, x_0) = x_0$ specified is given by

$$x(t, t_0, x_0) = \Phi(t, t_0)x_0, \qquad \text{for all} \quad t \in J.$$

The state transition matrix is also used to formulate the unique solution of (2.2). If $t_0 \in J$, and $(t_0, x_0) \in D$ then the unique solution $x(t, t_0, x_0)$ of (2.4) satisfying $x(t, t_0, x_0) = x_0$ is given by

$$x(t, t_0, x_0) = \Phi(t, t_0)x_0 + \int_{t_0}^{t} \Phi(t, s)g(s)ds,$$

Having introduced linear systems, a general way to study nonlinear systems to a certain extent is carried out by the so-called *linearization*. In this context, we assume that $f \in C^1(\mathbb{R} \times D)$ where D is a domain in $\mathbb{R}^n$ and $\varphi(t)$ is a given solution of (2.2) defined for all $t \geq t_0 \geq 0$, then the linearization can be applied as follows: define $y = x - \varphi(t)$ so that

$$\begin{aligned} y' &= f(t, x) - f(t, \varphi(t)) = f(t, y + \varphi(t)) - f(t, \varphi(t)) \\ &= \frac{\partial f}{\partial x}(t, \varphi(t))y + G(t, y), \end{aligned}$$

where $G(t, y) = f(t, y + \varphi(t)) - f(t, \varphi(t)) - \frac{\partial f}{\partial x}(t, \varphi(t))y$ is $o(|y|)$ as $|y| \to 0$ uniformly in t.

2.3 Stability

Stability is one of the fundamental topics of both differential equations and dynamical systems. Its great importance comes from its place in analyzing behavior of systems. What is meant by stability of a solution φ of a differential equation is that solutions with inital data close to initial data of φ will remain close to φ for future times. In other words, a solution φ is stable if solutions start nearby solution φ stay nearby for all times.

In this section, first, we introduce the basic definitions of stability for general differential equations. Next, we restrict the theory to stability of linear differential equations since we examine the stability of linearized form of systems in proceeding chapters. Beside the usual definitions of stability we provide, there is another way to describe and examine the stability: *Lyapunov second method for stability*. Although this method provides theoretically a huge understanding of stability, its application is not practical because of the difficulty of finding a Lyapunov function. Therefore, our study does not include this method but we suggest readers who are interested in this method should read Miller [22] and Liu [19].

Furthermore, the studies in the sequel have applications in constant coefficients systems, hence, the stability of linear system with constant coefficients needs particular attention as well. All information in this section is a summary of the related parts of Miller [22] and Liu [19].

2.3.1 Introduction to Stability of General Differential Equations

We start with an assumption to make sure that differential equation has a unique solution and $t = 0$ is included in the interval of existence and uniqueness. Specifically, we consider the differential equation (2.2) in $D = [0, \infty) \times Q$, where $Q \subset \mathbb{R}^n$ is a domain containing the zero solution vector. Assume that for any $(t_0, x_0) \in D = [0, \infty) \times Q$, the initial value problem in (2.2) has a unique solution $x(t, t_0, x_0)$ existing on $[t_0, \infty)$ with $x(t_0) = x_0$. We introduce the fundamental definitions of stability.

Definition 2.1 (Stability)**.** Let $x(t) = \varphi(t, t_0)$ denote a solution of (2.2) on $[t_0, \infty)$, $t_0 \geq 0$ for the following definitions.

(a) $\varphi(t, t_\varphi)$ is said to be *stable* if for any $t_0 \geq t_\varphi$ and any $\epsilon > 0$, there exists a $\delta = \delta(\epsilon, t_0) > 0$ such that $\|x_0 - \varphi(t_0)\| \leq \delta$ implies $\|x(t, t_0, x_0) - \varphi(t)\| \leq \epsilon$ for $t \geq t_0$.

(b) $\varphi(t, t_\varphi)$ is said to be *uniformly stable* if it is stable and δ in the definition of "stable" can be choosen to be independent of $t_0 \geq t_\varphi$. That is for any $\epsilon > 0$, there exists a $\delta = \delta(\epsilon) > 0$, such that $t_0 \geq t_\varphi$ and $\|x(t, t_0, x_0) - \varphi(t)\| \leq \epsilon$ for $t \geq t_0$.

(c) $\varphi(t, t_\varphi)$ is said to be *asymptotically stable* if it is stable and in addition, for any $t_0 \geq t_\varphi$, there exists an $r(t_0) > 0$ such that $\|x_0 - \varphi(t_0)\| \leq r(t_0)$ implies $\lim_{t\to\infty} \|x(t, t_0, x_0) - \varphi(t)\| = 0$.

(d) $\varphi(t, t_\varphi)$ is said to be *uniformly asymptotically stable* if it is uniformly stable and in addition, there exists an $r > 0$ independent of $t_0 \geq t_\varphi$, such that $\|x_0 - \varphi(t_0)\| \leq r$ implies that $\lim_{t\to\infty} \|x(t, t_0, x_0) - \varphi(t)\| = 0$ uniformly for $t_0 \geq t_\varphi$ in the following sense: for any $\epsilon > 0$, there exists a $\tau = \tau(\epsilon) > 0$ such that $t_0 \geq t_\varphi$, $\|x_0 - \varphi(t_0)\| \leq r$, $t \geq t_0 + \tau$ imply $\|x(t, t_0, x_0) - \varphi(t)\| \leq \epsilon$.

(e) $\varphi(t, t_\varphi)$ is said to be *unstable* if it is not stable.

(f) In particular, if $\varphi(t) = 0$, $t \geq 0$, is a solution of (2.2), or equivalently when $f(t, 0) = 0$, $t \geq 0$, then the above give the corresponding definitions concerning stability properties for the zero solution.

After giving the basics of stability, we consider the well-known approaches to analyze the stability of the linear system in (2.3) in the next section.

2.3.2 Stability of Linear Equations

In this section, we analyze the stability properties of systems of linear equations and consider (2.3) as a system of linear equations. We introduce the stability conditions for homogeneous linear equation (2.3) by the statement of Theorem 9.2.1 in Liu [19]. Assuming that $A(t)$ is continuous on $\mathbb{R}^n$ and letting Φ be the state transition matrix of (2.3), the stability of the zero solution $\varphi \equiv 0$ of (2.3) can be examined as in the following theorem.

Theorem 2.2. *The zero solution $\varphi \equiv 0$ of (2.3) is*

(i) stable if and only if there is a constant $C > 1$ such that $\|\Phi(t, 0)\| \leq C$, $0 \leq t < \infty$.

(ii) uniformly stable if and only if there is a constant $C > 1$ such that $\|\Phi(t, s)\| \leq C$, $0 \leq s \leq t < \infty$.

(iii) asymptotically stable if and only if $\|\Phi(t, 0)\| \longrightarrow 0$, as $t \to \infty$.

(iv) uniformly asymptotically stable if and only if there are constants $C > 1$ and $\alpha > 0$ such that $\|\Phi(t, s)\| \leq Ce^{-\alpha(t-s)}$, for $0 \leq s \leq t < \infty$.

For the nonhomogeneous linear systems such as (2.4), we present the statement of Theorem 9.2.3 in Liu [19] as follows: Assume that $A(t)$ and $g(t)$ are continuous on $\mathbb{R}^+$, then zero solution of (2.4) is stable if and only if every solution of (2.3) is stable. The same statement is valid for uniform stability, asymptotic stability, and uniform asymptotic stability. See, for instance, Liu [19] for more details on the stability of solutions.

As stated before, the present study will make use of the stability properties of systems with constant coefficients. Therefore, we consider the systems

$$x'(t) = Ax(t) \tag{2.5}$$

and

$$x'(t) = Ax(t) + g(t) \tag{2.6}$$

with inital data $x(t_0) = x_0$ and A being a constant matrix. For systems as in (2.5), a state transition matrix can be represented as

$$\Phi(t, t_0) = \exp\left(\int_{t_0}^{t} A ds\right) = e^{(t-t_0)A}$$

and a solution of (2.6) is simply formulated by the *variation of constants* formula,

$$x(t) = e^{(t-t_0)A}x_0 + \int_{t_0}^{t} e^{(t-s)A}g(s)ds.$$

As a summary of the main discussion about stability of this type of systems, we present the statement of Theorem 5.2.1 in Liu [19].

Theorem 2.3. *If $\varphi = 0$ is the zero solution of (2.5), then the stability of $\phi \equiv 0$ can be examined as in the following:*

(A) the following statements are equivalent:

- *(i) $\varphi = 0$ is stable or uniformly stable;*
- *(ii) for each eigenvalue λ of the matrix A, $\mathcal{R}e(\lambda) \leq 0$. If $\mathcal{R}e(\lambda) = 0$, then λ appears only in matrices J_i (in the Jordan canonical form for A) such that J_i is a 1×1 matrix;*
- *(iii) there is a constant $C > 1$ such that $\left\|e^{tA}\right\| \leq C$, for $0 \leq t < \infty$.*

(B) the following statements are equivalent:

- *(i) $\varphi = 0$ is asymptotically stable or uniformly asymptotically stable;*
- *(ii) each eigenvalue of matrix A has a negative real part;*
- *(iii) There are constants $C > 1$ and $\alpha > 0$ such that $\left\|e^{tA}\right\| \leq Ce^{-\alpha t}$, for $0 \leq t < \infty$.*

(C) the following statements are equivalent:

- *(i) $\varphi = 0$ is unstable;*
- *(ii) there is an eigenvalue λ of matrix A with $\mathcal{R}e(\lambda) = 0$ and λ appears in a matrix J_i that is at least 2×2 matrix;*
- *(iii) there is an eigenvalue of matrix A with a positive real part.*

Having introduced the essential parts of the stability for this study, in the sequel, we present another important concept: following chapter is devoted to the periodic solutions in continuous dynamical systems.

CHAPTER 3

PERIODIC SOLUTIONS IN CONTINUOUS DYNAMICAL SYSTEMS

The study of periodic systems and their periodic solutions is an extremely important subject in dynamical systems. The reason is simply that is they appear in many real-world problems: radio circuits, temperature distribution, or chemical and biological oscillations are some of the examples of periodic systems. In the sequel, we are interested in periodicity in population dynamics in terms of epidemiology. In the first part, we recall the basics of this concept, starting with introducing a general periodic differential equation. As we will make use of the Floquet theory, we further study this theory and its results. Although periodicity can be analyzed in nonlinear systems with its own theorems, we only recall in detail periodic solutions of linear systems as we use the linearized form of the nonlinear systems in the second part of this chapter. We suggest readers who are interested in periodic solutions in nonlinear systems should read Liu [19]. Unless otherwise is stated, the content in this section is based on Liu [19].

Consider the general differential equation (2.2) in $D = [0, \infty) \times \mathbb{R}^n$, where $f(t, x)$ is continuous and satisfies at least a local Lipschitz condition with respect to x on D. For simplicity, let us assume that $t_0 = 0$, and hence, for any $x_0 \in \mathbb{R}^n$, (2.2) has a unique solution $x(t, 0, x_0)$ existing on $[0, \infty)$ with $x(0, 0, x_0) = x_0$. In order to have a periodic system, a necessary condition is that the function f is periodic in t. That is, there is a constant $T > 0$ such that

$$f(t + T, x) = f(t, x)$$

for $(t, x) \in D$. It is important to note that this contains the case when f is autonomous for which periodic solutions can be obtained with periods that are not predetermined. A first basic result of periodic solutions can be given by the following lemma.

Lemma 3.1. *Assume that for a constant $T > 0$, $f(t+T, x) = f(t, x)$ for $(t, x) \in D$. Then, it holds:*

(i) If $x(t)$ is a solution of (2.2), then so is $x(t + T)$, $t \geq 0$.

(ii) Let $x(t, 0, x_0)$ be a solution of (2.2) with $x(0, 0, x_0) = x_0$. Then $x(t, 0, x_0)$ is T- periodic if and only if $x(T, 0, x_0) = x_0$.

In the following section, we introduce the linear periodic systems via Floquet theory.

3.1 Periodic Coefficients and Floquet Theory

As the simplest periodic systems appear as linear systems with periodic coefficients, we introduce the Floquet theory constructed on these systems. Consider the linear periodic differential equation as

$$x'(t) = A(t)x(t), \quad x(t_0) = x_0, \tag{3.1}$$

where $A(t)$ is T-periodic, that is,

$$A(t) = A(t+T), \quad t \in \mathbb{R}.$$

We then recall a lemma which is used in the proof of the Floquet theory. This lemma defines the natural logarithmic function for a nonsingular matrix. It states that any $n \times n$ constant nonsingular matrix B can be represented as $B = e^C$, where C is an $n \times n$ matrix. Because of this lemma, the fundamental matrix of $\Phi(t)$ of a linear periodic differential equation can be written in terms of an exponential matrix function. Consequently, we may transform (3.1) into a linear differential equation with constant coefficients using the Floquet theory. Accordingly, if $A(t) = A(t+T)$ for some constant $T > 0$ and $\Phi(t, t_0)$ is the fundamental matrix of (3.1), then there exists a constant C and a nonsingular, continuous, T-periodic matrix function $P(t)$, such that

$$\Phi(t) = P(t)e^{tC}.$$

Application of the Floquet theory to transform (3.1) into a constant coefficient system can be expressed via the statement of Theorem 3.4.4 in Liu [19]: If $A(t)$ is T-periodic and let C and $P(t)$ are given as above, and $y(t) = P^{-1}(t)x(t)$, where $x(t) = x(t, t_0, x_0)$ is the unique solution for (3.1), then $y(t)$ satisfies the linear differential equation with constant coefficients

$$y'(t) = Cy(t), \quad y(t_0) = P^{-1}(t_0)x_0. \tag{3.2}$$

In the study of the Floquet theory, there are some basic interpretations. If we consider the matrices $A(t)$ and C given as in Floquet theory, then

(a) The matrix e^{TC} is called the *monodromy matrix* of (3.1).

