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CONTINUOUS- AND DISCRETE-TIME STRUCTURED
MALARIA MODELS AND THEIR DYNAMICS

by

JUNLIANG LU

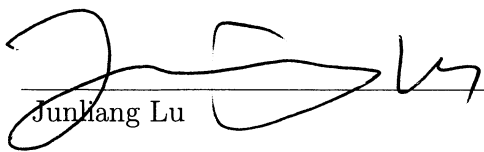
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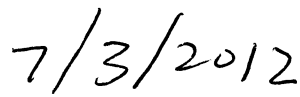
Submitted in partial fulfillment of the requirements
for the degree of Doctor of Philosophy
in
The Department of Mathematical Sciences
to
The School of Graduate Studies
of
The University of Alabama in Huntsville

HUNTSVILLE, ALABAMA

2012

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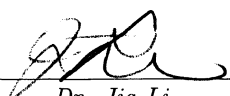

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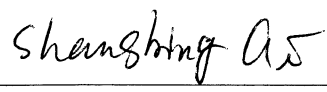

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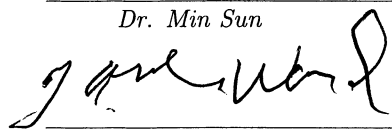
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We, the undersigned members of the Graduate Faculty of The University of Alabama in Huntsville, certify that we have advised and/or supervised the candidate of the work described in this dissertation. We further certify that we have reviewed the dissertation manuscript and approve it in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Mathematical Sciences.


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ABSTRACT

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Title Continuous- and Discrete-time Structured Malaria Models
and their Dynamics

Mosquito-borne diseases, including malaria, have been big concerns for the public health. No vaccines are available. An effective way to prevent the diseases is to control mosquitoes. To set any feasible optimal strategy in the control of mosquitoes and the diseases, we need to have a better understanding of the population dynamics of mosquitoes and transmission dynamics of the diseases. Mathematical models have been playing an important role to achieve our goals in this regard. Over the past century, considerable work has been done in modeling of malaria transmission, but, few of such studies have included the mosquitoes metamorphic stages structure, and most of the works are focused on continuous-time models. The aim of this dissertation is to formulate more stage-structured malaria models of continuous- as well as discrete-time, and provide more detailed investigations on dynamics of models with stage-structured mosquito populations.

We first formulate and study continuous-time models of the mosquito populations without infection. We determine the net reproductive number r_0 of the mosquito populations and investigate the mosquito population dynamics based on r_0 . We then study

continuous-time models of malaria with stage-structured mosquitoes, where we derive a formula for the reproductive number of infection R_0 , determine two critical numbers R_b and R_c , and then study the global dynamics of the disease transmission, based on R_0 , R_b , and R_c , including the appearance of a backward bifurcation.

We also formulate discrete-time stage-structured mosquito population models, based on difference equations. We include the four distinct mosquito metamorphic stages in the models, and investigate the existence and stability of all equilibria. We show that the models exhibit richer dynamics. We then formulate discrete-time models for malaria transmission, and determine threshold conditions for the epidemics. Incorporating the stage-structured mosquitoes, we formulate a discrete-time structured malaria model and study the model dynamics.

We finally provide summaries of our results and propose open problems for future research.

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LIST OF SYMBOLS

SYMBOL	DEFINITION
r_0	The inherent net reproductive number
R_0	The basic reproductive number
\mathbb{R}_+^n	The nonnegative orthant of space \mathbb{R}^n
$\text{int}(\mathbb{R}_+^n)$	The interior of \mathbb{R}_+^n
E	Eggs of mosquitoes
L	Larvae of mosquitoes
P	Pupae of mosquitoes
N_v (or M, N^v)	Adult mosquito populations
b (or b^v)	The birth rate of mosquitoes
μ_E	The natural death rate of eggs
μ_L	The natural death rate of larvae
μ_P	The natural death rate of pupae
μ_v	The natural death rate of adult mosquitoes
k_E, k_L and k_P	The stage progression rates

α	The larva density, causing larva death rate
β	The larva density, causing pupa death rate
N_h (or N^h)	The total human being populations
S_h (or S^h)	The susceptible human beings
E_h (or E^h)	The exposed or incubating human beings
I_h (or I^h)	The infectious human beings
R_h (or R^h)	The recovered human beings
S_v (or S^v)	The susceptible mosquitoes
E_v (or E^v)	The exposed or incubating mosquitoes
I_v (or I^v)	The infectious mosquitoes
Λ_h (or Λ)	The input flow of the susceptible human beings including birth rate
μ_h	The natural death rates of human beings
μ_v	The natural death rates of mosquitoes
δ_h	The disease-induced death rate for human beings
γ_h (or γ^h)	The developing rates of exposed human beings becoming infective
γ_v (or γ^v)	The developing rates of exposed mosquitoes becoming infective

η_h (or η^h)	The recovery rate of human beings
λ_h (or λ^h)	The infection rates for human beings
λ_v (or λ^v)	The infection rates for mosquitoes
r	The number of bites on a human by an individual mosquito per unit of time
β_v (or β^v)	The transmission probability per bite to a susceptible human being from an infective mosquito
β_h (or β^h)	The transmission probability per bite to a susceptible mosquito from an infective human being
V (or W)	Lyapunov functions
\dot{V} (or \dot{W})	The orbital derivative of V (or W)
\mathcal{E}^0	The infection-free equilibrium
\mathcal{E}^*	The endemic equilibrium
s_0	The survival probability of the eggs
$s_e(L)$	The surviving-adjusted hatching rate
$s_l(L)$	The surviving-adjusted pupation rate
s_p	The survival probability of pupae
$s_m(M)$	The survival probability of adult mosquitoes
$\alpha^{vb}(t)$	The survival probabilities of the newborn mosquitoes

$\alpha^v(t)$	The survival probabilities of the susceptible adult mosquitoes
α^{vE}	The survival probabilities of the incubating adult mosquitoes
$\alpha^{vI}(t)$	The survival probabilities of the infective adult mosquitoes
α^h	The survival probability of susceptible, latent, and recovered human beings
α^{hI}	The survival probability of infectious human beings
θ^h	The rate of partial immunity loss

To my wife and my parents

If I have seen further it is by standing on the shoulders of giants.

—Isaac Newton

CHAPTER 1

THE STUDY OF MALARIA AND ITS IMPACT

*Research is what I'm doing
when I don't know what I'm doing.*

—Wernher von Braun

1.1 What is malaria and its public health impact

Malaria is a mosquito infectious disease caused by a parasite plasmodium, which infects red blood cells. Historical records suggest that malaria has infected human beings from the beginning of mankind. The term “malaria” came from Italian and was first used in English in 1740 by H. Walpole to describe the disease. In the beginning, it was written as “mal aria”, whose meaning was “bad air” in Italian. “Mal aria” was shortened to “malaria” in 20th century. There are many obvious symptom characteristics to malaria like as flu-like illness, such as fever, chills, muscle aches, and headache. With the development of malaria, some patients become more serious, and appear nausea, vomiting, cough, and diarrhea. A typical characteristic is the cycles of chills, fever, and sweating that repeat every one, two, or three days. Because of destruction of red blood cells and liver cells by malaria, the patient’s skin and eyes become white. Some

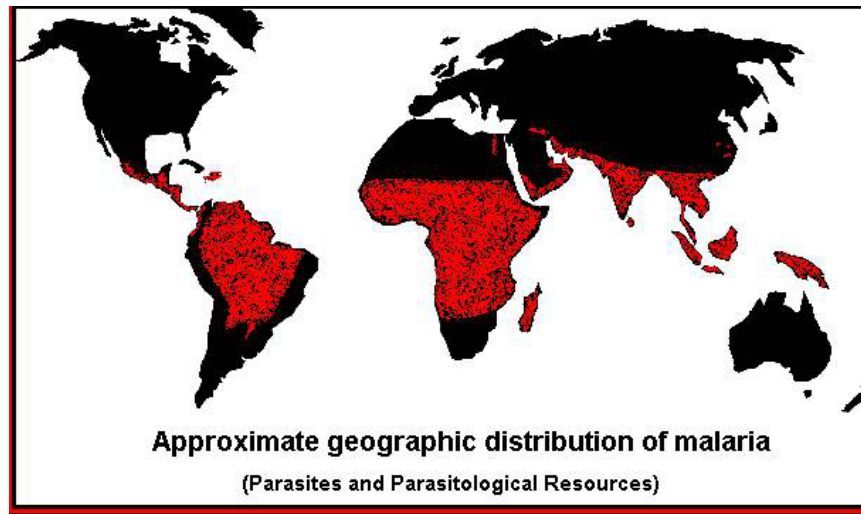


Figure 1.1: Geographic distribution of malaria in 2006

people with severe *Plasmodium Falciparum* malaria can develop more serious problems, such as coma, shock, liver or kidney failure, bleeding problems, central nervous system problems, and even can die from the infection or its complication. Severe *P.falciparum* infection can cause cerebral malaria (coma, or altered mental status or seizures). It is lethal if not treated quickly; even with treatment, about 15%–20% die [1].

Malaria is by far the world's most prevalent vector borne disease and it still remains among the most devastating diseases occurring in the world. It is the 5th cause of death from infectious diseases worldwide (after respiratory infections, HIV/AIDS, diarrheal disease, and tuberculosis). It is a public health problem today in more than 109 countries and territories inhabited by some 3.3 billion people, and approximately half of the world's populations is at risk of malaria, particularly those living in lower-

income countries, as shown in Figure 1.1 (The distribution of malaria in 2006). There were 247 million cases of malaria in 2006, causing nearly one million deaths, mostly among African, and 190–311 million clinical episodes, and 708,000–1,003,000 deaths in 2008. Malaria has been eradicated in the United States since the early 1950's. However, 63 outbreaks of locally transmitted mosquito-borne malaria have occurred between 1957 and 2009, and 1,500 cases of malaria, on average are reported every year in the United States [3, 68, 108].

Malaria is the 2nd leading cause of death from infectious diseases in Africa after HIV/AIDS. It represents 10% of Africa's overall disease burden [2]. The WHO reported that one in every five childhood deaths in Africa was due to the effects of malaria and an African child has on average between 1.6 to 5.4 times of malaria fever each year. There occurs a child death about every 30 seconds because of malaria. The latest estimate from the 2010 World Malaria Report is that malaria killed almost 800,000 people and afflicted 225 million others in 2009. A 2009 global malaria risk map [5, 6] (shown as Figure 1.2) suggests that while risks are worst in Africa, there are clear indications of dangers in many other countries too [5]. In the past three decades, malaria encroached upon areas where it had formerly been eradicated or had successfully been controlled [4] by use of chemicals, therapeutic drugs and insecticides, thus offsetting the gains attained in the latter half of the past century.

The prevalence of malaria has an enormous impact on a country's economy. It dramatically inhibits economic growth (by restricting individual worker productivity,

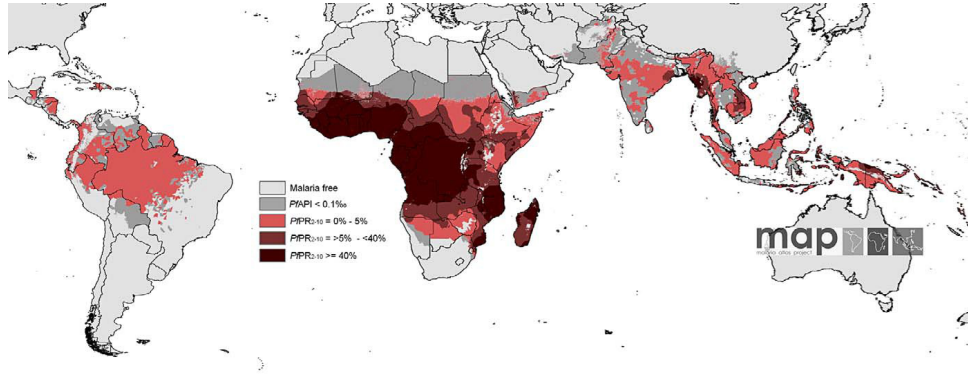


Figure 1.2: Comprehensive map of global malaria endemicity in 2009 [6]

tourism, transportation). In Africa malaria slows economic growth by up to 1.3% each year [7]. The explosiveness of malaria epidemics always strains the capacity of health facilities causing case fatality rates to increase five-fold or more during outbreaks. People of all ages remain susceptible to the full range of clinical effects. Malaria epidemics display the full explosive power of vector-borne infections, erupting with a suddenness and intensity that can overwhelm vulnerable communities. Malaria cases are being exacerbated by the high levels of HIV infection, which weakens the immune system rendering people with HIV more susceptible to contracting the disease [8]. It also enhances mortality in advanced HIV patients by a factor of about 25% in nonstable malaria areas [9]. In endemic areas the heaviest toll of morbidity and mortality falls on young children. This is due to (a slow) acquisition of immunity by children in endemic areas. Pregnant mothers, fetuses, and children are particularly vulnerable to malaria infection. In pregnancy, infections of malaria threaten both the survival of the mother and the

fetus through the infected placenta, leading to abortion, stillbirth or low-birth weight birth [10,11]. In children, around 20% mortality from cerebral malaria and a few residual effects from recovery, such as neurological defects in 10% of survival children, has substantially deepened children's vulnerability in future behavior and career development [10, 13]. Although campaigns against malaria were initially successful in some area, the emergence of resistance of the parasite to drugs and of the mosquito vector to insecticides, combined with difficulties in implementing and maintaining effective control schemes have led to a resurgence of the disease in many parts of the world [14,15]. Currently, 40% of the total human populations in the world is at risk for malaria and the proportion is projected to increase to 80% to 2080 [10].

1.2 Biology and life cycle of malaria

Malaria is a major tropical parasitic disease in areas of Asia, Africa, and central and South America. The life cycle of the disease is complicated. Malaria can be transmitted in human beings by the bite of an infected female *Anopheles* mosquito, through blood transfusion among people living in malarious areas, through organ transplantation, or vertically by infected mothers.

While there are about 3500 species of mosquito worldwide, of which 430 are in the genus *Anopheles* [16], the human malaria is caused by infection with one or more of four species of the plasmodium parasite: *P.falciparum* (tropics), *P.vivax* (tropical and temperate zones), *P.ovale*, and *P.malariae*. The first two are the main causes of the

disease, and animal malaria cannot spread to humans, nor can human malaria spread to animals [12]. These protozoan parasites are transmitted by the bites of an *Anopheles* mosquitoes.

An appreciation of the life cycle and transmission of *Plasmodia* and pathophysiology of infection is the key to understanding the disease. The biology of the four species of malaria parasites is generally similar and consists of two discrete phases—sexual and asexual.

Many stimuli, including high concentrations of carbon dioxide, lactic acid, sweat, moisture, certain body odors, body warmth and movement, can stimulate mosquitoes to target and identify human beings [17, 38]. Once human beings are attacked by a mosquito, the mosquito may bite human beings as many times as possible until it takes a blood meal. Depending on the disease status of both organisms, the mosquito will either infect human beings or be infected by human beings during its meal. When a mosquito alights on the skin of a human being, it attempts to pierce a small blood vessel with its proboscis in order to suck blood. The mosquito first injects some saliva together with anticoagulant (anti-clotting chemical) to prevent blood from clotting and closing the wound so that the mosquito can drink it. If the mosquito is infected with malaria parasites, the sporozoites are introduced into the human body together with saliva during the bite (see Figure 1.3, step (1), infective stage). The sporozoites, leave the site of the bite fairly rapidly, penetrate capillary and travel the bloodstream to gain access to liver cells (hepatocytes) (see Figure 1.3, step (2) and (3)), and develop into schizonts which

give rise, via asexual reproduction (see Figure 1.3, step (4)), to the form which invades the blood cells, the merozoites. These enter red blood cells and become first trophozoites and then erythrocytic schizonts (by a phase of asexual reproduction) (see Figure 1.3, step (5) and (6)). For each schizont, 12–24 merozoites are released to invade further blood cells. Some sporozoites may remain dormant in the liver as hypnozoites. They may later, after an interval of several months, develop into schizonts and then merozoites which enter the blood. Some merozoites develop into gametocytes and are ingested by a mosquito when it ingests human blood (see Figure 1.3, step (7)). Within the mosquito they develop into microgametes and macrogametes (the male and female gametes) that fuse to form a zygote (the sexual phase) (see Figure 1.3, step (8) and (9)). This becomes a motile ookinete form which bores through the gut wall of the vector (see Figure 1.3, step (10)) and forms an oocyst from which large numbers of sporozoites are released (see Figure 1.3, step (11) and (12)). These sporozoites then invade the salivary glands of the mosquitoes from which they are injected into a human host when the vector feeds. Such a life-cycle of the *Plasmodium* species (see Figure 1.3) causes the transmission of malaria between infected human beings and mosquitoes [18–20].

1.3 The history of mathematical malaria modeling

Mathematical models for the transmission dynamics of infectious diseases have proven useful for the purpose of providing a logical structure within which to incorporate knowledge and test assumptions about the complex epidemics, in a way that could not

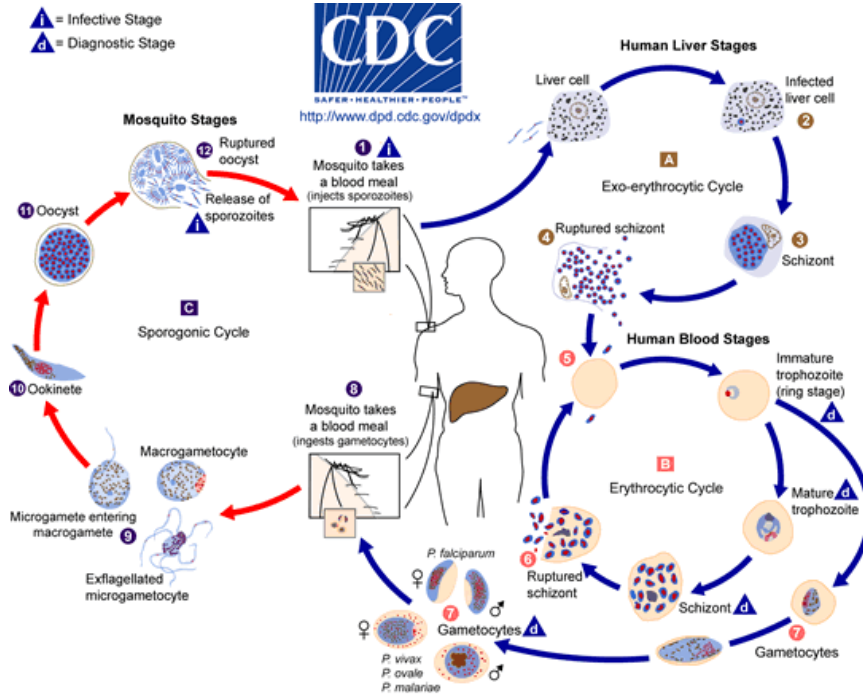


Figure 1.3: CDC illustration of the life cycles of malaria parasites, *Plasmodium* spp.

be done by simple thought processes. Mathematical models for malaria have played an important role in helping researchers to understand this epidemic, anticipate and plan for future, and design and analyze control strategies. The earliest malaria mathematical model can be traced to the model formulated by Ross in 1911 [21], in which he formulated a mathematical model of malaria after finding that the malaria parasite is transmitted from person to person by female mosquitoes each time the infected insect take a blood meal.

To the Ross model, George MacDonald made a major extension in his 1957 book [22], so that the Ross model is also called Ross-MacDonald model. The Ross-

MacDonald model is two-dimensional with one variable, $X(t)$, representing infective humans, and the other variable, $Y(t)$, representing infective mosquitoes. The model includes a pair of coupled differential equations which specify the time evolution of the human beings and mosquitoes. In particular, the Ross-MacDonald model assumes that the transmission of the plasmodium – from mosquito to human and from human to mosquito – depends jointly on the numbers of susceptible and infected individuals of humans and mosquitoes.

Let N and M be the total numbers of human beings and mosquitoes, respectively.

The Ross-MacDonald model is given as

$$\begin{aligned}\frac{dX}{dt} &= ABY (N - X) - rX, \\ \frac{dY}{dt} &= ACX (M - Y) - mY,\end{aligned}\tag{1.3.1}$$

where the parameters A is the mosquito biting rate, B the human infection rate, C the mosquito infection rate, m the mosquito death rate, and r the human recovery rate.

Equation (1.3.1) assumes constant human and mosquito populations, N and M . It is further assumed that infected human beings recover (and become immediately susceptible) at rate r , and that sporozoite-bearing mosquitoes die off at rate m – both loss processes are assumed to be exponential. As to the constants, A , B , and C , there relate transmission to biting by female mosquitoes– the event by which transfer occurs– and the probabilities of parasite transfer from vector to man and from man to vector.

Note that the products, AB and AC , are, respectively, the per mosquito production rate of newly infected humans and the per human production rate of newly infected mosquitoes [23].

Scaling the variables with

$$x = \frac{X}{N}, \quad y = \frac{Y}{M}, \quad q = \frac{M}{N}, \quad a = ACN, \quad b = \frac{B}{C}, \quad (1.3.2)$$

and substituting the new quantities (1.3.2) into system (1.3.1) yields

$$\begin{aligned} \frac{dx}{dt} &= abqy(1-x) - rx, \\ \frac{dy}{dt} &= ax(1-y) - my, \end{aligned} \quad (1.3.3)$$

which is the form that are most frequently encountered in the literatures (see, for example, Aron and May [24]).

For model (1.3.3), the basic reproductive rate of the disease R_0 is $R_0 = \frac{a^2 bq}{mr}$. If $R_0 < 1$, the disease dies out, and if $R_0 > 1$, the disease persists, with the proportion of infected humans and mosquitoes tending to their endemic values.

The model given by (1.3.1) or (1.3.3), is oversimplified, and it does not consider the developmental period of young mosquitoes into adult that transmit the infection. Among many biological details they omit the fact that parasites undergo a period of development within a mosquito's gut before entering her salivary glands and a period of development within the body of a human. In other words, the latent periods, t , during

which the mosquito is infected but not yet infectious, is omitted. Moreover, the model does not incorporate the intrinsic developmental period in the human, during which the human blood is free of the parasites, nor distinguishes between the pathological asexual merozoite blood stages and the infectious gametocyte sexual stage in the human.

After Ross and MacDonald, many other modeling attempts have been made to describe and to predict the transmission dynamics of malaria in literatures (e.g., [24–28]). More recently, more sophisticated, complex malaria models have been developed and studied. For example, compartmental SEIR (Susceptible-Exposed-Infected-Recovered) differential equation models including asymptomatic immune humans were studied in literatures, [29–31]. SEIRS (Susceptible-Exposed-Infected-Recovered-Susceptible) differential equation models with different levels of acquired immunity and the loss of immunity among human host populations were formulated in literatures [32–36]. Nevertheless, the life cycle of malaria is complex. It is affected by many factors, such as the ages of human beings, temporary immunity, incubation of the infection, environment temperature and humidity, the density of mosquitoes and the density of human beings. Due to the great difficulty of mathematical modeling and analysis, few of those factors have been included. As a result, the heterogeneity of mosquitoes has been ignored, so that the mosquito populations have been assumed homogeneous and the stage difference of mosquitoes prior to adults has been ignored in most of the work in the literature.

The life cycle of mosquito development is complex as well. Mosquitoes undergo complete metamorphosis, going through four distinct stages of development during a

lifetime: egg, pupa, larva, and adult. The reaction to environment and the roles in the disease transmission of mosquitoes at the distinct stages are different. To better understand, predict, and control malaria, more detailed investigations of mosquito dynamics in the malaria modeling are apparently necessary.

Furthermore, most of the existing mathematical models in the literature are of continuous-time. While this is to take the advantage of the well-developed theory and techniques of dynamical system, the significant difference of the time scales of the lifespan and development between human beings and mosquitoes makes it clear that the models with discrete-time, based on the time-steps of mosquitoes' development, seem more appropriate.

In this dissertation, we formulate both continuous- and discrete-time mathematical malaria models with stage-structured mosquitoes. We start with continuous- and discrete-time models for the mosquito populations, respectively. We fully analyze the population dynamics of the mosquitoes by investigating the existence and stability of all possible equilibria. Using the malaria model in [32, 66] as a baseline model, we incorporate the stage-structured mosquitoes and formulate more structured malaria models. We also formulate a discrete-time malaria model without the metamorphic stages of mosquitoes and then a discrete-time malaria model including the mosquitoes metamorphic stages. Existence and stability analysis of all equilibria are carried out. In particular, we establish conditions that determine whether a backward bifurcation could occur as the reproductive number of infection R_0 is at the critical value 1. Numerical examples

are provided to verify our theoretical results, and brief discussions of our findings and future study are also given.

CHAPTER 2

DYNAMICS OF CONTINUOUS-TIME MOSQUITO POPULATION MODELS

2.1 Introduction

Mosquitoes undergo complete metamorphosis, going through four distinct stages of development, egg, pupa, larva, and adult, during a lifetime. They are completely metamorphically as well as ecologically distinct. After drinking blood, a female mosquito can lay from 100 to 300 eggs at a time in standing water or very slow-moving water and will produce from 1,000 to 3,000 eggs throughout her lifetime [38]. Within a week, the eggs hatch into larvae (sometimes called wrigglers). Larvae breathe air through tubes which they poke above the surface of the water. Larvae eats bits of floating organic matter and each other. Larvae molt four times as they grow; after the fourth molt, they are called pupae. Pupae (also called tumblers) also live near the surface of the water, breathing through two horn-like tubes (called siphons) on their back. Pupae do not eat. When its skin splits after a few days from a pupa, an adult mosquito emerges.

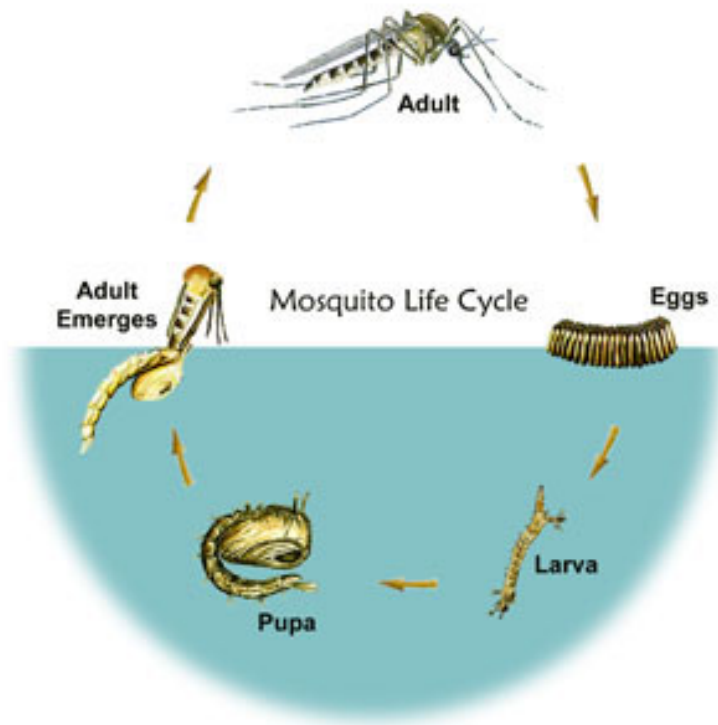


Figure 2.1: Mosquito life cycle

The adult lives for only a few weeks and the full life-cycle of a mosquito takes about a month [41, 99, 100] (as shown in Figure 2.1).

It is clear that, in order to have more realistic modeling of mosquitoes, we need to include the stage structure. In particular, different stages have different responses to environment and regulating factors to the population [77]. Some mosquito modeling work has included mosquito stages [65], and the four mosquito stages are included in the malaria model in [36], the analysis for which nevertheless seems mathematically untractable.

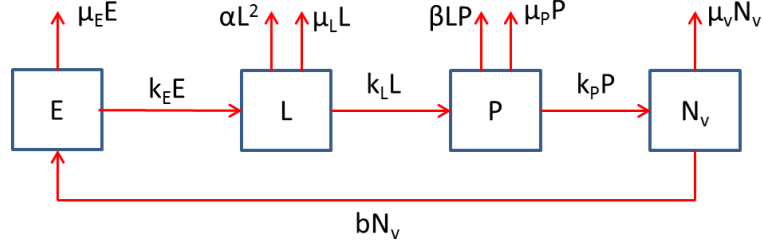


Figure 2.2: Graphic diagram of the four-stage-structured mosquito.

2.2 Continuous-time four-stage-structured mosquito population model

We assume the population of mosquitoes is sufficiently large so that it can be approximately assumed as a continuous function, and hence we develop our models as of continuous-time.

The life cycle of mosquito presents four distinct stages: egg (E), larva (L), pupa (P), and adult (N_v). Eggs, larvae and pupae live in water. Eggs are still, and pupae do not eat. we assume that the density-dependence is only based on the larvae population size, and it affects both of the survival rates of larvae and pupae with linear density functions αL and βL , respectively, where $\alpha > 0$ and $\beta > 0$. While interspecific competition and predation are rather rare events and could be discounted as major causes of larval mortality, interspecific competition could represent a major density dependent source for them, and hence the effect of crowding could be an important factor in the population dynamics of mosquitoes [36, 54, 57, 76]. Let $E(t)$, $L(t)$, $P(t)$ and $N_v(t)$ denote the number of eggs, larvae, pupae and adults of mosquitoes, respectively, at time t .

Following the life cycle of mosquitoes shown in Figure 2.1, we formulate the continuous-time four-stage-structured model of mosquito population, illustrated in Figure 2.2, as follows,

$$\begin{aligned}
\frac{dE}{dt} &= bN_v - k_E E - \mu_E E, \\
\frac{dL}{dt} &= k_E E - k_L L - (\mu_L + \alpha L)L, \\
\frac{dP}{dt} &= k_L L - k_P P - \mu_P P - \beta LP, \\
\frac{dN_v}{dt} &= k_P P - \mu_v N_v,
\end{aligned} \tag{2.2.1}$$

where b is the birth rate of mosquitoes, μ_E, μ_L, μ_P , and μ_v are natural death rate of eggs, larva, pupa and adult, respectively, and k_E, k_L , and k_P are the stage progression rates.

2.3 The preliminaries

Before we derive our main results, we give some preliminaries as follows.

Definition 2.3.1. *The class of Z-matrices are those matrices whose off-diagonal entries are less than or equal to zero; that is, a Z-matrix Z satisfies*

$$Z = (z_{ij}); \quad z_{ij} \leq 0, \quad i \neq j.$$

Definition 2.3.2. *An $n \times n$ Z-matrix $A = (a_{ij})$ is an M-matrix [42] if $a_{ii} > 0$, $i = 1, \dots, n$, $a_{ij} \leq 0$, for $i \neq j$, $i, j = 1, \dots, n$, and the leading principal minors satisfy*

$$\begin{vmatrix} a_{11} & \cdots & a_{1i} \\ \vdots & \ddots & \vdots \\ a_{i1} & \cdots & a_{ii} \end{vmatrix} > 0, \quad i = 1, \dots, n.$$

For M-matrices, there exist the following properties.

Theorem 2.3.1. [43, 44] *Let A be an M-matrix. Then it satisfies any one of the following equivalent conditions.*

- (1) *The leading principal minors of A are positive.*
- (2) *All principal minors of A are positive.*
- (3) *All real eigenvalues of A are positive.*
- (4) *The real part of any eigenvalue of A is positive.*
- (5) *A can be written in the form $A = kI - B$, where B is a non-negative matrix whose spectral radius is strictly less than k .*
- (6) *A is non-singular and the inverse of A is non-negative.*
- (7) *$Av \geq 0$ implies $v \geq 0$.*
- (8) *There exists a vector v with non-negative entries such that $Av > 0$.*
- (9) *$A + D$ is non-singular for every non-negative diagonal matrix D .*

- (10) $A + kI$ is non-singular for all $k > 0$.
- (11) For each nonzero vector v , $v_i(Av)_i > 0$ for some i .
- (12) There is a positive diagonal matrix D such that the matrix $DA + A^T D$ is positive definite.
- (13) A can be factorized as LU , where L is lower triangular, U is upper triangular, and the diagonal entries of both L and U are positive.
- (14) The diagonal entries of A are positive and AD is strictly diagonally dominant for some positive diagonal matrix D .