(b) The eigenvalues of the matrix C are called the *Floquet exponents* of (3.1).

(c) The eigenvalues of the monodromy matrix are called the *Floquet multipliers* of (3.1).

We note that transformation of (3.1) into (3.2) provides an easier way to analyze the behavior of the former, as the latter is a constant coefficient system. Therefore, boundedness and stability relations between these two systems are given as the statements of Theorem 3.4.6 in Liu [19].

Theorem 3.2. *If $A(t)$ is periodic and the matrix C is given in Floquet theory, then*

(A) The following statements are equivalent:

- *(i) There is a constant $C_1 > 0$ such that every solution of (3.1) satisfies $\|x(t, t_0, x_0)\| \leq C_1 \|x_0\|$, $t_0 \leq t < \infty$;*
- *(ii) There is a constant $C_2 > 0$ such that every solution of (3.2) satisfies $\|y(t, t_0, y_0)\| \leq C_2 \|y_0\|$, $t_0 \leq t < \infty$;*
- *(iii) For each Floquet exponent λ, $\mathcal{R}e(\lambda) \leq 0$. If $\mathcal{R}e(\lambda) = 0$, then λ appears only in the matrices J_i such that J_i is a 1×1 matrix of Jordan canonical form for C;*
- *(iv) For each Floquet multiplier η, $|\eta| \leq 1$. If $|\eta| = 1$, then η appears only in the matrices J_i such that J_i is a 1×1 matrix of Jordan canonical form for e^{TC}.*

(B) The following statements are equivalent:

- *(i) Every solution of (3.1) satisfies $\lim_{t\to\infty} \|x(t, t_0, x_0)\| = 0$;*
- *(ii) Every solution of (3.2) satisfies $\lim_{t\to\infty} \|y(t, t_0, y_0)\| = 0$;*
- *(iii) Each Floquet exponent has a negative real part;*
- *(iv) Each Floquet multiplier satisfies $|\eta| < 1$.*

(C) The following statements are equivalent:

- *(i) There is a solution x of (3.1) with $\lim_{t\to\infty} \|x(t, t_0, x_0)\| = \infty$;*
- *(ii) There is a solution y of (3.2) with $\lim_{t\to\infty} \|y(t, t_0, y_0)\| = \infty$;*
- *(iii) Either there is a Floquet exponent λ with $\mathcal{R}e(\lambda) = 0$ and λ appears in a matrix J_i that is at least 2×2, or there is a Floquet exponent with a positive real part;*
- *(iv) Either there is a Floquet multiplier η with $|\eta| = 1$ and η appears in a matrix J_i that is at least 2×2, or there is a Floquet multiplier η with $|\eta| > 1$.*

Beside the Floquet theory, there is another way to examine linear periodic systems. In the following section, we study the linear periodic systems via fixed points of a map Π.

3.2 Periodic Solutions of Linear Systems

In this part of the study, we make use of Lemma 3.1 and fixed point theorems in order to derive periodic solutions of linear periodic systems. Moreover, we analyze the stability of these systems by considering the eigenvalues of the monodromy matrix. Recall that a continuous function $x(t, 0, x_0)$ is a solution of the IVP (2.2) if and only if

$$x(t) = x_0 + \int_0^t f(s, x(s))ds, \quad \text{for all } \ t \geq 0.$$

Next, for $x_0 \in \mathbb{R}^n$ and the unique solution $x(t, 0, x_0)$ with $x(0, 0, x_0) = x_0$, we can define a mapping $\Pi : \mathbb{R}^n \to \mathbb{R}^n$ such that

$$\Pi(x_0) = x(T) = x_0 + \int_0^T f(s, x(s))ds. \tag{3.3}$$

Considering Lemma 3.1, we conclude that (2.2) has a T-periodic solution if and only if the mapping Π has a fixed point, that is, $\Pi(x_0) = x_0$. This result is stated by the following lemma.

Lemma 3.3. *Assume that for a constant $T > 0$, $f(t+T, x) = f(t, x)$ for $(t, x) \in D$, then* (2.2) *has a T-periodic solution if and only if mapping $\Pi : \mathbb{R}^n \to \mathbb{R}^n$ defined in* (3.3) *has a fixed point.*

The results for linear differential equations for deriving periodic solutions are given by Theorems 11.2.1 and 11.2.2 in Liu [19]. Liu states that if $A(t)$ is continuous and T-periodic, then (2.3) has a nonzero T-periodic solution if and only if 1 is an eigenvalue of $\Phi(T, 0)$. Accordingly, for nonhomogeneous case, if $A(t)$ is continuous and T-periodic, then (2.4) has a T-periodic solution for any continuous and T-periodic function f if and only if 1 is not an eigenvalue of $\Phi(T, 0)$.

Now, consider the linear homogeneous systems with linear or nonlinear perturbations, which can also be regarded as a linearization of a general differential equation:

$$\dot{x} = A(t)x(t) + g(t, x(t)), \quad \text{for all } t \geq 0, \tag{3.4}$$

where $x \in \mathbb{R}^n$ and $g(t, x(t))$ is also T-periodic in t. Again, the results for differential equations as in (3.4) for deriving periodic solutions are given by the statements of Theorem 11.2.3 and Theorem 11.2.4 in Liu [19]. Assuming that (3.4) is T-periodic in t and that $g(t, x)$ is continuous on $[0, \infty) \times \mathbb{R}^n$ and satisfies a weak Lipschitz condition with respect to x, first statement asserts that if 1 is not an eigenvalue of $\Phi(T, 0)$ and if $\|f(t, x)\| \leq C, \quad (t, x) \in [0, \infty) \times \mathbb{R}^n$, for some constant $C > 0$, then (3.4) has a T-periodic solution. Additionally, second statement asserts that if 1 is not an eigenvalue of $\Phi(T, 0)$ and if

$$\lim_{\|x\| \to \infty} \frac{\|g(t, x)\|}{\|x\|} = 0, \tag{3.5}$$

uniformly for $t \in [0, T]$, then (3.4) has a T-periodic solution.

CHAPTER 4

THRESHOLD DYNAMICS FOR A GENERAL COMPARTMENTAL EPIDEMIC MODEL

In this chapter, we introduce the threshold dynamics for a general compartmental epidemic model. Theoretical background of this chapter is provided by Driessche and Watmough [26].

For many epidemiology models, threshold dynamics is governed by the basic reproduction ratio, R_0. Formally, the basic reproduction ratio is defined by Hethcote [17] as the average number of secondary infections produced when one infected individiual is introduced into a host population where everyone is susceptible. According to this definition, the dynamics of disease transmission is determined by the following: if the basic reproduction ratio is less than unity then diease dies out, on the other hand, if it is greater than unity then disease is established in the population. Following this idea, we examine a compartmental epidemic model which is represented by a system of autonomous ordinary differential equations.

4.1 A General Compartmental Epidemic Model

In this section, we analyze a heteregeneous population whose individuals can be divided into n homogeneous compartments with respect to their age, behavior, spatial position, stage of disease, etc.. We establish a general epidemic model for such a population dynamics as in Driessche and Watmough [26].

Let $x = (x_1, \ldots, x_n)^T$, with each $x_i \geq 0$ be the state of individuals in each compartment. We categorize the compartments into two types: infected compartments, labeled by $i = 1, \ldots, m$, and uninfected compartments, labeled by $i = m+1, \ldots, n$. We specify $\mathcal{X}_s$ to be the set of all disease-free states

$$\mathcal{X}_s = \{x \geq 0 : \quad x_i = 0 \text{ for all } i = 1, \ldots, m\}.$$

In [26], Driessche and Watmough state that while getting R_0, distinguishing new infection from all other changes in population becomes an important issue. Therefore they examine the system of ordinary differential equations in this respect.

Thus, some new variables and definitions given in this respect are

$\mathcal{F}_i(x)$: the rate of appearence of new infections in compartment i,
$\mathcal{V}_i^+(x)$: the rate of transfer of individuals in a compartment i by all other means,
$\mathcal{V}_i^-(x)$: the rate of transfer of individuals out of compartment i.

Having defined these rates, the disease transmission model is constructed by the following system of equations (together with nonnegative initial conditions)

$$\dot{x}_i = f_i(x) = \mathcal{F}_i(x) - \mathcal{V}_i(x), \quad i = 1, \ldots, n. \tag{4.1}$$

where $\mathcal{V}_i = \mathcal{V}_i^- - \mathcal{V}_i^+$. Surely, this system of equations is accompanied by nonnegative initial contitions, such as $x_i(0) = \alpha_i \geq 0$ for each i.

Assumptions and Clarifications.

Below we present and clarify some of the necessary assumptions in order to analyze disease transmission models.

(A1) if $x \geq 0$, then $\mathcal{F}_i, \mathcal{V}_i^+, \mathcal{V}_i^- \geq 0$ for $i = 1, \ldots, n$. The first part of this assumption comes from the fact that each function represents a directed transfer of individuals.

(A2) if $x_i = 0$ then $\mathcal{V}_i^- = 0$. In particular, if $x \in \mathcal{X}_s$ then $\mathcal{V}_i^- = 0$ for $i = 1, \ldots, m$. This assumption means that if a compartment is empty then there is no transfer of individuals out of the compartment.

(A3) $\mathcal{F}_i = 0$ if $i > m$. This assumption states that the incidence of infection for uninfected compartment is zero.

(A4) if $x \in \mathcal{X}_s$ then $\mathcal{F}_i(x) = 0$ and $\mathcal{V}_i^+ = 0$ for $i = 1, \ldots, m$. By this assumption, our aim is to make the disease-free subspace be invariant, so that if the population is free of the disease, then the population continues to be free of the disease. In other words, there is no immigration of infected individuals.

We assume that the model has a disease-free solution $x^0 = (0, \ldots, 0, x_{m+1}^0, \ldots, x_n^0)^T$ with $x_i^0 > 0$ for $m+1 \leq i \leq n$ and it is locally asymptotically stable equilibrium solution. This helps us investigate the linearized system about the equilibrium solution x^0, that is,

$$\dot{x} = Df(x^0)(x - x^0), \tag{4.2}$$

where $Df(x^0)$ is the Jacobian of f evaluated at x^0. Our main concern is, therefore, systems for which the disease-free equilibrium is stable in the absence of new infection. Therefore, the next assumption is also necesary.

(A5) if $\mathcal{F}(x)$ is set to zero, then all eigenvalues of $Df(x^0)$ have negative real parts.

According to Driessche and Watmough in [26], the Jacobian of f, $Df(x^0)$, can be partitioned by the help of the conditions and assumptions listed above.

Lemma 4.1. *If x^0 is a disease-free equilibrium of (4.1) and $f_i(x)$ satisfies (A1)-(A5), then the derivatives $D\mathcal{F}(x^0)$ and $D\mathcal{V}(x^0)$ are partitioned as*

$$D\mathcal{F}(x^0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}, \qquad D\mathcal{V}(x^0) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix},$$

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

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x^0)\right] \quad \text{and} \quad V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x^0)\right]$$

for $1 \leq i, j \leq m$. Furthermore, F is non-negative, V is non-singular M-matrix, and all eigenvalues of J_4 have positive real part.

Proof. Assume that x^0 is a disease-free equilibrium solution of (4.1). First, for the partitioning of $D\mathcal{F}(x^0)$, consider all cases for i, j indices:

If $i > m$ and $1 \leq j \leq n$, then, by (A3), $\mathcal{F}_i = 0$, thus $\frac{\partial \mathcal{F}_i}{\partial x_j}(x^0) = 0$.

If $i \leq m$ and $j > m$, then, by (A4),

$$\frac{\partial \mathcal{F}_i}{\partial x_j}(x^0) = \lim_{h \to 0^+} \frac{\mathcal{F}_i(x^0 + he_j) - \mathcal{F}_i(x^0)}{h} = 0,$$

where e_j is the jth column of the $n \times n$ identity matrix and $x^0 + he_j \in \mathcal{X}_s$.