Definition 2.3.3. (A) Let $y = (y_1, \dots, y_n)$ and $z = (z_1, \dots, z_n) \in \mathbb{R}^n$. We write

$$y \leq z \quad \Longleftrightarrow \quad y_i \leq z_i, \quad \forall i, \quad i = 1, 2, \dots, n,$$

$$y < z \quad \Longleftrightarrow \quad y_i < z_i, \quad \forall i, \quad i = 1, 2, \dots, n.$$

- (B) An $n \times n$ matrix A is called irreducible if, for every (nontrivial) partition $I \cup J$ of the index set $\{1, 2, \dots, n\}$, there exist $i \in I$ and $j \in J$ such that $(A)_{ij} \neq 0$, or equivalently, for every pair $i, j \in \{1, 2, \dots, n\}$, there exists a positive integer k such that $(A^k)_{ij} > 0$.
- (C) A matrix A is called quasi-positive if all of the off-diagonal entries of A are non-negative.

(D) A smooth system $y' = f(y)$ is called cooperative on an open convex domain $\mathcal{U} \subseteq \mathbb{R}^n$ if the Jacobian matrix $Df(y)$ is quasi-positive for every $y \in \mathcal{U}$ (P. 34, [79]).

Theorem 2.3.2. (P. 112, [82]) Assume that $f : \mathcal{U} \rightarrow \mathbb{R}^n$ is cooperative, where \mathcal{U} is open and convex, and that $y, z : [t_0, t_0 + a] \rightarrow \mathcal{U}$ are differentiable. If

$$y(t_0) \leq z(t_0), \quad y'(t) \leq f(y(t)), \quad z'(t) = f(z(t)) \quad \forall t \in [t_0, t_0 + a],$$

then $y \leq z$, on $[t_0, t_0 + a]$.

Theorem 2.3.3. (P.62, [79]) Assume that $y' = f(y)$ is cooperative in an open convex set $\mathcal{U} \subseteq \mathbb{R}^n$ and that y^0 and y^1 , with $y^0 < y^1$, are the only equilibria in \mathcal{U} . If the Jacobian matrix $Df(y^0)$ is irreducible and $s(Df(y^0)) := \max\{\operatorname{Re} \lambda : \lambda \text{ is an eigenvalue of } A\} > 0$, then there exists a unique solution $y(t)$ (up to translation) satisfying $y'(t) > 0$, for all $t \in \mathbb{R}$, $y(t) \rightarrow y^0$, as $t \rightarrow -\infty$, and $y(t) \rightarrow y^1$, as $t \rightarrow \infty$.

2.4 The inherent net reproductive number of mosquitoes

First, we use the following notations, \mathbb{R}_+^4 for the nonnegative orthant of space \mathbb{R}^4 , $\operatorname{int}(\mathbb{R}_+^4)$ for the interior of \mathbb{R}_+^4 .

For system (2.2.1), there exists a trivial equilibrium point $(E^0, L^0, P^0, N_v^0) = (0, 0, 0, 0)$. The Jacobian matrix at the trivial equilibrium is

$$J_0 = \begin{pmatrix} -(\mu_E + k_E) & 0 & 0 & b \\ k_E & -(\mu_L + k_L) & 0 & 0 \\ 0 & k_L & -(\mu_P + k_P) & 0 \\ 0 & 0 & k_P & -\mu_v \end{pmatrix}.$$

Then, the trivial equilibrium is locally asymptotically stable if all eigenvalues of J_0 have negative real parts. Noting that all off-diagonal elements of $-J_0$ are non-positive, and the leading principal minors of $-J_0$ are

$$(\mu_E + k_E),$$

$$(\mu_E + k_E)(\mu_L + k_L),$$

$$(\mu_E + k_E)(\mu_L + k_L)(\mu_P + k_P),$$

$$(\mu_E + k_E)(\mu_L + k_L)(\mu_P + k_P)\mu_v - bk_E k_L k_P.$$

If

$$(\mu_E + k_E)(\mu_L + k_L)(\mu_P + k_P)\mu_v - bk_E k_L k_P > 0,$$

then all leading principal minors are larger than zero. Hence $-J_0$ is an M-matrix, and all eigenvalues of J_0 have negative real parts. Thus, the trivial equilibrium is locally asymptotically stable.

Define

$$r_0 := \frac{bk_E k_P k_L}{\mu_v \sigma_E \sigma_P \sigma_L} \tag{2.4.1}$$

where

$$\sigma_E := \mu_E + k_E, \quad \sigma_L := \mu_L + k_L, \quad \sigma_P := \mu_P + k_P,$$

which is the so-called inherent net reproductive number [49, 50]. Then the trivial equilibrium is locally asymptotically stable if $r_0 < 1$.

2.5 Global dynamics of the continuous-time mosquito population model

We now investigate the global dynamics of the model system and have the following results for system (2.2.1).

Theorem 2.5.1. *Every solution $(E(t), L(t), P(t), N_v(t))$ of (2.2.1) with its initial value in $\mathbb{R}_+^4 \setminus \{0\}$ is defined and lies in $\text{int}(\mathbb{R}_+^4)$ for all $t > 0$. Moreover,*

(i) *if $r_0 < 1$, the trivial equilibrium $(0, 0, 0, 0)$ of (2.2.1) is globally asymptotically stable;*

(ii) *if $r_0 > 1$, the trivial equilibrium is unstable, and there exists a unique positive equilibrium (E^*, L^*, P^*, N_v^*) of (2.2.1), given by*

$$\begin{aligned} E^* &= \frac{bk_L k_P}{\mu_v \sigma_E (\sigma_P + \beta L^*)} L^*, \quad P^* = \frac{k_L}{\sigma_P + \beta L^*} L^*, \quad N_v^* = \frac{k_L k_P}{\mu_v (\sigma_P + \beta L^*)} L^*, \\ L^* &= \frac{2\sigma_P \sigma_L (r_0 - 1)}{\alpha \sigma_P + \beta \sigma_L + \sqrt{(\alpha \sigma_P + \beta \sigma_L)^2 + 4\alpha \beta \sigma_P \sigma_L (r_0 - 1)}}, \end{aligned} \tag{2.5.1}$$

which is globally asymptotically stable in $\mathbb{R}_+^4 \setminus \{0\}$.

Note: As $r_0 < 1$, the trivial equilibrium is globally asymptotically stable; that is, all mosquitoes will eventually die out; as $r_0 > 1$, the trivial equilibrium is unstable, and there exists a globally asymptotically stable positive equilibrium, which implies that the mosquitoes will survive to a positive steady state.

We first establish several lemmas to prove the Theorem 2.5.1.

For simplicity, we use $\psi(t) := (E(t), L(t), P(t), N_v(t))$ to denote the solution of (2.2.1), $0 := (0, 0, 0, 0)$ to denote the trivial equilibrium of (2.2.1), and let f denote the right-hand side of (2.2.1). The Jacobian matrix of f is

$$Df(E, L, P, N_v) = \begin{pmatrix} -\sigma_E & 0 & 0 & b \\ k_E & -\sigma_L - 2\alpha L & 0 & 0 \\ 0 & k_L - \beta P & -\sigma_P - \beta L & 0 \\ 0 & 0 & k_P & -\mu_v \end{pmatrix}. \quad (2.5.2)$$

Lemma 2.5.2. *If $\psi(0) \in \mathbb{R}_+^4 \setminus \{0\}$, then $\psi(t) \in \text{int}(\mathbb{R}_+^4)$, for all $t > 0$.*

Proof. Since (2.2.1) is a smooth system in \mathbb{R}_0^4 , $\psi(t)$ exists on a maximal interval $[0, T^+)$, for $0 < T^+ \leq \infty$.

Step 1. We first show that $\psi(t) > 0$, for $0 \leq t < T^+ < \infty$. Using the variation of parameters formula, we have, for $t \in [0, T^+)$,

$$E(t) = E(0)e^{-\sigma_E t} + b \int_0^t N_v(\tau)e^{-\sigma_E(t-\tau)} d\tau,$$

$$\begin{aligned}
L(t) &= L(0)e^{-\int_0^t (\sigma_L + \alpha L(\tau)) d\tau} + k_E \int_0^t E(\tau) e^{-\int_\tau^t (\sigma_L + \alpha L(\eta)) d\eta} d\tau, \\
P(t) &= P(0)e^{-\int_0^t (\sigma_P + \beta L(\tau)) d\tau} + k_L \int_0^t L(\tau) e^{-\int_\tau^t (\sigma_P + \beta L(\eta)) d\eta} d\tau, \\
N_v(t) &= N_v(0)e^{-\mu_v t} + k_P \int_0^t P(\tau) e^{-\mu_v (t-\tau)} d\tau.
\end{aligned} \tag{2.5.3}$$

Since $\psi(0) \in \mathbb{R}_+^4 \setminus \{0\}$, we have either $E(0) > 0$, $L(0) > 0$, $P(0) > 0$, or $N_v(0) > 0$. If $E(0) > 0$, it follows from the continuity of E that $E(t) > 0$, for $t \in (0, \delta)$, for small $\delta > 0$. Then it follows from (2.5.3) that $L > 0$, on $(0, \delta]$, which in turn implies that $P > 0$, on $(0, \delta]$, and then $N_v > 0$, on $(0, \delta]$. Note that for any $t \in [\delta, T^+)$, as long as E, L, P, N_v are positive on $(0, t)$, all the integrals on the right-hand of (2.5.3) are positive. It then follows from (2.5.3) that $E(t) > 0$, $L(t) > 0$, $P(t) > 0$, and $N_v(t) > 0$, for any $t \in [\delta, T^+)$, as long as E, L, P, N_v are positive on $(0, t)$. This yields that E, L, P , and N_v are positive on $(0, T^+)$. The same assertion holds in the cases where $L(0) > 0$, $P(0) > 0$, or $N_v(0) > 0$.

Step 2. We next show that $\psi(t) > 0$, for $0 \leq t \leq \infty$. For this, we compare $\psi(t)$ with a solution of the variational system of (2.2.1) at its trivial equilibrium $0 := (0, 0, 0, 0)$:

$$z' = Df(0)z \tag{2.5.4}$$

which is a cooperative system in \mathbb{R}^4 . Let $z(t)$ be the solution of $z' = Df(0)z$, with $z(0) = \psi(0)$. Since $\psi(t) \in \mathbb{R}_+^4$, for $t \in [0, T^+)$, it follows, for $t \in [0, T^+)$,

$$\psi'(t) = f(\psi(t)) = Df(0)\psi(t) - (0, \alpha L^2(t), -\beta L(t)P(t), 0)^\top \leq Df(0)\psi(t).$$

Then, from Theorem 2.3.2 it follows that $\psi(t) \leq z(t)$, for $t \in [0, T^+)$. Since $z(t)$ is defined for all $t \geq 0$, it follows that $\psi(t)$ is defined for all $t \in (0, \infty)$.

Combining the results from Steps 1-2, we conclude the assertion of the lemma. \square

Lemma 2.5.3. *Let*

$$\mathcal{C} = \left\{ (E, L, P, N_v) \in \text{int}(\mathbb{R}_+^4) : P < \frac{k_L}{\beta} \right\},$$

which is an open and convex set in \mathbb{R}_+^4 . Then we have the following,

(i) \mathcal{C} *is positively invariant for the flows of (2.2.1), where (2.2.1) is a cooperative system; that is, the Jacobian matrix $Df(E, L, P, N_v)$ of the right-hand side of (2.2.1) has nonnegative off-diagonal entries on \mathcal{C} .*

(ii) *Let $\psi(t)$ be a solution of (2.2.1) with $\phi(0) \in \mathbb{R}_+^4 \setminus \mathcal{C}$. Then there is $\bar{t} > 0$ such that $\psi(t) \in \mathcal{C}$, for $t > \bar{t}$.*

Proof. Let $\psi(0) \in \mathcal{C}$. At $P = \frac{k_L}{\beta}$, then

$$P' = k_L L - k_P P - \mu_P P - \beta L P$$

$$\begin{aligned}
&= k_L L - k_P \frac{k_L}{\beta} - \mu_P \frac{k_L}{\beta} - \beta L \frac{k_L}{\beta} \\
&= -k_P \frac{k_L}{\beta} - \mu_P \frac{k_L}{\beta} \\
&= -\sigma_P \frac{k_L}{\beta} < 0,
\end{aligned}$$

hence $\psi(t)$ cannot reach the boundary $P = \frac{k_L}{\beta}$ of \mathcal{C} . This together with Lemma 2.5.2 implies that \mathcal{C} is positively invariant.

Let $\psi(0) \in \mathbb{R}_+^4 \setminus \mathcal{C}$. Then, as long as $\psi \in \mathbb{R}_+^4 \setminus \mathcal{C}$ on $[0, t)$, we have, from the equation of P ,

$$\begin{aligned}
P' &= k_L L - k_P P - \mu_P P - \beta L P \\
&\leq k_L L - k_P P - \mu_P P - \beta L \frac{k_L}{\beta} \\
&= -k_P P - \mu_P P = -\sigma_P P \\
&\leq -\sigma_P \frac{k_L}{\beta},
\end{aligned}$$

which implies that there is \bar{t} ,

$$0 < \bar{t} < \frac{\beta(P(0) - k_P/\beta)}{\sigma_P k_P},$$

such that

$$P(\bar{t}) < k_P/\beta,$$

that is,

$$\psi(\bar{t}) \in \mathcal{C}.$$

It then follows from (i) that $\psi(t) \in \mathcal{C}$, for all $t > \bar{t}$. □

Lemma 2.5.4. *The trivial equilibrium point $(0, 0, 0, 0)$ of (2.2.1) is globally asymptotically stable in \mathbb{R}_+^4 if $r_0 < 1$, and is unstable if $r_0 > 1$.*

Proof. Since, from (2.5.2), the leading principal minors of the matrix $-Df(0)$ are

$$\sigma_E, \quad \sigma_E \sigma_L, \quad \sigma_E \sigma_L \sigma_P,$$

$$\det(-Df(0)) = \sigma_E \sigma_L \sigma_P \mu_v - b k_E k_L k_P = \sigma_E \sigma_L \sigma_P \mu_v (1 - r_0),$$

it follows that they are all positive if and only if $r_0 < 1$. Since the diagonal entries of $-Df(0)$ are all positive and the off-diagonal entries are non-positive, we then conclude, from the definition 2.3.2, that $-Df(0)$ is an M-matrix if and only if $r_0 < 1$. Thus, all eigenvalues of $-Df(0)$ has positive real parts if $r_0 < 1$, and at lease one of the eigenvalues has negative real part if $r_0 > 1$. Consequently, the linear system (2.5.4) is exponentially asymptotically stable at 0. Hence, (2.2.1) is locally asymptotically stable at 0 if $r_0 < 1$, and is unstable if $r_0 > 1$.

Assume $r_0 < 1$. It remains to show that if $\psi(0) \in \mathbb{R}_+^4 \setminus \{0\}$, then $\psi(t) \rightarrow 0$ as $t \rightarrow \infty$. Note that, for such a solution, we have shown in the proof of Lemma 2.5.2 that $0 < \psi(t) \leq z(t)$ for all $t > 0$, where $z(t)$ is the solution of (2.5.4) with $z(0) = \psi(0)$.

Since $z(t) \rightarrow 0$, as $t \rightarrow \infty$ (since $r_0 < 1$), it follows that $\psi(t) \rightarrow 0$ as $t \rightarrow \infty$. The proof is complete. \square

Lemma 2.5.5. *If $r_0 > 1$, then there exists a positive equilibrium $\mathcal{V}^* := (E^*, L^*, P^*, N_v^*)$, given in (2.5.1), which is globally asymptotically stable in $\mathbb{R}_+^4 \setminus \{0\}$.*

Proof. It is trivial to check that \mathcal{V}^* is an equilibrium of (2.2.1), and, from the expression of \mathcal{V}^* , that $\mathcal{V}^* \in \mathbb{R}_+^4$ exists if and only if $r_0 > 1$. Furthermore,

$$P^* = \frac{k_L}{\sigma_P + \beta L} L^* < \frac{k_L}{\beta L^*} L^* = \frac{k_L}{\beta}.$$

Hence, $\mathcal{V}^* \in \mathcal{C} = \left\{ (E, L, P, N_v) \in \text{int}(\mathbb{R}_+^4) : P < \frac{k_L}{\beta} \right\}$.

To determine the local stability of \mathcal{V}^* , we consider the variational system of (2.2.1) at \mathcal{V}^* :

$$z' = Df(\mathcal{V}^*)z. \tag{2.5.5}$$

Using the expression of $Df(E, L, P, N_v)$ in (2.5.2) with $(E, L, P, N_v) = \mathcal{V}^*$ and the formulas in (2.5.1), we have

$$k_L - \beta P^* = k_L - \beta \frac{k_L}{k_P + \mu_P + \beta L^*} L^* = \frac{k_L (k_P + \mu_P)}{k_P + \mu_P + \beta L^*} > 0.$$

Hence, the diagonal entries of $-Df(\mathcal{V}^*)$ are all positive and the off-diagonal entries are non-positive. It is easy to check that the leading principal minors of the matrix $-Df(\mathcal{V}^*)$

are

$$\begin{aligned}
& \sigma_E > 0, \quad \sigma_E(\sigma_L + 2\alpha L^*) > 0, \quad \sigma_E(\sigma_L + 2\alpha L^*)(\sigma_P + \beta L^*) > 0, \\
& \det(-Df(\mathcal{V}^*)) = \sigma_E(\sigma_L + 2\alpha L^*)(\sigma_P + \beta L^*)\mu_v - bk_E(k_L - \beta P^*)k_P \\
& = \sigma_E\alpha L^*(\sigma_P + \beta L^*)\mu_v + \sigma_E(\sigma_L + \alpha L^*)(\sigma_P + \beta L^*)\mu_v \\
& \quad - bk_E k_L k_P + bk_E \beta P^* k_P \\
& = \sigma_E\alpha L^*(\sigma_P + \beta L^*)\mu_v + \sigma_E \frac{bk_E k_L k_P}{\sigma_E \mu_v} \mu_v - bk_E k_L k_P + bk_E \beta P^* k_P \\
& = \sigma_E\alpha L^*(\sigma_P + \beta L^*)\mu_v + bk_E \beta P^* k_P > 0.
\end{aligned}$$

Then it follows from Definition 2.3.2 that $-Df(\mathcal{V}^*)$ is an M-matrix so that all the eigenvalues of $-Df(\mathcal{V}^*)$ have positive real part. This shows that (2.5.5) is asymptotically stable at 0, and (2.2.1) is locally asymptotically stable at \mathcal{V}^* .

From Lemmas 2.5.2 and 2.5.3, it remains to show that if $\psi(0) \in \mathcal{C}$, then $\psi(t) \rightarrow \mathcal{V}^*$ as $t \rightarrow \infty$. To this end, we divide \mathcal{C} into three subsets:

$$\mathcal{C}_1 = \{0 \leq (E, L, P, N_v) \leq \mathcal{V}^*\} \cap \mathcal{C}, \quad \mathcal{C}_2 = \{(E, L, P, N_v) \geq \mathcal{V}^*\} \cap \mathcal{C}, \quad \mathcal{C}_3 = \mathcal{C} \setminus (\mathcal{C}_1 \cup \mathcal{C}_2).$$

Step 1. Let $\psi(0) \in \mathcal{C}_1$. We show that $\psi(t) \rightarrow \mathcal{V}^*$, as $t \rightarrow \infty$. We first show, by Theorem 2.3.3, that there is a unique solution $\psi_0(t)$ of (2.2.1) such that $0 < \psi_0(t) < \mathcal{V}^*$, for all $t \in \mathbb{R}$, $\psi_0(t) \rightarrow 0$, as $t \rightarrow -\infty$, and $\psi_0(t) \rightarrow \mathcal{V}^*$ as $t \rightarrow \infty$. It suffices to check that the conditions of Theorem 2.3.3 are satisfied.

First, note from (2.5.2) that, for sufficiently small $\delta > 0$, Df is quasi-positive, (that is, all of whose elements are nonnegative except for those on the main diagonal), in a larger open convex domain $\tilde{\mathcal{C}}$ (larger than \mathcal{C}):

$$\tilde{\mathcal{C}} = \left\{ (E, L, P, N_v) \in \mathbb{R}^4 : (E, L, P, N_v) > -(\delta, \delta, \delta, \delta), \quad P < \frac{k_L}{\beta} \right\},$$

so that (2.2.1) is cooperative in $\tilde{\mathcal{C}}$. Next, by using Definition 2.3.3 (B), it is trivial to verify that $Df(0)$ is irreducible. Since $r_0 > 1$, it follows that 0 is an unstable equilibrium of (2.2.1) and $s(Df(0)) = \max\{Re\lambda : \lambda \text{ are the eighvalues of } Df(0)\} > 0$. Applying Theorem 2.3.3 yields the existence of ψ_0 .

Now, since $\psi(0) \in \mathcal{C}_1$, taking t_0 sufficiently negative, we have $\psi_0(t_0) \leq \psi(0) \leq \mathcal{V}^*$, and applying Theorem 2.3.2, we have that $\psi_0(t + t_0) \leq \psi(t) \leq \mathcal{V}^*$, for all $t > 0$. Letting $t \rightarrow \infty$ gives $\psi(t) \rightarrow \mathcal{V}^*$, as expected.

Step 2. Let $\psi(0) \in \mathcal{C}_2$. We show that $\psi(t) \rightarrow \mathcal{V}^*$ as $t \rightarrow \infty$. First, since (2.2.1) is a cooperative system in \mathcal{C} , it follows that $\psi(t) \geq \mathcal{V}^*$ and thus $\psi(t) \in \mathcal{C}_2$, for all $t > 0$. Therefore, from (2.2.1), for $t > 0$,

$$\psi(t)' = Df(V^*)(\psi(t) - V^*) - \begin{pmatrix} 0 \\ \alpha(L(t) - L^*)^2 \\ \beta(L(t) - L^*)(P(t) - P^*) \\ 0 \end{pmatrix} \leq Df(\mathcal{V}^*)(\psi(t) - \mathcal{V}^*). \quad (2.5.6)$$

Let $z(t)$ be the solution of the variational system $z' = Df(\mathcal{V}^*)z$ with $z(0) = \psi(0) - \mathcal{V}^*$. Since $Df(\mathcal{V}^*)$ is quasi-positive, it follows from Theorem 2.3.2 that $\psi(t) - \mathcal{V}^* \leq z(t)$, i.e., $\psi(t) \leq \mathcal{V}^* + z(t)$ for all $t > 0$. Since $z(t) \rightarrow 0$ as $t \rightarrow \infty$, this together with $\mathcal{V}^* \leq \psi(t)$ yields $\psi(t) \rightarrow \mathcal{V}^*$ as $t \rightarrow \infty$.

Step 3. Let $\psi(0) \in \mathcal{C}_3$. We show that $\psi(t) \rightarrow \mathcal{V}^*$ as $t \rightarrow \infty$. From Step 1, $\psi_0(t) \rightarrow 0$ as $t \rightarrow -\infty$, and so for sufficiently negative t_0 , $\psi_0(t_0) \leq \psi(0)$, which yields, by Theorem 2.3.2, that $\psi_0(t + t_0) \leq \psi(t)$ for all $t > 0$. On the other hand, let $\psi_1(t)$ be the solution of (2.2.1) with the initial condition

$$\psi_1(0) = \max\{E(0), L(0), P(0), N_v(0)\}(1, 1, 1, 1).$$

Note that $\psi(0) \in \mathcal{C}_3$ implies that $\psi_1(0) \in \mathcal{C}_2$. Applying Theorem 2.3.2 again gives $\psi(t) \leq \psi_1(t)$ for all $t > 0$. Since from Steps 1-2 both $\psi_0(t + t_0) \rightarrow \mathcal{V}^*$ and $\psi_1(t) \rightarrow \mathcal{V}^*$ as $t \rightarrow \infty$, it follows that $\psi(t) \rightarrow \mathcal{V}^*$ as $t \rightarrow \infty$. The proof of Lemma 2.5.5 is complete. \square

Proof of Theorem 2.5.1 It is clear that it follows from Lemmas 2.5.2, 2.5.4, and 2.5.5 that Theorem 2.5.1 is proved. \square

2.6 Numerical examples

We provide simple numerical examples to confirm our analytic results and demonstrate the dynamics of system (2.2.1) as follows.

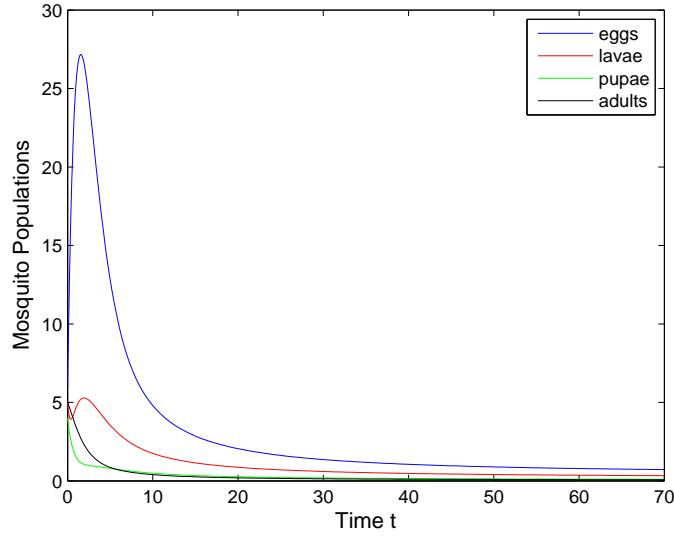


Figure 2.3: The function forms and parameters are given in Example 2.4.1. Since $r_0 = 0.6944 < 1$, E_0 is globally asymptotically stable. Solutions approach E_0 , as $t \rightarrow \infty$.

Example 2.6.1. In this example, we assume the following parameters:

$$\begin{aligned}
 b &= 5; & k_E &= 0.4; & \mu_E &= 0.4; & k_L &= 0.3; & \mu_L &= 0.5; \\
 k_P &= 0.4; & \mu_P &= 0.5; & \mu_v &= 0.6; & \alpha &= 0.23; & \beta &= 0.15.
 \end{aligned}$$

Then the inherent net reproductive number $r_0 = 0.6944 < 1$, such that the trivial equilibrium point E_0 is globally stable; that is, the mosquito population goes extinct, which is shown in Figure 2.3.

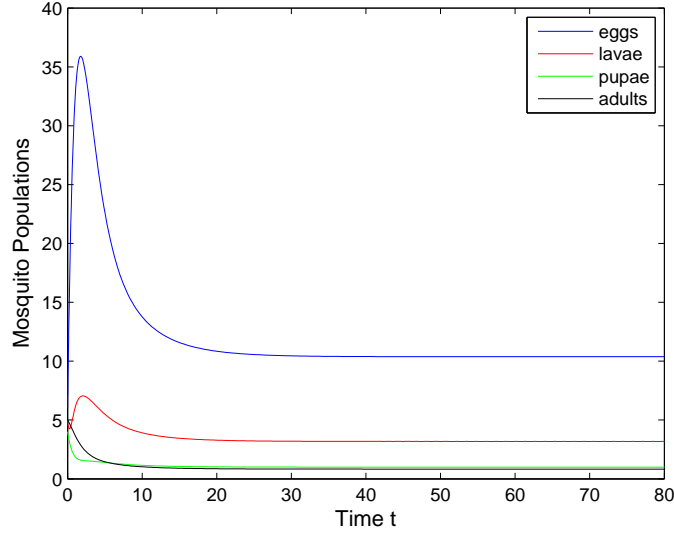


Figure 2.4: The function forms and parameters are given in Example 2.4.2. Since $r_0 = 2.8935 > 1$, E_0 is unstable and the positive equilibrium $E_1 = (10.3763, 3.1790, 0.9963, 0.8300)$ is globally asymptotically stable. Solutions approach E_1 , as $t \rightarrow \infty$.

Example 2.6.2. In this example, we assume the following parameters:

$$b = 10; \quad k_E = 0.5; \quad \mu_E = 0.3; \quad k_L = 0.4; \quad \mu_L = 0.4;$$

$$k_P = 0.5; \quad \mu_P = 0.3; \quad \mu_v = 0.6; \quad \alpha = 0.23; \quad \beta = 0.15;$$

Then the inherent net reproductive number $r_0 = 2.8935 > 1$, such that the trivial equilibrium point E_0 is unstable and the positive equilibrium point E_1 exists and is globally stable, as shown in Figure 2.4.

CHAPTER 3

MOSQUITO-STAGE-STRUCTURED MALARIA MODELS AND THEIR DYNAMICS

3.1 Introduction

While mathematical models for the malaria transmission growth abound in the literature, the mosquito population has been assumed to be homogeneous, or its stage structure has been simplified in most of the models [29–32, 66, 69, 70]. (See the malaria life cycle in Figure 3.1 and the graphic diagram in Figure 3.2, the homogeneous malaria models were formulated based on the two figures). Moreover, because of the complexity of the models, mathematical analysis is far from complete in many of the studies.

Mosquitoes undergo complete metamorphosis going through four distinct stages of development during a lifetime as described in Chapter 2. While it is appropriate to assume that only mosquito adults are involved in the malaria transmission, the dynamics of the juvenile stages (pupae and larvae) have significant effects on the dynamics of the mosquito population, and hence the disease transmission dynamics [65].

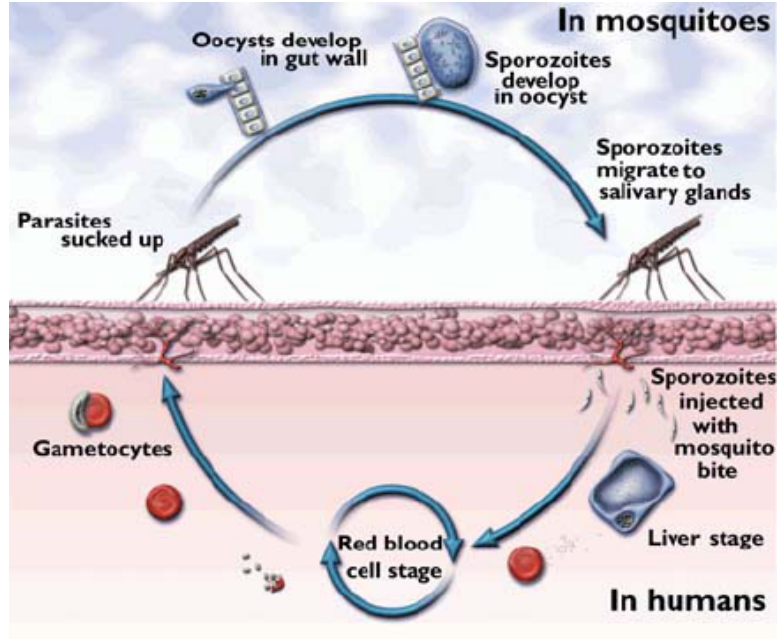


Figure 3.1: Malaria life cycle

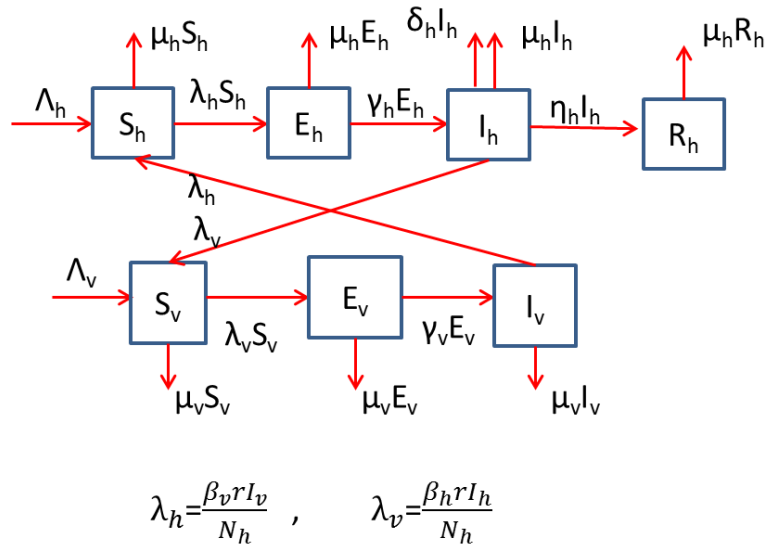


Figure 3.2: Graphic diagram of homogeneous compartmental malaria models

Using the malaria model in [66] as our baseline model, we include the four distinct metamorphic stages of mosquitoes to formulate a mosquito-stage-structured malaria model and study the model dynamics in this chapter.