If $1 \leq i, j \leq m$, then

$$F = \frac{\partial \mathcal{F}_i}{\partial x_j}(x^0) = \lim_{h \to 0^+} \frac{\mathcal{F}_i(x^0 + he_j) - \mathcal{F}_i(x^0)}{h} \geq 0$$

since $\mathcal{F}_i(x^0) = 0$ by (A4) and $\mathcal{F}_i(x^0 + he_j) \geq 0$ by (A1). This result shows the nonnegativity of F and partitioning of zero blocks.

Now, consider the partitioning of the matrix $D\mathcal{V}(x^0)$: if $i \leq m$ and $j > m$, then by (A2) and (A4), $\mathcal{V}_i(x^0) = 0$ and $\mathcal{V}_i(x^0 + he_j) = 0$ since $x^0 \in \mathcal{X}_s$ and $x^0 + he_j \in \mathcal{X}_s$. Therefore,

$$\frac{\partial \mathcal{V}_i}{\partial x_j}(x^0) = \lim_{h \to 0^+} \frac{\mathcal{V}_i(x^0 + he_j) - \mathcal{V}_i(x^0)}{h} = 0$$

gives the zero block.

Next, in order to show that V is a non-singular M-matrix, we should show that V satisfies the Z-sign pattern (that is, $V_{ij} \leq 0$ for $i \leq m$ and $j \neq i$), and all eigenvalues of V have positive real parts. In fact, if $V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x^0)\right]$ with $1 \leq i, j \leq m$, then for $i \neq j$ we have

$$V_{ij} = \frac{\partial \mathcal{V}_i}{\partial x_j}(x^0) = \lim_{h \to 0^+} \frac{\mathcal{V}_i(x^0 + he_j) - \mathcal{V}_i(x^0)}{h} \leq 0,$$

since $\mathcal{V}_i(x^0) = 0$ by (A2) and (A4), $\mathcal{V}_i^-(x_0+he_j) = 0$ by (A2), and $\mathcal{V}_i^+(x^0+he_j) \geq 0$ by (A1). This shows that V has the Z-sign pattern. Moreover, by (A5) all eigenvalues of V have positive real parts. Owing to these conditions, V is a non-singular M-matrix.

Again by (A5), the eigenvalues of J_4 have positive real parts. Hence the proof is completed. □

By the help of the proof of Lemma 4.1, we are now able to construct the formulation of the basic reproduction ratio.

The Basic Reproduction Ratio

Considering an infective individual introduced into the population and assuming that reinfection is turned off, the dynamics of the linearized system (4.2) reduces to

$$\dot{x} = -D\mathcal{V}(x^0)(x - x^0). \tag{4.3}$$

By the assumption (A5), we conclude that the disease-free equilibrium is locally asymptotically stable in this system. Therefore, it is possible to use (4.3) to determine the effect of a small number of the infected individuals introduced to the disease-free population.

Let $\psi_i(0)$ be the number of infected individuals initially in compartment i, and $\psi(t) = (\psi_1(t), \ldots, \psi_m(t))^T$ be the number of these initially infected individuals remaining in the infected compartments at time t. Due to the partitioning of $-D\mathcal{V}(x^0)$, $\psi(t)$ satisfies

$$\psi'(t) = -V\psi(t)$$

and hence, is uniquely determined by

$$\psi(t) = e^{-Vt}\psi(0).$$

Owing to Lemma 4.1, V is a nonsingular M-matrix and so invertible and all of its eigenvalues have positive real part. Therefore, integrating $F\psi(t)$ from zero to infinity, the expected number of new infections produced by the initially infected individuals can be found as

$$\begin{aligned}\int_0^\infty F\psi(s)ds &= \int_0^\infty Fe^{-Vs}\psi(0)ds \\ &= FV^{-1}\psi(0).\end{aligned}$$

We then define the basic reproduction ratio as

$$R_0 = \rho(FV^{-1}), \tag{4.4}$$

where $\rho(A)$ denotes the spectral radius of a matrix A.

According to the stability theory, a disease-free equilibrium is locally asymptotically stable if all eigenvalues of the matrix $Df(x^0)$ have negative real parts and unstable if any eigenvalues of $Df(x^0)$ has a positive real part. As a consequence of Lemma 4.1, the eigenvalues of $Df(x^0)$ can also be partitioned into two sets corresponding to the infected and uninfected compartments. These two sets are the eigenvalues of $F - V$ and those of $-J_4$. As we have proven that (by Lemma 4.1) the eigenvalues of $-J_4$ all have negative real part, the stability of disease-free equilibrium is determined by the eigenvalues of $F - V$.

The relation between the stability of the desease-free equalibrium x^0 and the basic reproduction ratio R_0 is given by the following theorem.

Theorem 4.2 (Driessche, Watmough [26])**.** *Consider the disease transmission model given by* (4.1) *with* $f(x)$ *satisfying conditions (A1)–(A5). Then,* x^0 *is locally asymptotically stable if* $R_0 < 1$*, and it is unstable if* $R_0 > 1$*, where* R_0 *is defined by* (4.4)*.*

Proof. Assume that $R_0 < 1$ then from the definiton of R_0, $\rho(FV^{-1}) < 1$. Because of the nonnegativity of FV^{-1}, all eigenvalues of FV^{-1} have magnitude that are less than or equal to $\rho(FV^{-1})$. Therefore, $s(I - FV^{-1}) > 0$ where $s(A)$ denotes the maximum real part of all the eigenvalues of a matrix A (the spectral abscissa).

Again because of the nonnegativity of FV^{-1}, if $B = I - FV^{-1} = [b_{ij}]$, then $b_{ij} \leq 0$ for $i \neq j$, that is, $I - FV^{-1}$ has the Z-sign pattern. These two properties of $I - FV^{-1}$ ensures it a non-singular M-matrix.

Since we can express $I - FV^{-1}$ as $(V - F)V^{-1}$ and by the theorem in appendix A of Driessche an Watmough [5], $V - F$ is also a non-singular M-matrix. Accordingly, all eigenvalues of $F - V$ has negative real parts and thence x^0 is asymptotically stable.

Similarly, if $R_0 = 1$ we have $\rho(FV^{-1}) = 1$ and $s(I - FV^{-1}) = 0$. As we have that $I - FV^{-1}$ has the Z-sign pattern and $s(I - FV^{-1}) = 0$, the matrix $I - FV^{-1}$ becomes a singular M-matrix. Using $I - FV^{-1} = (V - F)V^{-1}$ and the theorem in appendix A of Driessche an Watmough [5], $V - F$ is a singular M-matrix. Hence, $s(V - F) = 0$ and $s(F - V) = 0$.

Combining these two results, we have $s(F - V) < 0$ if $R_0 < 1$ and $s(F - V) = 0$ if $R_0 = 1$. Therefore, we can conclude that $s(F - V) > 0$ if $R_0 > 1$, that is, if $R_0 > 1$ then all eigenvalues of matrix $F - V$ have positive real parts. As a result, x^0 is unstable if $R_0 > 1$. The proof is completed. □

4.2 Applications on an Autonomous Vector Host Model

In this part, we introduce an epidemic model which is called the vector-host model and apply the theory given within this chapter to analyze its dynamics. First, let us present the vector-host model: in this context, a *vector* may be regarded

as a *carrier*, as in the situation that an animal which transfers an infective agent from one host to another. A host is an organism that harbors or nourishes another organism. As we study epidemic diseases, we consider the modelling of the Dengue fever which is an infectious disease of the tropics transmitted by mosquitos and characterized by rash and aching head and joints.

Dengue virus is primarily transmitted by Aedes mosquitos. They typically bite during the day, particularly in the early morning and in the evening. Humans are the primary host of the virus, but it also circulates in nonhuman primates. An infection can be acquired via a single bite. A female mosquito that takes blood meal from a person infected with Dengue fever becomes itself infected with the virus in the cells lining its gut. The virus seems to have no-detrimental effect on the mosquito, which remains infected for life. There are no approved vaccines for the Dengue virus. Prevention thus depends on control of and protection from the bites of the mosquito that transmits it.

For many reasons, such as population growth, increased international travel and global warming, the incidence of Dengue increased between 1960-2010. Therefore, this particular disease attracts attention of many scientists, not only from medical societies, but also from different branches of applied sciences, engineering, and mathematics, who are interested in mathematical modelling.

4.2.1 An analysis on Dengue Fever

Now, we formulate the dynamics of the disease transmisson model of Dengue Fever as a coupled system of ordinary differential equations

$$\begin{aligned} \dot{I} &= \beta_s SV - (b+\gamma)I, \\ \dot{V} &= \beta_m MI - cV, \\ \dot{S} &= b - bS + \gamma I - \beta_s SV, \\ \dot{M} &= c - cM - \beta_m MI, \end{aligned} \tag{4.5}$$

where I, V, S and M, named as compartments, and denote the infected hosts, infected vectors, susceptible hosts and susceptible vectors, respectively. In this model, hosts are infected by contacts with vectors, and vectors are in turn infected by contacts with infected hosts. The contact rates of host and vectors are given by the two terms $\beta_s SV$ and $\beta_m MI$.

Other parameters in the system can be interpreted as
b : birth and death rates for the host,
c : birth and death rates for the vector,
γ : recovery rate for the host .

Clearly, the disease-free equilibrium for this model is $x^0 = (0, 0, 1, 1)^T$ where $x = (I, V, S, M)$. Before finding the partitioned linearized system, we formulate

the Jacobian of f as

$$D_x f(x) = \begin{pmatrix} -(b+\gamma) & \beta_s S & 0 & 0 \\ \beta_m M & -c & 0 & \beta_m I \\ \gamma & -\beta_s S & -b-\beta_s V & 0 \\ -\beta_m M & 0 & 0 & -c-\beta_m I \end{pmatrix},$$

and by substituting x^0, we find

$$D_x f(x^0) = \begin{pmatrix} -(b+\gamma) & \beta_s & 0 & 0 \\ \beta_m & -c & 0 & 0 \\ \gamma & -\beta_s & -b & 0 \\ -\beta_m & 0 & 0 & -c \end{pmatrix}.$$

Now, considering the way of transmisson of Dengue fever between compartments and following assumptions, functions $\mathcal{F}_i$, $\mathcal{V}_i^-$ and $\mathcal{V}_i^+$ are formulated as

$$\begin{array}{lll} \mathcal{F}_1(x) = \beta_s SV, & \mathcal{V}_1^-(x) = (b+\gamma)I, & \mathcal{V}_1^+(x) = 0, \\ \mathcal{F}_2(x) = \beta_m MI, & \mathcal{V}_2^-(x) = cV, & \mathcal{V}_2^+(x) = 0, \\ \mathcal{F}_3(x) = 0, & \mathcal{V}_3^-(x) = bS + \beta_s SV, & \mathcal{V}_3^+(x) = b+\gamma I, \\ \mathcal{F}_4(x) = 0, & \mathcal{V}_4^-(x) = cM + \beta_m MI, & \mathcal{V}_4^+(x) = c. \end{array}$$

After stating these functions, we present the matrices F and V introduced in Lemma 4.1:

$$\left(\frac{\partial \mathcal{V}_i}{\partial x_j}\right)(x^0) = \begin{pmatrix} b+\gamma & 0 \\ 0 & c \end{pmatrix}, \quad \left(\frac{\partial \mathcal{F}_i}{\partial x_j}\right)(x^0) = \begin{pmatrix} 0 & \beta_s \\ \beta_m & 0 \end{pmatrix}$$

for any $1 \leq i, j \leq 2$.

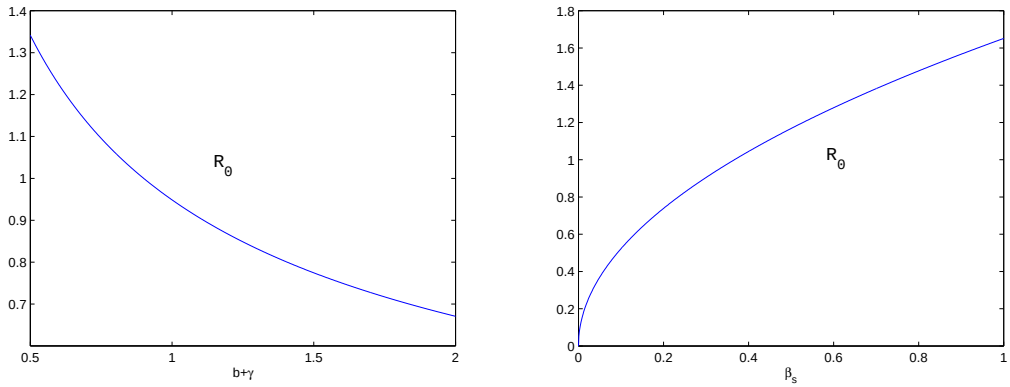
Now as we have the matrices F and V at hand, it is not difficult to calculate the basic reproduction ratio $R_0 = \rho(FV^{-1})$: it follows from

$$FV^{-1} = \begin{pmatrix} 0 & \frac{\beta_s}{c} \\ \frac{\beta_m}{b+\gamma} & 0 \end{pmatrix},$$

that

$$R_0 = \sqrt{\frac{\beta_m \beta_s}{c(b+\gamma)}}.$$

Biologically, the basic reproduction ratio means that each infected host results in $\frac{\beta_m}{c}$ new infected vectors over its expected period and each infected vector results in $\frac{\beta_s}{b+\gamma}$ new infected hosts over its expected period. Moreover, the square root appears from the two 'resources' required for an infected vector or host to 'generate' itself [26].