3.2 The model formulation

Based on the malaria life cycle shown in Figure 1.3 and the life cycle of mosquitoes shown in Figure 2.1, we follow the line in [29–32, 66] to formulate our malaria model with stage-structured mosquitoes as follows.

We divide the human population into groups of susceptible, exposed or incubating, infective, and recovered individuals, and let $S_h(t)$ be the number of susceptible human beings, $E_h(t)$ be the number of exposed or incubating human beings, who are infected but not infectious yet, $I_h(t)$ be the number of infective human beings, who are infected and also infectious, and $R_h(t)$ be the number of human beings who have recovered from infection. To account the transmission dynamics between human beings and mosquitoes, we divide the adult mosquito population into groups of susceptible, exposed, and infective individuals, denoted by $S_v(t)$, $E_v(t)$, and $I_v(t)$, respectively. Due to the short lifespan of mosquitoes, we assume that infective mosquitoes die, that is, mosquitoes cannot recover. While most of the existing malaria transmission models only include adult mosquitoes, because mosquitoes undergo complete metamorphosis going through four distinct stages of development during a lifetime, and the reactions from those distinct stages to environment and other factors are significantly different, it

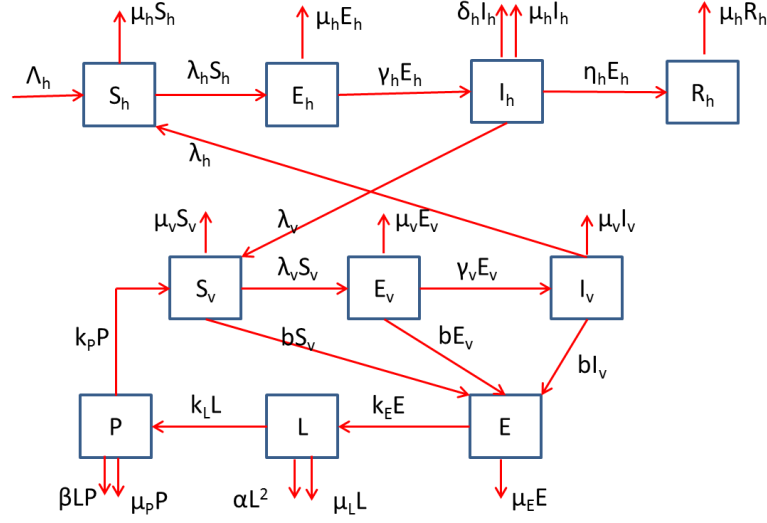


Figure 3.3: Graphic diagram of mosquito-stage-structured malaria models

is more appropriate to consider those stages in malaria models [36, 77]. Hence to include the four metamorphic stages in our model formulation we let the sizes of mosquito eggs, larvae, and pupae, at time t , be $E(t)$, $L(t)$, and $P(t)$, respectively. Then, illustrated by the graphic diagram in Figure 3.3, the dynamics of the malaria transmission in human beings and in stage-structured mosquitoes are models (3.2.1) and (3.2.2), respectively,

$$\begin{aligned}
 \frac{dS_h}{dt} &= \Lambda_h - (\mu_h + \lambda_h) S_h, \\
 \frac{dE_h}{dt} &= \lambda_h S_h - (\mu_h + \gamma_h) E_h, \\
 \frac{dI_h}{dt} &= \gamma_h E_h - (\mu_h + \delta_h + \eta_h) I_h, \\
 \frac{dR_h}{dt} &= \eta_h I_h - \mu_h R_h,
 \end{aligned} \tag{3.2.1}$$

and

$$\begin{aligned}
\frac{dE}{dt} &= bN_v - (k_E + \mu_E)E, \\
\frac{dL}{dt} &= k_E E - (k_L + \mu_L + \alpha L)L, \\
\frac{dP}{dt} &= k_L L - (k_P + \mu_P + \beta L)P, \\
\frac{dS_v}{dt} &= k_P P - \mu_v S_v - \lambda_v S_v, \\
\frac{dE_v}{dt} &= \lambda_v S_v - (\mu_v + \gamma_v)E_v, \\
\frac{dI_v}{dt} &= \gamma_v E_v - \mu_v I_v,
\end{aligned} \tag{3.2.2}$$

where Λ_h is the input flow of the susceptible human beings including birth; μ_h and μ_v are the natural death rates of human beings and mosquitoes; δ_h is the disease-induced death rate for human beings; γ_h and γ_v are the developing rates of exposed human beings and mosquitoes becoming infective, such that $1/\gamma_h$ is the incubation period of infected human beings, and $1/\gamma_v$ is the extrinsic incubation period of the parasite within the mosquitoes or the period of sporogony; η_h is the recovery rate of human beings, λ_h and λ_v are the infection rates for human beings and mosquitoes, respectively. Different from the model in [66], we assume that there is no loss of immunity for recovered human beings.

The infection rate of a human host, λ_h , is given by

$$\lambda_h = \beta_v r \frac{I_v}{N_h}, \tag{3.2.3}$$

where β_v is the transmission probability to a human per infected bite, r the number of bites on a human by an individual mosquito per unit of time, and

$$N_v = S_v + E_v + I_v, \quad N_h = S_h + E_h + I_h + R_h.$$

Similarly, the infection rate for mosquitoes is given by

$$\lambda_v = \beta_h r \frac{I_h}{N_h}, \quad (3.2.4)$$

where β_h is the transmission probability per bite to a susceptible mosquito from an infective human [32, 66].

The parameters in the equations for the eggs, larvae, and pupae, are b , the birth rate of mosquitoes, μ_i , the natural death rates, and k_i , $i = E, L, P$, the stage progression rates.

As stated in Chapter 2, we assume that the density-dependence is only based on the larvae size, and it affects both of the survival rates of larvae and pupae with linear density functions αL and βL , respectively, where $\alpha > 0$ and $\beta > 0$.

3.3 Positive invariant sets of the model system

For convenience of our study, we rewrite systems(3.2.1) and (3.2.2) as

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - (\mu_h + \lambda_h) S_h, \\
\frac{dE_h}{dt} &= \lambda_h S_h - (\mu_h + \gamma_h) E_h, \\
\frac{dI_h}{dt} &= \gamma_h E_h - (\mu_h + \delta_h + \eta_h) I_h, \\
\frac{dR_h}{dt} &= \eta_h I_h - \mu_h R_h, \\
\frac{dE_v}{dt} &= \lambda_v S_v - (\mu_v + \gamma_v) E_v, \\
\frac{dI_v}{dt} &= \gamma_v E_v - \mu_v I_v, \\
\frac{dE}{dt} &= bN_v - (k_E + \mu_E) E, \\
\frac{dL}{dt} &= k_E E - (k_L + \mu_L + \alpha L) L, \\
\frac{dP}{dt} &= k_L L - (k_P + \mu_P + \beta L) P, \\
\frac{dS_v}{dt} &= k_P P - \mu_v S_v - \lambda_v S_v.
\end{aligned} \tag{3.3.1}$$

We now show that the system (3.3.1) is mathematically well-defined and biologically reasonable. We use the following notations, \mathbb{R}_+^n for the nonnegative orthant of space \mathbb{R}^n , $\text{int}(\mathbb{R}_+^n)$ for the interior of \mathbb{R}_+^n , $\phi(t)$ and $\omega(\phi(t))$ for a solution of (3.3.1) and its omega limit set, respectively. We write

$$\sigma_1 := \mu_h + \gamma_h, \quad \sigma_2 := \mu_h + \delta_h + \eta_h, \quad \sigma_v := \mu_v + \gamma_v.$$

Note that the system (3.3.1) is a smooth system in the open set Ω of \mathbb{R}_+^{10} given by

$$\Omega := \{(S_h, E_h, I_h, R_h, E_v, I_v, E, L, P, S_v) \in \mathbb{R}_+^{10} : N_h > 0\}.$$

Thus, every solution $\phi(t)$ of (3.3.1), with $\phi(0) \in \Omega$, is defined for t in a maximal interval (T^-, T^+) , with $-\infty \leq T^- < 0 < T^+ \leq \infty$, such that $\phi(t) \in \Omega$, for all t in (T^-, T^+) . Moreover, we are mainly interested in the solutions of (3.3.1) in the following subset \mathcal{D} of Ω :

$$\mathcal{D} := \mathbb{R}_+^{10} \setminus (\{E = L = P = N_v = 0\} \cup \{N_h = 0\}).$$

Note that \mathcal{D} is the manifold on which both vectors and hosts have non-zero population size.

Using Theorem 2.5.1 we have the following basic results that describes the positive invariance of \mathbb{R}_+^{10} and a compact attractor for solutions of system (3.3.1).

Theorem 3.3.1. *Assume the inherent net reproductive number $r_0 > 1$.*

(i) *Let \mathcal{D}_0 be a subset of \mathcal{D} , defined by*

$$\mathcal{D}_0 := \{E_h = I_h = E_v = I_v = 0\} \cap \mathcal{D}.$$

Then every solution $\phi(t)$ of (3.3.1), with $\phi(0) \in \mathcal{D}_0$, is defined for all $t \in [0, \infty)$, and satisfies

$$\begin{aligned}
\phi(t) &\in \mathcal{D}_0, & 0 \leq t < \infty, \\
(S_h(t), S_v(t), E(t), L(t), P(t)) &\in \text{int}(\mathbb{R}_+^5), & 0 < t < \infty, \\
R_h(t) &> 0, & 0 \leq t < \infty, \quad \text{or} \quad R_h \equiv 0, \\
\phi(t) &\rightarrow \mathcal{E}^0, & t \rightarrow \infty,
\end{aligned} \tag{3.3.2}$$

where

$$\begin{aligned}
\mathcal{E}^0 &:= (S_h, E_h, I_h, R_h, E_v, I_v, E, L, P, S_v) \\
&= (N_h^0, 0, 0, 0, 0, 0, E^*, L^*, P^*, N_v^*),
\end{aligned} \tag{3.3.3}$$

with $N_h^0 := \Lambda_h/\mu_h$, E^*, L^*, P^* and N_v^* defined as (2.5.1), is the infection-free equilibrium of (3.3.1). That is, \mathcal{D}_0 is positively invariant for solutions of (3.3.1) and lies on the stable manifold of \mathcal{E}^0 [60, 83].

(ii) Every solution $\phi(t)$ of (3.3.1) with $\phi(0) \in \mathcal{D} \setminus \mathcal{D}_0$ is defined and bounded for $t \in [0, \infty)$, $\phi(t) \in \text{int}(\mathbb{R}_+^{10})$ for $t \in (0, \infty)$, and its omega limit set lies in the compact set

$$\begin{aligned}
\mathcal{A} &:= \mathcal{D} \cap \left\{ (E, L, P, N_v, N_h + \frac{\delta_h}{\eta_h} R_h) \right. \\
&= (E^*, L^*, P^*, N_v^*, N_h^0) : \frac{\Lambda_h}{\mu_h + \delta_h} \leq N_h \leq N_h^0 \left. \right\},
\end{aligned}$$

which is positively invariant for the flows of (3.3.1).

Proof. Note that if

$$E_h(t) = I_h(t) = E_v(t) = I_v(t) = 0,$$

then $S_v(t) = N_v(t)$ and system (3.3.1) can be written as

$$\begin{aligned}\frac{dS_h}{dt} &= \Lambda_h - \mu_h S_h, \\ \frac{dR_h}{dt} &= -\mu_h R_h, \\ \frac{dE}{dt} &= bN_v - (k_E + \mu_E)E, \\ \frac{dL}{dt} &= k_E E - (k_L + \mu_L + \alpha L)L, \\ \frac{dP}{dt} &= k_L L - (k_P + \mu_P + \beta L)P, \\ \frac{dN_v}{dt} &= k_P P - \mu_v N_v.\end{aligned}\tag{3.3.4}$$

The solution of the first two equations of system (3.3.4) are

$$S_h(t) = S_h(0)e^{-\mu_h t} + N_h^0(1 - e^{-\mu_h t}),$$

$$R_h(t) = R_h(0)e^{-\mu_h t},$$

for $t \geq 0$. We observe that if $(E(t), L(t), P(t), N_v(t))$ is a solution of system (2.2.1), then

$(S_h(t), E_h(t), I_h(t), R_h(t), E_v(t), I_v(t), E(t), L(t), P(t), N_v(t))$ is a solution of (3.3.1). There-

fore, as $t \rightarrow \infty$, $S_h(t) \rightarrow N_h^0, R_h(t) \rightarrow 0, E(t) \rightarrow E^*, L(t) \rightarrow L^*, P(t) \rightarrow P^*$, and

$N_v(t) \rightarrow N_v^*$, that is, $\phi(t) \rightarrow \mathcal{E}^0 = (N_h^0, 0, 0, 0, 0, 0, E^*, L^*, P^*, N_v^*)$. The conclusion in (i) then follows from the uniqueness of the initial value problem of (3.3.1).

We next show (ii) via three steps, and let $\phi(0) \in \mathcal{D} \setminus \mathcal{D}_0$.

Step 1. We first show that $\phi(t) \in \text{int}(\mathbb{R}_+^{10})$, $\forall t \in (0, T^+)$. It follows from Theorem 2.5.1 that $E(t) > 0$, $L(t) > 0$, $P(t) > 0$, and $N_v(t) > 0$, $\forall t \in (0, T^+)$. We express the rest of components of $\phi(t)$ as follows. For $t \in [0, T^+)$,

$$\begin{aligned}
S_h(t) &= S_h(0)e^{-\int_0^t (\mu_h + \lambda_h) d\tau} + \Lambda_h \int_0^t e^{-\int_\tau^t (\mu_h + \lambda_h) ds} d\tau, \\
E_h(t) &= E_h(0)e^{-\sigma_1 t} + r\beta_v \int_0^t e^{-\sigma_1(t-\tau)} \frac{I_v(\tau)}{N_h(\tau)} S_h(\tau) d\tau, \\
I_h(t) &= I_h(0)e^{-\sigma_2 t} + \int_0^t e^{-\sigma_2(t-\tau)} E_h(\tau) d\tau, \\
R_h(t) &= R_h(0)e^{-\mu_h t} + \int_0^t e^{-\mu_h(t-\tau)} I_h(\tau) d\tau, \\
E_v(t) &= E_v(0)e^{-\sigma_v t} + r\beta_h \int_0^t e^{-\sigma_v(t-\tau)} \frac{I_h(\tau)}{N_h(\tau)} S_v(\tau) d\tau, \\
I_v(t) &= I_v(0)e^{-\mu_v t} + \int_0^t e^{-\mu_v(t-\tau)} E_v(\tau) d\tau, \\
S_v(t) &= S_v(0)e^{-\int_0^t (\mu_v + \lambda_h) d\tau} + k_P \int_0^t e^{-\int_\tau^t (\mu_v + \lambda_v) ds} P(\tau) d\tau.
\end{aligned} \tag{3.3.5}$$

It follows that, for $t \in (0, T^+)$,

$$S_v(t) \geq k_P \int_0^t e^{-\int_s^t (\mu_v + \lambda_v) d\tau} P(s) ds > 0, \quad S_h(t) \geq \Lambda_h \int_0^t e^{-\int_s^t (\mu_h + \lambda_h) d\tau} ds > 0.$$

Since $\phi(0) \notin \mathcal{D}_0$, it follows that at least one of the components $E_h(0)$, $I_h(0)$, $E_v(0)$, and $I_v(0)$ is nonzero. For example, if $E_h(0) > 0$, then from the continuity of E_h , $E_h > 0$ on $[0, \delta]$ for small $\delta > 0$. This together with the fact that $N_h > 0$ on $[0, T^+)$ yields that, for $t \in (0, \delta]$,

$$\begin{aligned}
I_h(t) &\geq \int_0^t e^{-\sigma_2(t-\tau)} E_h(\tau) d\tau > 0, \\
R_h(t) &\geq \int_0^t e^{-\mu_h(t-\tau)} I_h(\tau) d\tau > 0, \\
E_v(t) &\geq r\beta_h \int_0^t e^{-\sigma_v(t-\tau)} \frac{I_h(\tau)}{N_h(\tau)} S_v(\tau) d\tau > 0, \\
I_v(t) &\geq \int_0^t e^{-\mu_v(t-\tau)} E_v(\tau) d\tau > 0.
\end{aligned} \tag{3.3.6}$$

Clearly, the integrals on the right-hand side of (3.3.6) and the second equation of (3.3.5) remain positive at any t in (δ, T^+) , as long as E_h , I_h , R_h , E_v , and I_v are positive on (δ, t) . This implies that E_h , I_h , R_h , E_v , and I_v are positive on $(0, T^+)$. In a similar manner we show that in the case $I_h(0) > 0$, $E_v(0) > 0$, or $I_v(0) > 0$, each component of $\phi(t)$ is strictly positive for $t \in (0, T^+)$.

Step 2. Then we show $T^+ = \infty$. Adding the first four equations of (3.3.1), we have

$$\begin{aligned}
\frac{dN_h}{dt} &= \Lambda_h - \mu_h N_h - \delta_h I_h, \\
\frac{d\left(N_h + \frac{\delta_h}{\eta_h} R_h\right)}{dt} &= \Lambda_h - \mu_h \left(N_h + \frac{\delta_h}{\eta_h} R_h\right).
\end{aligned} \tag{3.3.7}$$

The nonnegativity of S_h , E_h , I_h , and R_h on $[0, T^+)$, from Step 1, leads to $I_h \leq N_h$, on $[0, T^+)$, and thus

$$\Lambda_h - (\mu_h + \delta_h)N_h \leq \frac{dN_h}{dt} \leq \Lambda_h - \mu_h N_h, \quad (3.3.8)$$

on $[0, T^+)$. Solving the differential equation

$$\frac{dN_h}{dt} = \Lambda_h - (\mu_h + \delta_h)N_h,$$

we obtain the solution

$$N_h(t) = \frac{\Lambda_h}{\mu_h + \delta_h} + [N_h(0) - \frac{\Lambda_h}{\mu_h + \delta_h}]e^{-(\mu_h + \delta_h)t}.$$

Solving the differential equation

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

we then obtain the solution

$$N_h(t) = N_h^0 + [N_h(0) - N_h^0]e^{-\mu_h t}.$$

Consequently, for $t \in [0, T^+)$, by comparison theorem, we have

$$\begin{aligned}
\frac{\Lambda_h}{\mu_h + \delta_h} + [N_h(0) - \frac{\Lambda_h}{\mu_h + \delta_h}]e^{-(\mu_h + \delta_h)t} &\leq N_h(t) \\
&\leq N_h^0 + [N_h(0) - N_h^0]e^{-\mu_h t},
\end{aligned} \tag{3.3.9}$$

which yields that

$$N_h(0)e^{-(\mu_h + \delta_h)t} \leq N_h(t) < N_h^0 + |N_h(0) - N_h^0|, \tag{3.3.10}$$

for $t \in [0, T^+)$. This together with the boundedness of (E, L, P, N_v) from Theorem 2.5.1 yields that ϕ is bounded on $[0, T^+)$, which implies that $T^+ = \infty$. Now letting $t \rightarrow \infty$ in (3.3.9) gives $\frac{\Lambda_h}{\mu_h + \delta_h} \leq \liminf_{t \rightarrow \infty} N_h(t) \leq \limsup_{t \rightarrow \infty} N_h(t) \leq N_h^0$, from which and Theorem 2.5.1 we conclude that $\omega(\phi)$ lies in \mathcal{A} .

Step 3. Finally, we show that \mathcal{A} is positively invariant for the solutions of (3.3.1). Let $\phi(0) \in \mathcal{A}$. It follows from the results in Steps 1 and 2 that $\phi(t)$ is defined on $[0, \infty)$ and lies in \mathcal{D} , with $(E, L, P, N_v) \equiv (E^*, L^*, P^*, N_v^*)$, and the associated $N_h(t)$ satisfying (3.3.9). The estimate in (3.3.9) together with $\phi(0) \in \mathcal{A}$ yields $\Lambda_h/(\mu_h + \delta_h) \leq N_h(t) \leq N_h^0$, for all $t \in [0, \infty)$, thereby $\phi(t) \in \mathcal{A}$ for all $t \in [0, \infty)$. This completes the proof of Theorem 3.3.1. \square

3.4 Infection-free equilibrium and reproductive number R_0

Similarly as in [39,66], we can easily derive a formula for the reproductive number of infection R_0 as follows.

It is clear that system (3.3.1) and the new system by replacing S_v by N_v have the same dynamics. Then the Jacobian matrix of the new system at the infection-free equilibrium \mathcal{E}^0 in (3.3.1) has the form of

$$A_0 = \begin{pmatrix} A_{11} & 0 \\ A_{21} & A_{22} \end{pmatrix},$$

where

$$A_{11} = \begin{pmatrix} -\mu_h & 0 & 0 & 0 & 0 & -\beta_v r \\ 0 & -\sigma_1 & 0 & 0 & 0 & \beta_v r \\ 0 & \gamma_h & -\sigma_2 & 0 & 0 & 0 \\ 0 & 0 & \eta_h & -\mu_h & 0 & 0 \\ 0 & 0 & \frac{\beta_h r N_v^*}{N_h^0} & 0 & -\sigma_v & 0 \\ 0 & 0 & 0 & 0 & \gamma_v & -\mu_v \end{pmatrix},$$

$$A_{21} = \begin{pmatrix} 0 & 0 & 0 & 0 & b & b \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\frac{\beta_h r N_v^*}{N_h^0} & 0 & 0 & 0 \end{pmatrix},$$

and $A_{22} := Df(E^*, L^*, P^*, N_v^*)$ is the Jacobian matrix at (E^*, L^*, P^*, N_v^*) , given in (2.5.2) in chapter 2.

The eigenvalues of A_0 consist of those of A_{11} and A_{22} . The eigenvalues of A_{11} except μ_h are the eigenvalues of the following matrix A ,

$$A = \begin{pmatrix} -\sigma_1 & 0 & 0 & \beta_v r \\ \gamma_h & -\sigma_2 & 0 & 0 \\ 0 & r\beta_h \frac{N_v^*}{N_h^0} & -\sigma_v & 0 \\ 0 & 0 & \gamma_v & -\mu_v \end{pmatrix}. \quad (3.4.1)$$

The leading principal minors of matrix $-A$ are

$$\begin{aligned} & \sigma_1, \quad \sigma_1\sigma_2, \quad \sigma_1\sigma_2\sigma_v, \\ \det(-A) &= \sigma_1\sigma_2\sigma_v\mu_v - \frac{r^2\beta_h\beta_v\gamma_h\gamma_vN_v^*}{N_h^0} = \sigma_1\sigma_2\sigma_v\mu_v \left(1 - \frac{r^2\beta_h\beta_v\gamma_h\gamma_vN_v^*}{\sigma_1\sigma_2\sigma_v\mu_vN_h^0} \right). \end{aligned}$$

Hence, if $\det(-A) > 0$, then matrix $-A$ is an M-matrix.

Define the reproductive number of infection R_0 by

$$R_0 := \sqrt{\frac{r^2\beta_h\beta_v\gamma_h\gamma_vN_v^*}{\sigma_1\sigma_2\sigma_v\mu_vN_h^0}}. \quad (3.4.2)$$

Then, all eigenvalues of A have negative real part if and only if $R_0 < 1$ [66]. On the other hand, since $r_0 > 1$, it follows from Theorem 2.5.1 that all eigenvalues of A_{22} have negative real part. Hence we have the following results.

Theorem 3.4.1. *Assume $r_0 > 1$. The infection-free equilibrium \mathcal{E}^0 is locally asymptotically stable if $R_0 < 1$, and is unstable if $R_0 > 1$.*

3.5 Endemic equilibria and backward bifurcation

We then investigate the existence of endemic equilibria of (3.3.1), whose components are all positive.

Assume E^*, L^*, P^* , and N_v^* are given in (2.5.1). Then it follows from the fourth equation of (2.5.1), $k_P P^* = \mu_v N_v^*$, and E^*, L^*, P^* , and N_v^* are the components of any biologically meaningful equilibrium of system (3.3.1). Therefore, the rest of the components, at an endemic equilibrium of system (3.3.1), are the components of the endemic of the following limiting system:

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - (\mu_h + \lambda_h) S_h, \\
\frac{dE_h}{dt} &= \lambda_h S_h - \sigma_1 E_h, \\
\frac{dI_h}{dt} &= \gamma_h E_h - \sigma_2 I_h, \\
\frac{dR_h}{dt} &= \eta_h I_h - \mu_h R_h, \\
\frac{dS_v}{dt} &= \mu_v N_v^* - (\mu_v + \lambda_v) S_v, \\
\frac{dE_v}{dt} &= \lambda_v S_v - \sigma_v E_v, \\
\frac{dI_v}{dt} &= \gamma_v E_v - \mu_v I_v.
\end{aligned} \tag{3.5.1}$$

Hence, an endemic equilibrium satisfies

$$\begin{aligned}
\Lambda_h - (\mu_h + \lambda_h) S_h &= 0, \\
\lambda_h S_h - \sigma_1 E_h &= 0, \\
\gamma_h E_h - \sigma_2 I_h &= 0, \\
\eta_h I_h - \mu_h R_h &= 0, \\
\mu_v N_v^* - (\mu_v + \lambda_v) S_v &= 0, \\
\lambda_v S_v - \sigma_v E_v &= 0, \\
\gamma_v E_v - \mu_v I_v &= 0.
\end{aligned} \tag{3.5.2}$$

Solving (3.5.2), we have

$$\begin{aligned}
S_h^* &= N_h^0 - \left(1 + \frac{\gamma_h}{\sigma_2} + \frac{\gamma_h \eta_h}{\sigma_2 \mu_h}\right) E_h^*, \quad I_h^* = \frac{\gamma_h}{\sigma_2} E_h^*, \quad R_h^* = \frac{\gamma_h \eta_h}{\sigma_2 \mu_h} E_h^*, \\
E_h^* &= \frac{N_h^0 \mu_v \sigma_2 \mu_h}{R_0^2 \mu_v (\sigma_2 \sigma_3 + \gamma_h \mu_h + \gamma_h \eta_h) + r \beta_h \gamma_h \mu_h} (R_0^2 - 1), \\
S_v^* &= N_v^* - \frac{(\mu + \gamma_v) r \beta_h \gamma_h N_v^*}{(r \beta_h \gamma_h + N_h^0 \mu_v \sigma_2) \sigma_v} E_h^*, \quad E_v^* = \frac{r \beta_h \gamma_h N_v^* \mu_v}{(r \beta_h \gamma_h + N_h^0 \mu_v \sigma_2) \sigma_v} E_h^*, \\
I_v^* &= \frac{r \beta_h \gamma_h N_v^* \mu_v \gamma_v}{(r \beta_h \gamma_h + N_h^0 \mu_v \sigma_2) \sigma_v \mu_v} E_h^*.
\end{aligned}$$

Therefore, if $R_0 > 1$, then system (3.3.1) has a unique endemic equilibrium

$$\mathcal{E}^* = (S_h^*, E_h^*, I_h^*, R_h^*, E_v^*, I_v^*, E^*, L^*, P^*, S_v^*).$$

The existence of an endemic equilibrium, for $R_0 < 1$, is related to the transcritical bifurcation at $R_0 = 1$ [66]. We give a full investigation for the model system (3.3.1) as follows. From equations (3.5.2), we obtain

$$\begin{aligned}
S_h &= \frac{\Lambda_h}{\mu_h + \lambda_h} \\
E_h &= \frac{\lambda_h}{\sigma_1} S_h = \frac{\lambda_h}{\sigma_1} \frac{\Lambda_h}{\mu_h + \lambda_h}, \\
I_h &= \frac{\gamma_h}{\sigma_2} E_h = \frac{\gamma_h \lambda_h}{\sigma_2 \sigma_1} \frac{\Lambda_h}{\mu_h + \lambda_h}, \\
R_h &= \frac{\eta_h}{\mu_h} I_h = \frac{\eta_h \gamma_h \lambda_h}{\mu_h \sigma_2 \sigma_1} \frac{\Lambda_h}{\mu_h + \lambda_h}, \\
S_v &= \frac{\mu_v N_v^*}{\mu_v + \lambda_v}, \\
E_v &= \frac{\lambda_v}{\sigma_v} S_v = \frac{\lambda_v}{\sigma_v} \frac{\mu_v N_v^*}{\mu_v + \lambda_v}, \\
I_v &= \frac{\gamma_v}{\mu_v} E_v = \frac{\gamma_v \lambda_v}{\mu_v \sigma_v} \frac{\mu_v N_v^*}{\mu_v + \lambda_v}.
\end{aligned} \tag{3.5.3}$$

Hence,

$$\begin{aligned}
N_h &= S_h + E_h + I_h + R_h \\
&= \frac{\Lambda_h}{\mu_h + \lambda_h} \left(1 + \frac{\lambda_h}{\sigma_1} + \frac{\gamma_h \lambda_h}{\sigma_2 \sigma_1} + \frac{\eta_h \gamma_h \lambda_h}{\mu_h \sigma_2 \sigma_1} \right) \\
&= \frac{\Lambda_h}{\mu_h + \lambda_h} (1 + K_2 \lambda_h),
\end{aligned} \tag{3.5.4}$$

where

$$K_2 = \frac{1}{\sigma_1} + \frac{\gamma_h}{\sigma_1 \sigma_2} + \frac{\eta_h \gamma_h}{\mu_h \sigma_1 \sigma_2}.$$

It follows from the definitions of λ_h and λ_v , we have

$$\lambda_h = \beta_v r \frac{I_v}{N_h} = \frac{\beta_v r \frac{\gamma_v \lambda_v N_v^*}{\sigma_v(\mu_v + \lambda_v)}}{\frac{\Lambda_h}{\mu_h + \lambda_h} (1 + K_2 \lambda_h)} = \frac{\beta_v r \gamma_v \lambda_v N_v^* (\mu_h + \lambda_h)}{\Lambda_h (1 + K_2 \lambda_h) \sigma_v (\mu_v + \lambda_v)}$$

and

$$\lambda_v = \beta_h r \frac{I_h}{N_h} = \frac{\beta_h r \frac{\gamma_h \lambda_h \Lambda_h}{\sigma_1 \sigma_2 (\mu_h + \lambda_h)}}{\frac{\Lambda_h}{\mu_h + \lambda_h} (1 + K_2 \lambda_h)} = \frac{\beta_h r \gamma_h \lambda_h}{\sigma_1 \sigma_2 (1 + K_2 \lambda_h)}.$$

By substituting λ_v into λ_h , we have

$$\begin{aligned} \lambda_h &= \frac{\beta_v r \gamma_v N_v^* (\mu_h + \lambda_h) \frac{\beta_h r \gamma_h \lambda_h}{\sigma_1 \sigma_2 (1 + K_2 \lambda_h)}}{\Lambda_h (1 + K_2 \lambda_h) \sigma_v \left(\mu_v + \frac{\beta_h r \gamma_h \lambda_h}{\sigma_1 \sigma_2 (1 + K_2 \lambda_h)} \right)} \\ &= \frac{r^2 \beta_h \beta_v \gamma_h \gamma_v N_v^*}{N_h^0 \sigma_1 \sigma_2 \sigma_v \mu_v} \frac{\left(1 + \frac{\lambda_h}{\mu_h} \right) \lambda_h}{(1 + K_2 \lambda_h)^2 \left(1 + \frac{\beta_h r \gamma_h \lambda_h}{\sigma_1 \sigma_2 \mu_v (1 + K_2 \lambda_h)} \right)} \\ &= R_0^2 \frac{(1 + K_3 \lambda_h) \lambda_h}{(1 + K_2 \lambda_h)(1 + K_4 \lambda_h)}, \end{aligned} \tag{3.5.5}$$

where $K_3 = \frac{1}{\mu_h}$ and $K_4 = K_2 + \frac{\beta_h r \gamma_h}{\sigma_1 \sigma_2 \mu_v}$. Thus, equation (3.5.5) can be simplified as

$$1 = \frac{R_0^2 (1 + K_3 \lambda_h)}{(1 + K_2 \lambda_h)(1 + K_4 \lambda_h)},$$

that is,

$$(1 + K_2 \lambda_h)(1 + K_4 \lambda_h) = R_0^2 (1 + K_3 \lambda_h).$$

Equivalently,

$$K_2 K_4 \lambda_h^2 + (K_2 + K_4) \lambda_h + 1 = R_0^2 + R_0^2 K_3 \lambda_h. \tag{3.5.6}$$

Let $c = R_0^2 - 1$. Equation (3.5.6) becomes

$$K_2 K_4 \lambda_h^2 + (K_2 + K_4 - (c + 1)K_3)\lambda_h - c = 0. \quad (3.5.7)$$

Solving c leads to

$$c(\lambda_h) = \frac{K_2 K_4 \lambda_h^2 + (K_2 + K_4 - K_3)\lambda_h}{1 + K_3 \lambda_h}. \quad (3.5.8)$$

Equation $c(\lambda_h) = 0$ has positive real root

$$\lambda_h^* = \frac{K_3 - (K_2 + K_4)}{K_2 K_4}, \quad (3.5.9)$$

if and only if $K_2 + K_4 - K_3 < 0$, that is,

$$\frac{1}{\mu_h} - \frac{2(\mu_h \sigma_2 + \gamma_h \mu_h + \eta_h \gamma_h)}{\mu_h \sigma_1 \sigma_2} - \frac{\beta_h r \gamma_h}{\sigma_1 \sigma_2 \mu_v} > 0. \quad (3.5.10)$$

Substituting $\sigma_1 = \mu_h + \gamma_h$ and $\sigma_2 = \mu_h + \delta_h + \eta_h$ into (3.5.10), we have

$$\delta_h(\gamma_h - \mu_h) > \mu_h \left(\mu_h + \eta_h + \gamma_h + \frac{\beta_h r \gamma_h}{\mu_v} \right) + \eta_h \gamma_h. \quad (3.5.11)$$

Hence, if $\gamma_h > \mu_h$, we define

$$\Delta := \frac{\mu_h(\mu_h + \eta_h + \gamma_h + \frac{r\beta_h\gamma_h}{\mu_v}) + \gamma_h\eta_h}{\gamma_h - \mu_h}. \quad (3.5.12)$$

It is clear that, if $\delta_h > \Delta$, then

$$D := K_3 - K_2 - K_4 > 0.$$

Next, we calculate the global minimum value of the function

$$c(\lambda_h) = \frac{K_2 K_4 \lambda^2 - D \lambda}{1 + K_3 \lambda}, \quad \lambda \in (-1/K_3, \infty).$$

Taking the derivative $c'(\lambda_h)$ of $c(\lambda_h)$ and letting $c'(\lambda_h) = 0$, we have

$$c'(\lambda_h) = \frac{K_2 K_3 K_4 \lambda_h^2 + 2K_2 K_4 \lambda_h + K_2 + K_4 - K_3}{(1 + K_3 \lambda_h)^2} = 0,$$

that is

$$K_2 K_3 K_4 \lambda_h^2 + 2K_2 K_4 \lambda_h + K_2 + K_4 - K_3 = 0. \quad (3.5.13)$$

The roots of equation (3.5.13) are

$$\bar{\lambda}_h = \frac{-2K_2 K_4 \pm \sqrt{4K_2^2 K_4^2 - 4K_2 K_3 K_4 (K_2 + K_4 - K_3)}}{2K_2 K_3 K_4},$$

it follows from $K_2 + K_4 < K_3$ that

$$\begin{aligned} \bar{\lambda}_h &= \frac{-2K_2 K_4 + \sqrt{4K_2^2 K_4^2 - 4K_2 K_3 K_4 (K_2 + K_4 - K_3)}}{2K_2 K_3 K_4} \\ &= \frac{-K_2 K_4 + \sqrt{K_2 K_4 (K_3 - K_2)(K_3 - K_4)}}{K_2 K_3 K_4} = \frac{1}{K_3} \left(\sqrt{1 + K_5} - 1 \right), \end{aligned}$$

where, $K_5 = \frac{K_3 D}{K_2 K_4}$. Therefore, the global minimum value of $c(\lambda_h)$ is

$$\begin{aligned}
c(\bar{\lambda}_h) &= \frac{\bar{\lambda}_h(K_2 K_4 \lambda_h + K_2 + K_4 - K_3)}{1 + K_3 \bar{\lambda}_h} \\
&= K_2 K_4 \bar{\lambda}_h \frac{\sqrt{K_2 K_4 (K_3 - K_2)(K_3 - K_4)} - (K_3 - K_2)(K_3 - K_4)}{K_3 \sqrt{K_2 K_4 (K_3 - K_2)(K_3 - K_4)}} \\
&= K_2 K_4 \bar{\lambda}_h \frac{K_2 K_4 - \sqrt{K_2 K_4 (K_3 - K_2)(K_3 - K_4)}}{K_2 K_3 K_4} = -K_2 K_4 \bar{\lambda}_h^2 \\
&= -1 + \frac{K_3(K_2 + K_4) - 2K_2 K_4 + 2\sqrt{K_2 K_4 (K_3 - K_2)(K_3 - K_4)}}{K_3^2},
\end{aligned} \tag{3.5.14}$$

which implies $-1 < c(\bar{\lambda}_h) < 0$. Hence,

$$\begin{aligned}
|c(\bar{\lambda}_h)| &= K_2 K_4 \left(\frac{1}{K_3} (\sqrt{1 + K_5} - 1) \right)^2 \\
&= D K_3 \frac{K_2 K_4}{D K_3} \left(\frac{1}{K_3} \frac{K_5}{\sqrt{1 + K_5} + 1} \right)^2 \\
&= D K_3 \frac{1}{K_5} \frac{K_5^2}{K_3^2 (\sqrt{1 + K_5} + 1)^2} \\
&= \frac{D}{K_3} \frac{K_5}{(\sqrt{1 + K_5} + 1)^2} \\
&= \frac{D}{K_3} \left(\sqrt{1 + \frac{1}{K_5}} + \sqrt{\frac{1}{K_5}} \right)^{-2}
\end{aligned} \tag{3.5.15}$$

Similarly as in [66], we let $R_b^2 := 1 + c(\bar{\lambda}_h)$. Then

$$\begin{aligned}
R_b^2 &= 1 + c(\bar{\lambda}_h) \\
&= \frac{K_3(K_2 + K_4) - 2K_2 K_4 + 2\sqrt{K_2 K_4 (K_3 - K_2)(K_3 - K_4)}}{K_3^2} \\
&\geq \frac{K_3 2\sqrt{K_2 K_4} - 2K_2 K_4 + 2\sqrt{K_2 K_4 (K_3 - K_2)(K_3 - K_4)}}{K_3^2}
\end{aligned}$$

$$\begin{aligned}
&= \frac{2\sqrt{K_2 K_4}(K_3 - \sqrt{K_2 K_4} + \sqrt{(K_3 - K_2)(K_3 - K_4)})}{K_3^2} \\
&\geq \frac{2\sqrt{K_2 K_4}(K_3 - \frac{K_2 + K_4}{2} + \sqrt{(K_3 - K_2)(K_3 - K_4)})}{K_3^2} \\
&> \frac{2\sqrt{K_2 K_4}(K_3 - \frac{K_3}{2} + \sqrt{(K_3 - K_2)(K_3 - K_4)})}{K_3^2} \\
&\quad (\text{since } K_2 + K_4 < K_3) \\
&> \frac{\sqrt{K_2 K_4}}{K_3} \quad (\text{since } K_4 = K_2 + \frac{\beta_h r \gamma_h}{\sigma_1 \sigma_2 \mu_v}) \\
&> \frac{K_2}{K_3} = \frac{\frac{\mu_h \sigma_2 + \mu_h \gamma_h + \eta_h \gamma_h}{\mu_h \sigma_1 \sigma_2}}{\frac{1}{\mu_h}} \\
&= \frac{\mu_h \sigma_2 + \mu_h \gamma_h + \eta_h \gamma_h}{\sigma_1 \sigma_2}.
\end{aligned}$$

Since $c(\bar{\lambda}_h) < 0$,

$$\begin{aligned}
R_b &= (1 + c(\bar{\lambda}_h))^{1/2} = (1 - |c(\bar{\lambda}_h)|)^{1/2} \\
&= \left(1 - \frac{D}{K_3} \frac{1}{\left(\sqrt{1 + \frac{K_2 K_4}{D K_3}} + \sqrt{\frac{K_2 K_4}{D K_3}} \right)^2} \right)^{1/2} \\
&= \left(1 - \frac{D^2}{\left(\sqrt{D K_3} + K_2 K_4 + \sqrt{K_2 K_4} \right)^2} \right)^{1/2}.
\end{aligned} \tag{3.5.16}$$

It is easy to see that, R_b is monotone decreasing for δ_h in the interval (Δ, ∞) , when all other parameters are fixed, from the fact that while K_3 is independent of δ_h , D is increasing, and both K_2 and K_4 are decreasing such that $\frac{K_2 K_4}{D K_3}$ is also decreasing. At the same time, we see that R_b has a limit when $\delta_h \rightarrow \infty$, since $K_2 \rightarrow \frac{1}{\mu_h + \gamma_h}$ and $K_4 \rightarrow \frac{1}{\mu_h + \gamma_h}$ as $\delta_h \rightarrow \infty$.

In summary, we have the following results.

Theorem 3.5.1. *Assume $\gamma_h > \mu_h$, $\delta_h > \Delta$. Define R_b as in (3.5.16). Then it has the following properties.*

(a) $\sqrt{\frac{\mu_h \sigma_2 + \mu_h \gamma_h + \eta_h \gamma_h}{\sigma_1 \sigma_2}} < R_b < 1.$

(b) *Regard R_b as a function of δ_h with other parameters fixed. Then R_b is monotone decreasing for δ_h in (Δ, ∞) .*

(c) *As $\delta_h \rightarrow \infty$,*

$$\lim_{\delta_h \rightarrow \infty} R_b^2 = 1 - \left(\frac{\gamma_h - \mu_h}{\gamma_h + \mu_h} \right)^2 = \frac{4\gamma_h \mu_h}{(\gamma_h + \mu_h)^2} := \left(R_b^{min} \right)^2 \quad (3.5.17)$$

in a monotone decreasing manner.

The following result in [66] describes the endemic equilibria of the system (3.5.1), which is the limiting system of (3.3.1).

Lemma 3.5.2. (Theorem 5.1 [66]) *System (3.5.1) has a unique endemic equilibrium if $R_0 > 1$. Under the condition of $K_2 + K_4 < K_3$, there exists $R_b \in (0, 1)$ such that (3.5.1) has no endemic equilibrium if $R_0 < R_b$, a unique endemic equilibrium if $R_0 = R_b$, and two endemic equilibria if $R_b < R_0 < 1$, which implies a backward bifurcation at $R_0 = 1$. On the other hand, if $K_2 + K_4 > K_3$, there exists no endemic equilibrium, and backward bifurcation cannot occur for $R_0 < 1$.*

Now we present the main results on endemic equilibria of (3.3.1) for $R_0 \leq 1$.

Theorem 3.5.3. *Let all coefficients in (3.3.1) be positive with $\gamma_h > \mu_h$. Then we have the following.*

- (I) *Assume $\delta_h \leq \Delta$ and $R_0 \leq 1$. Then (3.3.1) has no endemic equilibrium, and a forward transcritical bifurcation occurs at $R_0 = 1$ [62, 83].*
- (II) *Assume $\delta_h > \Delta$ and $R_0 \leq 1$. Then*
 - (i) *at $R_0 = 1$, there is a unique endemic equilibrium of (3.3.1), and a backward transcritical bifurcation occurs;*
 - (ii) *for $R_b < R_0 < 1$, (3.3.1) has two endemic equilibria, one of which is locally asymptotically stable and one of which is unstable;*
 - (iii) *at $R_0 = R_b$, (3.3.1) has a unique endemic equilibrium, and a saddle-node bifurcation occurs;*
 - (iv) *if $R_0 < R_b$, then (3.3.1) has no endemic equilibrium.*

Remark 1. We note that all cases in Theorem 3.5.3 can happen. For example, the conditions

$$R_b < R_0 < 1$$

are equivalent to

$$\frac{\sigma_1 \sigma_2 \mu_v^2}{r^2 \beta_h \gamma_h \mu_h} R_b^2 < \frac{\beta_v N_v^*}{\Lambda_h \left(\frac{1}{\mu_v} + \frac{1}{\gamma_v} \right)} < \frac{\sigma_1 \sigma_2 \mu_v^2}{r^2 \beta_h \gamma_h \mu_h}, \quad (3.5.18)$$

and the left and right terms in (3.5.18) do not depend on Λ_h , μ_v , and γ_v . Thus, if $\delta_h > \Delta$, we can choose parameters so that the inequalities in (3.5.18) are satisfied, and then Case (III) (ii) occurs. We demonstrate such a case in Example (3.5.1), based on the limiting system (3.5.1).

Example 3.5.1. We first use the following parameters for the mosquito population

$$\begin{aligned} b = 2000, \quad k_E = 0.8, \quad \mu_E = 0.7, \quad k_L = .8, \quad \mu_L = 0.7, \\ \alpha = 0.2, \quad k_P = 0.4, \quad \mu_P = 0.4, \quad \mu_v = 0.6. \end{aligned}$$

Then $r_0 = 474 > 1$ and hence $N_v(t) \rightarrow N_v^* = 2,365$. We then consider the limiting system (3.5.1), and select the parameters for the human population and the disease transmission as

$$\begin{aligned} \mu_h = 0.011, \quad \delta_h = 0.4, \quad \gamma_h = 0.03, \quad \eta_h = 0.06, \\ r = 5, \quad \beta_h = 0.032, \quad \beta_v = 0.199, \end{aligned}$$

such that $R_b = 0.9712$. A backward bifurcation then occurs and the bifurcation diagram is shown in Figure 3.4. We then let $\Lambda_h = 6$ and $\gamma_v = 0.7$ such that $R_0 = 0.9811$. With the initial value $(2, 0.001, 0.001, 0.001, 2, 0.001, 0.001)$, the solution approaches the infection-free equilibrium $(545.5, 0, 0, 0, 2, 365.4, 0, 0)$, as shown in Figure 3.5; while the solution with the initial value $(1, 1, 1, 0.5, 10, 10, 10)$ approaches the endemic equilibrium $(247.2, 79.7, 5.1, 27.8, 2, 356.5, 4.1, 4.8)$ as shown in Figure 3.6.

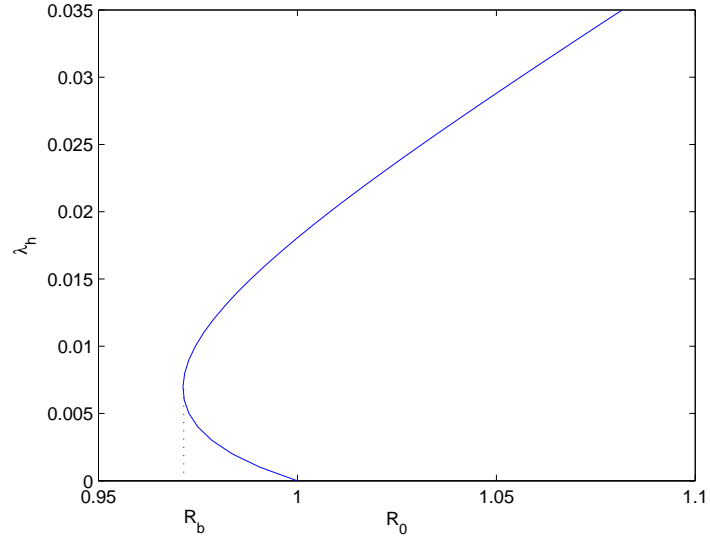


Figure 3.4: The parameters are given in Example (3.5.1). A backward bifurcation occurs with $R_b = 0.9712$.

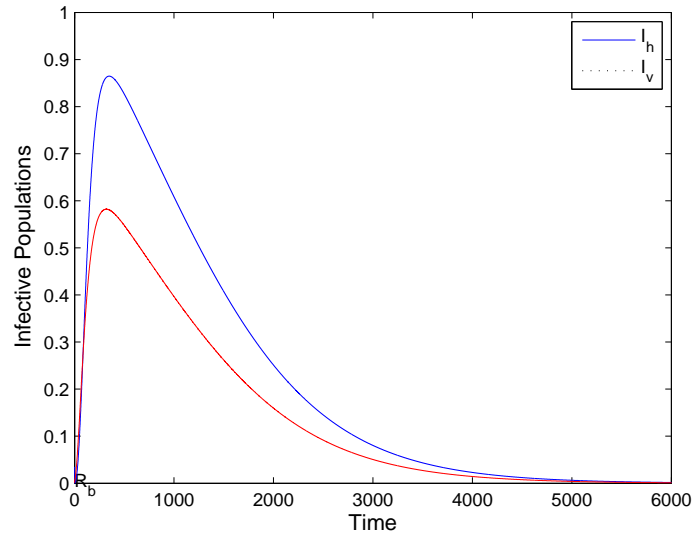


Figure 3.5: With the initial value $(2, 0.001, 0.001, 0.001, 2, 0.001, 0.001)$, the solution approaches the infection-free equilibrium $(545.5, 0, 0, 0, 2,365.4, 0, 0)$.

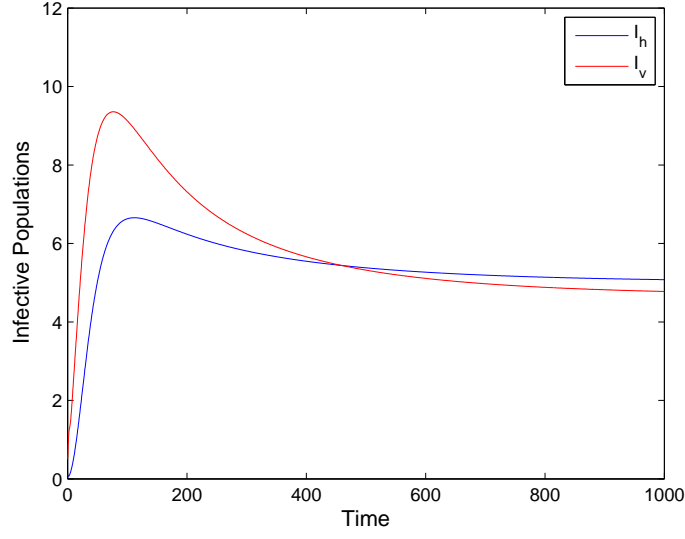


Figure 3.6: With the initial value $(1, 1, 1, 0.5, 10, 10, 10)$ approaches the endemic equilibrium $(247.2, 79.7, 5.1, 27.8, 2,356.5, 4.1, 4.8)$.

3.6 Global stability of the infection-free equilibrium \mathcal{E}^0

In this section we investigate the global stability of the infection-free equilibrium point \mathcal{E}^0 .

It is clear that a necessary condition for the infection-free equilibrium to be globally stable is $R_0 < R_b$. While we have not been able to prove the general case, we establish the following results, using the following LaSalle's invariance principle.

Theorem 3.6.1. (LaSalle's Invariance Principle [61, 64, 83]) *Consider the system*

$$z' = f(z), \quad z \in \mathcal{U}, \quad (3.6.1)$$

where \mathcal{U} is an open set in \mathbb{R}^n and $f : \mathcal{U} \rightarrow \mathbb{R}^n$ is C^1 . Let $z = \phi(t)$ be a solution of (3.6.1) such that for all $t \geq t_0 \geq 0$, $\phi(t)$ lies in a compact set of $\text{int}(\mathcal{U})$. If there is a C^1 function $V : \mathcal{U} \rightarrow \mathbb{R}$ such that its orbital derivative on $\phi(t)$ satisfies

$$\dot{V}(z) = \nabla V(z) \cdot f(z) \leq 0, \quad \forall z = \phi(t), \quad t \geq t_0,$$

then,

$$\omega(\phi(t)) \subseteq \text{cl}(\{\phi(t) : t \in [t_0, \infty)\}) \cap \{z \in \mathcal{U} : \dot{V}(z) = 0\}.$$

Theorem 3.6.2. Assume $r_0 > 1$ and define

$$R_c =: \max \left\{ \left(\frac{\mu_h}{\mu_h + \delta_h} \right)^{1/2}, \left(\frac{\eta_h}{\eta_h + \delta_h} \right)^{1/2} \right\}.$$

If $R_0 < R_c$, then \mathcal{E}^0 is globally asymptotically stable in \mathcal{D} .

Proof. It follows from Theorem 3.4.1 that \mathcal{E}^0 is locally asymptotically stable. It remains to show that $\phi(t) \rightarrow \mathcal{E}^0$, as $t \rightarrow \infty$, for any $\phi(0) \in \mathcal{D}$.

Step 1. We show that if $\phi(0) \in \mathcal{A}$, then $\phi(t) \rightarrow \mathcal{E}^0$ as $t \rightarrow \infty$. To this end, we define a Lyapunov function [73, 83]

$$V := \sigma_v \mu_v (\gamma_h E_h + \sigma_1 I_h) + r \beta_v \gamma_h (\gamma_v E_v + \sigma_v I_v). \quad (3.6.2)$$

Since, from Theorem 3.3.1 (ii), \mathcal{A} is a positive invariant set of (3.3.1), we have $\phi(t) \in \mathcal{A}$ for $t \in [0, \infty)$, and thus its components satisfy $N_v \equiv N_v^*$, $N_h + \frac{\delta_h R_h}{\eta_h} \equiv N_h^0$, $\frac{\Lambda_h}{\mu_h + \delta_h} \leq N_h \leq N_h^0$, and $S_v \equiv N_v^* - (E_v + I_v)$, on $[0, \infty)$. Taking the orbital derivative of V on $\phi(t)$ and using the assumption on R_0 , we have, on $[0, \infty)$,

$$\begin{aligned}
\dot{V} &= \sigma_v \mu_v \gamma_h (\lambda_h S_h - \sigma_1 E_h) + \sigma_v \mu_v \sigma_1 (\gamma_h E_h - \sigma_2 I_h) \\
&\quad + r \beta_v \gamma_h \gamma_v (\lambda_v S_v - \sigma_v E_v) + r \beta_v \gamma_h \sigma_v (\gamma_v E_v - \mu_v I_v) \\
&= \sigma_v \mu_v \gamma_h \frac{\beta_v r I_v}{N_h} S_h - \sigma_v \mu_v \sigma_1 \sigma_2 I_h + r \beta_v \gamma_h \gamma_v \frac{\beta_h r I_h}{N_h} S_v - r \beta_v \gamma_h \sigma_v \mu_v I_v \\
&= \sigma_v \mu_v \gamma_h \frac{\beta_v r I_v}{N_h} (N_h - (E_h + I_h + R_h)) - \sigma_v \mu_v \sigma_1 \sigma_2 I_h \\
&\quad + r \beta_v \gamma_h \gamma_v \frac{\beta_h r I_h}{N_h} (N_v^* - (E_v + I_v)) - r \beta_v \gamma_h \sigma_v \mu_v I_v \\
&= - \left(\sigma_1 \sigma_2 \sigma_v \mu_v - \frac{r^2 \beta_h \beta_v \gamma_h \gamma_v N_v^*}{N_h} \right) I_h \\
&\quad - \frac{\sigma_v \mu_v \gamma_h r \beta_v (E_h + I_h + R_h) I_v}{N_h} - \frac{r^2 \beta_v \beta_h \gamma_h \gamma_v (E_v + I_v) I_h}{N_h} \\
&= - \sigma_1 \sigma_2 \sigma_v \mu_v \left(1 - R_0^2 \frac{N_h^0}{N_h} \right) I_h - \frac{\sigma_v \mu_v \gamma_h r \beta_v (E_h + I_h + R_h) I_v}{N_h} \\
&\quad - \frac{r^2 \beta_v \beta_h \gamma_h \gamma_v (E_v + I_v) I_h}{N_h} \leq 0.
\end{aligned} \tag{3.6.3}$$

It thus follows from Theorem 3.6.1 that $\omega(\phi(t)) \subseteq \mathcal{A} \cap \{\dot{V} = 0\}$. Note that since $\Lambda_h/(\mu_h + \delta_h) \leq N_h \leq N_h^0$ and $R_0 < R_c$ imply that $1 - \frac{R_0^2 N_h^0}{N_h} > 0$, it follows from (3.6.3) that $\mathcal{A} \cap \{\dot{V} = 0\} \subseteq \mathcal{A} \cap \{I_h = 0\}$. Thus, $\omega(\phi(t)) \subseteq \mathcal{A} \cap \{I_h = 0\}$.

Now let $\tilde{\phi}(t) = (\tilde{S}_h, \tilde{E}_h, \tilde{I}_h, \tilde{R}_h, \tilde{E}_v, \tilde{I}_v, \tilde{E}, \tilde{L}, \tilde{P}, \tilde{S}_v,)$ be an arbitrary orbit in $\omega(\phi(t))$, which is defined for all $t \in (-\infty, \infty)$. It follows from Theorem 2.5.1 that $(\tilde{E}, \tilde{L}, \tilde{P}, \tilde{N}_v) \equiv$

(E^*, L^*, P^*, N_v^*) , and from the last statement of the above paragraph, $\tilde{I}_h \equiv 0$ on $(-\infty, \infty)$. Then, using the equations in (3.3.1), we can derive with no difficulty that $\tilde{S}_h \equiv N_h^0$, $\tilde{S}_v \equiv N_v^*$, $\tilde{E}_h = \tilde{R}_h = \tilde{E}_v = \tilde{I}_v \equiv 0$ on $(-\infty, \infty)$. This shows that $\tilde{\phi} = \{\mathcal{E}^0\}$. We thus conclude $\omega(\phi(t)) = \{\mathcal{E}^0\}$.

Step 2. We then assume $\phi(0) \in \mathcal{D}$. Let $\bar{\phi}(t)$ be an orbit of (3.3.1) lying in $\omega(\phi(t))$. Since, from Theorem 3.3.1 (ii), $\bar{\phi}(t) \in \mathcal{A}$ for all t in $(-\infty, \infty)$, we have, from Step 1 above, $\omega(\bar{\phi}(t)) = \{\mathcal{E}^0\}$ so that $\bar{\phi}(t) \rightarrow \mathcal{E}^0$ as $t \rightarrow \infty$. This yields that for some sufficiently large t_0 , $\phi(t_0)$ lies in a local attraction domain of \mathcal{E}^0 (since \mathcal{E}^0 is locally asymptotically stable from Theorem 3.4.1), and consequently $\phi(t) \rightarrow \mathcal{E}^0$ as $t \rightarrow \infty$. The proof of the theorem is then complete. \square

Corollary 3.6.3. *Assume $r_0 > 1$ and $\delta_h = 0$. If $R_0 < 1$, then \mathcal{E}^0 is globally asymptotically stable in \mathcal{D} .*

3.7 Global stability of the endemic equilibrium \mathcal{E}^* when $\delta_h = 0$

The determination of stability of the endemic equilibrium is not an easy task. Even investigating locations of the eigenvalues of the Jacobian matrix at an endemic equilibrium for its local stability is not trivial because of the high dimension of system (3.3.1). Thus we only consider the case of $\delta_h = 0$ and study the stability of the endemic equilibrium \mathcal{E}^* , by using a Volterra-Goh type Lyapunov function.

The main results are given as follows.

Theorem 3.7.1. *Assume $r_0 > 1$ and $\delta_h = 0$. If $R_0 > 1$, then \mathcal{E}^* is globally asymptotically stable in $\mathcal{D} \setminus \mathcal{D}_0$.*

To prove Theorem 3.7.1 we first establish several lemmas. For notational convenience, we write solution $\phi(t)$ of (3.3.1) as $\phi(t) = (\phi_1(t), \phi_2(t))$, where

$$\phi_1(t) = (S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), E_v(t), I_v(t)), \quad \phi_2(t) = (E(t), L(t), P(t)),$$

and write $\mathcal{E}^* = (\mathcal{E}_1^*, \mathcal{E}_2^*)$, where $\mathcal{E}_1^* = (S_h^*, E_h^*, I_h^*, R_h^*, S_v^*, E_v^*, I_v^*)$ and $\mathcal{E}_2^* := (E^*, L^*, P^*)$. It follows from Theorem 2.5.1 that $\phi_2(t) \rightarrow \mathcal{E}_2^*$ as $t \rightarrow \infty$. We then need to show the local stability of \mathcal{E}^* and $\phi_1(t) \rightarrow \mathcal{E}_1^*$, as $t \rightarrow \infty$, if $\phi(0) \in \mathcal{D} \setminus \mathcal{D}_0$. We use a Volterra-Goh type Lyapunov function [58, 63] to accomplish this.

In order to simplify the notation for the Lyapunov function and its derivative along $\phi(t)$, we introduce the following new variables for $S_h, E_h, I_h, R_h, S_v, E_v, I_v$:

$$x_1 = \frac{S_h}{S_h^*}, \quad x_2 = \frac{E_h}{E_h^*}, \quad x_3 = \frac{I_h}{I_h^*}, \quad x_4 = \frac{R_h}{R_h^*}, \quad y_1 = \frac{S_v}{S_v^*}, \quad y_2 = \frac{E_v}{E_v^*}, \quad y_3 = \frac{I_v}{I_v^*}.$$

The resulting equations for the new variables are

$$\begin{aligned}
\frac{dx_1}{dt} &= \mu_h + \frac{r\beta_v I_v^*}{N_h^0} - \left(\mu_h + r\beta_v I_v^* \frac{y_3}{N_h} \right) x_1, \\
\frac{dx_2}{dt} &= \sigma_1(N_h^0 \frac{y_3}{N_h} x_1 - x_2), \\
\frac{dx_3}{dt} &= \sigma_2(x_2 - x_3), \\
\frac{dx_4}{dt} &= \mu_h(x_3 - x_4), \\
\frac{dy_1}{dt} &= \frac{1}{S_v^*} k_P(P - P^*) + \mu_v + \frac{r\beta_h I_h^*}{N_h^0} - (\mu_v + r\beta_h I_h^* \frac{x_3}{N_h}) y_1, \\
\frac{dy_2}{dt} &= \sigma_v(N_h^0 \frac{x_3}{N_h} y_1 - y_2), \\
\frac{dy_3}{dt} &= \mu_v(y_2 - y_3).
\end{aligned} \tag{3.7.1}$$

Let $x = (x_1, x_2, x_3, x_4)$, $y := (y_1, y_2, y_3)$, $x^* = (1, 1, 1, 1)$, and $y^* = (1, 1, 1)$. It follows that \mathcal{E}_1^* is transformed into (x^*, y^*) , and $\phi_1(t) \rightarrow \mathcal{E}_1^*$, as $t \rightarrow \infty$, if and only if the corresponding solution $(x(t), y(t))$ of (3.7.1) approaches (x^*, y^*) , as $t \rightarrow \infty$.

We define the Volterra-Goh type Lyapunov function $W : \text{int}(\mathbb{R}_+^7) \mapsto \mathbb{R}$ as

$$\begin{aligned}
W(x, y) &:= x_1 - 1 - \ln x_1 + \frac{r\beta_v I_v^*}{\sigma_1 N_h^0} (x_2 - 1 - \ln x_2) \\
&\quad + \frac{r\beta_v I_v^*}{\sigma_2 N_h^0} (x_3 - 1 - \ln x_3) \\
&\quad + k \left(y_1 - 1 - \ln y_1 + \frac{r\beta_h I_h^*}{\sigma_v N_h^0} (y_2 - 1 - \ln y_2) \right. \\
&\quad \left. + \frac{r\beta_h I_h^*}{\mu_v N_h^0} (y_3 - 1 - \ln y_3) \right),
\end{aligned} \tag{3.7.2}$$

where $k = \frac{\beta_v I_v^*}{\beta_h I_h^*}$. Using such properties of the function $f(\eta) := \eta - 1 - \ln \eta$, $\eta > 0$, as $f(\eta) > f(1) > 0$, for $\eta \neq 1$, $\lim_{\eta \rightarrow 0^+} f(\eta) = \lim_{\eta \rightarrow \infty} f(\eta) = \infty$, and $\frac{1}{4}(\eta - 1)^2 \leq f(\eta) \leq (\eta - 1)^2$, for $1/2 \leq \eta \leq 2$, we obtain the following preliminary results for $W(x, y)$.