(a) (b)

Figure 4.1: The change of R_0 as (a) $b + \gamma$, (b) β_s varies.

As a contribution to the work of Watmough and Driessche [26], we investigate and understand the behavior of R_0 with respect to the parameters of the system. Since c and $b + \gamma$ are included in the denominator as factors, behaviour of the basic reproduction ratio is depicted in Figure 4.1a only with respect to the sum of b and γ. Considering the numerator in the representation of R_0, which consists of the factors β_s and β_m, it is sufficient to illustrate the changes of the basic reproduction ratio with respect to β_s as in Figure 4.1b.

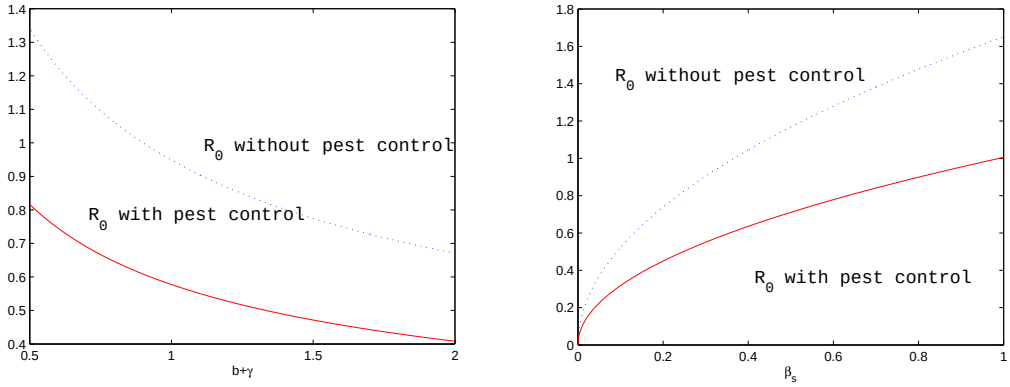
From Figure 4.1a, it is clear that R_0 decreases as the sum $b + \gamma$ increases. In other words, an increase of the birth and/or the recovery rate of the host leads to diminishing of the disease.

It is also apparent in Figure 4.1b that R_0 increases provided that β_s (or β_m) increases. That is, an increment of any contact rates causes the spread of the disease.

These two observations indicate that the method considered is consistent with the natural phenomena of this particular infectious disease and is suitable for other diseases which have similar transmission way in population.

4.2.2 An Analysis on Pest Control for Dengue Fever

After analyzing dynamics of Dengue fever, it is reasonable to seek a way to control of the disease in some way. Since there has not been developed a vaccine for the Dengue virus, pest control on the vectors can be studied as an eradication policy. Thus, as another additional piece to the work of Watmough and Driessche [26], we model the dynamics of Dengue fever with pest control and compare the basic reproduction ratio for the systems with and without the pest control. To do so, a new parameter d, which indicates the effect of pesticide on the vector, is adjusted to the equations for the dynamics of V and M, respectively, infected and susceptible vectors, of the system (4.5). The renewed system is then formulated



(a) (b)

Figure 4.2: The change of R_0 with and without pest control as (a) $b+\gamma$, (b) β_s varies.

as

$$\begin{aligned} \dot{I} &= \beta_s SV - (b+\gamma)I, \\ \dot{V} &= \beta_m MI - cV - dV, \\ \dot{S} &= b - bS + \gamma I - \beta_s SV, \\ \dot{M} &= c - cM - \beta_m MI - dM. \end{aligned} \tag{4.6}$$

As a result of this modification, the matrix V is now computed as

$$V = \begin{pmatrix} b+\gamma & 0 \\ 0 & c+d \end{pmatrix},$$

and, accordingly, the basic reproduction ratio R_0 is found to be

$$R_0 = \sqrt{\frac{\beta_m \beta_s}{(c+d)(b+\gamma)}}.$$

In Figure 4.2, the dynamics of the renewed system (4.6) is shown as a function of the sum $b+\gamma$ and β_s, respectively. The effect of d on the basic reproduction ratio is obvious: pest control has a great effect on the eradication of the disease.

Additionally, one can determine the minimum level of pesticide to apply on vector as long as the other parameters included in the system are prescribed. For example, if the parameters in the system were $\beta_s = \beta_m = 0.5$, $c = \gamma = 0.1$, and $b = 1$, then the minimum value of d is calculated as 0.1273. The change of the basic reproduction ratio as a function of the parameter d is depicted in Figure 4.3: if $d > 0.1273$, then R_0 is less than 1, conversely, if $d < 0.1273$ then R_0 is greater than 1. In other words, if $d > 0.1273$ then disease will be extinct, and if $d < 0.1273$, then disease will invade the population despite the effect of the pest control on the vectors (carriers). This anaylsis enables ust to prevent the spread of the disease.

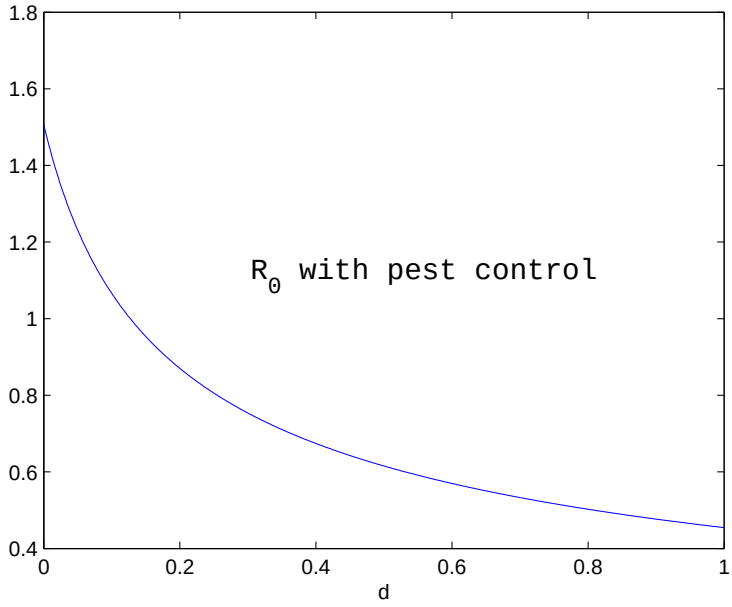


Figure 4.3: The change of R_0 with pest control as d varies.

CHAPTER 5

THRESHOLD DYNAMICS FOR A PERIODIC COMPARTMENTAL EPIDEMIC MODEL

In this chapter, we introduce the threshold dynamics for a compartmental epidemic model with the difference of periodic environment. In the previous chapter, disease transmisson model is considered for the autonomous case, however, in this chapter we analyze this model for the nonautonomous case based on the theory provided by Wang and Zhao [27].

In real life, many epidemic diseases show seasonal behavior for many reasons. For example, seasonal contact rates because of the opening and closing schools, periodic changes in birth rates and vaccination programs can be considered as a source of periodicity. Therefore, in order to analyze threshold dynamics for a disease transmisson, it is important to consider periodicity as well. We establish the basic reproduction ratio, defined in the preceding chapter, for the periodic epidemic model and analyze the threshold dynamics of the periodic system.

5.1 A Periodic Compartmental Epidemic Model

In this part, we consider again a heteregenous population, cited in Chapter 4, but now within a periodic environmental setting. We make some modifications to the given definitions and additions to the previous assumptions to have a system of nonautonomous, but periodic, ordinary differential equations.

We classify the population in n homogeneous compartments as before, and seperate them into two types: infected compartments, labeled by $i = 1, \ldots, m$, and uninfected compartments, labeled by $i = m+1, \ldots, n$. The brief description of variables can be given as follows: we denote again the state of individuals in each compartment by $x = (x_1, \ldots, x_n)^T$, and the set of all disease-free states by

$$\mathcal{X}_s = \{x \geq 0 : x_i = 0, \text{ for } i = 1, \ldots, m\}.$$

Furthermore, we define

$\mathcal{F}_i(t,x)$: the input rate of newly infected individuals in the ith compartment,
$\mathcal{V}_i^+(t,x)$: the input rate of individuals by other means,
$\mathcal{V}_i^-(t,x)$: the rate of transfer of individuals out of the the compartment i.

The disease transmission model is constructed by the nonautonomous differential system

$$\frac{dx_i}{dt} = \mathcal{F}_i(t,x) - \mathcal{V}_i(t,x) = f_i(t,x), \qquad i = 1,\dots,n. \tag{5.1}$$

where $\mathcal{V}_i = \mathcal{V}_i^- - \mathcal{V}_i^+$. As Wang and Zhao [27] did, using the information for autonomous compartment model in Driesshe and Watmough [26], we make the following assumptions for nonautonomous case in the sequel.

Assumptions and Clarifications.

(A1) For each $1 \le i \le n$, the functions $\mathcal{F}_i(t,x)$, $\mathcal{V}_i^+(t,x)$ and $\mathcal{V}_i^-(t,x)$ are non-negative and continuous on $\mathbb{R} \times \mathbb{R}_+^n$ and continuously differentiable with respect to x. This assumption represents the idea of that each function denotes a directed non-negative transfer of individuals.

(A2) There is a real number $\omega > 0$ such that for $1 \le i \le n$, the functions $\mathcal{F}_i(t,x)$, $\mathcal{V}_i^+(t,x)$ and $\mathcal{V}_i^-(t,x)$ are ω-periodic in t in order to define a periodic system.

(A3) If $x_i = 0$, then $\mathcal{V}_i^- = 0$. Particularly, if $x \in \mathcal{X}_s$, then $\mathcal{V}_i^- = 0$ for $i = 1,\dots,m$. This means that if a compartment is empty, then there is no transfer of individuals out of the compartment.

(A4) $\mathcal{F}_i = 0$ for $i > m$. That is, the incidence of infection for uninfected compartment is zero.

(A5) If $x \in \mathcal{X}_s$, then $\mathcal{F}_i(x) = \mathcal{V}_i^+(x) = 0$ for $i = 1,\dots,m$. This assumption states that the population will remain free of disease if it is so initially.

In [27], Wang and Zhao assume that the model (5.1) has a disease-free periodic solution $x^0(t) = (0,\dots,0,x_{m+1}^0(t),\dots,x_n^0(t))$ with $x_i^0(t) > 0$, $m+1 \le i \le n$ for all t. Let $f = (f_1,\dots,f_n)^T$ and define an $(n-m)\times(n-m)$ matrix

$$M(t) = \left[\frac{\partial f_i(t,x^0(t))}{\partial x_j}\right]_{m+1\le i,j\le n}.$$

Let $\Phi_M(\omega)$ be the monodromy matrix of the linear ω-periodic system

$$\frac{dz}{dt} = M(t)z.$$

Then, we impose another condition that $x^0(t)$ is linearly asymptotically stable in the disease-free subspace $\mathcal{X}_s$:

(A6) $\rho(\Phi_M(\omega)) < 1$, where $\rho(\Phi_M(\omega))$ is the spectral radius of $\Phi_M(\omega)$.

Following the similar arguments of Chapter 4, specifically by Lemma 4.1, we are able to state that

$$D_x\mathcal{F}(t,x^0(t)) = \begin{pmatrix} F(t) & 0 \\ 0 & 0 \end{pmatrix}, \qquad D_x\mathcal{V}(t,x^0(t)) = \begin{pmatrix} V(t) & 0 \\ J(t) & -M(t) \end{pmatrix},$$

where $F(t)$ and $V(t)$ are two $m \times m$ matrices defined by

$$F(t) = \left[\frac{\partial \mathcal{F}_i(t, x^0(t))}{\partial x_j}\right]_{1\le i,j\le m}, \qquad V(t) = \left[\frac{\partial \mathcal{V}_i(t, x^0(t))}{\partial x_j}\right]_{1\le i,j\le m},$$

respectively, and $J(t)$ is an $(n-m) \times m$ matrix. From their definitions, it is clear that $F(t)$ is nonnegative and $-V(t)$ is cooperative in the sense that the off-diagonal elements of $-V(t)$ are nonnegative.

The Basic Reproduction Ratio

Now, in order to define the basic reproduction ratio, let us consider an infective individual introduced into the population and assume that reinfection is turned off. Therefore, the dynamics of the linearized system for (5.1) is represented by

$$\dot{x} = -D_x \mathcal{V}(t, x^0(t))(x - x^0).$$

First, let $\phi(s)$ be the initial distribution of infectious individuals, that is, $\phi(s)$ shows the first m component of x at time s. Because of the partitioning of $-D_x \mathcal{V}(t, x^0(t))$, solution of the system

$$\frac{dy}{dt} = -V(t)y \tag{5.2}$$

with initial condition $\phi(s)$ gives the distribution of infectious individuals newly infected at time s and remain in the infected compartment at time t. Thus, if $Y(t, s)$ is the evolution operator for (5.2) and satisfy

$$\frac{d}{dt}Y(t, s) = -V(t)Y(t, s), \quad Y(s, s) = I,$$

then $Y(t, s)\phi(s)$ is the solution of (5.2).