- (i) $W(x, y) > 0$, for all $(x, y) \in \text{int}(\mathbb{R}_+^7)$, except $x_i = y_i = 1$, $i = 1, 2, 3$.
- (ii) If $W(x, y) \leq M$, for some $M > 0$, then there exist $0 < m_1 < m_2 < \infty$, such that $m_1 \leq y_i \leq m_2$ and $m_1 \leq x_i \leq m_2$, for $i = 1, 2, 3$.
- (iii) If $|x_i - 1| \leq 1/2$ and $|y_i - 1| \leq 1/2$, for $i = 1, 2, 3$, then

$$M_1 \sum_{i=1}^3 [(x_i - 1)^2 + (y_i - 1)^2] \leq W(x, y) \leq M_2 \sum_{i=1}^3 [(x_i - 1)^2 + (y_i - 1)^2], \quad (3.7.3)$$

where

$$\begin{aligned} M_1 &:= \frac{1}{4} \min \mathcal{M}, \quad M_2 := \max \mathcal{M}, \\ \mathcal{M} &:= \left\{ \frac{r\beta_v I_v^*}{\sigma_1 N_h^0}, \frac{r\beta_v I_v^*}{\sigma_2 N_h^0}, k, \frac{kr\beta_h I_h^*}{\sigma_v N_h^0}, \frac{kr\beta_h I_h^*}{\mu_v N_h^0} \right\}. \end{aligned} \quad (3.7.4)$$

Recall from Theorem 3.3.1 (ii) that $\phi(0) \in \mathcal{D} \setminus \mathcal{D}_0$ implies $\phi(t) \in \text{int}(\mathbb{R}_+^{10})$, for $t > 0$, and thus each component of the corresponding solution $(x(t), y(t))$ of (3.7.1) is positive on $(0, \infty)$. Thus, $W(x(t), y(t))$ is well defined for all $t > 0$, and its orbital derivative is, for $t > 0$,

$$\dot{W}(x, y) = x'_1 - \frac{1}{x_1} x'_1 + \frac{r\beta_v I_v^*}{\sigma_1 N_h^0} \left(x'_2 - \frac{1}{x_2} x'_2 \right) + \frac{r\beta_v I_v^*}{\sigma_2 N_h^0} \left(x'_3 - \frac{1}{x_3} x'_3 \right)$$

$$\begin{aligned}
& + k \left(y'_1 - \frac{1}{y_1} y'_1 + \frac{r\beta_h I_h^*}{\sigma_v N_h^0} (y'_2 - \frac{1}{y_2} y'_2) + \frac{r\beta_h I_h^*}{\mu_v N_h^0} (y'_3 - \frac{1}{y_3} y'_3) \right) \\
= & \left(1 - \frac{1}{x_1} \right) x'_1 + \frac{r\beta_v I_v^*}{\sigma_1 N_h^0} \left(1 - \frac{1}{x_2} \right) x'_2 + \frac{r\beta_v I_v^*}{\sigma_2 N_h^0} \left(1 - \frac{1}{x_3} \right) x'_3 \\
& + k \left(\left(1 - \frac{1}{y_1} \right) y'_1 + \frac{r\beta_h I_h^*}{\sigma_v N_h^0} \left(1 - \frac{1}{y_2} \right) y'_2 + \frac{r\beta_h I_h^*}{\mu_v N_h^0} \left(1 - \frac{1}{y_3} \right) y'_3 \right) \\
= & \left(1 - \frac{1}{x_1} \right) \left(\mu_h + \frac{r\beta_v I_v^*}{N_h^0} - \left(\mu_h + r\beta_v I_v^* \frac{y_3}{N_h} \right) x_1 \right) \\
& + \frac{r\beta_v I_v^*}{\sigma_1 N_h^0} \left(1 - \frac{1}{x_2} \right) \left(\sigma_1 (N_h^0 \frac{y_3}{N_h} x_1 - x_2) \right) \\
& + \frac{r\beta_v I_v^*}{\sigma_2 N_h^0} \left(1 - \frac{1}{x_3} \right) (\sigma_2 (x_2 - x_3)) \\
& + k \left(\left(1 - \frac{1}{y_1} \right) \left(\frac{1}{S_v^*} k_P (P - P^*) + \mu_v + \frac{r\beta_h I_h^*}{N_h^0} \right. \right. \\
& \quad \left. \left. - (\mu_v + r\beta_h I_h^* \frac{x_3}{N_h}) y_1 \right) + \frac{r\beta_h I_h^*}{\sigma_v N_h^0} \left(1 - \frac{1}{y_2} \right) \left(\sigma_v (N_h^0 \frac{x_3}{N_h} y_1 - y_2) \right) \right. \\
& \quad \left. + \frac{r\beta_h I_h^*}{\mu_v N_h^0} \left(1 - \frac{1}{y_3} \right) (\mu_v (y_2 - y_3)) \right) \\
= & \mu_h \left(2 - x_1 - \frac{1}{x_1} \right) + k\mu_v \left(2 - y_1 - \frac{1}{y_1} \right) \\
& + \frac{r\beta_v I_v^*}{N_h^0} \left(6 - \frac{1}{x_1} - \frac{y_3 x_1}{x_2} - \frac{x_2}{x_3} - \frac{1}{y_1} - \frac{x_3 y_1}{y_2} - \frac{y_2}{y_3} \right) \\
& + r\beta_v I_v^* \left(\frac{1}{N_h} - \frac{1}{N_h^0} \right) \left(\frac{(x_2 - x_1)y_3}{x_2} + \frac{(y_2 - y_1)x_3}{y_2} \right) \\
& + \frac{k_P k}{S_v^*} (P - P^*) \left(1 - \frac{1}{y_1} \right).
\end{aligned} \tag{3.7.5}$$

Applying the arithmetic-geometric mean inequality

$$a_1 + a_2 + \cdots + a_n \geq n \sqrt[n]{a_1 a_2 \cdots a_n}, \tag{3.7.6}$$

$$\text{for } a_k \geq 0, \quad k = 1, 2, \dots, n,$$

where the equality holds if and only if $a_1 = a_2 = \dots = a_n$, to \dot{W} yields

$$\begin{aligned} \dot{W}(x, y) \leq & r\beta_v I_v^* \left(\frac{1}{N_h} - \frac{1}{N_h^0} \right) \left(\frac{(x_2 - x_1)y_3}{x_2} + \frac{(y_2 - y_1)x_3}{y_2} \right) \\ & + \frac{k_P k}{S_v^*} (P - P^*) \left(1 - \frac{1}{y_1} \right). \end{aligned} \quad (3.7.7)$$

Integrating (3.7.7) over $[0, t]$, for $t > 0$, yields

$$\begin{aligned} W(x(t), y(t)) \leq & W(x(0), y(0)) \\ & + \frac{r\beta_v I_v^*}{N_h^0} \int_0^t \frac{N_h^0 - N_h}{N_h} \left(\frac{(x_2 - x_1)y_3}{x_2} + \frac{(y_2 - y_1)x_3}{y_2} \right) ds \\ & + \frac{k_P k}{S_v^*} \int_0^t (P - P^*) \left(1 - \frac{1}{y_1} \right) ds. \end{aligned} \quad (3.7.8)$$

Based on these preliminary results, we have the following results.

Lemma 3.7.2. *Assume $r_0 > 1$ and $\delta_h = 0$. Then*

(i) *the ω -limit set of every solution $\phi(t)$ of (3.3.1), with $\phi(0) \in \mathcal{D}$, lies in the set \mathcal{A}*

$$\mathcal{A} := \{E = E^*, L = L^*, P = P^*, N_v = N_v^*, N_h = N_h^0\} \cap \mathcal{D},$$

which is an invariant set of system (3.3.1);

(ii) *if $\phi(0) \in \mathcal{A} \setminus \mathcal{D}_0$, then $\phi(t) \rightarrow \mathcal{E}^*$ as $t \rightarrow \infty$.*

Proof. Since $\delta_h = 0$, we have $N_h' = \Lambda_h - \mu_h N_h$, and thus $N_h(t) = N_h^0 + N_h(0)e^{-\mu_h t}$, for t in $(-\infty, \infty)$. The assertion of (i) then follows from Theorem 3.3.1 (ii).

We assume that $\phi(0) \in \mathcal{A} \setminus \mathcal{D}_0$, and need to show $\phi_1(t) \rightarrow \mathcal{E}_1^*$ as $t \rightarrow \infty$. Since \mathcal{A} is invariant, it follows that $(E, L, P, N_v, N_h) \equiv (E^*, L^*, P^*, N_v^*, N_h^0)$ along $\phi(t)$, that is, $E = E^*, L = L^*, P = P^*, N_v = N_v^*, N_h = N_h^0$. Then, along $(x(t), y(t))$, (3.7.5) is reduced to

$$\begin{aligned} \dot{W}(x, y) = & \mu_h \left(2 - x_1 - \frac{1}{x_1}\right) + k\mu_v \left(2 - y_1 - \frac{1}{y_1}\right) \\ & + \frac{r\beta_v I_v^*}{N_h^0} \left(6 - \frac{1}{x_1} - \frac{y_3 x_1}{x_2} - \frac{x_2}{x_3} - \frac{1}{y_1} - \frac{x_3 y_1}{y_2} - \frac{y_2}{y_3}\right) \leq 0, \end{aligned} \quad (3.7.9)$$

which implies that $W(x(t), y(t)) \leq W(x(1), y(1))$, for $t \geq 1$, and thus from the properties of W , we have, for some $m_2 > m_1 > 0$, $m_1 \leq x_i(t) \leq m_2$ and $m_1 \leq y_i(t) \leq m_2$ for $i = 1, 2, 3$ and $t \geq 1$. On the other hand, from the equation of x_4 in system (3.7.1) we have

$$x_4(t) = x_4(1)e^{-\mu_h(t-1)} + \mu_h \int_1^t x_3(\tau)e^{-\mu_h(t-\tau)} d\tau, \quad t \geq 1,$$

which implies $m_1[1 - e^{-\mu_h}] \leq x_4(t) \leq x_4(1) + m_2$, for $t \geq 2$. Thus, we conclude that for $t \geq 2$, $(x(t), y(t))$ lies in a compact set of $\text{int}(\mathbb{R}_+^7)$. Applying Theorem 3.6.1 (LaSalle's Invariance Principle), then yields

$$\omega(x(t), y(t)) \subseteq \mathcal{B}_0 = \left\{ (x, y) \in \text{int}(\mathbb{R}_+^7) : \dot{W}(x, y) = 0 \right\}.$$

Now applying the arithmetic-geometric mean inequality to (3.7.9), with $\dot{W} = 0$, yields

$$x_1 = 1, \quad y_1 = 1, \quad \frac{1}{x_1} = \frac{y_3 x_1}{x_2} = \frac{x_2}{x_3} = \frac{1}{y_1} = \frac{x_3 y_1}{y_2} = \frac{y_2}{y_3},$$

and this gives that

$$\mathcal{B}_0 = \{(x, y) \in \text{int}(\mathbb{R}_+^7) : x_1 = y_1 = 1, x_2 = x_3 = y_2 = y_3\}.$$

Then using these equalities and the first and fifth equations in (3.7.1), we conclude that the equilibrium point (x^*, y^*) is the only full orbit of (3.7.1), lying in \mathcal{B}_0 . Thus, it follows that $\omega(x(t), y(t)) = \{(x^*, y^*)\}$, and consequently, $\omega(\phi_1(t)) = \{\mathcal{E}_1^*\}$. \square

Lemma 3.7.3. *If $\phi(0) \in \mathcal{D} \setminus \mathcal{D}_0$ and $\phi(0) \in \text{int}(\mathbb{R}_+^{10})$, then $\omega(\phi(t))$ lies in a compact set of $\text{int}(\mathbb{R}_+^{10})$.*

Proof. Without loss of generality, we assume $\phi(0) \in \text{int}(\mathbb{R}_+^{10})$. It suffices to show that, for $t \in [0, \infty)$, each component of $\phi_1(t)$ is bounded below by a positive number. We first prove this is true for the components $S_j, E_j, I_j, j = h, v$, by showing that, along its corresponding solution $(x(t), y(t))$ of (3.7.1), $W(x(t), y(t))$ is bounded, and then prove it is true for $R_h(t)$.

Step 1. We show that $W(x(t), y(t))$ is bounded for $[0, \infty)$. Writing the expressions

$$\frac{(x_2 - x_1)y_3}{x_2} \quad \text{and} \quad \frac{(y_2 - y_1)x_3}{y_2}$$

in the integrand of (3.7.8) as

$$\frac{(x_2 - x_1)y_3}{x_2} = y_3 - \frac{x_1}{x_2}y_3, \quad \frac{(y_2 - y_1)x_3}{y_2} = x_3 - \frac{y_1}{y_2}x_3. \quad (3.7.10)$$

From the equation for x_2 in (3.7.1), we have

$$\frac{x_2'}{\sigma_1} = N_h^0 \frac{y_3}{N_h} x_1 - x_2,$$

simplifying it, we can obtain

$$y_3 \frac{x_1}{x_2} = \frac{N_h}{N_h^0} \left(\frac{1}{\sigma_1} \frac{x_2'}{x_2} + 1 \right). \quad (3.7.11)$$

Similarly, from the equation for y_2 in (3.7.1), we have

$$x_3 \frac{y_1}{y_2} = \frac{N_h}{N_h^0} \left(\frac{1}{\sigma_v} \frac{y_2'}{y_2} + 1 \right). \quad (3.7.12)$$

Inserting (3.7.10), (3.7.11) and (3.7.12) into (3.7.8), we have, for $t \geq 0$,

$$\begin{aligned} W(x(t), y(t)) &\leq W(x(0), y(0)) \\ &+ \frac{r\beta_v I_v^*}{N_h^0} \int_0^t \frac{N_h^0 - N_h}{N_h} \left(y_3 - \frac{x_1 y_3}{x_2} + x_3 - \frac{y_1 x_3}{y_2} \right) ds \\ &+ \frac{k_P k}{S_v^*} \int_0^t (P - P^*) \left(1 - \frac{1}{y_1} \right) ds \end{aligned}$$

$$\begin{aligned}
&= W(x(0), y(0)) + \frac{r\beta_v I_v^*}{N_h^0} \int_0^t \frac{N_h^0 - N_h}{N_h} (x_3 + y_3) ds \\
&\quad - \frac{r\beta_v I_v^*}{N_h^0} \int_0^t \frac{N_h^0 - N_h}{N_h} \left(\frac{x_1 y_3}{x_2} + \frac{y_1 x_3}{y_2} \right) ds \\
&\quad + \frac{k_P k}{S_v^*} \int_0^t (P - P^*) \left(1 - \frac{1}{y_1} \right) ds \\
&\leq W(x(0), y(0)) + \frac{r\beta_v I_v^*}{N_h^0} \int_0^t \frac{N_h^0 - N_h}{N_h} (x_3 + y_3) ds \\
&\quad + \frac{r\beta_v I_v^*}{N_h^0} \int_0^t \frac{N_h^0 - N_h}{N_h} \frac{N_h}{N_h^0} \left(\frac{1}{\sigma_1} \frac{x_2'}{x_2} + \frac{1}{\sigma_v} \frac{y_2'}{y_2} \right) ds \\
&\quad + \frac{k_P k}{S_v^*} \int_0^t (P - P^*) \left(1 - \frac{1}{y_1} \right) ds \\
&= W(x(0), y(0)) + \frac{r\beta_v I_v^*}{N_h^0} \int_0^t \frac{N_h^0 - N_h}{N_h} (y_3 + x_3) ds \\
&\quad + \frac{r\beta_v I_v^*}{(N_h^0)^2} \int_0^t (N_h^0 - N_h) \left(\frac{1}{\sigma_1} \frac{x_2'}{x_2} + 1 + \frac{1}{\sigma_v} \frac{y_2'}{y_2} + 1 \right) ds \\
&\quad + \frac{k_P k}{S_v^*} \int_0^t (P - P^*) \left(1 - \frac{1}{y_1} \right) ds.
\end{aligned} \tag{3.7.13}$$

Since $N_h(t) - N_h^0 \rightarrow 0$ exponentially as $t \rightarrow \infty$, it follows that the first integral of (3.7.13)

is bounded. Integration by parts for the second integral then yields

$$\begin{aligned}
&\int_0^t (N_h^0 - N_h(s)) \left(\frac{1}{\sigma_1} \frac{x_2'(s)}{x_2(s)} + 1 + \frac{1}{\sigma_v} \frac{y_2'(s)}{y_2(s)} + 1 \right) ds \\
&= \int_0^t (N_h^0 - N_h(s)) d \left(\frac{1}{\sigma_1} \ln(x_2(s)) + s + \frac{1}{\sigma_v} \ln(y_2(s)) + s \right) \\
&= (N_h^0 - N_h(t)) \left(\frac{1}{\sigma_1} \ln(x_2(t)) + t + \frac{1}{\sigma_v} \ln(y_2(t)) + t \right) \\
&\quad - (N_h^0 - N_h(0)) \left(\frac{1}{\sigma_1} \ln(x_2(0)) + \frac{1}{\sigma_v} \ln(y_2(0)) \right) \\
&\quad + \int_0^t N_h'(s) \left(\frac{1}{\sigma_1} \ln(x_2(s)) + \frac{1}{\sigma_v} \ln(y_2(s)) + 2s \right) ds.
\end{aligned} \tag{3.7.14}$$

On the other hand, it follows from the equation for x_2 in (3.7.1) that $x_2' \geq -\sigma_1 x_2$, and integrating it gives $\frac{1}{\sigma_1} \ln x_2(t) + t \geq \frac{1}{\sigma_1} \ln x_2(0)$, for $t \geq 0$. Since $\ln x_2(t) \leq \ln \|x_2\|_\infty$, where $\|x_2\|_\infty := \sup_{0 \leq t < \infty} |x_2(t)|$, it follows that $\frac{1}{\sigma_1} \ln x_2(0) \leq \frac{1}{\sigma_1} \ln x_2(t) + t \leq t + \ln \|x_2\|_\infty$, for all $t \geq 0$. Employing a similar argument to y_2 then yields $\frac{1}{\sigma_v} \ln y_2(0) \leq \frac{1}{\sigma_v} \ln y_2(t) + t \leq t + \ln \|y_2\|_\infty$, for all $t \geq 0$. We see that $t + \ln \|x_2\|_\infty$ and $t + \ln \|y_2\|_\infty$ are algebraically increasing, while $N_h(t)$ is exponential decay, hence $(N_h^0 - N_h(t)) \left(\frac{1}{\sigma_1} \ln(x_2(t)) + t + \frac{1}{\sigma_v} \ln(y_2(t)) + t \right)$ is bounded. Clearly, these estimates together with the exponential decay of $N_h'(t)$ and (3.7.14) imply that the integrals on the right-hand side of (3.7.13) are bounded, for $t \geq 0$.

We next show that the third integral in (3.7.13) is bounded on $[0, \infty)$. Since

$$\frac{x_3}{N_h} = \frac{x_3}{x_1 S_h^* + x_2 E_h^* + x_3 I_h^* + x_4 R_h^*} \leq \frac{1}{I_h^*},$$

it follows from the equation for y_1 in (3.7.1) that

$$y_1' \geq \frac{1}{S_v^*} k_P (P - P^*) + \mu_v + \frac{r \beta_h I_h^*}{N_h^0} - (\mu_v + r \beta_h) y_1.$$

Since $P(t) - P^* \rightarrow 0$ as $t \rightarrow \infty$, it follows that there is a positive t_0 , such that for $t > t_0$,

$$y_1' \geq \frac{1}{S_v^*} k_P (P - P^*) + \mu_v + \frac{r \beta_h I_h^*}{N_h^0} - (\mu_v + r \beta_h) y_1 \geq \mu_v - (\mu_v + r \beta_h) y_1,$$

and then

$$y_1(t) \geq y_1(t_0)e^{-(\mu_v+r\beta_h)(t-t_0)} + \frac{\mu_v}{\mu_v+r\beta_h} (1 - e^{-(\mu_v+r\beta_h)(t-t_0)}), \quad \forall t \geq t_0.$$

Hence, in addition to $y_1 > 0$ on $[0, t_0]$, we conclude that there exists a positive constant m , such that $y_1(t) \geq m$ for $t \geq 0$, and thus $|1 - \frac{1}{y_1}| \leq 1 + \frac{1}{m}$ for $t \geq 0$. This estimate together with the exponential decay of $P(t) - P^*$ as $t \rightarrow \infty$, yields that the third integral in (3.7.13) is bounded for $t \geq 0$. It then follows from (3.7.13) that $W(x(t), y(t))$ is bounded for $t \geq 0$.

Step 2. We show that R_h is bounded below by a positive number on $[0, \infty)$. It follows from Step 1 that $I_h(t) \geq \delta$, for $t \in [0, \infty)$ and some $\delta > 0$. Then using the fourth equation in (3.3.5), we have, for $t \geq 1$,

$$R_h(t) \geq \int_0^t e^{-\mu_h(t-\tau)} I_h(\tau) d\tau \geq (1 - e^{-\mu_h})\delta/\mu_h.$$

This together with $R_h(t) > 0$, for $t \in [0, 1]$, yields the desired property for R_h . \square

Lemma 3.7.4. *There exist positive constants ρ , K_0 , and δ_0 such that each solution (E, L, P, N_v) of (2.2.1), with $|E(0) - E^*| + |L(0) - L^*| + |P(0) - P^*| + |N_v(0) - N_v^*| < \delta_0$, satisfies, for $t \geq 0$,*

$$\begin{aligned}
& |E(t) - E^*| + |L(t) - L^*| + |P(t) - P^*| + |N_v(t) - N_v^*| \\
& \leq K_0 \left[|E(0) - E^*| + |L(0) - L^*| + |P(0) - P^*| + |N_v(0) - N_v^*| \right] e^{-\rho t}.
\end{aligned} \tag{3.7.15}$$

Proof. As in the Chapter 2, we let $\psi(t) = (E(t), L(t), P(t), N_v(t))$ denote the solution of (2.2.1) and f be the right-hand side of the vector field of (2.2.1)). Let $\mathcal{V}^* := (E^*, L^*, P^*, N_v^*)$ and write (2.2.1) as

$$\psi' = A(\psi - \mathcal{V}^*) + \mathcal{N}(\psi), \quad A := Df(\mathcal{V}^*),$$

where $\mathcal{N} = f(\psi) - A(\psi - \mathcal{V}^*)$ satisfies that, for every $\delta > 0$, there is $\varepsilon(\delta)$ with $\varepsilon(\delta) \rightarrow 0$, as $\delta \rightarrow 0$, such that $\|\mathcal{N}(\psi)\| \leq \varepsilon(\delta)\|\psi - \mathcal{V}^*\|$ if $\|\psi - \mathcal{V}^*\| < \delta$. Using the variation of parameters formula, we get, for $t > 0$,

$$\psi(t) - \mathcal{V}^* = e^{At}(\psi(0) - \mathcal{V}^*) + \int_0^t e^{A(t-\tau)} \mathcal{N}(\psi(\tau)) d\tau. \tag{3.7.16}$$

From Theorem 2.5.1 we know that all eigenvalues of A have negative real part. Let $0 < 2\rho < \min\{|Re \lambda|\}$, where λ are the eigenvalues of A . Then there exist a constant $K_0 > 0$, such that $\|e^{At}\| \leq K_0 e^{-2\rho t}$, for $t \geq 0$. We now fix $\delta > 0$ such that $K_0 \varepsilon(\delta) < \rho$ and let $\delta_0 := \delta/K_0$. Assume that $\|\psi(0) - \mathcal{V}^*\| < \delta_0$. It follows from (3.7.16) that, for

$t > 0$, as long as $\|\psi - \mathcal{V}^*\| < \delta$ on $[0, t]$,

$$\|\psi(t) - \mathcal{V}^*\| \leq K_0 \|\psi(0) - \mathcal{V}^*\| e^{-2\rho t} + K_0 \varepsilon(\delta) \int_0^t e^{-2\rho(t-\tau)} \|\psi(\tau) - \mathcal{V}^*\| d\tau,$$

and applying the Gronwall's inequality leads to

$$\begin{aligned} \|\psi(t) - \mathcal{V}^*\| &\leq K_0 \|\psi(0) - \mathcal{V}^*\| e^{-(2\rho - K_0 \varepsilon(\delta))t} \\ &\leq K_0 \|\psi(0) - \mathcal{V}^*\| e^{-\rho t} < K_0 \delta_0 = \delta, \end{aligned} \tag{3.7.17}$$

for all $t > 0$, which implies (3.7.15). □

Lemma 3.7.5. *Let \mathbb{R}^n be an n -dimensional vector space. Given vectors $u = (u_1, u_2, \dots, u_n)$*

and $v = (v_1, v_2, \dots, v_n)$, we define the inner product $\langle u, v \rangle = \sum_{i=1}^n u_i v_i$ and define norms

$\|v\|_1 := \sum_{i=1}^n |v_i|$ and $\|v\|_2 := \sqrt{\sum_{i=1}^n v_i^2}$, then $\|v\|_1 \leq \sqrt{n} \cdot \|v\|_2$.

Proof. Let vector $v_0 = (1, 1, \dots, 1) \in \mathbb{R}^n$. Then, $\|v_0\|_2 = \sqrt{n}$ and

$$\begin{aligned} \|v\|_1 &= \sum_{i=1}^n |v_i| = |v_1| + |v_2| + \dots + |v_n| \\ &= |v_1| \cdot 1 + |v_2| \cdot 1 + \dots + |v_n| \cdot 1 = \langle v, v_0 \rangle \leq |\langle v, v_0 \rangle| \\ &\leq \|v_0\|_2 \|v\|_2 = \sqrt{n} \cdot \|v\|_2 \end{aligned}$$

by the Cauchy-Schwartz inequality. □

Lemma 3.7.6. *For $v = (v_1, \dots, v_n) \in \mathbb{R}^n$, we define norm $\|v\| := \sum_{i=1}^n |v_i|$.*

(i) Let \mathcal{O} be the neighborhood of \mathcal{E}^* , defined by

$$\mathcal{O} = \{u = (u_1, u_2) \in \mathbb{R}^7 \times \mathbb{R}^3 : \|u_1 - \mathcal{E}_1^*\| < \delta_1, \|u_2 - \mathcal{E}_2^*\| < \delta_1\},$$

where

$$\delta_1 := \frac{1}{2} \min\{\delta_0, S_h^*, E_h^*, S_v^*, E_v^*, N_h^0\},$$

with δ_0 given in Lemma 3.7.4. Then there exists positive constant $M > 0$ such that, for every solution $\phi(t)$ of (3.3.1) with $\phi(0) \in \mathcal{O}$ and any $T > 0$, as long as $\phi(t) \in \mathcal{O}$, for $t \in [0, T]$, we have, for $0 \leq t \leq T$,

$$\|\phi_1(t) - \mathcal{E}_1^*\| \leq M \sqrt{\|\phi_1(0) - \mathcal{E}_1^*\| + \|\phi_2(0) - \mathcal{E}_2^*\|}. \quad (3.7.18)$$

(ii) The endemic equilibrium \mathcal{E}^* is locally stable.

Proof. To show (i), we let $\phi(0) \in \mathcal{O}$ and $T > 0$ such that $\phi(t) \in \mathcal{O}$, for $0 \leq t \leq T$. Let $(x(t), y(t))$ be the solution of (3.7.1) associated with $\phi(t)$. We first use (3.7.8) to estimate $W(t)$. Since $\phi(t) \in \mathcal{O}$, for $0 \leq t \leq T$, we have, by the definition of δ_1 ,

$$\begin{aligned} |N_h(t) - N_h^0| &= |N_h(0) - N_h^0| e^{-\mu_h t} \leq \|\phi_1(0) - \mathcal{E}_1^*\| e^{-\mu_h t} \leq \delta_1, \\ |x_1(t) - 1| &= \frac{1}{S_h^*} |S_h(t) - S_h^*| \leq \frac{1}{S_h^*} \delta_1 \leq \frac{1}{2}, \\ |x_2(t) - 1| &= \frac{1}{E_h^*} |E_h(t) - E_h^*| \leq \frac{1}{E_h^*} \delta_1 \leq \frac{1}{2}, \end{aligned} \quad (3.7.19)$$

$$\begin{aligned}
|x_3(t) - 1| &= \frac{1}{I_h^*} |I_h(t) - I_h^*| \leq \frac{1}{I_h^*} \delta_1 \leq \frac{1}{2}, \\
|y_1(t) - 1| &= \frac{1}{S_v^*} |S_v(t) - S_v^*| \leq \frac{1}{S_v^*} \delta_1 \leq \frac{1}{2}, \\
|y_2(t) - 1| &= \frac{1}{E_v^*} |E_v(t) - E_v^*| \leq \frac{1}{E_v^*} \delta_1 \leq \frac{1}{2}, \\
|y_3(t) - 1| &= \frac{1}{I_v^*} |I_v(t) - I_v^*| \leq \frac{1}{I_v^*} \delta_1 \leq \frac{1}{2}.
\end{aligned}$$

Thus,

$$\begin{aligned}
N_h(t) &\geq \frac{1}{2} N_h^0, \quad \frac{1}{2} \leq x_i(t) \leq \frac{3}{2}, \quad \frac{1}{2} \leq y_i(t) \leq \frac{3}{2} \quad i = 1, 2, 3, \\
|x_2(t) - x_1(t)| &\leq 1, \quad |y_2(t) - y_1(t)| \leq 1, \quad \left| 1 - \frac{1}{y_1(t)} \right| \leq 1.
\end{aligned} \tag{3.7.20}$$

It follows from (3.7.19), with $t = 0$, and the second inequality in (3.7.3) that, for $0 \leq t \leq T$,

$$\begin{aligned}
W(x(0), y(0)) &\leq M_2 \sum_{i=1}^3 [(x_i(0) - 1)^2 + (y_i(0) - 1)^2] \\
&= M_2 \left[\left(\frac{S_h(0)}{S_h^*} - 1 \right)^2 + \left(\frac{E_h(0)}{E_h^*} - 1 \right)^2 + \left(\frac{I_h(0)}{I_h^*} - 1 \right)^2 \right. \\
&\quad \left. + \left(\frac{S_v(0)}{S_v^*} - 1 \right)^2 + \left(\frac{E_v(0)}{E_v^*} - 1 \right)^2 + \left(\frac{I_v(0)}{I_v^*} - 1 \right)^2 \right] \\
&= M_2 \left[\left(\frac{S_h(0) - S_h^*}{S_h^*} \right)^2 + \left(\frac{E_h(0) - E_h^*}{E_h^*} \right)^2 + \left(\frac{I_h(0) - I_h^*}{I_h^*} \right)^2 \right. \\
&\quad \left. + \left(\frac{S_v(0) - S_v^*}{S_v^*} \right)^2 + \left(\frac{E_v(0) - E_v^*}{E_v^*} \right)^2 + \left(\frac{I_v(0) - I_v^*}{I_v^*} \right)^2 \right] \\
&\leq \frac{1}{2} M_2 \left(\frac{|S_h(0) - S_h^*|}{S_h^*} + \frac{|E_h(0) - E_h^*|}{E_h^*} + \frac{|I_h(0) - I_h^*|}{I_h^*} \right.
\end{aligned} \tag{3.7.21}$$

$$\begin{aligned}
& + \frac{|S_v(0) - S_v^*|}{S_v^*} + \frac{|E_v(0) - E_v^*|}{E_v^*} + \frac{|I_v(0) - I_v^*|}{I_v^*} \Big) \\
& \leq M_3 (|S_h(0) - S_h^*| + |E_h(0) - E_h^*| + |I_h(0) - I_h^*| \\
& \quad + |S_v(0) - S_v^*| + |E_v(0) - E_v^*| + |I_v(0) - I_v^*|) \\
& \leq M_3 (|S_h(0) - S_h^*| + |E_h(0) - E_h^*| + |I_h(0) - I_h^*| + |R_h(0) - R_h^*| \\
& \quad + |S_v(0) - S_v^*| + |E_v(0) - E_v^*| + |I_v(0) - I_v^*|) \\
& = M_3 \|\phi_1(0) - \mathcal{E}_1^*\|,
\end{aligned}$$

where

$$M_3 := \frac{1}{2} M_2 \max \left\{ \frac{1}{S_h^*}, \frac{1}{E_h^*}, \frac{1}{I_h^*}, \frac{1}{S_v^*}, \frac{1}{E_v^*}, \frac{1}{I_v^*} \right\}.$$

with M_2 given in (3.7.4). Using (3.7.19) and (3.7.20), we have

$$\begin{aligned}
& \frac{r\beta_v I_v^*}{N_h^0} \int_0^t \frac{N_h^0 - N_h}{N_h} \left(\frac{(x_2 - x_1)y_3}{x_2} + \frac{(y_2 - y_1)x_3}{y_2} \right) ds \\
& \leq \frac{r\beta_v I_v^*}{N_h^0} \int_0^t \frac{|N_h^0 - N_h|}{N_h} \left(\frac{|x_2 - x_1|y_3}{x_2} + \frac{|y_2 - y_1|x_3}{y_2} \right) ds \\
& \leq \frac{12r\beta_v I_v^*}{\mu_h (N_h^0)^2} \int_0^t \|\phi_1(0) - \mathcal{E}_1^*\| e^{-\mu_h t} ds \\
& \leq \frac{12r\beta_v I_v^*}{\mu_h (N_h^0)^2} \|\phi_1(0) - \mathcal{E}_1^*\|.
\end{aligned} \tag{3.7.22}$$

From Lemma 3.7.4, we have $|P(t) - P^*| \leq K_0 \|\phi_2(0) - \mathcal{E}_2^*\| e^{-\rho t}$ for $t \geq 0$, which together with (3.7.20) yields

$$\frac{k_P k}{S_v^*} \int_0^t (P - P^*) \left(1 - \frac{1}{y_1} \right) ds$$

$$\begin{aligned}
&\leq \frac{k_P k}{S_v^*} \int_0^t |P - P^*| \left| 1 - \frac{1}{y_1} \right| ds \\
&\leq \frac{k_P k}{S_v^*} \int_0^t K_0 \|\phi_2(0) - \mathcal{E}_2^*\| e^{-\rho t} ds \\
&\leq \frac{k_P k K_0}{S_v^* \rho} \|\phi_2(0) - \mathcal{E}_2^*\|.
\end{aligned} \tag{3.7.23}$$

Inserting (3.7.21), (3.7.22), and (3.7) into (3.7.8) gives

$$W(x(t), y(t)) \leq M_4 \left(\|\phi_1(0) - \mathcal{E}_1^*\| + \|\phi_2(0) - \mathcal{E}_2^*\| \right), \tag{3.7.24}$$

where

$$M_4 := M_3 + \frac{12r\beta_v I_v^*}{\mu_h (N_h^0)^2} + \frac{k_P k K_0}{S_v^* \rho}.$$

Then it follows from the first inequality in (3.7.3) that

$$\sum_{i=1}^3 [(x_i(t) - 1)^2 + (y_i(t) - 1)^2] \leq \frac{M_4}{M_1} \left(\|\phi_1(0) - \mathcal{E}_1^*\| + \|\phi_2(0) - \mathcal{E}_2^*\| \right), \tag{3.7.25}$$

and consequently,

$$\begin{aligned}
&(S_h(t) - S_h^*)^2 + (E_h(t) - E_h^*)^2 + (I_h(t) - I_h^*)^2 \\
&\quad + (S_v(t) - S_v^*)^2 + (E_v(t) - E_v^*)^2 + (I_v(t) - I_v^*)^2 \\
&\leq \frac{M_4}{M_2 M_5} \left(\|\phi_1(0) - \mathcal{E}_1^*\| + \|\phi_2(0) - \mathcal{E}_2^*\| \right),
\end{aligned}$$

where

$$M_5 := \min \left\{ \frac{1}{(S_h^*)^2}, \frac{1}{(E_h^*)^2}, \frac{1}{(I_h^*)^2}, \frac{1}{(S_v^*)^2}, \frac{1}{(E_v^*)^2}, \frac{1}{(I_v^*)^2} \right\}.$$

Thus, according to lemma 3.7.5, for $t \in [0, T]$,

$$\begin{aligned} & |S_h(t) - S_h^*| + |E_h(t) - E_h^*| + |I_h(t) - I_h^*| \\ & + |S_v(t) - S_v^*| + |E_v(t) - E_v^*| + |I_v(t) - I_v^*| \\ & \leq \sqrt{\frac{6M_4}{M_2M_5}} \left(\|\phi_1(0) - \mathcal{E}_1^*\| + \|\phi_2(0) - \mathcal{E}_2^*\| \right). \end{aligned} \quad (3.7.26)$$

We next estimate $R_h(t) - R_h^*$. Writing the equation for R_h in (3.3.1) as $R_h' = \eta_h(I_h - I_h^*) - \mu_h(R_h - R_h^*)$, and applying the variation of parameters formula, we have, for $t \in [0, T]$,

$$R_h(t) - R_h^* = [R_h(0) - R_h^*]e^{-\mu_h t} + \eta_h \int_0^t (I_h(s) - I_h^*)e^{-\mu_h(t-s)} ds,$$

and thus

$$\begin{aligned} |R_h(t) - R_h^*| & \leq |R_h(0) - R_h^*| + \frac{\eta_h}{\mu_h} \max_{0 \leq s \leq t} |I_h(s) - I_h^*| \\ & \leq \sqrt{\|\phi_1(0) - \mathcal{E}_1^*\|} + \frac{\eta_h}{\mu_h} \sqrt{\frac{6M_4}{M_2M_5}} \left(\|\phi_1(0) - \mathcal{E}_1^*\| + \|\phi_2(0) - \mathcal{E}_2^*\| \right), \end{aligned}$$

where we use $\|\phi_1(0) - \mathcal{E}_1^*\| < 1$. This combining with (3.7.26) yields, for $t \in [0, T]$,

$$\|\phi_1(t) - \mathcal{E}_1^*\| \leq M_6 \sqrt{\|\phi_1(0) - \mathcal{E}_1^*\| + \|\phi_2(0) - \mathcal{E}_2^*\|},$$

where

$$M_6 := \sqrt{\frac{6M_4}{M_2M_5}} + 1 + \frac{\eta_h}{\mu_h} \sqrt{\frac{6M_4}{M_2M_5}}.$$

We note that M_6 does not depend on $\phi(0)$ and $T > 0$. The proof of (i) is then complete by letting $M := M_6$ in (3.7.18).

We now show that \mathcal{E}_1^* is locally stable. Give an arbitrarily small $\varepsilon \in (0, \delta_1)$ and let $\delta := \min\{\delta_1, \frac{\varepsilon^2}{4M^2}, \frac{\varepsilon}{2K_0}\}$. If $\phi(0) \in \mathbb{R}_+^{10}$ is in the δ -neighborhood of \mathcal{E}^* , that is, $\|\phi(0) - \mathcal{E}^*\| = \|\phi_1(0) - \mathcal{E}_1^*\| + \|\phi_2(0) - \mathcal{E}_2^*\| < \delta$, then it follows from (3.7.15) and (3.7.18) that

$$\|\phi(t) - \mathcal{E}^*\| = \|\phi_1(t) - \mathcal{E}_1^*\| + \|\phi_2(t) - \mathcal{E}_2^*\| \leq M \sqrt{\frac{\varepsilon^2}{4M^2}} + K_0 \frac{\varepsilon}{2K_0} = \varepsilon,$$

for all $t \geq 0$. This shows that \mathcal{E}^* is locally stable. \square

Proof of Theorem 3.7.1 It follows from Lemma 3.7.6 that \mathcal{E}^* is locally stable. Thus it remains to show that if $\phi(0) \in \mathcal{D} \setminus \mathcal{D}_0$, then $\omega(\phi(t)) = \{\mathcal{E}^*\}$. Let $\phi(0) \in \mathcal{D} \setminus \mathcal{D}_0$. Lemmas 3.7.2 (i) and 3.7.3 imply that $\omega(\phi(t))$ lies in a compact set of $\mathcal{A} \cap \text{int}(\mathbb{R}_+^{10})$, and in particular, $\omega(\phi(t)) \subseteq \mathcal{A} \setminus \mathcal{D}_0$. Let $\tilde{\phi}(t)$ be an arbitrary full orbit lying in $\omega(\phi(t))$. Then it follows from Lemma 3.7.2 (ii) that $\tilde{\phi}(t) \rightarrow \mathcal{E}^*$, as $t \rightarrow \infty$, which implies that

there exists a sequence $\{t_k\}$ such that $t_k \rightarrow \infty$ and $\phi(t_k) \rightarrow \mathcal{E}^*$, as $k \rightarrow \infty$. Together with the local stability of \mathcal{E}^* it shows that $\tilde{\phi}(t) \equiv \mathcal{E}^*$, and hence $\omega(\phi(t)) = \{\mathcal{E}^*\}$.

CHAPTER 4

DYNAMICS OF DISCRETE-TIME STAGE-STRUCTURED MOSQUITO POPULATION MODELS

4.1 Introduction

The time scales of the lifespan and development of human beings and mosquitoes are significantly different. Hence, using the time-steps for mosquitoes as a basis seems more natural, and thus, discrete-time models seem to be more appropriate to describe the dynamics. In this chapter, we formulate a discrete-time model for the mosquito population with stage structure. As for the continuous-time models, we derive a formula for the inherent net reproductive number r_0 , and investigate the model dynamics, including existence and stability of positive equilibria.

4.2 The model formulation

Let $E(t), L(t), P(t)$ and $M(t)$ denote the numbers of eggs, larvae, pupae, and adults of mosquitoes, respectively, at time t . We then assume that the oviposition rate, denoted by b , and the survival probability of the eggs, denoted by s_0 , are con-

stants. As in the study of continuous-time mosquito population models, we assume the density-dependence for the first three stages is on the size of the larvae and the density-dependence for adults is on the adult size. Hence we have that the surviving-adjusted hatching rate, denoted by $s_e = s_e(L)$, and the surviving-adjusted pupation rate, denoted by $s_l = s_l(L)$, are functions of larvae L , and the adults survival probability, denoted by $s_m = s_m(M)$, is a function of the adults M . The equations for four-stage-structured mosquito population model are given by the following system.

$$\begin{aligned}
E(t+1) &= bs_0M(t), \\
L(t+1) &= s_e(L(t))E(t), \\
P(t+1) &= s_l(L(t))L(t), \\
M(t+1) &= s_pP(t) + s_m(M(t))M(t).
\end{aligned} \tag{4.2.1}$$

Comparing the different lifespan for the four stages, we assume function $s_m(M)$ satisfies the following conditions (H1) [85].

$$\begin{aligned}
s_i(z) &\in C^1[0, \infty), \quad s_i(0) := \alpha_i, \quad 0 < \alpha_i \leq 1, \quad s'_i(z) \leq 0, \quad (s_i(z)z)' > 0, \\
\lim_{z \rightarrow \infty} s_i(z) &= 0, \quad \lim_{z \rightarrow \infty} s_i(z)z := k_i, \quad 0 < k_i < \infty.
\end{aligned} \tag{H1}$$

The density-dependent functions $s_e(L)$ and $s_l(L)$ are assumed to satisfy either conditions (H1), or conditions (H2) given below.

$$\begin{aligned}
& s_i(z) \in C^1[0, \infty), \quad s_i(0) := \alpha_i, \quad 0 < \alpha_i \leq 1, \quad s'_i(z) \leq 0, \quad \lim_{z \rightarrow \infty} s_i(z) = 0, \\
& \exists k_i > 0, \quad (s_i(z)z)' \begin{cases} > 0, & z < k_i, \\ < 0, & z > k_i, \end{cases} \quad \lim_{z \rightarrow \infty} s_i(z)z = 0.
\end{aligned} \tag{H2}$$

Conditions (H1) assume that the surviving-adjusted hatching and pupation rates and the adult survival rate are all decreasing, but the total numbers of eggs, pupae, and adults are increasing and saturating to fixed numbers, as the number of individuals increases. For example, these rates may have the Beverton-Holt form such that $s_i(z) = (\alpha_i k_i)/(k_i + \alpha_i z)$, [88]. On the other hand, conditions (H2) characterize the fact that while those rates are decreasing, as the number of individuals increases, the total numbers increase to certain levels, k_i , but then decrease as the number of individuals exceeds the threshold. The Ricker-type function $s_i(z) = \alpha_i e^{-z/k_i}$ has such properties.

Define $x(t) := (E(t), L(t), P(t), M(t))^T$. System (4.2.1) can be written as the following matrix form:

$$x(t+1) = A(x(t))x(t), \tag{4.2.2}$$

where the projection matrix $A(x)$ is given by

$$A(x) = \begin{pmatrix} 0 & 0 & 0 & bs_0 \\ s_e(L) & 0 & 0 & 0 \\ 0 & s_l(L) & 0 & 0 \\ 0 & 0 & s_p & s_m(M) \end{pmatrix}.$$

Let $A = (a_{ij}) \in \mathbb{R}^{n \times m}$ and $B = (b_{ij}) \in \mathbb{R}^{n \times m}$. We say that $A \leq B$ if and only if $a_{ij} \leq b_{ij}$ for all $i = 1, \dots, n$, and $j = 1, \dots, m$, (refer to Definition 2.3.3 (A)). Hence, from assumption (H1) or (H2), we have $A(x) \geq A(y)$, for any $x \leq y$.

Furthermore, it is easy to see that system (4.2.1) or (4.2.2) is point dissipative [93, 96]. In fact, under assumption (H1) or (H2), it follows that

$$\begin{aligned} M(t+1) &= s_p P(t) + s_m(M(t))M(t) = s_p s_e(L(t))L(t) + s_m(M(t))M(t) \\ &\leq s_p \bar{k}_e + k_m := \omega_4, \end{aligned}$$

for all $t \geq 0$. Then, it follows from system (4.2.1) that

$$E(t+1) \leq bs_0(s_p \bar{k}_e + k_m) := \omega_1,$$

$$L(t+1) \leq s_e(0)bs_0(s_p \bar{k}_e + k_m) := \omega_2,$$

$$P(t+1) \leq \bar{k}_l,$$

for all $t \geq 0$, where $\bar{k}_i = k_i$ if (H1) is assumed, or $\bar{k}_i = s_i(k_i)k_i$, if (H2) is assumed.

We summarize the basic properties of the system as follows.

Theorem 4.2.1. *System (4.2.1) or (4.2.2) is point dissipative. Define set Ω by*

$$\begin{aligned} \Omega := \{x(t) = (E, L, P, M)^T \in \mathbb{R}_+^4 : 0 \leq E \leq \omega_1, 0 \leq L \leq \omega_2, \\ 0 \leq P \leq \bar{k}_l, 0 \leq M \leq \omega_4\}. \end{aligned} \quad (4.2.3)$$

Then Ω is positively invariant under the flows of system (4.2.2) and is attracting to all solutions of (4.2.2) if conditions (H1) or (H2) hold.

4.3 The inherent net reproductive number and dynamics of the trivial equilibrium

System (4.2.2) has the trivial equilibrium, $E_0 := (0, 0, 0, 0)^T$, and its linearization at the trivial equilibrium is an age-structured linear Leslie population model. As is well-known, one of the important characterizations for a linear Leslie matrix model is the inherent net reproductive number which is the expected number of offspring per mosquito over the course of its lifetime, and the inherent net reproductive number also determines the asymptotic dynamics of the linear system [50, 90, 91]. Using the techniques in [50, 84, 86], we find the inherent net reproductive number, r_0 , for system (4.2.2) as follows.

Define the fertility matrix F and the transition matrix T , respectively, as

$$F = \begin{pmatrix} 0 & 0 & 0 & bs_0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad T = \begin{pmatrix} 0 & 0 & 0 & 0 \\ \alpha_1 & 0 & 0 & 0 \\ 0 & \alpha_2 & 0 & 0 \\ 0 & 0 & \alpha_3 & \alpha_4 \end{pmatrix}.$$

Then the inherent projection matrix of the nonlinear system (4.2.2) is

$$A(0) = \begin{pmatrix} 0 & 0 & 0 & bs_0 \\ \alpha_1 & 0 & 0 & 0 \\ 0 & \alpha_2 & 0 & 0 \\ 0 & 0 & \alpha_3 & \alpha_4 \end{pmatrix} = F + T,$$

and thus, the inherent net reproductive number is the positive, simple, and strictly dominant eigenvalue of $F(I - T)^{-1}$, denoted by r_0 . Simple calculation show that

$$r_0 = \frac{bs_0\alpha_1\alpha_2\alpha_3}{1 - \alpha_4} = \frac{bs_0s_e(0)s_l(0)s_p}{1 - s_m(0)}.$$

We then determine the stability of the trivial equilibrium.

Since $x(t) \geq 0$ for all $t \geq 0$, it follows from (4.2.2) and conditions (H1) that

$$x(1) = A(x(0))x(0) \leq A(0)x(0),$$

and

$$x(2) = A(x(1))x(1) \leq A(0)x(1) \leq A^2(0)x(0).$$

Continuing in this manner, we have

$$x(t) \leq A^t(0)x(0).$$

Note that $A(0)$ is non-negative, irreducible, and primitive. Then $A(0)$ has a positive, simple, and strictly dominant eigenvalue, which is the inherent net reproductive number, r_0 . If $r_0 < 1$, then it follows, [94], that

$$\lim_{t \rightarrow \infty} A^t(0) = 0.$$

If $r_0 > 1$, $A(0)$ has a positive strictly dominant eigenvalue greater than one. That is, the linearization of system (4.2.2) at the trivial equilibrium has a positive eigenvalue greater than one, which implies the instability of the trivial equilibrium. Therefore, we arrive at the following stability result for the trivial equilibrium.

Theorem 4.3.1. *Let b be a positive constant. The trivial equilibrium of system (4.2.1) or (4.2.2), $E_0 = (0, 0, 0, 0)^T$, is globally asymptotically stable if the inherent net reproductive number $r_0 < 1$, and is unstable if $r_0 > 1$.*

4.4 The positive equilibrium

System (4.2.1) or (4.2.2) may have positive equilibria. We first determine its existence and uniqueness, and then find conditions that ensure the stability of the positive equilibrium.

4.4.1 Existence of the positive equilibrium

Let $E_1 = (\bar{E}, \bar{L}, \bar{P}, \bar{M})^T$ be a positive equilibrium. Then its components satisfy the following system

$$E = bs_0M, \tag{4.4.1a}$$

$$L = s_e(L)E, \tag{4.4.1b}$$

$$P = s_l(L)L, \tag{4.4.1c}$$

$$M = s_pP + s_m(M)M. \tag{4.4.1d}$$

It follows from (4.4.1b) that

$$\frac{L}{s_e(L)} = E = bs_0M. \tag{4.4.2}$$

Define $F(L) = \frac{L}{s_e(L)}$. Then

$$F'(L) = \frac{1}{s_e(L)} - \frac{Ls'_e(L)}{s_e^2(L)} > 0.$$

Note that $F(0) = 0$ and $\lim_{L \rightarrow \infty} F(L) = \lim_{L \rightarrow \infty} \frac{L}{s_e(L)} = \lim_{L \rightarrow \infty} \frac{L^2}{s_e(L)L} = \infty$ under assumption (H1) or (H2). Then there exists a unique positive solution, $L(M)$, to equation (4.4.2).

We also note that, as a function of M ,

$$L'(M) = bs_0s_e(L(M)) + s'_e(L(M))L'(M)bs_0M. \quad (4.4.3)$$

Solving (4.4.3) for $L'(M)$, we have

$$L'(M) = \frac{bs_0s_e(L(M))}{1 - bs_0Ms'_e(L(M))} > 0. \quad (4.4.4)$$

That is, L is a monotone increasing function of M and we have

$$L(M) = s_e(bs_0M)bs_0M.$$

Substituting this solution $L(M)$ into (4.4.1c) and then into (4.4.1d), we obtain

$$M = s_p s_l(L(M))s_e(L(M))bs_0M + s_m(M)M. \quad (4.4.5)$$

To solve for a positive solution $M > 0$ to equation (4.4.5), we define function

$$H(M) := bs_0s_p s_l(L(M))s_e(L(M)) + s_m(M) - 1. \quad (4.4.6)$$

Then system (4.2.1) or (4.2.2) has a positive equilibrium if and only if there exists a positive root of $H(M) = 0$.

Since

$$H'(M) = bs_0s_p(s'_l(L(M))s_e(L(M)) + s_l(L(M))s'_e(L(M))L'(M) + s'_m(M)), \quad (4.4.7)$$

it follows from conditions (H1), or conditions (H2), and (4.4.4) that $H'(M) < 0$; that is, $H(M)$ is a monotone decreasing function with respect to M .

Since $\lim_{M \rightarrow \infty} H(M) = -1$ from assumption (H1) or (H2), then $H(M) = 0$ has a unique positive root if and only if $H(0) > 0$, which is equivalent to

$$r_0 = \frac{bs_0s_ps_l(0)s_e(0)}{1 - s_m(0)} > 1,$$

that is the inherent net number $r_0 > 1$.

In summary, we obtain the following existence result.

Theorem 4.4.1. *System (4.2.1) or (4.2.2) has a unique positive equilibrium $E_1 = (\bar{E}, \bar{L}, \bar{P}, \bar{M})^T$ if and only if the inherent net reproductive number $r_0 > 1$.*

4.4.2 The stability of the positive equilibrium

Suppose $r_0 > 1$. Then there exists a unique positive equilibrium $E_1 = (\bar{E}, \bar{L}, \bar{P}, \bar{M})^T$ to the system (4.2.2), where \bar{M} satisfies $H(M) = 0$, that is:

$$1 = bs_0s_ps_e(L(\bar{M}))s_l(L(\bar{M})) + s_m(\bar{M}) \quad (4.4.8)$$

and

$$\bar{E} = bs_0\bar{M},$$

$$\bar{L} = s_e(L(\bar{M})) \cdot b\bar{M},$$

$$\bar{P} = s_l(L(\bar{M})) \cdot s_e(L(\bar{M})) \cdot b\bar{M}.$$

We focus on the case where conditions (H1) are satisfied, and have the following local stability results for the positive equilibrium.

Theorem 4.4.2. *Let $r_0 > 1$. Then the unique positive equilibrium E_1 of system (4.2.1) or (4.2.2) is locally asymptotically stable, if either condition*

$$s'_e(\bar{L})bs_0\bar{M} + (s_m(\bar{M})\bar{M})' > 0 \quad (\text{H3})$$

holds, or condition

$$\begin{aligned} 0 &< -s'_e(\bar{L})bs_0\bar{M} - (s_m(\bar{M})\bar{M})' \\ &< s_m(\bar{M}) - bs_0s_ps_es'_l(\bar{L})\bar{L} + s'_e(\bar{L})bs_0\bar{M}(s_m(\bar{M})\bar{M})' \end{aligned} \quad (\text{H4})$$

is satisfied, where \bar{E} , \bar{L} , \bar{P} , and \bar{M} are the components of the positive equilibrium E_1 .

Proof: The linearized system at $E_1 = (\bar{E}, \bar{L}, \bar{P}, \bar{M})^T$ has the following coefficient matrix:

$$J = \begin{pmatrix} 0 & 0 & 0 & bs_0 \\ s_e(\bar{L}) & s'_e(\bar{L})\bar{E} & 0 & 0 \\ 0 & s_l(\bar{L}) + s'_l(\bar{L})\bar{L} & 0 & 0 \\ 0 & 0 & s_P & s_m(\bar{M}) + s'_m(\bar{M})\bar{M} \end{pmatrix}.$$

The characteristic polynomial associated with this matrix is given by

$$f(\lambda) = \lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_4,$$

where

$$\begin{aligned} a_1 &= -(s'_e(\bar{L})\bar{E} + s_m(\bar{M}) + s'_m(\bar{M})\bar{M}), \quad a_2 = s'_e(\bar{L})\bar{E}(s_m(\bar{M}) + s'_m(\bar{M})\bar{M}), \\ a_3 &= 0, \quad a_4 = -bs_0s_Ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}). \end{aligned}$$

Define

$$\begin{aligned} b_4 &:= 1 - a_4^2 = 1 - (bs_0s_Ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}))^2, \\ b_3 &:= a_1 - a_4a_3 = -(s'_e(\bar{L})\bar{E} + s_m(\bar{M}) + s'_m(\bar{M})\bar{M}), \\ b_2 &:= a_2 - a_4a_2 = s'_e(\bar{L})\bar{E}(s_m(\bar{M}) + s'_m(\bar{M})\bar{M})(1 + bs_0s_Ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L})), \\ b_1 &:= a_3 - a_4a_1 = -(s'_e(\bar{L})\bar{E} + s_m(\bar{M}) + s'_m(\bar{M})\bar{M})(bs_0s_Ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L})), \end{aligned}$$

and

$$\begin{aligned}
c_4 &:= b_4^2 - b_1^2 = (b_4 - b_1)(b_4 + b_1) \\
&= (1 - (bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}))^2 + \\
&\quad (s'_e(\bar{L})\bar{E} + s_m(\bar{M}) + s'_m(\bar{M})\bar{M})(bs_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}))) \\
&\quad \times (1 - (bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}))^2 - \\
&\quad (s'_e(\bar{L})\bar{E} + s_m(\bar{M}) + s'_m(\bar{M})\bar{M})(bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}))), \\
c_3 &:= b_4b_3 - b_1b_2 \\
&= - (1 + bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}))(s'_e(\bar{L})\bar{E} + s_m(\bar{M}) + s'_m(\bar{M})\bar{M}) \\
&\quad \times (1 - bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}) - s'_e(\bar{L})\bar{E}(s_m(\bar{M}) + s'_m(\bar{M})\bar{M}) \\
&\quad \times bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L})), \\
c_2 &:= b_4b_2 - b_1b_3 \\
&= (1 + bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}))^2(1 - bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L})) \\
&\quad \times s'_e(\bar{L})\bar{E}(s_m(\bar{M}) + s'_m(\bar{M})\bar{M}) - (s'_e(\bar{L})\bar{E} + s_m(\bar{M}) + s'_m(\bar{M})\bar{M})^2 \\
&\quad \times bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L})).
\end{aligned}$$

It follows from the Jury stability criterion [97, 101] that the roots of the characteristic polynomial $f(\lambda)$ all have magnitudes less than one if

$$f(1) > 0, \quad f(-1) > 0, \quad |a_4| < 1, \quad |b_4| > |b_1|, \quad |c_4| > |c_2|.$$

Since

$$f(\pm 1) = 1 \pm a_1 + a_2 + a_4,$$

$$f(1) - f(-1) = 2a_1. \quad (4.4.9)$$

Assume condition (H3) holds. Then $a_1 < 0$, and

$$\begin{aligned} f(1) &= 1 + a_1 + a_2 + a_4 \\ &= 1 - (s'_e(\bar{L})bs_0\bar{M} + s_m(\bar{M}) + s'_m(\bar{M})\bar{M}) + s'_e(\bar{M})bs_0\bar{M}(s_m(\bar{M}) + s'_m(\bar{M})\bar{M}) \\ &\quad - bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}) \\ &= s'_e(\bar{L})bs_0\bar{M}(s'_m(\bar{M})\bar{M} - bs_0s_ps_e(\bar{L})s_l(\bar{L})) - s'_m(\bar{M})\bar{M} \\ &\quad - bs_0s_ps_e(\bar{L})s'_l(\bar{L})\bar{L} > 0. \end{aligned}$$

Furthermore, it follows from (4.4.9) that $f(-1) > 0$.

Notice that, at the positive equilibrium from (4.4.6),

$$1 = s_m(\bar{M}) + bs_0s_ps_e(\bar{L})s_l(\bar{L}) > bs_0s_ps_e(\bar{L})s_l(\bar{L}) > |a_4|.$$

Then

$$|b_4| - |b_1| = 1 - a_4^2 - |a_4||a_1| > |a_4|(1 - |a_4| - |a_1|). \quad (4.4.10)$$

If assumption (H3) holds, then

$$\begin{aligned} 1 - |a_4| - |a_1| &= 1 - bs_0s_ps_e(\bar{L})(s_l(\bar{L}) + s'_l(\bar{L})\bar{L}) - s'_e(\bar{L})bs_0\bar{M} - s_m(\bar{M}) - s'_m(\bar{M})\bar{M} \\ &= -bs_0s_ps_e(\bar{L})s'_l(\bar{L})\bar{L} - s'_e(\bar{L})bs_0M - s'_m(M)M > 0, \end{aligned}$$

and hence $|b_4| > |b_1|$.

Suppose $|b_4| > |b_1|$. Then $c_4 > 0$, and it follows from $a_2 < 0$ and $-1 < a_4 < 0$ that

$$\begin{aligned} c_2 &= b_4b_2 - b_1b_3 = (1 - a_4^2)(a_2 - a_4a_2) + a_4a_1^2 \\ &= (1 - a_4^2)(1 - a_4)a_2 + a_1^2a_4 < 0. \end{aligned}$$

Then

$$\begin{aligned} |c_4| - |c_2| &= c_4 + c_2 = b_4^2 - b_1^2 + b_2b_4 - b_1b_3 \\ &= b_4(b_2 + b_4) - b_1(b_1 + b_3) \\ &= (1 - a_4^2)(1 - a_4^2 + a_2(1 - a_4)) + a_4a_1^2(1 - a_4) \\ &= (1 - a_4)((1 - a_4^2)(1 + a_4 + a_2) + a_1^2a_4). \end{aligned}$$

Suppose (H3) holds and hence $f(1) > 0$. Then $-a_1 > 0$ and it follows, in addition from $-1 < a_4 < 0$, that $|c_4| - |c_2| > 0$, if $1 - a_4^2 - a_1a_4 > 0$. However,

$$1 - a_4^2 - a_1a_4 = 1 - a_4(a_4 + a_1) = 1 - a_4(f(1) - 1 - a_2)$$

$$= 1 + a_4 - a_4 f(1) + a_2 a_4 > 0.$$

Hence $|c_4| - |c_2| > 0$.

Therefore, if (H3) holds, the positive equilibrium is locally asymptotically stable.

We next assume

$$s'_e(L)bs_0M + (s_m(M)M)' < 0.$$

Then $a_1 > 0$, and $f(1) > 0$ provided $f(-1) > 0$. It follows from $f(-1) = 1 - a_1 + a_2 + a_4$

that if $0 < a_1 < 1 + a_2 + a_4$, that is, if (H4) holds, then $f(-1) > 0$.

Suppose assumption (H4) holds. Then $a_1 > 0$ and it follows from (4.4.10) that

$$|b_4| - |b_1| = 1 - a_4^2 - |a_4||a_1| = 1 - a_4(a_4 + a_1) = 1 - a_4 f(1) + a_4 + a_4 a_2 > 0.$$

Moreover, since

$$\begin{aligned} |c_4| - |c_2| &= (1 - a_4)((1 - a_4^2)f(-1) + (1 - a_4^2)a_1 + a_1^2 a_4) \\ &= (1 - a_4)((1 - a_4^2)f(-1) + a_1(1 - a_4^2 + a_1 a_4)), \end{aligned}$$

$|c_4| - |c_2| > 0$, if $1 - a_4^2 + a_1 a_4 > 0$. It is easy to see that

$$\begin{aligned} 1 - a_4^2 + a_1 a_4 &= 1 - a_4(a_4 - a_1) \\ &= 1 - a_4(a_4 - a_1 + 1 + a_2 - 1 - a_2) \\ &= 1 - a_4 f(-1) + a_4 + a_2 a_4 > 0. \end{aligned}$$

Hence $|c_4| > |c_2|$. Therefore, positive fixed E_1 is locally asymptotically stable. The proof is complete. \square

The dynamics of system (4.2.2) are richer and more complex if s_e and s_l satisfy conditions (H2). We give local stability results for the positive equilibrium in the following theorem.

Theorem 4.4.3. *Let $s_m(M)$ satisfy conditions (H1), and $s_e(\bar{L})$ and $s_l(\bar{L})$ both satisfy conditions (H2). Then we have the following stability results.*

1. *Assume $(s_l(\bar{L})\bar{L})' > 0$. Then E_1 is locally asymptotically stable if conditions (H3) or (H4) are satisfied.*
2. *Assume $(s_l(\bar{L})\bar{L})' < 0$ and $(s_m(\bar{M})\bar{M})' < -s'_e(\bar{L})bs_0\bar{M}$. Then E_1 is locally asymptotically stable if*

$$\begin{aligned} -s'_e(\bar{L})bs_0\bar{M} - (s_m(\bar{M})\bar{M})' &< 1 + bs_0s_ps_e(\bar{L})s_l(\bar{L}) + bs_0s_ps_e(\bar{L})s'_l(\bar{L})\bar{L} \\ &+ s'_e(\bar{L})bs_0\bar{M}(s_m(\bar{L}\bar{M})\bar{M})'. \end{aligned} \quad (\text{H5})$$

3. *Assume $(s_l(\bar{L})\bar{L})' < 0$ and $-s'_e(\bar{L})bs_0\bar{M} < (s_m(\bar{M})\bar{M})'$. Then E_1 is locally asymptotically stable if*

$$-bs_0s_ps_e(\bar{L})s'_l(\bar{L})\bar{L} < 2bs_0s_ps_e(\bar{L})s_l(\bar{L}) - s'_e(\bar{L})bs_0\bar{M} - s'_m(\bar{M})\bar{M}. \quad (\text{H6})$$

Here $\bar{E}, \bar{L}, \bar{P}$, and \bar{M} are the components of the positive equilibrium E_1 .