Next, $F(s)Y(t, s)\phi(s)$ describes the distribution of new infections produced by the infected individuals who were introduced at time s and remain in the infected compartment at time t. Furthermore,

$$\psi(t) = \int_{-\infty}^{t} F(s)Y(t, s)\phi(s)ds = \int_{0}^{\infty} F(t-a)Y(t, t-a)\phi(t-a)da \tag{5.3}$$

gives the distribution of accumulative new infections at time t produced by all those infected individuals $\phi(s)$ introduced at previous times till time t.

Meanwhile, we note that the internal evolution of individuals in the infection compartments is dissipative and exponentially decreasing in many cases due to the loss of infective members from natural mortalities and disease-induced mortalities. Therefore, another assumption becomes

(A7) $\rho(\Phi_{-V}(\omega)) < 1$.

Considering the last assumption and the standard Floquet theory, there exist $K > 0$ and $\alpha > 0$ such that

$$\|Y(t,s)\| \leq Ke^{-\alpha(t-s)} \tag{5.4}$$

for $t \geq s$ and $s \in \mathbb{R}$. This follows that

$$\|Y(t,t-a)F(t-a)\| \leq K \|F(t-a)\| e^{-\alpha a}$$

for $t \geq s$, and $a \in [0,\infty)$.

Now, we introduce the next infection operator L: let C_ω be the ordered Banach space of all ω-periodic functions from $\mathbb{R}$ to $\mathbb{R}^m$, which is equipped with the maximum norm $\|\cdot\|$ and the positive cone $C_\omega^+ = \{\phi \in C_\omega : \phi(t) \geq 0, \text{ for } t \in \mathbb{R}\}$. Then, the linear operator $L : C_\omega \to C_\omega$ is defined by

$$(L\phi)(t) = \int_0^\infty Y(t,t-a)F(t-a)\phi(t-a)da \tag{5.5}$$

for every $t \in \mathbb{R}$ and $\phi \in C_\omega$.

Operator L is called the next infection operator and its spectral radius is defined to be the basic reproduction ratio:

$$R_0 = \rho(L)$$

of the epidemic model (5.1). Note that we can state (5.3) as a linear operator by defining

$$(\tilde{L}\phi)(t) = \int_{-\infty}^t F(s)Y(t,s)\phi(s)ds = \int_0^\infty F(t-a)Y(t,t-a)\phi(t-a)da,$$

where $\tilde{L} : C_\omega \to C_\omega$. Although the kernel in the operator L is different from the one in the operator $\tilde{L}$, the two operators have the same spectral radius. Using this fact and following the study in [27], we choose to work with the operator L.

If we take into account the case where $V(t)$ is reducible, then we define

$$V_\epsilon(t) = V(t) - \epsilon E$$

for $\epsilon \in [0,\infty)$, where E is the $m \times m$ matrix with each element being unity. In this case, $-V_\epsilon(t)$ becomes cooperative and irreducible for each $t \in \mathbb{R}$. By this modification, $Y_\epsilon(t,s)$ represents the evolution operator of the linear system (5.2) with $V(t)$ replaced by $V_\epsilon(t)$. This follows that there exists an $\epsilon_0 > 0$ such that for any $\epsilon \in [0,\epsilon_0)$, $Y_\epsilon(t,s)$ admits a similar property as in Hale [15], by the theory of perturbed linear systems. As a consequence, we introduce the linear operator L_ϵ by replacing $Y(t,s)$ in (5.5) with $Y_\epsilon(t,s)$ and set $R_0^\epsilon = \rho(L_\epsilon)$ for $\epsilon \in [0,\epsilon_0)$.

Lemma 5.1 (Wang, Zhao [27])**.** *Let the assumptions (A1)–(A7) hold. Then,*

(i) the operator L is positive, continuous and compact on C_ω.

(ii) $\lim_{\epsilon\to 0^+} \rho(\Phi_{F-V_\epsilon}(\omega)) = \rho(\Phi_{F-V}(\omega))$, *and* $\lim_{\epsilon\to 0^+} R_0^\epsilon = R_0$.

Lemma 5.1 will be useful in the proofs of the following theorems.

Now, in the search of calculating the basic reproduction ratio R_0, but not directly form the spectral radius of L, we investigate the following linear ω-periodic equation

$$\frac{dw}{dt} = \left[-V(t) + \frac{F(t)}{\lambda}\right] \tag{5.6}$$

with parameter $\lambda \in (0, \infty)$. Moreover, let $W(t, s, \lambda)$, $t \geq s$, $s \in \mathbb{R}$ be the evolution operator of the system (5.6) on $\mathbb{R}^m$.

It is easy to see that if $\lambda = 1$ then $W(t, 0, 1) = \Phi_{F-V}(t)$, $t \geq 0$ and for each $\lambda \in (0, \infty)$ the matrix $-V(t)+\frac{F(t)}{\lambda}$ is cooperative. Then, the linear operator $W(t, s, \lambda)$ is positive in $\mathbb{R}^m$ for each $t \geq s$, $s \in \mathbb{R}$. Therefore, the Perron Frobenius theorem in [5] states that $\rho(W(\omega, 0, \lambda))$ is an eigenvalue of $W(\omega, 0, \lambda)$ with a nonnegative eigenvector. Another observation can be noticed from the Floquet theory. Since the matrix $W(s + \omega, s, \lambda)$ is similar to the matrix $W(\omega, 0, \lambda)$, clearly, $\sigma(W(s + \omega, s, \lambda)) = \sigma(W(\omega, 0, \lambda))$ for any $s \in \mathbb{R}$, where $\sigma(D)$ denotes the spectrum of the matrix D.

Theorem 5.2 (Wang, Zhao [27])**.** *Let the assumptions (A1)–(A7) hold. Then,*

(i) if $\rho(W(\omega, 0, \lambda)) = 1$ *has a positive solution* λ_0*, then* λ_0 *is an eigenvalue of* L*, and* $R_0 > 0$*;*

(ii) if $R_0 > 0$*, then* $\lambda = R_0$ *is the unique solution of* $\rho(W(\omega, 0, \lambda)) = 1$*;*

(iii) $R_0 = 0$ *if and only if* $\rho(W(\omega, 0, \lambda)) < 1$ *for all* $\lambda > 0$.

Proof. We consider the cases separately:

(i) Let us consider the case $\rho(W(\omega, 0, \lambda)) = 1$ for some $\lambda_0 > 0$. As stated before the theorem, 1 is an eigenvalue of $W(\omega, 0, \lambda)$ with a nonnegative eigenvector ϕ_0. So, $W(\omega, 0, \lambda)\phi_0 = \phi_0$ and this means that system (5.6) with $\lambda = \lambda_0$ has an ω-periodic solution which is represented by $\phi(t) = W(t, 0, \lambda_0)\phi_0$. By treating system (5.6) as a nonhomogeneous ordinary differential equations in the form of $\frac{dw}{dt} = -V(t)w + \frac{F(t)}{\lambda}w$ and using constant-variation formula, we are able to express $\phi(t)$ as

$$\phi(t) = Y(t, \tau)\phi(\tau) + \int_\tau^t Y(t, s)\frac{F(s)}{\lambda_0}\phi(s)ds$$

for $t \geq \tau$, and $\tau \in \mathbb{R}$. Then we take the limit as $\tau \to -\infty$ in order to reach L in terms of the integral form. Due to the boundedness of $\phi(t)$ on $\mathbb{R}$ and the inequality in (5.4), $Y(t, \tau)\phi(\tau) \longrightarrow 0$ as $\tau \to -\infty$, we obtain

$$\phi(t) = \int_{-\infty}^t Y(t, s)\frac{F(s)}{\lambda_0}\phi(s)ds$$

for $t \in \mathbb{R}$, that is, $L\phi = \lambda_0\phi$. In other words, $\lambda_0 \in \sigma(L)\setminus\{0\}$ and from the definition of R_0, $\rho(L) = R_0 > 0$.

(ii) Now, let R_0 be positive. Due to the Lemma 5.1, there exists $\epsilon_1 \in (0, \epsilon_0]$ such that $R_0^\epsilon = \rho(L_\epsilon) > 0$ for all $\epsilon \in [0, \epsilon_1]$. Because L_ϵ is positive, bounded and compact, by using the Krein Rutman theorem we conclude that R_0^ϵ is an eigenvalue of L_ϵ with an eigenvector $w > 0$ in C_ω, $w \in C_\omega^+\setminus\{0\}$. Therefore, there exists a $s_0 \geq 0$ such that $w(s_0) > 0$ in $\mathbb{R}^m$. If we call $W_\epsilon(t, s, \lambda)$ for $t \geq s$, $s \in \mathbb{R}$ as the evolution operator of the linear periodic system

$$\frac{dw}{dt} = \left[-V_\epsilon(t) + \frac{F(t)}{\lambda}\right] \tag{5.7}$$

with parameter $\lambda \in (0, \infty)$ then $w(t)$ satisfies the system (5.7) with $\lambda = R_0^\epsilon$ since $L_\epsilon w = R_0^\epsilon$. Therefore, we have $w(t) = W_\epsilon(t, s_0, R_0^\epsilon)w(s_0)$, for all $t \geq s_0$. Especially, having $w(s_0) = w(s + \omega)$ we conclude that

$$w(s_0 + \omega) = W_\epsilon(s_0 + \omega, s_0, R_0^\epsilon)w(s_0) = w(s_0).$$

This shows that 1 (unity) is an eigenvalue of $W_\epsilon(s_0 + \omega, s_0, R_0^\epsilon)$ with the eigenvector $w(s_0) > 0$ corresponding to that. Since $W_\epsilon(s_0 + \omega, s_0, R_0^\epsilon)$ is compact and strongly positive on $\mathbb{R}^m$, by the Krein Rutman theorem we have $\rho(W_\epsilon(s_0 + \omega, s_0, R_0^\epsilon)) = 1$. Then, $\rho(W_\epsilon(\omega, 0, R_0^\epsilon)) = 1$ because $\sigma(W_\epsilon(s_0 + \omega, s_0, R_0^\epsilon)) = \sigma(W_\epsilon(\omega, 0, R_0^\epsilon))$. If we let $\epsilon \to 0^+$, then we get $\rho(W(\omega, 0, R_0)) = 1$. The remaining part to prove is that $\rho(W(\omega, 0, \lambda)) = 1$ has at most one positive solution for λ. Firstly, the fact that $F(t)$ is nonnegative and $-V(t)$ is cooperative implies that $\rho(W(\omega, 0, \lambda))$ is nonincreasing in $\lambda \in (0, \infty)$ by the standard comparison theorem. By contradiction, assume that $\rho(W(\omega, 0, \lambda)) = 1$ has two positive solutions $\lambda_1 < \lambda_2$. Then, since $\rho(W(\omega, 0, \lambda))$ is nonincreasing in $\lambda \in (0, \infty)$, $\rho(W(\omega, 0, \lambda)) = 1$ for all $\lambda \in [\lambda_1, \lambda_2]$. By part (i) each λ in $[\lambda_1, \lambda_2]$ is an eigenvalue of L, however, this contradicts with the fact that L is a compact linear operator and has countably eigenvalues. Therefore, $\lambda = R_0$ is the unique solution of $\rho(W(\omega, 0, \lambda)) = 1$.

(iii) By part(i) and (ii), we conclude that $\rho(W(\omega, 0, \lambda)) = 1$ has a positive solution for some λ if and only if $R_0 > 0$. Hence, $R_0 = 0$ if and only if $\rho(W(\omega, 0, \lambda)) \neq 1$ for all $\lambda \in (0, \infty)$. The continuity of spectrum for matrices implies that $\rho(W(\omega, 0, \lambda))$ is continous in $\lambda \in (0, \infty)$ and

$$\lim_{\lambda\to\infty} \rho(W(\omega, 0, \lambda)) = \rho(\Phi_{-V}(\omega)) < 1.$$

This shows that $R_0 = 0$ if and only if $\rho(W(\omega, 0, \lambda)) < 1$ for all $\lambda \in (0, \infty)$.

The proof is completed. □

In order to give an explicit formula for R_0 in a special case of the periodic setting of (5.1), we introduce the average of a continuous periodic function as

$$[g] = \frac{1}{\omega}\int_0^\omega g(t)dt \tag{5.8}$$

where $g(t)$ is a continuous ω-periodic function.

Lemma 5.3 (Wang, Zhao [27]). *Let the assumptions (A1)–(A7) hold. If* $V(t) = \operatorname{diag}(V_1(t), \ldots, V_m(t))$ *and* $F(t) = \operatorname{diag}(F_1(t), \ldots, F_m(t))$, *then* $R_0 = \max_{1 \le i \le m} \left\{ \frac{[F_i]}{[V_i]} \right\}$.

Proof. If the matrices $F(t)$ and $V(t)$ are in the diagonal form, then the monodromy matrix of the system (5.6) is represented by

$$W(\omega, 0, \lambda) = \operatorname{diag}\left(\exp \int_0^\omega \left(-V_1(t) + \frac{1}{\lambda} F_1(t) \right) dt, \right.$$
$$\left. \ldots, \exp \int_0^\omega \left(-V_m(t) + \frac{1}{\lambda} F_m(t) \right) dt \right)$$

for all $\lambda > 0$. Thus,

$$\rho(W(\omega, 0, \lambda)) = \max_{1 \le i \le m} \left\{ \exp \int_0^\omega \left(-V_i(t) + \frac{1}{\lambda} F_i(t) \right) dt \right\}.$$

In order to find R_0 we are looking for a λ which satisfies

$$\rho(W(\omega, 0, \lambda)) = \max_{1 \le i \le m} \left\{ \exp \int_0^\omega \left(-V_i(t) + \frac{1}{\lambda} F_i(t) \right) dt \right\} = 1$$

and this is valid if and only if

$$\max_{1 \le i \le m} \left\{ \int_0^\omega \left(-V_i(t) + \frac{1}{\lambda} F_i(t) \right) dt \right\} = 0,$$

If we consider the integrals interms of a average of a function, then we obtain

$$\max_{1 \le i \le m} \left\{ -\omega \, [V_i] + \frac{\omega}{R_0} \, [F_i] \right\} = 0.$$

Consequently, we see that $R_0 = \max_{1 \le i \le m} \left\{ \frac{[F_i]}{[V_i]} \right\}$, which completes the proof. □

By Lemma 5.3 we give an expression of R_0 for a special case in which $V(t)$ and $F(t)$ are diagonal matrices. Now, in the following theorem, we present an interpretation of R_0 for any form of $V(t)$ and $F(t)$ by considering the spectral radius of the monodromy matrix of system (5.6) with $\lambda = 1$.

Theorem 5.4 (Wang, Zhao [27]). *Let the assumptions (A1)–(A7) hold. Then,*

(i) $R_0 = 1$ *if and only if* $\rho(\Phi_{F-V}(\omega)) = 1$.

(ii) $R_0 > 1$ *if and only if* $\rho(\Phi_{F-V}(\omega)) > 1$.

(iii) $R_0 < 1$ *if and only if* $\rho(\Phi_{F-V}(\omega)) < 1$.

In particular, $x^0(t)$ *is asymptotically stable if* $R_0 < 1$*, and unstable if* $R_0 > 1$.

Proof. Particular case is trivial, and the proofs of the statements are below.

(i) Assume that $R_0 = 1$, then by Theorem 5.2(ii), we obtain $\rho(W(\omega, 0, 1) = 1$. On the other hand, if $\rho(W(\omega, 0, 1) = 1$ then again by Theorem 5.2(i) and (ii) provide that $R_0 = 1$.

(ii) If $R_0 > 1$ then it means that $R_0 > 0$. Thus, due to the Krein Rutman theorem, there exists $w > 0$ in C_ω such that $Lw = R_0 w$. This implies that $w(t_0) > 0$ in $\mathbb{R}^m$ for some $t_0 \in [0, \omega]$ and $w(t)$ satisfies (5.6) with $\lambda = R_0$. Then we rearrange this system as

$$\frac{dw}{dt} = (F(t) - V(t))\, w(t) + \left(\frac{1}{R_0} - 1\right) F(t)w(t). \tag{5.9}$$

In this manner, first claim is that $F(t)w(t) \neq 0$. By contradiction let us assume that $F(t)w(t) = 0, \forall t \in \mathbb{R}$. Accordingly, system (5.9) reduces to

$$\frac{dw}{dt} = -V(t)w(t). \tag{5.10}$$

If $\Phi_{-V}(t, s), t \geq s, s \in \mathbb{R}$ is the evolution operator of the linear system (5.10), then

$$w(t_0) = w(t_0 + \omega) = \Phi_{-V}(t_0 + \omega, t_0)w(t_0).$$

That is, $1 \in \sigma(\Phi_{-V}(t_0 + \omega, t_0)) = \sigma(\Phi_{-V}(\omega))$ since $\Phi_{-V}(t_0 + \omega, t_0) = \Phi_{-V}(\omega, 0)$ and $\Phi_{-V}(t) = \Phi_{-V}(t, 0)$. But this contradicts with the assumption (A7) which says that $\Phi_{-V}(\omega) < 1$. Therefore, $F(t)w(t) \neq 0$.

Next, we use the constant-variation formula for the linear system (5.9) and we obtain

$$w(t_0) = w(t_0 + \omega) = W(t_0 + \omega, t_0, 1)w(t_0) + h,$$

where

$$h = \left(\frac{1}{R_0} - 1\right) \int_{t_0}^{t_0+\omega} W(t_0 + \omega, s, 1)F(s)w(s)ds.$$

Thus,

$$w(t_0) - W(t_0 + \omega, t_0, 1)w(t_0) = h. \tag{5.11}$$

If $V(t)$ is irreducible for each $t \in [0, \omega]$, then $W(t, s, 1)$ is strongly positive for each $t > s, s \in \mathbb{R}$. Since we see that $F(t)w(t) \neq 0$, we get

$$\int_{t_0}^{t_0+\omega} W(t_0 + \omega, s, 1)F(s)w(s)ds \gg 0$$

in $\mathbb{R}^m$. Then by the assumption $R_0 > 1$, we obtain that $h < 0$. Hence, we see that $1 < \rho(W(t_0 + \omega, t_0, 1)) = \rho(\Phi_{F-V}(\omega))$. In the reducible case of $V(t)$, we replace $V(t)$ with $V_\epsilon(t)$ and use the limit as $\epsilon \to 0$ and obtain $\rho(\Phi_{F-V}(\omega)) \geq 1$. However, $\rho(\Phi_{F-V}(\omega)) \neq 1$ by the conclusion (i), then we obtain $\rho(\Phi_{F-V}(\omega)) > 1$. Now, assume that $\rho(\Phi_{F-V}(\omega)) > 1$. Because of the result of (i), we have $R_0 \neq 1$. Theorem 5.2(iii) indicates that $R_0 > 0$ since $\rho(W(\omega, 0, 1)) = \rho(\Phi_{F-V}(\omega)) > 1$. In this concept, (5.11) is still valid. It is necessary to prove that $R_0 > 1$. By contradiction, suppose that $R_0 \in (0, 1)$. If $V(t)$ is irreducible for each $t \in [0, \omega]$, then (5.11) holds with $h >> 0$ in $\mathbb{R}^m$. Therefore, $1 > \rho(W(t_0 + \omega, t_0, 1) = \rho(\Phi_{F-V}(\omega))$. In the reducible case of $V(t)$, again we replace $V(t)$ with $V_\epsilon(t)$ and use the limit as $\epsilon \to 0$ and obtain $\rho(\Phi_{F-V}(\omega)) \leq 1$ which is a contradiction since we have $R_0 > 1$.

(iii) This statement is a consequence of (i) and (ii). Linearized form of the system in (5.1) yields

$$D_x f(t, x^0(t)) = \begin{pmatrix} F(t) - V(t) & 0 \\ -J(t) & M(y) \end{pmatrix}.$$

By (A6), we have $\rho(\Phi_M(\omega)) < 1$ and now adding the new result of this observation, we see that $x^0(t)$ is asymptotically stable if $\rho(\Phi(_{F-V}(\omega))) < 1$ and unstable if $\rho(\Phi(_{F-V}(\omega))) > 1$.

The proof is completed. □

5.2 Applications on a Periodic Vector Host Model

In this section, we present applications of the theory given through this chapter. We consider the vector-host model, however, in the case of a periodic setting.

Firstly, we examine the Dengue fever in a periodic environment since contact rates for this disease are sensitive to weather changes. Then, we study time-averaged system for Dengue fever and compare the results of both systems. Next, as a contribution of this work, we introduce a periodic vector-host model for avian influenza. Again, after analyzing the threshold dynamics of the model, we study time-averaged model and compare these results with periodic system.

5.2.1 An Analysis on Dengue Fever in a Periodic Environment

In this part of the study, we analyze the threshold dynamics of Dengue fever within a vector-host model considering periodic contact rates. Since we are familiar with this model, we give only the differences from the previous application in Chapter 4.

The model (4.5) has some parameters changing with time:

$$\begin{aligned}\dot{I} &= \beta_s(t)SV - (b+\gamma)I,\\ \dot{V} &= \beta_m(t)MI - cV,\\ \dot{S} &= b - bS + \gamma I - \beta_s(t)SV,\\ \dot{M} &= c - cM - \beta_m(t)MI,\end{aligned} \tag{5.12}$$

where $\beta_s(t)$ and $\beta_m(t)$ are functions of time. If we choose them as in Wang and Zhao [27]

$$\begin{aligned}\beta_s(t) &= k(1+\delta\cos(2\pi t)),\\ \beta_m(t) &= \beta_0(1+\delta\cos(2\pi t)),\end{aligned}$$

with δ being a constant parameter, then system (5.12) becomes a 1-periodic system because of including 1-periodic functions as $\beta_s(t)$ and $\beta_m(t)$. According to this modification, the partitioning of the linearized system give the matrices

$$F(t) = \begin{pmatrix} 0 & \beta_s(t) \\ \beta_m(t) & 0 \end{pmatrix} \quad \text{and} \quad V(t) = \begin{pmatrix} b+\gamma & 0 \\ 0 & c \end{pmatrix}.$$

If we further formulate the system of differential equation, we get

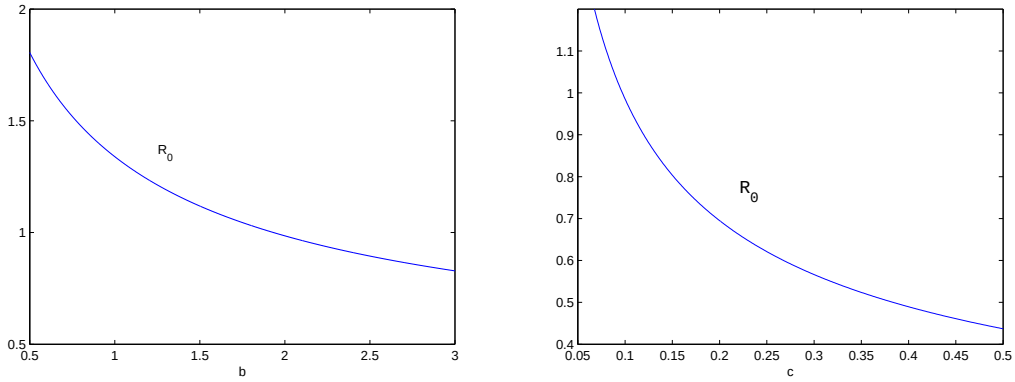
$$\frac{dw}{dt} = \begin{pmatrix} -(b+\gamma) & \frac{\beta_s(t)}{\lambda} \\ \frac{\beta_m(t)}{\lambda} & -c \end{pmatrix} w.$$

To begin with, we examine the general behavior of the periodic system with respect to its parameters. As an additional work to the paper of Wang and Zhao [27], we consider the birth rate b for the host and birth rate c for the vector as well. The change of R_0 is depicted in the following graphs with respect to the parameters b, c, k and δ, respectively.

Figure 5.1a analyses the behavior of R_0 according to the birth and death rate of the host b. It shows that R_0 is decreasing while b is increasing. In Figure 5.1b, the birth and death rate of the vector is considered. Clearly, an increment of c causes to spreading of the disease since vector is the main source of the disease.

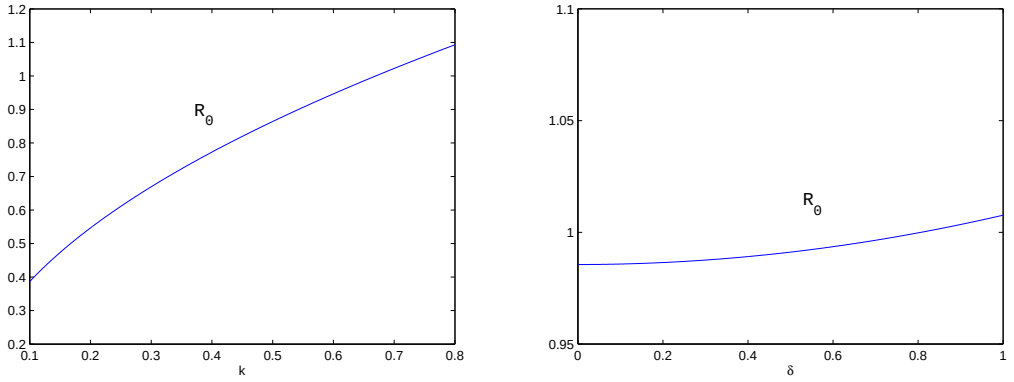
Further, in Figure 5.2a we figured the change of R_0 with respect to the parameter k included in the contact rate between host and vector. Since increment of k implies increment of the contact rate $\beta_s(t)$, this leads to increment of R_0 as well. Similarly, in Figure 5.2b a change of δ causes to spread of the disease as k does.