The proof, with tedious algebra, is similar to that of Theorem 4.4.2, and is omitted.

4.4.3 Uniform persistence

We have shown that if $r_0 > 1$, the trivial equilibrium is unstable and there exists a unique positive equilibrium. Moreover, employing the technique shown in [84, 85], we can show that if $r_0 > 1$, system (4.2.2) is uniformly persistent; that is, there exists a positive number $\rho \in \mathbb{R}_+^4$, such that for every solution, $x(t)$, of (4.2.2) with $x(0) > 0$, $\liminf_{t \rightarrow \infty} x(t) \geq \rho > 0$. This is equivalent to say that the trivial equilibrium is a uniform repeller [92, 95].

4.4.3.1 Preliminaries

Definition 4.4.1. *Let X be a metric space with metric d . A map $f : X \rightarrow X$ defines a discrete semi-dynamical system $T : Z_+ \times X \rightarrow X$ by $T(n, x) = f^n(x)$, where Z_+ denotes the set of nonnegative integers and $f^n(x)$ denotes the n^{th} iterate of x under f . Let Y be a subspace of X . We say that f is uniformly persistent (with respect to Y) if there exists $\eta > 0$ such that for all $x \in X \setminus Y$, $\liminf_{n \rightarrow \infty} f^n(x) \geq \eta$.*

Remark : In applications to ecological equations, X will be the set of all possible states of the system and Y the set of extinction states. In that case, uniform persistence captures the idea of non-extinction of the system.

Definition 4.4.2. *If (a) X is a compact metric space, (b) $f : X \rightarrow X$ is a continuous map and (c) $M \subset X$ is compact invariant, that is, $f(M) = M$, then, M is said to be a repeller if there exists a neighborhood U of M such that for all $x \in U$ there exists $n_0 = n_0(x) > 0$ satisfying $f^n(x) \in U$ for all $n \geq n_0$. U is called a repeller neighborhood of M .*

Theorem 4.4.4. [95] *M is a repeller if and only if*

(1) M is isolated, that is, there exists a closed neighborhood U of M (U is called an isolating neighborhood of M) such that M is the largest invariant set in U , and

(2) $W^s(M) \subset M$, where $W^s(M) = \{x \in X : f^n(x) \rightarrow M \text{ as } n \rightarrow \infty\}$ is the stable set of M .

Corollary 4.4.5. [95] *Let $X \setminus M$ be positively invariant. Then M is a repeller if there exists a continuous function $P : X \rightarrow \mathbb{R}_+$ satisfying the conditions:*

(1) $P(x) = 0$ for $x \in M$ and
(2) there exists a neighborhood U of M such that $\forall x \in U \setminus M, \exists n > 0$, such that $P(f^n(x)) > P(x)$.

Theorem 4.4.6. [95] *f is uniformly persistent (w. r. t. Y) if and only if*

(1) M is isolated in X and
(2) $W^s(M) \subset Y$.

Let X be a complete metric space (with metric d) and suppose that $T(t) : X \rightarrow X, t \geq 0$ is a C^0 -semigroup on X ; that is, $T(0) = I, T(t+s) = T(t)T(s)$ for $t, s \geq 0$, and

$T(t)x$ is continuous in t, x . The positive orbit $\gamma^+(x)$ through x is defined as $\gamma^+(x) = \bigcup_{t \geq 0} \{T(t)x\}$.

Definition 4.4.3. *The semigroup $T(t)$ is said to be asymptotically smooth if for any bounded subset B of X , for which $T(t)B \subset B$, for $t \geq 0$, there exists a compact set K such that the distance $d(T(t)B, K) \rightarrow 0$ as $t \rightarrow \infty$. The semigroup $T(t)$ is said to be point dissipative in X if there is a bounded nonempty set B in X such that, for any $x \in X$, there is a $t_0 = t_0(x, B)$ such that $T(t)x \in B$ for $t \geq t_0$.*

Theorem 4.4.7. [94] *if*

- (i) $T(t)$ is asymptotically smooth,
 - (ii) $T(t)$ is point dissipative in X ,
 - (iii) $\gamma^+(U)$ is bounded in X if U is bounded in X ,
- then there is a nonempty global attractor A in X .*

4.4.3.2 Uniform persistence

Let $G := A(x(t))x(t)$ be the map from \mathbb{R}_+^4 to \mathbb{R}_+^4 and let D be the boundary of Ω defined in (4.2.3). Then it follows from Theorem 4.2.1 that $G^t(\Omega \setminus D) \subset \Omega \setminus D$, where $G^t(x)$ denotes the t th iteration of x under G , and hence there exists a global attract X in Ω [94].

For $r_0 > 1$, the trivial equilibrium is unstable. Let $M := \{(0, 0, 0, 0)\} \subset X$. Then M is a compact subset of Ω and $\Omega \setminus M$ is positively invariant. Set M is also isolated in X .

Since $A(0)$ is nonnegative and irreducible, it has a dominant positive eigenvalue, $r > 1$, which has a corresponding positive left eigenvector, $\eta > 0$, such that

$$\eta^T A(0) = r\eta^T.$$

Let $1 < r^* < r$. Then

$$\eta^T A(0) > r^* \eta^T.$$

We define a vector norm $\|\cdot\|$ such that $\|x\| := \eta^T x$. Clearly this norm is equivalent to the 2- norm, $\|x\|_2 = (\sum_{i=1}^n x_i^2)^{1/2}$. Since $A(x)$ is continuous, there exists $\rho > 0$, such that

$$\eta^T A(x) > r^* \eta^T, \tag{4.4.11}$$

for all $x \in N_\rho(0) := \{x \in \mathbb{R}_+^4, \|x\| \leq \rho\}$.

Let $x(t)$ be a solution of system (4.2.1) or (4.2.2). If $x(t) \in N_\rho(0)$, then it follows from (4.4.11) that

$$p^T x(t+1) = \eta^T A(x(t))x(t) > r^* \eta^T x(t),$$

that is, $\|x(t+1)\| > r^*\|x(t)\| > \|x(t)\|$, for all $x(t) \in N_\rho(0)$. Hence $\liminf_{t \rightarrow \infty} x(t) \geq \rho$, which implies that the trivial equilibrium is a uniform repeller and then system (4.2.1) or (4.2.2) is uniformly persistent. In summary, we have the following result.

Theorem 4.4.8. *The trivial equilibrium is a uniform repeller and system (4.2.1) or (4.2.2) is uniformly persistence if $r_0 > 1$.*

4.5 Numerical examples

We provide simple numerical examples to demonstrate the dynamics of system (4.2.1) or (4.2.2) as follows.

Table II. Basic Parameter Values

Parameters	Values
b	$3 \leq b \leq 80$
α_e	$0 < \alpha_e \leq 1$
α_l	$0 < \alpha_e \leq 1$
α_m	$0 < \alpha_e \leq 1$
k_e	$100 < k_e \leq 1500$
k_l	$100 < k_l \leq 1500$
k_m	$100 < k_m \leq 1500$
s_0	$0 < s_0 \leq 1$
s_p	$0 < s_p \leq 1$

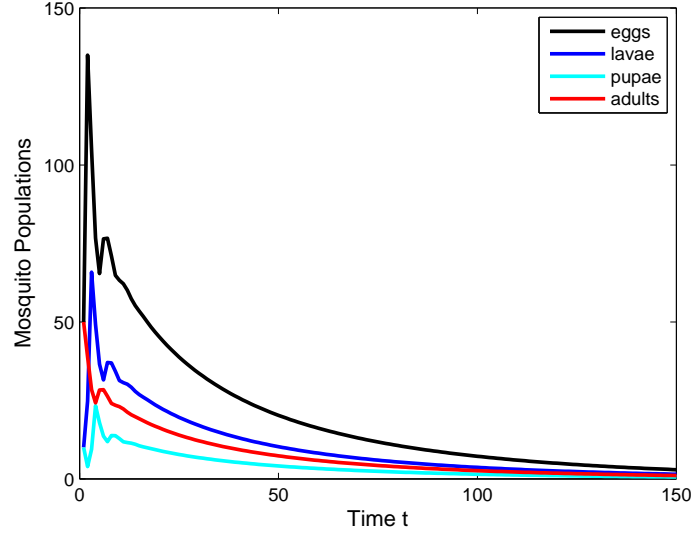


Figure 4.1: The function forms and parameters are given in Example 4.5.1. As $b = 4.5$, the inherent net reproductive number $r_0 = 0.9 < 1$. E_0 is globally asymptotically stable. Solutions approach E_0 as $t \rightarrow \infty$.

Example 4.5.1. In this example, we assume s_e , s_l , and s_m all have the Beverton-Holt form such that $s_i(z) = \frac{\alpha_i k_i}{k_i + \alpha_i z}$, $i = e, l, m$, and use the following parameters

$$\begin{aligned} s_0 &= 0.6, \quad \alpha_e = 0.5, \quad \alpha_l = 0.4, \quad \alpha_m = 0.7, \\ k_e &= 500, \quad k_l = 200, \quad k_m = 1000, \quad s_p = 0.5. \end{aligned}$$

If $b = 4.5$, the inherent net reproductive number $r_0 = 0.9 < 1$. Trivial equilibrium E_0 is globally stable and the mosquito population goes extinct, the case is shown in Figure 4.1. If $b = 8$, the inherent net reproductive number $r_0 = 1.6 > 1$. The trivial equilibrium becomes unstable and there exists a positive equilibrium, $E_1 =$

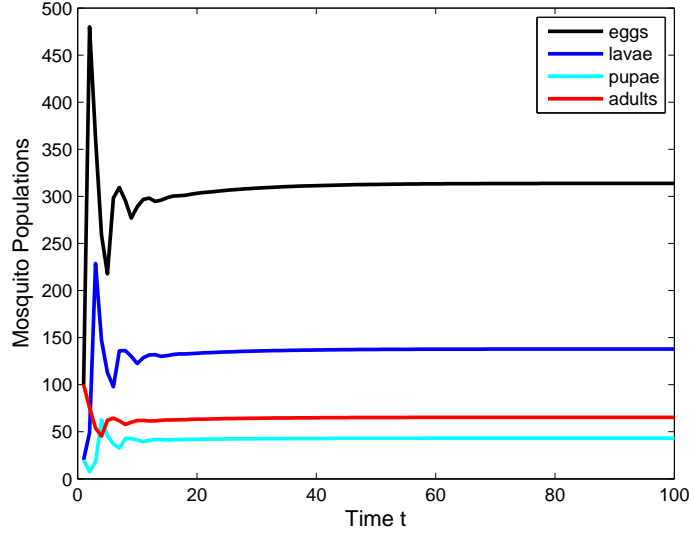


Figure 4.2: The function forms and parameters are given in Example 4.5.1 As $b = 8$, the inherent net reproductive number $r_0 = 1.6 > 1$. E_0 is unstable and $E_1 = (313.8399, 137.9042, 43.2367, 65.3841)^T$ is asymptotically stable. Solutions approach E_1 , as $t \rightarrow \infty$.

$(313.8399, 137.9042, 43.2367, 65.3841)^T$, which is asymptotically stable, the case is shown in Figure 4.2

Example 4.5.2. We assume, in this example, that $s_m(M)$ still has the Beverton-Holt form such that $s_m(z) = \frac{\alpha_m k_m}{k_m + \alpha_m z}$, but $s_i(L)$, $i = e, l$, have the Ricker-type nonlinearity such that $s_i(L) = \alpha_i e^{-L/k_i}$, $i = e, l$. We use the following set of parameters

$$\begin{aligned} s_0 &= 0.6, & \alpha_e &= 0.3, & \alpha_l &= 0.8, & \alpha_m &= 0.01, \\ k_e &= 500, & k_l &= 200, & k_m &= 1000, & s_p &= 0.8. \end{aligned}$$

If $b = 13$, the inherent net reproductive number $r_0 = 0.9455 < 1$. Trivial equilibrium E_0 is globally stable and the mosquito population goes extinct, as shown

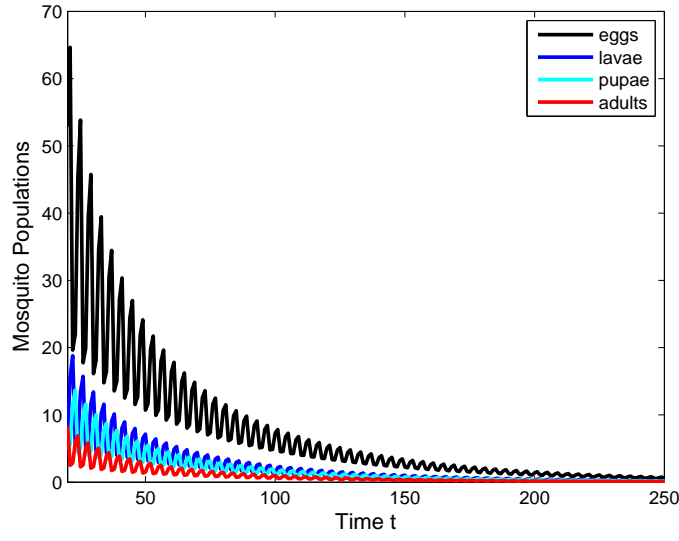


Figure 4.3: The function forms and parameters are given in Example 4.5.2 As $b = 13$, the inherent net reproductive number $r_0 = 0.9455 < 1$. E_0 is globally asymptotically stable. Solutions approach E_0 as $t \rightarrow \infty$.

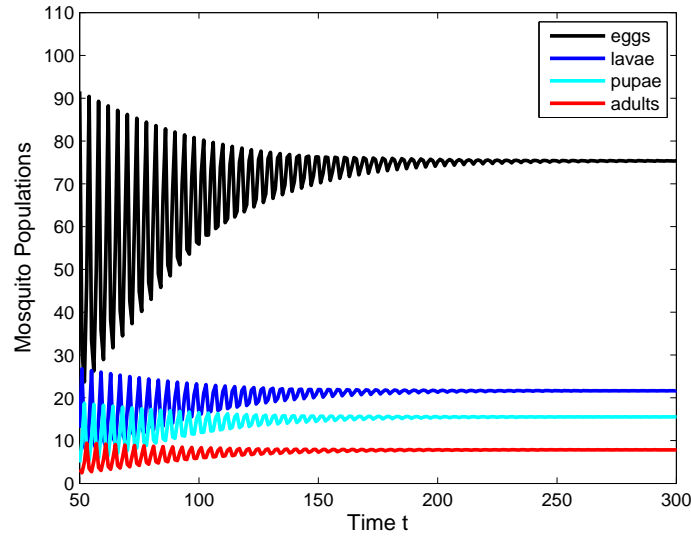


Figure 4.4: The function forms and parameters are given in Example 4.5.2. As $b = 16$, the inherent net reproductive number $r_0 = 1.1636 > 1$. E_0 is unstable and $E_1 = (75, 3596, 21.6499, 15.5429, 7.8500)^T$ is asymptotically stable. Solutions approach E_1 , as $t \rightarrow \infty$.

in Figure 4.3. As $b = 16$, the inherent net reproductive number $r_0 = 1.1636 > 1$. The trivial equilibrium becomes unstable and there exists a positive equilibrium $E_1 = (75, 3596, 21.6499, 15.5429, 7.8500)^T$ which is asymptotically stable, as shown in Figure 4.4.

Example 4.5.3. Population models with the Ricker-type nonlinearity have richer and more complex dynamics [49, 66, 98]. We assume, in this example, the same structure as that given in Example 2 that is, $s_m(z) = \frac{\alpha_m k_m}{k_m + \alpha_m z}$, and $s_i(L) = \alpha_i e^{-L/k_i}$, $i = e, l$. We use the following set of parameters

$$\begin{aligned} s_0 &= 0.8, \quad \alpha_e = 0.8, \quad \alpha_l = 0.8, \quad \alpha_m = 0.2, \\ k_e &= 300, \quad k_l = 350, \quad k_m = 500, \quad s_p = 0.8, \end{aligned}$$

and let b vary, but keep all $r_0 > 1$. The period-doubling bifurcation appears as expected.

If $b = 5$, the inherent net reproductive number $r_0 = 2.56$. There exists a unique positive equilibrium, E_1 , which is asymptotically stable, as shown Figure 4.5. If $b = 15$, we have $r_0 = 7.68$. A stable 2-cycle appears, as shown Figure 4.6. As $b = 21.5$, we have $r_0 = 11.008$. A cycle with a large period exists, as shown Figure 4.7. As $b = 70$, we have $r_0 = 35.84$. The system exhibits chaotic behavior, as shown Figure 4.8.

Remark: All populations shown in the figures 4.5-4.8. are only larvae for clearer views.

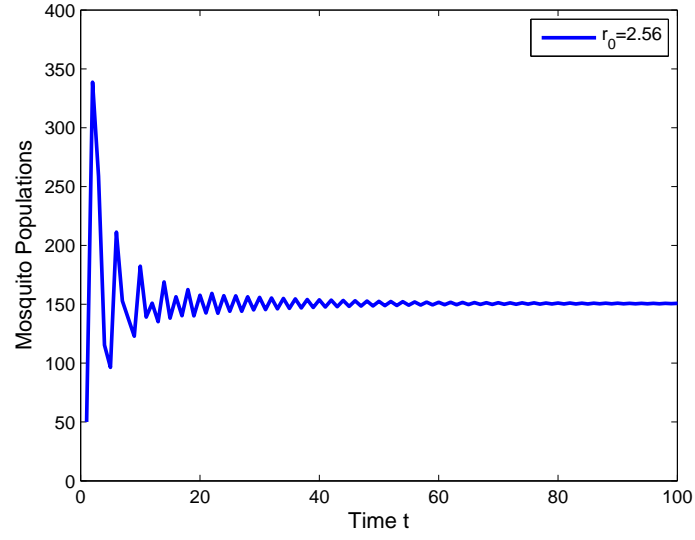


Figure 4.5: The function forms and parameters are given in Example 4.5.3 As $b = 5$, $r_0 = 2.56$. Positive equilibrium E_1 is asymptotically stable.

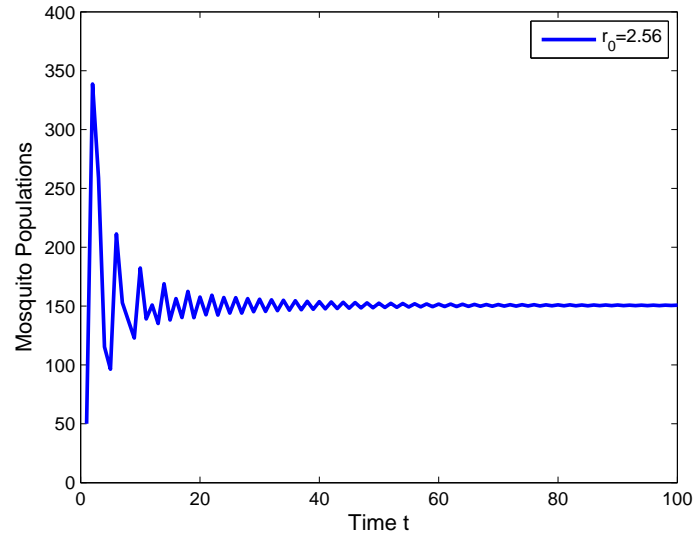


Figure 4.6: The function forms and parameters are given in Example 4.5.3. At $b = 15$, $r_0 = 7.68$, a stable 2-cycle appears.

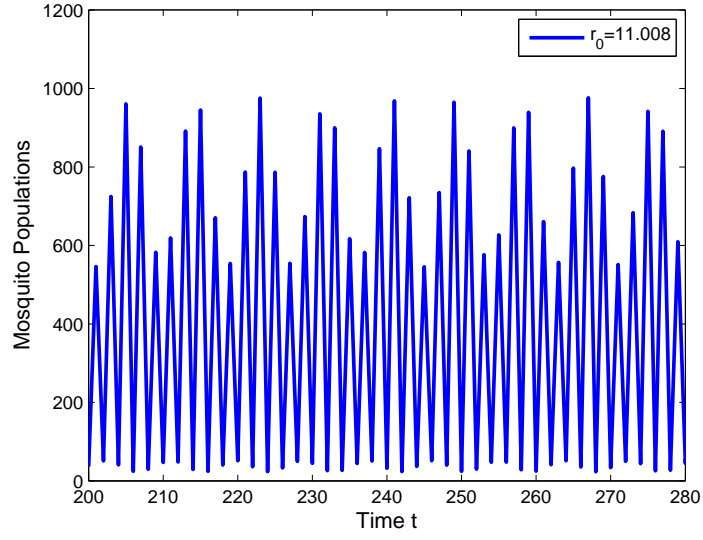


Figure 4.7: The function forms and parameters are given in Example 4.5.3. If $b = 21.5$, $r_0 = 11.008$, and a cycle with a large period exists.

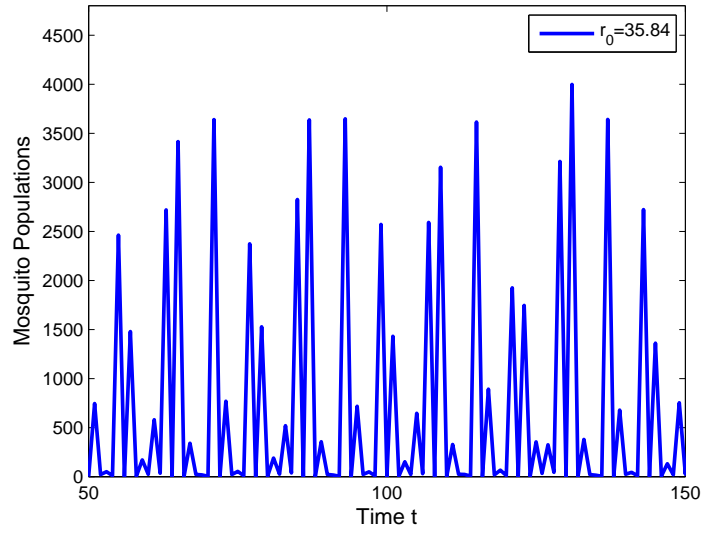


Figure 4.8: The function forms and parameters are given in Example 4.5.3. As $b = 70$, $r_0 = 35.84$, and the system exhibits chaotic behavior.

CHAPTER 5

SIMPLE DISCRETE-TIME MALARIA MODELS

Due to the significant difference on the time scales of the lifespan and development between human beings and mosquitoes, the models with discrete-time, based on the time-steps of mosquitoes' development, are more appropriate in certain cases. Hence we formulate discrete-time malaria models in this chapter.

5.1 Population dynamics for mosquitoes and humans without infection

We start with the model formulation for the mosquito population as follows. We first assume the mosquito population dynamics, in the absence of infection, are described by the following equation

$$N^v(t+1) = b^v \alpha^{vb}(t) N^v(t) + \alpha^v(t) N^v(t), \quad (5.1.1)$$

where b^v is the per capita birth rate of mosquitoes, $\alpha^{vb}(t)$ and $\alpha^v(t)$ are the survival probabilities of the mosquito newborns and adults at time t , respectively.

We assume that the survival probabilities are density-dependent and are given by

$$\alpha^{vb}(t) = \frac{k_0^v}{1 + \eta_0^v N^v(t)} \quad \text{and} \quad \alpha^v(t) = \frac{k_1^v}{1 + \eta_1^v N^v(t)}. \quad (5.1.2)$$

Then equation (5.1.1) becomes

$$N^v(t+1) = \left(\frac{b^v k_0^v}{1 + \eta_0^v N^v(t)} + \frac{k_1^v}{1 + \eta_1^v N^v(t)} \right) N^v(t). \quad (5.1.3)$$

Equation (5.1.3) has a trivial solution $N^v \equiv 0$. If $b^v k_0^v + k_1^v < 1$, it follows from

$$N^v(t+1) \leq (b^v k_0^v + k_1^v) N^v(t),$$

for $N^v(t) \geq 0$, that the trivial solution is globally asymptotically stable. It is clear that the trivial solution is unstable if $b^v k_0^v + k_1^v > 1$.

Let

$$F(N^v) := \frac{b^v k_0^v}{1 + \eta_0^v N^v} + \frac{k_1^v}{1 + \eta_1^v N^v}. \quad (5.1.4)$$

Then $F'(N^v) < 0$, $F''(N^v) > 0$, and $F(0) = b^v k_0^v + k_1^v$. Hence if $b^v k_0^v + k_1^v < 1$, there exists no positive solution to $F(N^v) = 1$, and thus no positive equilibrium to equation (5.1.3). If $b^v k_0^v + k_1^v > 1$, there exists a unique positive equilibrium

$$N^{v*} = \frac{B^v + \sqrt{\Delta^v}}{2\eta_0^v \eta_1^v}, \quad (5.1.5)$$

where

$$B^v = (b^v k_0^v - 1)\eta_1^v + (k_1^v - 1)\eta_0^v,$$

and

$$\begin{aligned}\Delta^v &= (B^v)^2 - 4\eta_0^v \eta_1^v (1 - b^v k_0^v - k_1^v) \\ &= (b^v k_0^v - 1)^2 (\eta_1^v)^2 + (k_1^v - 1)^2 (\eta_0^v)^2 + 2\eta_0^v \eta_1^v (b^v k_0^v k_1^v + b^v k_0^v + k_1^v - 1) \\ &= ((b^v k_0^v - 1)\eta_1^v - (k_1^v - 1)\eta_0^v)^2 + 4b^v k_0^v k_1^v \eta_0^v \eta_1^v.\end{aligned}$$

Suppose there exists a unique positive equilibrium N^{v*} . The the positive equilibrium is locally asymptotically stable if $|F(N^{v*}) + F'(N^{v*})N^{v*}| < 1$, that is $-F'(N^{v*})N^{v*} < 2$.

Notice that

$$\begin{aligned}-F'(N^{v*})N^{v*} &= \frac{b^v k_0^v \eta_0^v N^{v*}}{(1 + \eta_0^v N^{v*})^2} + \frac{k_1^v \eta_1^v N^{v*}}{(1 + \eta_1^v N^{v*})^2} \\ &= \frac{\eta_0^v N^{v*}}{1 + \eta_0^v N^{v*}} \frac{b^v k_0^v}{1 + \eta_0^v N^{v*}} + \frac{\eta_1^v N^{v*}}{1 + \eta_1^v N^{v*}} \frac{k_1^v}{1 + \eta_1^v N^{v*}} \\ &< \frac{b^v k_0^v}{1 + \eta_0^v N^{v*}} + \frac{k_1^v}{1 + \eta_1^v N^{v*}} = 1,\end{aligned}\tag{5.1.6}$$

since $F(N^{v*}) = 1$. Therefore, the positive equilibrium is locally asymptotically stable if it exists.

Because the difference between the time scales of the population dynamics of mosquitoes and humans, we assume the human population has a simple stable steady

state. That is, in the absence of infection, the dynamics of the humans satisfy the equation

$$N^h(t+1) = \Lambda + \alpha^h N^h(t), \quad (5.1.7)$$

where Λ is the constant input flow and $0 \leq \alpha^h < 1$ is the survival probability of humans. It is easy to check that the population approaches the unique stable equilibrium $N^{h*} = \Lambda/(1 - \alpha^h)$ globally, as $t \rightarrow \infty$.

5.2 Discrete-time malaria transmission model

We then consider the transmission dynamics of malaria between mosquitoes and humans. We divide the mosquito population into groups of susceptible, latent, and infective individuals. Since the mosquito lifespan is usually shorter than their infective period, we assume that there is no group of recovered mosquitoes, and denote the numbers of susceptible, latent, and infective mosquitoes at time t by $S^v(t)$, $E^v(t)$, and $I^v(t)$, respectively. Let $\lambda^v(t)$ be the mosquito infection rate, $\gamma^v(t)$ the rate of incubating individuals becoming infectious, $b^v(t)$ the per capita birth rate, $\alpha^{vb}(t)$, $\alpha^v(t)$, α^{vE} , $\alpha^{vI}(t)$, the survival probabilities of the newborns, susceptible adults, incubating adults, and infective adults, respectively. We assume that the infection has no effects on the birth and all newborns are susceptible. Let $N^v(t) = S^v(t) + E^v(t) + I^v(t)$ be the total population number of mosquitoes. Then the model equations for the mosquitoes are given by

$$\begin{aligned}
S^v(t+1) &= b^v(t)\alpha^{vb}(t)N^v(t) + (1 - \lambda^v(t))S^v(t)\alpha^v(t), \\
E^v(t+1) &= (\lambda^v(t)S^v(t) + (1 - \gamma^v(t))E^v(t))\alpha^{vE}(t), \\
I^v(t+1) &= (\gamma^v(t)E^v(t) + I^v(t))\alpha^{vI}(t).
\end{aligned} \tag{5.2.1}$$

We note that as we describe the model dynamics from t to $t+1$, we mean from time t to the next time step. The time step plays an important role in our model formulation. For example, if the time step is larger than the incubating period, no exposed individuals at time t will stay in this class at time $t+1$. On the other hand, if the time step is shorter than the incubating period, a certain proportion of exposed individuals will survive but have not become infectious so that they will stay in the E^v class. To make our model formulation in a more general setting, we keep the terms for those retaining individuals.

We then divide the human population into groups of susceptible, latent or incubating, infective, and recovered individuals. Here the latent or incubating period is defined as the time from the initial infection to the appearance of gametocytes in the blood [18]. The infection dynamics among humans during the same period of time are relatively simpler than the dynamics among mosquitoes. Then let $S^h(t)$ be the number of susceptible humans, $E^h(t)$ the number of latent or incubating humans, who are infected but not infectious yet, $I^h(t)$ the number of infective humans, who are infected and also infectious, $R^h(t)$ the number of the humans who are recovered from infection

but partly lose immunity [29–32], and $N^h(t) = S^h(t) + E^h(t) + I^h(t) + R^h(t)$, at time t . We assume the susceptible, latent, and recovered humans have the same survival probability α^h , but the infectives have survival probability $\alpha^{hI} \leq \alpha^h$. The model equations for humans are given by

$$\begin{aligned}
S^h(t+1) &= \Lambda + ((1 - \lambda^h(t))S^h(t) + \theta^h R^h(t)) \alpha^h, \\
E^h(t+1) &= (\lambda^h(t)S^h(t) + (1 - \gamma^h)E^h(t)) \alpha^h, \\
I^h(t+1) &= (\gamma^h E^h(t) + (1 - \eta^h)I^h(t)) \alpha^{hI}, \\
R^h(t+1) &= (\eta^h I^h(t) + (1 - \theta^h)R^h(t)) \alpha^h.
\end{aligned} \tag{5.2.2}$$

where γ^h is the developing rate of incubating humans to become infectious, such that $1/\gamma^h$ is the incubation period, η^h is the recovery rate for infectious humans, and θ^h is the rate of partial immunity loss.

The infection rates in the malaria model given by (5.2.1) and (5.2.2), are determined as follows.

We let r be the number of average bites by a single mosquito on all human hosts, and β^h be the transmission probability per bite to a mosquito from an infective human. Then the infection rate for mosquitoes is given by

$$\lambda^v(t) = \beta^h r \frac{I^h(t)}{N^h(t)}, \tag{5.2.3}$$

where we assume $\beta^h r < 1$. Similarly, the infection rate for humans is given by

$$\lambda^h(t) = \beta^v r' \frac{I^v(t)}{N^v(t)},$$

where β^v is the transmission probability from an infective mosquito to a susceptible human per infected bite and r' is the average bites on a human host by all mosquitoes.

Notice that r and r' need to satisfy the following balance constraint

$$rN^v(t) = r'N^h(t).$$

Hence the infection rate for humans becomes

$$\lambda^h(t) = \beta^v r \frac{N^v(t)}{N^h(t)} \frac{I^v(t)}{N^v(t)} = \beta^v r \frac{I^v(t)}{N^h(t)}, \quad (5.2.4)$$

where as assume $\beta^v r < 1$.