After insight of this work, we look for any extension of this theory and application. In this sense, since it is easier to work with an autonomous system instead of a periodic system, we consider the time-averaged one. However, the theory constructed for a periodic system can be unsuccesfull when the time-averaged system is used instead. For example, R_0 may be overestimated or underestimated by the time-averaged system. Therefore, we compare the basic reproduction ratio of the periodic system and the time-averaged system for this example in order to see



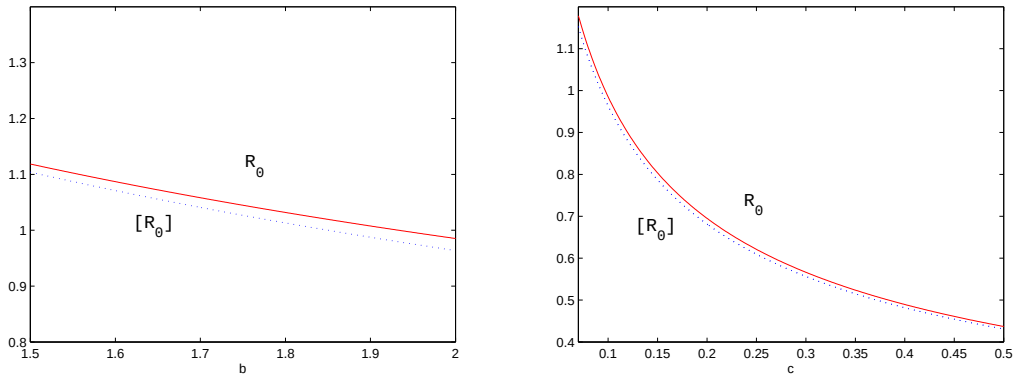
(a) (b)

Figure 5.1: The change of R_0 as (a) b, (b) c varies.



(a) (b)

Figure 5.2: The change of R_0 as (a) k, (b) δ varies.



(a) (b)

Figure 5.3: The changes of R_0 and $[R_0]$ as (a) b, (b) c varies.

whether there is a difference between them. In the time-averaged system, instead of $\beta_s(t)$ and $\beta_m(t)$, the averages $[\beta_s]$ and $[\beta_m]$ are used. By the definition given in (5.8)

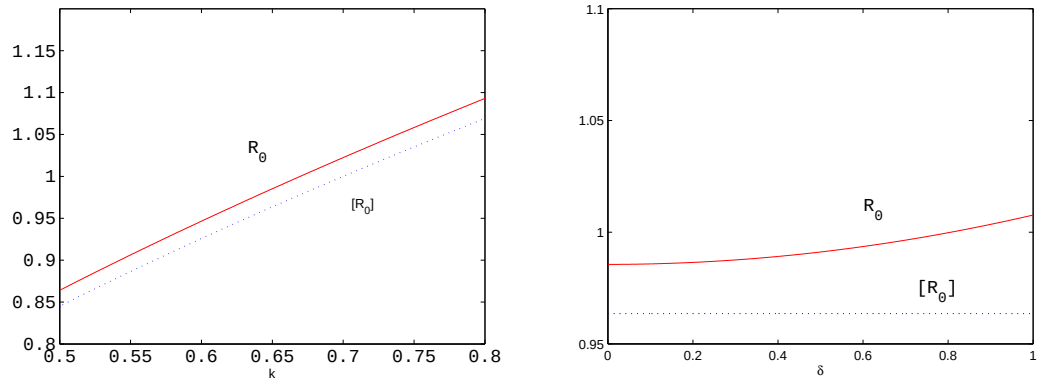
$$[\beta_s] = \frac{1}{1}\int k(1+\delta\cos(2\pi t))dt = k,$$
$$[\beta_m] = \frac{1}{1}\int \beta_0(1+\delta)\cos(2\pi t)dt = \beta_0.$$

Now, the system turns out to be an autonomous system and therefore the theory given in Chapter 4 is applicable for it. So, as an additional work to the paper of Wang and Zhao [27], we compare the results of these two systems according to the birth rate for the host b and birth rate for the vector c as well.

Meanwhile, let $[R_0]$ represent the basic reproduction ratio of the time-averaged system and be called as the average basic reproduction ratio.

For Figure 5.3a, we fix $\gamma = 0.1$, $k = 0.65$, $\delta = 1$, $\beta_0 = 0.3$, $c = 0.1$ and let b varies in $[0, 3]$. Numerical calculations shows that $[R_0] = 1$ when $b = 1,85$ and $R_0 = 1$ when $b = 1.993$. Further, $[R_0] = 0,9794$ when $b = 1,933$. This indicates that the average basic reproduction ratio underestimates the disease transmission risk. After that, we fix $b = 2$, $\gamma = 0.1$, $k = 0.65$, $\delta = 1$, $\beta_0 = 0.3$ and let c varies in $[0.07, 0.8]$. By Figure 5.3b, we infer that $[R_0] = 1$ when $c = 0,092$, $R_0 = 1$ when $c = 0,097$ and $[R_0] = 0.09784$ when $c = 0.097$. It is noted that there is an underestimation of the disease transmission risk by the average basic reproduction ratio.

Another proof of underestimation is obtained by numerical calculation in Figure 5.4a. If we fix $b = 2$, $\gamma = 0.1$, $\delta = 1$, $\beta_0 = 0.3$, $c = 0.1$ and let k varies in $[0, 1]$. We obtain that $[R_0] = 1$ when $k = 0.7$, $R_0 = 1$ when $k = 0.67$ and $[R_0] = 0.9783$ when $k = 0.67$. Therefore, it is clear that the averaged basic reproduction ratio underestimates the disease transmisson risk. Last but not the simplest result is



(a) (b)

Figure 5.4: The changes of R_0 and $[R_0]$ as (a) k, (b) δ varies.

obtained in Figure 5.4b. One can definitely notice that $[R_0]$ is always 0.9636 when δ varies in $[0, 1]$ if we fix $k = 0.68$ and other parameters are unchanged as above. However, R_0 is 1 when $\delta = 0.808$ and greater than 1 when $0.81 < \delta < 1$.

Consequently, all numerical calculations and figures imply the underestimation of the disease transmisson risk in the case of using the time-averaged system instead of using the periodic system.

5.2.2 An Analysis on Avian Influenza in a Periodic Environment

In this part of the work, we study another epidemic disease avian influenza, which can occur periodically, through a vector-host model. Avian influenza is known informally as avian flu or bird flu and refers to an ifluenza caused by viruses adapted to birds. However, adaptation is not restricted and viruses responsible for influenza outbreaks are adapted to both humans and birds. There are many subtypes of avian influenza viruses, but only some strains of four subtypes have been higly pathogenic in humans. These are the types H5N1, H7N3, H7N7 and H9N2. The most well known is the H5N1 subtype virus and it causes to death of at least 300 humans in Azerbaijan, Turkey and many countries. Currently, virus H5N1 is not transmitted easily from human to human. If the transmission rate from human to human increases, then another pandemic could occur. Therefore, people and organizations interested in this area work for developing strategies to prevent the spread of H5N1. So, this disease is also worthy of consideration in terms of examining its dynamics and making some progress of predicting its behavior.

As a contribution, we formulate the dynamics of the disease avian influenza in conjuction with vector-host model as the following system of ordinary differential

equations

$$\begin{aligned}
\dot{I} &= \eta(t)SV + \mu(t)SI - (b+\gamma)I, \\
\dot{V} &= \beta(t)MV - cV, \\
\dot{S} &= b + \gamma I - bS - \eta(t)SV - \mu(t)SI, \\
\dot{M} &= c - cM - \beta(t)MV,
\end{aligned} \tag{5.13}$$

where I, V, S, and M compartments denote the infected humans, infected birds, susceptible humans and susceptible birds respectively. Here,

$\eta(t)$	:	the disease transmission rate between humans and birds,
$\mu(t)$	:	the disease transmission rate between humans,
$\beta(t)$	:	the disease transmisson rate between birds,
b	:	the birth and death rate for the humans,
c	:	the birth and death rate for the birds,
γ	:	the recovery rate for the humans.

In order to use the theory given in this chapter, first we find the partitions of (5.13) as functions $\mathcal{F}_i(t,x)$ and $\mathcal{V}_i(t,x)$ where $x = (I,V,S,M)^T$ for $i = 1,\ldots,4$.

$$\begin{aligned}
&\mathcal{F}_1(t,x) = \eta(t)SV + \mu(t)SI, && \mathcal{V}_1^-(t,x) = (b+\gamma), && \mathcal{V}_1^+(t,x) = 0, \\
&\mathcal{F}_2(t,x) = \beta(t)MV, && \mathcal{V}_2^-(t,x) = cV, && \mathcal{V}_2^+(t,x) = 0, \\
&\mathcal{F}_3(t,x) = 0, && \mathcal{V}_3^-(t,x) = bS + \eta(t)SV, && \mathcal{V}_3^+(t,x) = b + \gamma I, \\
&\mathcal{F}_4(t,x) = 0, && \mathcal{V}_4^-(t,x) = cM + \beta(t)MV, && \mathcal{V}_4^+(t,x) = c.
\end{aligned}$$

Then (5.13) can be studied in the form of

$$\frac{dx_i}{dt} = \mathcal{F}_i(t,x) - \mathcal{V}_i(t,x)$$

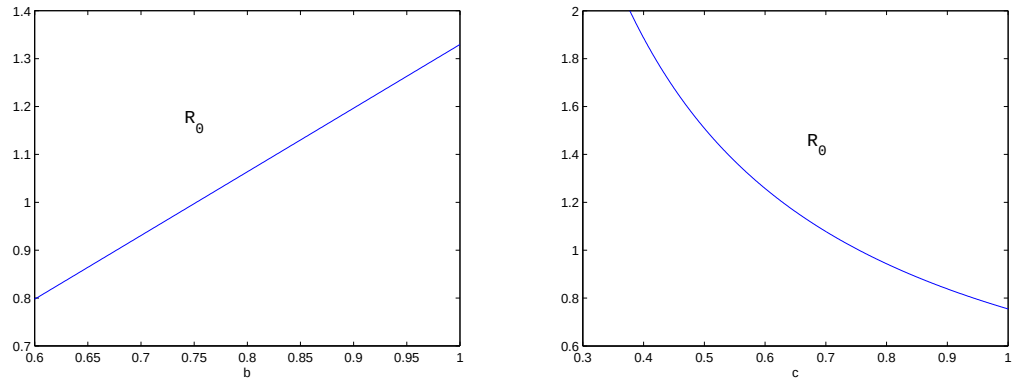
where $\mathcal{V}_i(t,x) = \mathcal{V}_i^-(t,x) - \mathcal{V}_i^+(t,x)$ for $i = 1,\ldots,4$. Next, since the disease-free equilibrium of this model is $x^0 = (0,0,1,1)^T$, two partitions of the linearized system at x^0 is formulated as $F(t)$ and $V(t)$ matrices where

$$F(t) = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(t,x^0)\right]_{1\le i,j\le 2} = \begin{pmatrix} \mu(t) & \eta(t) \\ 0 & \beta(t) \end{pmatrix},$$

$$V(t) = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(t,x^0)\right]_{1\le i,j\le 2} = \begin{pmatrix} b+\gamma & 0 \\ 0 & c \end{pmatrix}$$

so that we arrange (5.6) for this model as

$$\begin{aligned}
\frac{dw_1}{dt} &= \left(-(b+\gamma) + \frac{\mu(t)}{\lambda}\right) w_1 + \frac{\eta(t)}{\lambda} w_2, \\
\frac{dw_2}{dt} &= \left(-c + \frac{\beta(t)}{\lambda}\right) w_2.
\end{aligned}$$



(a) (b)

Figure 5.5: The change of R_0 as (a) b, (b) c varies.

For this application we consider the $\eta(t)$, $\mu(t)$, and $\beta(t)$ as

$$\eta(t) = \eta_0(1 + \alpha_1 \sin(2\pi t)),$$
$$\mu(t) = \mu_0(1 + \alpha_2 \sin(2\pi t)),$$
$$\beta(t) = \beta_0(1 + \alpha_3 \sin(2\pi t)).$$

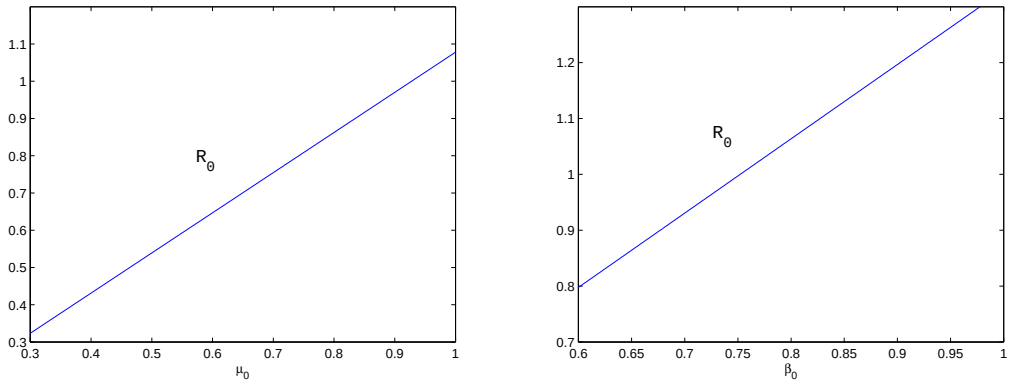
Now that we have a periodic system with period 1, as a contribution, using Theorem 5.2, the basic reproduction ratio of the system is calculated, and stability of the disease-free equilibrium can be analysed.

First, we consider all of the parameters of system to perform an analysis of the stability. However, we see that three of them, η_0, α_1 and α_2 do not have any notable effect on the change of stability when other parameters unchanged. Therefore we take into account of b, c, γ, β_0, μ_0 and α_3. By numerical calculations, we find a threshold parameter of each of them which determines that R_0 is greater or less than unity.

By Figure 5.5a, R_0 is considered according to parameter b. We see that if we fix other parameters, then $R_0 = 1$ when $b = 0.7520$. That is, if $b < 0.7520$ then disease free equilibrium is asymptotically stable and if $b > 0.7520$ then disease free equilibrium is unstable. In Figure 5.5b, we are interested with parameter c. It is observed that keeping c greater than 0.7540 satisifes the asymptotic stability of disease free equilibrium, otherwise disease free equilibrium is unstable.

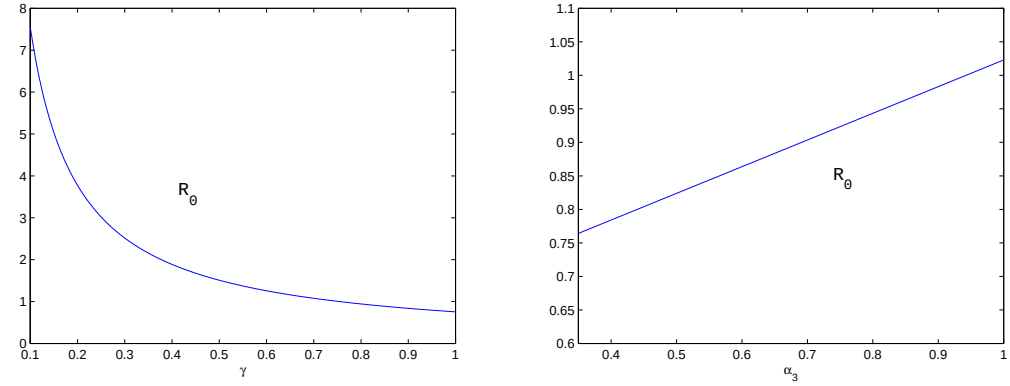
In Figure 5.6a, while μ_0 changes from 0.3 to 1, R_0 increases accordingly. Further, when $\mu_0 > 0.9280$, $R_0 > 1$ and when $\mu_0 < 0.9280$, $R_0 < 1$. Numerical calculations for Figure 5.6b imply that if β_0 is greater than 0.7520 then $R_0 > 1$ and if $\beta_0 < 0.7520$ then $R_0 > 1$ as in the case of b.

Next, the effect of γ is analyzed in Figure 5.7a and the observation says that if $\gamma > 0.7540$ then disease free equilibrium is asymptotically stable, and if $\gamma <$



(a) (b)

Figure 5.6: The change of R_0 as (a) μ_0, (b) β_0 varies.



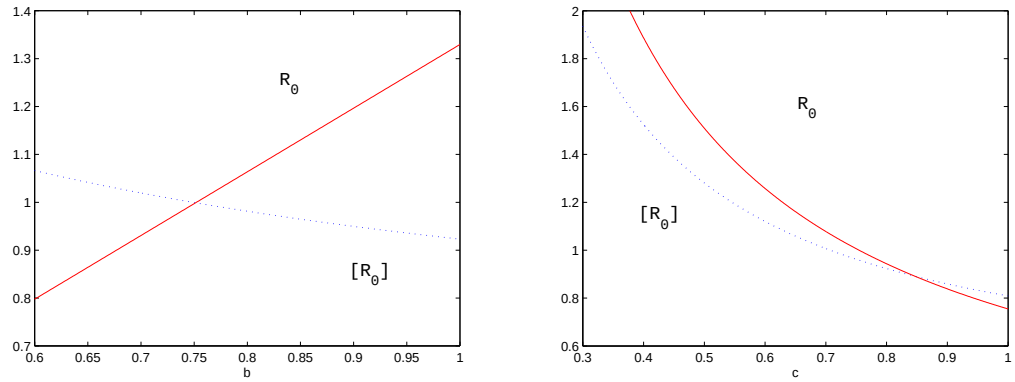
(a) (b)

Figure 5.7: The change of R_0 as (a) γ, (b) α_3 varies.

0.7540 then disease free equilibriums unstable. Finally, in Figure 5.7b we analyze α_3 and notice that when $\alpha_3 = 0.9430$, $R_0 = 1$. That is, if $\alpha_3 > 0.9430$ then $R_0 > 1$, and if $\alpha_3 < 0.9430$ then $R_0 < 1$.

Briefly, all the parameters are analyzed and their effects on the stability of disease free equilibrium are observed. After getting this general inspect about the system, we investigate how the time-averaged system is close to the periodic system in terms of the stabillity of disease free equilibrium. Therefore, averages of the function $\eta(t)$, $\mu(t)$ and $\beta(t)$ are found as

$$[\eta] = \frac{1}{1}\int_0^1 \eta_0(1+\alpha_1\sin(2\pi t))dt = \eta_0$$
$$[\mu] = \frac{1}{1}\int_0^1 \mu_0(1+\alpha_2\sin(2\pi t))dt = \mu_0$$
$$[\beta] = \frac{1}{1}\int_0^1 \beta_0(1+\alpha_3\sin(2\pi t))dt = \beta_0$$



(a) (b)

Figure 5.8: The changes of R_0 and $[R_0]$ as (a) b, (b) c varies.

so that we have an autonomous form of the system that can be solved via the theory summarized in Chapter 4.

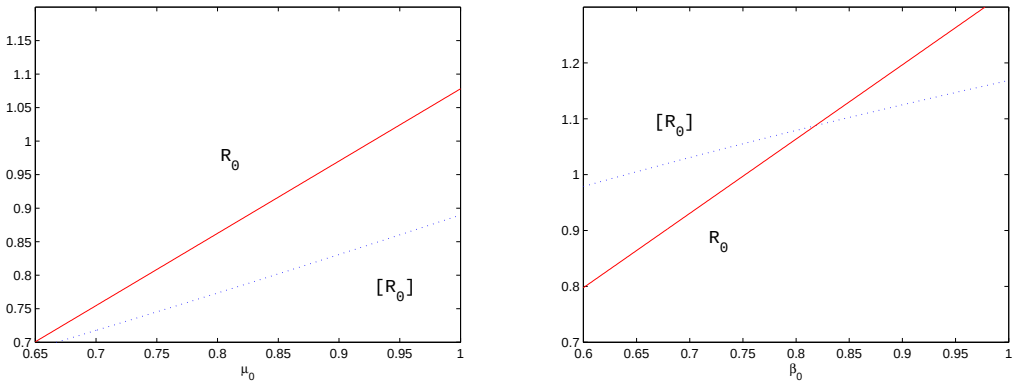
Clearly, for analysis of avian influenza, the case more tragic than the case of Dengue fever. Although in analysis of Dengue fever the time-averaged system only underestimates the disease transmisson risk, now it both underestimates and overestimates. This can be seen from the following figures of the comparison of the time-averaged and periodic system. Through these six figures, R_0 is analyzed with respect to the parameters b, c, μ_0, β_0, γ, and α_3.

Figure 5.8a proves the overestimation for $b < 0.7540$ and underestimation for $b > 0.7540$, clearly. Also, R_0 and $[R_0]$ show different types of characteristics since $[R_0]$ is decreasing function and R_0 is increasing function according to b. In Figure 5.8b, it is noted that $[R_0]$ and R_0 have same types of behaviors according to c but there is an underestimation for $c < 0.8470$ and an overestimation for $c > 0.8470$.

In Figure 5.9a, we observed that while for all $\mu_0 \in [0, 1]$, $[R_0]$ can not reach 1, $R_0 = 1$ when $\mu_0 = 0.9280$ and $R_0 > 1$ when $\mu_0 > 0.9280$. Moreover, for $0.65 \leq \mu_0 \leq 1$ the time averaged system underestimates the disease transmisson risk. In Figure 5.9b, the graph of β_0 resembles the graph of b, that is, both graphs imply the same behavior.

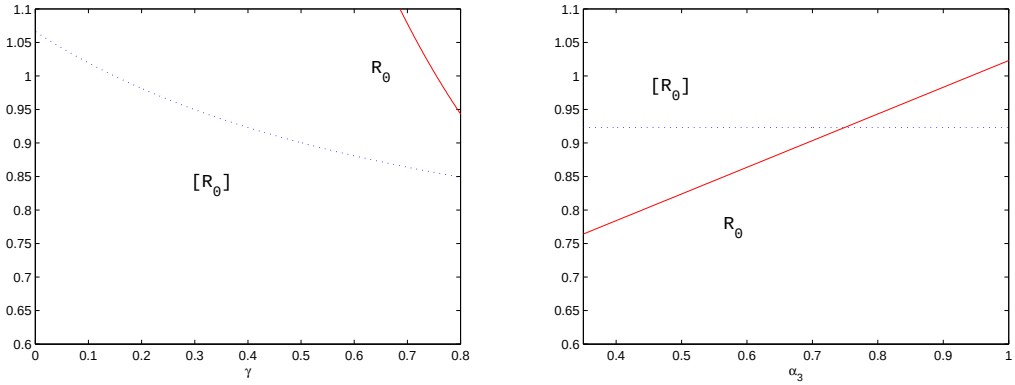
More apparent difference occurs in Figure 5.10a since $R_0 = 1$ when $\gamma = 0.7540$ and $[R_0] = 1$ when $\gamma = 0.1490$. There is a huge difference between the values of R_0 and $[R_0]$ for $\gamma \in [0, 1]$. Lastly by Figure 5.10b, as in the analysis of Dengue fever, definite proof of underestimation of the disease transmission risk is observed on the graph of α_3. Despite the fact that $R_0 > 1$ for $\alpha_3 > 0.9430$ and $R_0 < 1$ for $\alpha_3 < 0.9430$, $[R_0]$ is always 0.9231 for all $\alpha_3 \in [0, 1]$.

Consequently, all of the numerical calculations imply that the time-averaged system underestimates or overestimates the disease transmisson risk. Therefore, the time-average system is not appropriate to use it instead of a periodic system.



(a) (b)

Figure 5.9: The changes of R_0 and $[R_0]$ as (a) μ_0, (b) β_0 varies.



(a) (b)

Figure 5.10: The changes of R_0 and $[R_0]$ as (a) γ, (b) α_3 varies.

CHAPTER 6

CONCLUSION AND OUTLOOK

In this thesis, we have reviewed several works that analyze the threshold dynamics for compartmental epidemic models for both autonomous and periodic systems. Moreover, we have made some additional works to the paper of Driessche and Watmough [26], and as a contribution, we model the dynamics of the disease transmission model of avian influenza.

First of all, we have reviewed the study of Driessche and Watmough [26], in which the threshold dynamics is examined for Dengue fever via autonomous systems. As an additional application of this theory, we have applied a strategy to control the spread of the disease, which is called pest control. The observations have showed the positive effect of pest control as an eradication policy, since it reduces the basic reproduction ratio of the disease. We conclude that due to this strategy one can determine the minimum level of pesticide to prevent the spread of the disease.

Next, we have presented a detailed study of Wang and Zhao [27]. Application of this theory consists of two main parts. Considering periodic vector-host model for Dengue fever, firstly, as an additional piece to the work of Wang and Zhao, we analyze the threshold dynamics of this model with respect to the birth rate of humans and mosquitos as well. Then, we have made a comparison between time-averaged and periodic systems and accordingly, results show the underestimation of the disease transmission risk by the time-averaged system. In the second part, as a contribution, we have proposed a vector host model for avian influenza. We examine the threhold dynamics of this disease with respect to all parameters included in the model. Moreover, we have implemented the calculation of R_0 in time-averaged system for avian influenza and compared this result with periodic case. As a result, the implementations clearly indicate the proof of the underestimation and overestimation of the time-averaged basic reproduction ratio, which clearly implies the risky assessment of the disease transmission prediction by the averaged basic reproduction ratio.

We believe that this study could also be investigated using stochasticity in the contact rates in order to further extend the theiry and to mimic the real world applications. Additionaly, approaches by delay differential equations or impulsive differential equations may improve the analysis of the models in terms of

consistency with the real world.

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