5.3 Constant birth rate and survival rates for incubating and infective mosquitoes

We only consider a simple case where it is assumed that b^v , α^{vE} , α^{vI} and γ^v are all constants. We rewrite system (5.2.1) and (5.2.2) as

$$\begin{aligned}
E^v(t+1) &= (\lambda^v(t)S^v(t) + (1 - \gamma^v(t))E^v(t))\alpha^{vE}(t), \\
I^v(t+1) &= (\gamma^v(t)E^v(t) + I^v(t))\alpha^{vI}(t), \\
E^h(t+1) &= (\lambda^h(t)S^h(t) + (1 - \gamma^h(t))E^h(t))\alpha^h, \\
I^h(t+1) &= (\gamma^h(t)E^h(t) + (1 - \eta^h(t))I^h(t))\alpha^{hI}, \\
S^v(t+1) &= b^v(t)\alpha^{vb}(t)N^v(t) + (1 - \lambda^v(t))S^v(t)\alpha^v(t), \\
S^h(t+1) &= \Lambda + ((1 - \lambda^h(t))S^h(t) + \theta^h R^h(t))\alpha^h, \\
R^h(t+1) &= (\eta^h(t)I^h(t) + (1 - \theta^h(t))R^h(t))\alpha^h.
\end{aligned} \tag{5.3.1}$$

5.3.1 The infection-free equilibrium and reproductive number

The unique infection-free equilibrium to system (5.3.1) given by

$$(E^v, I^v, E^h, I^h, S^v, S^h, R^h) = (0, 0, 0, 0, S_0^v, S_0^h, 0), \tag{5.3.2}$$

where $S_0^v = N^{v*}$ as the same in (5.1.5) and $S_0^h = N^{h*} = \frac{\Lambda}{1-\alpha^h}$ as the same in (5.1.7).

For system (5.3.1) we use the next generation matrix approach to calculate the reproductive number R_0 [86, 88] as follows.

The Jacobian matrix J evaluated at the infection-free equilibrium is

$$J = \begin{pmatrix} F + T & 0 \\ J_{21} & C \end{pmatrix},$$

where

$$F = \begin{pmatrix} 0 & 0 & 0 & \frac{\alpha^{vE} \beta^h r S_0^v}{S_0^h} \\ 0 & 0 & 0 & 0 \\ 0 & \alpha^h \beta^v r & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$T = \begin{pmatrix} (1 - \gamma^v) \alpha^{vE} & 0 & 0 & 0 \\ \alpha^{vI} \gamma^v & \alpha^{vI} & 0 & 0 \\ 0 & 0 & (1 - \mu^h) \alpha^h & 0 \\ 0 & 0 & \alpha^h I \gamma^h & (1 - \eta^h) \alpha^{hI} \end{pmatrix},$$

$$J_{21} = \begin{pmatrix} \frac{b^v k_0^v}{(1 + \eta_0^v S_0^v)^2} - \frac{\eta_1^v k_1^v S_0^h}{(1 + \eta_1^v S_0^v)^2} & \frac{b^v k_0^v}{(1 + \eta_0^v S_0^v)^2} - \frac{\eta_1^v k_1^v S_0^h}{(1 + \eta_1^v S_0^v)^2} & 0 & -\frac{\beta^h r k_1 S_0^v}{S_0^h (1 + \eta_1^v S_0^v)} \\ 0 & -\alpha^h \beta^v r & 0 & 0 \\ 0 & 0 & 0 & \alpha^h \eta^h \end{pmatrix},$$

and

$$C = \begin{pmatrix} \frac{b^v k_0^v}{(1 + \eta_0^v S_0^v)^2} + \frac{k_1^v}{(1 + \eta_1^v S_0^v)^2} & 0 & 0 \\ 0 & \alpha^h & \alpha^h \theta^h \\ 0 & 0 & (1 - \theta^h) \alpha^h \end{pmatrix}.$$

To determine the spectral radius of the next generation matrix, we first have the following lemma.

Lemma 5.3.1.

$$\frac{b^v k_0^v}{(1 + \eta_0^v S_0^v)^2} + \frac{k_1^v}{(1 + \eta_1^v S_0^v)^2} < 1$$

Proof. Since $S_0^v > 0$ satisfies equation

$$\frac{b^v k_0^v}{1 + \eta_0^v S_0^v} + \frac{k_1^v}{1 + \eta_1^v S_0^v} = 1$$

and $\eta_0^v > 0, \eta_1^v > 0$, then

$$\begin{aligned} 0 &< \frac{b^v k_0^v}{(1 + \eta_0^v S_0^v)^2} + \frac{k_1^v}{(1 + \eta_1^v S_0^v)^2} \\ &= \frac{1}{1 + \eta_0^v S_0^v} \frac{b^v k_0^v}{1 + \eta_0^v S_0^v} + \frac{1}{1 + \eta_1^v S_0^v} \frac{k_1^v}{1 + \eta_1^v S_0^v} \\ &< \frac{b^v k_0^v}{1 + \eta_0^v S_0^v} + \frac{k_1^v}{1 + \eta_1^v S_0^v} = 1, \end{aligned}$$

which completes the proof. □

Since $0 < \gamma^v < 1$, $0 < \alpha^{vE} < 1$, $0 < \alpha^h < 1$, $0 < \eta^h < 1$, $0 < \theta^h < 1$, and $0 < \alpha^{hI} < 1$, hence, the spectral radii $\rho(T) < 1$ and $\rho(C) < 1$

For matrix T , the inverse matrix $(I - T)^{-1}$ is

$$(I - T)^{-1} = \begin{pmatrix} \frac{1}{1-(1-\gamma^v)\alpha^{vE}} & 0 & 0 & 0 \\ \frac{\alpha^{vI}\gamma^v}{(1-\alpha^{vI})(1-(1-\gamma^v)\alpha^{vE})} & \frac{1}{1-\alpha^{vI}} & 0 & 0 \\ 0 & 0 & \frac{1}{1-(1-\gamma^h)\alpha^h} & 0 \\ 0 & 0 & \frac{\alpha^{hI}\gamma^h}{(1-(1-\gamma^h)\alpha^h)(1-(1-\eta^h)\alpha^{hI})} & \frac{1}{(1-(1-\eta^h)\alpha^{hI})} \end{pmatrix}.$$

Then the next generation matrix

$$Q = F(I - T)^{-1} = \begin{pmatrix} 0 & 0 & \frac{\alpha^{hI}\gamma^h\alpha^{vE}\beta^h r \gamma^h S_0^v}{(1-(1-\gamma^h)\alpha^h)(1-(1-\eta^h)\alpha^{hI})S_0^h} & \frac{\alpha^{vE}\beta^h r S_0^v}{(1-(1-\eta^h)\alpha^{hI})S_0^h} \\ 0 & 0 & 0 & 0 \\ \frac{\alpha^h\beta^v r \alpha^{vI}\gamma^v}{(1-(1-\gamma^v)\alpha^{vE})(1-\alpha^{vI})} & \frac{\alpha^h\beta^v r}{1-\alpha^{vI}} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

has its the characteristic equation

$$\det(\lambda I - Q) = \lambda^2 \left(\lambda^2 - \frac{\alpha^h\alpha^{hI}\alpha^{vE}\alpha^{vI}\beta^h\beta^v r^2 \gamma^h \gamma^v S_0^v}{(1-(1-\gamma^v)\alpha^{vE})(1-\alpha^{vI})(1-(1-\gamma^h)\alpha^h)(1-(1-\eta^h)\alpha^{hI})S_0^h} \right).$$

Define the reproductive number of infection R_0 for system (5.3.1) by

$$R_0 := \sqrt{\frac{\alpha^h\alpha^{hI}\alpha^{vE}\alpha^{vI}\beta^h\beta^v r^2 \gamma^h \gamma^v S_0^v}{(1-(1-\gamma^v)\alpha^{vE})(1-\alpha^{vI})(1-(1-\gamma^h)\alpha^h)(1-(1-\eta^h)\alpha^{hI})S_0^h}}. \quad (5.3.3)$$

We then have the following results.

Theorem 5.3.2. *The infection-free equilibrium of system (5.3.1), given in (5.3.2), is locally asymptotically stable if the basic reproductive number $R_0 < 1$, and is unstable if $R_0 > 1$.*

5.3.2 Endemic equilibria

We only study the existence of endemic equilibria in this section.

The components of the endemic equilibrium need to satisfy the following equations:

$$\begin{aligned}
S^v &= b^v \alpha^{vb}(t) N^v + (1 - \lambda^v(t)) S^v \alpha^v(t), \\
E^v &= (\lambda^v(t) S^v + (1 - \gamma^v) E^v) \alpha^{vE}, \\
I^v &= (\gamma^v E^v + I^v) \alpha^{vI}, \\
S^h &= \Lambda + ((1 - \lambda^h(t)) S^h + \theta^h R^h) \alpha^h, \\
E^h &= (\lambda^h(t) S^h + (1 - \gamma^h) E^h) \alpha^h, \\
I^h &= (\gamma^h E^h + (1 - \eta^h) I^h) \alpha^{hI}, \\
R^h &= (\eta^h I^h + (1 - \theta^h) R^h) \alpha^h,
\end{aligned} \tag{5.3.4}$$

where $\alpha^{vb}(t)$ and $\alpha^v(t)$ are given in (5.1.2).

Solving the last three equations in (5.3.4) in terms of S^h , we have

$$\begin{aligned}
E^h &= \frac{\alpha^h \lambda^h S^h}{1 - (1 - \gamma^h) \alpha^h}, \\
I^h &= \frac{\alpha^{hI} \gamma^h E^h}{1 - (1 - \eta^h) \alpha^h} = \frac{\alpha^{hI} \gamma^h \alpha^h \lambda^h S^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})} \\
R^h &= \frac{\alpha^h \eta^h I^h}{1 - (1 - \theta^h) \alpha^h} = \frac{(\alpha^h)^2 \alpha^{hI} \eta^h \gamma^h \lambda^h S^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})(1 - (1 - \theta^h) \alpha^h)}.
\end{aligned} \tag{5.3.5}$$

Substituting (5.3.5) into the fourth equation in (5.3.4), we get the equation about S^h

$$S^h = \Lambda + \left((1 - \lambda^h(t)) S^h + \frac{(\alpha^h)^2 \alpha^{hI} \eta^h \gamma^h \lambda^h S^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})(1 - (1 - \theta^h) \alpha^h)} \right) \alpha^h.$$

Solving S^h , in terms of λ^h , we obtain

$$S^h = \frac{\Lambda}{1 - \alpha^h + A \lambda^h},$$

where

$$A := \alpha^h - \frac{(\alpha^h)^3 \alpha^{hI} \gamma^h \eta^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})(1 - (1 - \theta^h) \alpha^h)} > 0.$$

Substituting it into the other equations in (5.3.4), we have

$$\begin{aligned}
S^h &= \frac{\Lambda}{1 - \alpha^h + A \lambda^h}, \\
E^h &= \frac{\alpha^h \lambda^h}{1 - (1 - \gamma^h) \alpha^h} \frac{\Lambda}{1 - \alpha^h + A \lambda^h},
\end{aligned}$$

$$\begin{aligned}
I^h &= \frac{\lambda^h \alpha^{hI} \gamma^h \lambda^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})} \frac{\Lambda}{1 - \alpha^h + A \lambda^h}, \\
R^h &= \frac{(\alpha^h)^2 \alpha^{hI} \eta^h \gamma^h \lambda^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})(1 - (1 - \theta^h) \alpha^h)} \frac{\Lambda}{1 - \alpha^h + A \lambda^h},
\end{aligned} \tag{5.3.6}$$

and thus

$$\begin{aligned}
N^h &= S^h + E^h + I^h + R^h \\
&= \frac{\Lambda}{1 - \alpha^h + A \lambda^h} + \frac{\alpha^h \lambda^h}{1 - (1 - \gamma^h) \alpha^h} \frac{\Lambda}{1 - \alpha^h + A \lambda^h} \\
&\quad + \frac{\lambda^h \alpha^{hI} \gamma^h \lambda^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})} \frac{\Lambda}{1 - \alpha^h + A \lambda^h} \\
&\quad + \frac{(\alpha^h)^2 \alpha^{hI} \eta^h \gamma^h \lambda^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})(1 - (1 - \theta^h) \alpha^h)} \frac{\Lambda}{1 - \alpha^h + A \lambda^h} \\
&= \frac{\Lambda}{1 - \alpha^h + A \lambda^h} \times \left(1 + \frac{(1 - (1 - \theta^h) \alpha^h)[(1 - (1 - \eta^h) \alpha^{hI}) \alpha^h + \gamma^h \alpha^{hI} \eta^h] + (\alpha^h)^2 \alpha^{hI} \eta^h \gamma^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})(1 - (1 - \theta^h) \alpha^h)} \lambda^h \right) \\
&= \frac{\Lambda}{1 - \alpha^h + A \lambda^h} (1 + B \lambda^h),
\end{aligned} \tag{5.3.7}$$

where

$$B := \frac{(1 - (1 - \theta^h) \alpha^h)[(1 - (1 - \eta^h) \alpha^{hI}) \alpha^h + \gamma^h \alpha^{hI} \eta^h] + (\alpha^h)^2 \alpha^{hI} \eta^h \gamma^h}{(1 - (1 - \eta^h) \alpha^h)(1 - (1 - \gamma^h) \alpha^{hI})(1 - (1 - \theta^h) \alpha^h)}.$$

Similarly, solving the second and third equations of (5.3.4), in terms of S^v , we have

$$E^v = \frac{\alpha^{vE} \lambda^v S^v}{1 - (1 - \gamma^v) \alpha^{vE}}, \quad I^v = \frac{\gamma^v \alpha^{vI} E^v}{1 - \alpha^{vI}} = \frac{\alpha^{vE} \alpha^{vI} \gamma^v \lambda^v S^v}{(1 - \alpha^{vI}(1 - (1 - \gamma^v) \alpha^{vE}))}. \tag{5.3.8}$$

Substituting (5.3.8) into the first equation in (5.3.4), we obtain

$$S^v = \frac{b^v k_0^v \left(S^v + \frac{\alpha^{vE} \lambda^v S^v}{1-(1-\gamma^v)\alpha^{vE}} + \frac{\alpha^{vE} \alpha^{vI} \gamma^v \lambda^v S^v}{(1-\alpha^{vI})(1-(1-\gamma^v)\alpha^{vE})} \right)}{1 + \eta_0^v \left(S^v + \frac{\alpha^{vE} \lambda^v S^v}{1-(1-\gamma^v)\alpha^{vE}} + \frac{\alpha^{vE} \alpha^{vI} \gamma^v \lambda^v S^v}{(1-\alpha^{vI})(1-(1-\gamma^v)\alpha^{vE})} \right)} + \frac{(1-\lambda^v)k_1^v S^v}{1 + \eta_1^v \left(S^v + \frac{\alpha^{vE} \lambda^v S^v}{1-(1-\gamma^v)\alpha^{vE}} + \frac{\alpha^{vE} \alpha^{vI} \gamma^v \lambda^v S^v}{(1-\alpha^{vI})(1-(1-\gamma^v)\alpha^{vE})} \right)},$$

which leads to

$$1 = \frac{b^v k_0^v \left(1 + \frac{\alpha^{vE} \lambda^v}{1-(1-\gamma^v)\alpha^{vE}} + \frac{\alpha^{vE} \alpha^{vI} \gamma^v \lambda^v}{(1-\alpha^{vI})(1-(1-\gamma^v)\alpha^{vE})} \right)}{1 + \eta_0^v \left(S^v + \frac{\alpha^{vE} \lambda^v S^v}{1-(1-\gamma^v)\alpha^{vE}} + \frac{\alpha^{vE} \alpha^{vI} \gamma^v \lambda^v S^v}{(1-\alpha^{vI})(1-(1-\gamma^v)\alpha^{vE})} \right)} + \frac{(1-\lambda^v)k_1^v}{1 + \eta_1^v \left(S^v + \frac{\alpha^{vE} \lambda^v S^v}{1-(1-\gamma^v)\alpha^{vE}} + \frac{\alpha^{vE} \alpha^{vI} \gamma^v \lambda^v S^v}{(1-\alpha^{vI})(1-(1-\gamma^v)\alpha^{vE})} \right)}. \quad (5.3.9)$$

Write

$$C := 1 + \left(\frac{\alpha^{vE}}{1-(1-\gamma^v)\alpha^{vE}} + \frac{\alpha^{vE} \alpha^{vI}}{(1-\alpha^{vI})(1-(1-\gamma^v)\alpha^{vE})} \right) \lambda^v \\ = 1 + \frac{(1-\alpha^{vI})\alpha^{vE} + \alpha^{vE} \alpha^{vI}}{(1-\alpha^{vI})(1-(1-\gamma^v)\alpha^{vE})} \lambda^v.$$

Then equation (5.3.9) can be written as

$$1 = \frac{b^v k_0^v C}{1 + \eta_0^v C S^v} + \frac{(1-\lambda^v)k_1^v}{1 + \eta_1^v C S^v}.$$

Letting $z = C S^v$, we have

$$1 = \frac{b^v k_0^v C}{1 + \eta_0^v z} + \frac{(1-\lambda^v)k_1^v}{1 + \eta_1^v z}.$$

Hence,

$$(1 + \eta_0^v z)(1 + \eta_1^v z) = b^v k_0^v C(1 + \eta_1^v z) + (1 - \lambda^v) k_1^v (1 + \eta_0^v z),$$

i.e.,

$$\eta_0^v \eta_1^v z^2 - ((b^v k_0^v C - 1)\eta_1^v + ((1 - \lambda^v)k_1^v - 1)\eta_0^v)z - (b^v k_0^v C + (1 - \lambda^v)k_1^v - 1) = 0. \quad (5.3.10)$$

If there exists a positive root z to equation (5.3.10), there exists a positive S^v .

It follows from

$$\begin{aligned} b^v k_0^v C + (1 - \lambda^v)k_1^v - 1 &= b^v k_0^v \left(1 + \frac{(1 - \alpha^{vI})\alpha^{vE} + \alpha^{vE}\alpha^{vI}}{(1 - \alpha^{vI})(1 - (1 - \gamma^v)\alpha^{vE})} \lambda^v \right) + k_1^v - k_1^v \lambda^v - 1 \\ &= (b^v k_0^v + k_1^v - 1) + \left(\frac{b^v k_0^v (1 - \alpha^{vI})\alpha^{vE} + \alpha^{vE}\alpha^{vI}}{(1 - \alpha^{vI})(1 - (1 - \gamma^v)\alpha^{vE})} - k_1^v \right) \lambda^v, \end{aligned}$$

that if we assume

$$\frac{b^v k_0^v ((1 - \alpha^{vI})\alpha^{vE} + \alpha^{vE}\alpha^{vI})}{(1 - \alpha^{vI})(1 - (1 - \gamma^v)\alpha^{vE})} - k_1^v > 0,$$

that is,

$$b^v k_0^v ((1 - \alpha^{vI})\alpha^{vE} + \alpha^{vE}\alpha^{vI}) > k_1^v ((1 - \alpha^{vI})(1 - (1 - \gamma^v)\alpha^{vE})), \quad (A)$$

then, if we assume, in addition, $b^v k_0^v + k_1^v - 1 > 0$, we have $b^v k_0^v C + (1 - \lambda^v)k_1^v - 1 > 0$,

which implies that equation (5.3.10) has a unique positive root:

$$z = \frac{B_1^v + \sqrt{\Delta_1^v}}{2\eta_0^v \eta_1^v},$$

where

$$B_1^v = (b^v k_0^v C - 1)\eta_1^v + ((1 - \lambda^v)k_1^v - 1)\eta_0^v$$

and

$$\Delta_1^v = ((b^v k_0^v C - 1)\eta_1^v + ((1 - \lambda^v)k_1^v - 1)\eta_0^v)^2 + 4\eta_0^v \eta_1^v (b^v k_0^v C + (1 - \lambda^v)k_1^v - 1) > 0.$$

Substituting (5.3.8), (5.3.6) and (5.3.7) into (5.2.3) and (5.2.4), respectively, we obtain

$$\lambda^v = \frac{\beta^h r I_h}{N^h} = \frac{\alpha^h \alpha^{hI} \beta^h r \gamma^h \lambda^h}{(1 - (1 - \eta^h)\alpha^{hI})(1 - (1 - \gamma^h)\alpha^h)(1 + B\lambda^h)} \quad (5.3.11)$$

and

$$\lambda^h = \frac{\beta^v r I^v}{N^h} = \frac{\alpha^{vE} \alpha^{vI} \beta^v r \gamma^v \lambda^v S^v ((1 - \alpha^h) + A\lambda^h)}{(1 - \alpha^{vI})(1 - (1 - \gamma^v)\alpha^{vE})\Lambda(1 + B\lambda^h)}. \quad (5.3.12)$$

Clearly, $\lambda^v = 0$ if and only if $\lambda^h = 0$.

Substituting (5.3.11) into (5.3.12), we obtain

$$\lambda^h = \frac{\alpha^{vE} \alpha^{vI} \beta^v r \gamma^v \frac{\alpha^h \alpha^{hI} \beta^h r \gamma^h \lambda^h}{(1 - (1 - \eta^h)\alpha^{hI})(1 - (1 - \gamma^h)\alpha^h)(1 + B\lambda^h)} S_0^v ((1 - \alpha^h) + A\lambda^h)}{(1 - \alpha^{vI})(1 - (1 - \gamma^v)\alpha^{vE})\Lambda(1 + B\lambda^h)},$$

i.e.,

$$1 = \frac{\alpha^h \alpha^{hI} \alpha^{vE} \alpha^{vI} \beta^h \beta^v \gamma^h \gamma^v r^2 S_0^v}{(1 - \alpha^{vI})(1 - (1 - \gamma^v)\alpha^{vE})(1 - (1 - \eta^h)\alpha^{hI})(1 - (1 - \gamma^h)\alpha^h)S_0^h}$$

$$\times \frac{1 - \alpha^h + A\lambda^h}{(1 - \alpha^h)(1 + B\lambda^h)^2} = R_0^2 \times \frac{1 - \alpha^h + A\lambda^h}{(1 - \alpha^h)(1 + B\lambda^h)^2}. \quad (5.3.13)$$

Hence, there exists an endemic equilibrium if there exists a positive solution λ^h to equation (5.3.13).

Define function

$$H(\lambda^h) = R_0^2 \times \frac{1 - \alpha^h + A\lambda^h}{(1 - \alpha^h)(1 + B\lambda^h)^2} - 1. \quad (5.3.14)$$

Then there exists an endemic equilibrium for model (5.2.1) and (5.2.2) if and only if there is a positive solution to the equation $H(\lambda^h) - 1 = 0$.

Since

$$H(0) = R_0^2 - 1, \quad \lim_{\lambda^h \rightarrow \infty} H(\lambda^h) = -1$$

then, there exists an endemic equilibrium if $R_0 > 1$. In summary we have the existence result.

Theorem 5.3.3. *Under assumption (A) and $b^v k_0^v + k_1^v > 1$, system (5.2.1) and (5.2.2) has an endemic equilibrium if the basic reproductive number $R_0 > 1$.*

Unfortunately, it does not seem mathematically tractable to determine the stability of the endemic equilibrium analytically.

CHAPTER 6

DISCRETE-TIME MOSQUITO-STAGE-STRUCTURED MALARIA MODELS

As is well known, discrete-time models can have very rich dynamics and can exhibit chaotic behavior. Analysis for higher dimensional discrete-time models therefore becomes a mathematical challenge. Incorporating the discrete-time stage-structured mosquito populations into the malaria models we study in Chapters 5 and 6, respectively, we formulate a discrete-time mosquito-stage-structured malaria model in this chapter.

6.1 The model formulation

Using the same notations as in Chapters 5 and 6, we denote the numbers of mosquito eggs, pupae, larvae, at time t , as $E(t)$, $L(t)$, $P(t)$, the numbers of susceptible, exposed, infective mosquitoes as $S^v(t)$, $E^v(t)$, $I^v(t)$, and the numbers of susceptible, exposed, infective, recovered humans as $S^h(t)$, $E^h(t)$, $I^h(t)$, $R^h(t)$, respectively.

Then the dynamics of the malaria transmission with the stage-structured mosquitoes are then described by the following system:

$$\begin{aligned}
E(t+1) &= bs_0N^v(t), \\
L(t+1) &= s_e(L(t))E(t), \\
P(t+1) &= s_l(L(t))L(t), \\
S^v(t+1) &= s_pP(t) + s_v(N^v(t))N^v(t) + (1 - \lambda^v(t))S^v(t)\alpha^v(t), \\
E^v(t+1) &= (\lambda^v(t)S^v(t) + (1 - \gamma^v(t))E^v(t))\alpha^v(t), \\
I^v(t+1) &= (\gamma^v(t)E^v(t) + I^v(t))\alpha^v(t), \\
S^h(t+1) &= \Lambda + ((1 - \lambda^h(t))S^h(t) + \theta^h R^h(t))\alpha^h, \\
E^h(t+1) &= (\lambda^h(t)S^h(t) + (1 - \gamma^h(t))E^h(t))\alpha^h, \\
I^h(t+1) &= (\gamma^h(t)E^h(t) + (1 - \eta^h(t))I^h(t))\alpha^{hI}, \\
R^h(t+1) &= (\eta^h(t)I^h(t) + (1 - \theta^h)R^h(t))\alpha^h.
\end{aligned} \tag{6.1.1}$$

where, similarly as in Chapters 4 and 5, $\lambda^v(t)$ is the mosquito infection rate, $\gamma^v(t)$ is the rate of incubating individuals becoming infectious, $b^v(t)$ is the per capita birth rate, s_i , $i = 0, e, l, p$, are the development rates of mosquitoes, $\alpha^v(t)$ is the survival probability of mosquitoes, α^h is survival probability of susceptible, latent, and recovered humans, α^{hI} is the survival probability of infectious humans, with $\alpha^{hI} \leq \alpha^h$, γ^h is the progression rate of incubating humans to become infectious, η^h is the recovery rate for infectious humans, and θ^h is the rate of partial immunity loss.

The infection rate for mosquitoes is given by

$$\lambda^v(t) = \beta^h r \frac{I^h(t)}{N^h(t)}, \quad (6.1.2)$$

and infection rate for humans is given by

$$\lambda^h(t) = \beta^v r \frac{I^v(t)}{N^h(t)}, \quad (6.1.3)$$

where r is the number of average bites by a single mosquito on all human hosts, β^h the transmission probability per bite to a mosquito from an infective human, β^v the transmission probability from an infective mosquito to a susceptible human per infected bite.

The total populations of mosquitoes and humans are

$$N^v(t) = S^v(t) + E^v(t) + I^v(t), \quad N^h(t) = S^h(t) + E^h(t) + I^h(t) + R^h(t),$$

respectively.

We only consider the case where the mosquitoes survival probability of $\alpha^v(t) := \alpha^v$ is constant, but assume the survival probabilities $s_i(z)$, $i = 0, e, l, v$, satisfy the following conditions (A1).

$$\begin{aligned}
s_i(z) &\in C^1[0, \infty), \quad s_i(0) := \alpha_i, \quad 0 < \alpha_i \leq 1, \quad s'_i(z) \leq 0, \quad (s_i(z)z)' > 0, \\
\lim_{z \rightarrow \infty} s_i(z) &= 0, \quad \lim_{z \rightarrow \infty} s_i(z)z := k_i, \quad 0 < k_i < \infty, \quad 0 < s_m(0) + \alpha^v \leq 1.
\end{aligned} \tag{A1}$$

System (6.1.1) is well defined. Indeed, Adding the equations for S^v , E^v and I^v in (6.1.1) together, we have $N^v(t+1) = s_p P(t) + (s_v(N^v(t)) + \alpha^v)N^v(t)$, which together with the first three equations in (6.1.1) leads to the following closed system:

$$\begin{aligned}
E(t+1) &= bs_0 N^v(t), \\
L(t+1) &= s_e(L(t))E(t), \\
P(t+1) &= s_l(L(t))L(t), \\
N^v(t+1) &= s_p P(t) + (s_v(N^v(t)) + \alpha^v)N^v(t).
\end{aligned} \tag{6.1.4}$$

Let $x(t) := (E(t), L(t), P(t), M(t))^T$. System (6.1.4) can be written as in the following matrix form:

$$x(t+1) = J_1(x(t))x(t), \tag{6.1.5}$$

where the projection matrix $J_1(x)$ is given by

$$J_1(x) = \begin{pmatrix} 0 & 0 & 0 & bs_0 \\ s_e(L) & 0 & 0 & 0 \\ 0 & s_l(L) & 0 & 0 \\ 0 & 0 & s_p & s_v(N^v) + \alpha^v \end{pmatrix}.$$

Similarly as in Chapter 4, we derive the inherent net reproductive number of mosquitoes as

$$r_0 = \frac{bs_0s_e(0)s_l(0)s_p}{1 - (s_v(0) + \alpha^v)},$$

and obtain the following results for system (6.1.4). The proofs are similar to those in Chapter 4, and hence we omit them.

Theorem 6.1.1. *Every solution $(E(t), L(t), P(t), N^v(t))^T$ of (6.1.4) with its initial value in $\mathbb{R}_+^4 \setminus \{0\}$ is defined and lies in $\text{int}(\mathbb{R}_+^4)$ for all $t > 0$. Moreover,*

(i) *if $r_0 < 1$, the unique trivial equilibrium $(0, 0, 0, 0)^T$ of (6.1.4) is globally asymptotically stable;*

(ii) *if $r_0 > 1$, the trivial equilibrium is unstable, and there exists a unique positive equilibrium $E_1 = (E^*, L^*, P^*, N^{v*})^T$ of (6.1.4), where the components satisfy*

$$1 = bs_0s_ps_e(L(N^{v*}))s_l(L(N^{v*})) + s_v(N^{v*}) + \alpha^v$$

$$\begin{aligned}
E^* &= bs_0 N^{v*}, \\
L^* &= s_e(L(\bar{N}^{v*})) \cdot bs_0 N^{v*} \\
P^* &= s_l(L(N^{v*})) \cdot s_e(L(N^{v*})) \cdot bs_0 N^{v*}.
\end{aligned} \tag{6.1.6}$$

The positive equilibrium is locally asymptotically stable in $\mathbb{R}_+^4 \setminus \{0\}$, if either the condition

$$s'_e(L)bs_0 N^{v*} + ((s_v(N^{v*}) + \alpha^v)N^{v*})' > 0 \tag{A2}$$

holds, or the condition

$$\begin{aligned}
0 &< -s'_e(L^*)bs_0 N^{v*} - ((s_v(N^{v*}) + \alpha^v)N^{v*})' \\
&< s_v(N^{v*}) - bs_0 s_p s_e s'_l(L^*) + s'_e(L^*)bs_0 N^{v*}((s_v(N^{v*}) + \alpha^v)N^{v*})'
\end{aligned} \tag{A3}$$

is satisfied, where E^*, L^*, P^* , and N^{v*} are the components of the positive equilibrium E_1 .

We then study the dynamics of the infection-free equilibrium of system (6.1.1) and derive a formula for the reproductive number.

System (6.1.1) can be rewritten as follows.

$$\begin{aligned}
E(t+1) &= bs_0 N^v(t), \\
L(t+1) &= s_e(L(t))E(t), \\
P(t+1) &= s_l(L(t))L(t),
\end{aligned}$$

$$\begin{aligned}
S^v(t+1) &= s_p P(t) + s_v(N^v(t))N^v(t) + (1 - \lambda^v(t))S^v(t)\alpha^v, \\
S^h(t+1) &= \Lambda + ((1 - \lambda^h(t))S^h(t) + \theta^h R^h(t))\alpha^h, \\
R^h(t+1) &= (\eta^h I^h(t) + (1 - \theta^h)R^h(t))\alpha^h, \\
E^v(t+1) &= (\lambda^v(t)S^v(t) + (1 - \gamma^v(t))E^v(t))\alpha^v, \\
I^v(t+1) &= (\gamma^v(t)E^v(t) + I^v(t))\alpha^v, \\
E^h(t+1) &= (\lambda^h(t)S^h(t) + (1 - \gamma^h(t))E^h(t))\alpha^h, \\
I^h(t+1) &= (\gamma^h(t)E^h(t) + (1 - \eta^h)I^h(t))\alpha^h.
\end{aligned} \tag{6.1.7}$$

The infection-free equilibrium is given by

$$\mathcal{E}_0 = (E^*, L^*, P^*, N^{v*}, S_0^h, 0, 0, 0, 0, 0),$$

where $E^*, L^*, P^*, N^{v*} = S_0^v$ satisfy (6.1.6) and $S_0^h = \frac{\Lambda}{1-\alpha^h}$. The Jacobian matrix of the system (6.1.7) at the infection-free equilibrium \mathcal{E}_0 has the form of

$$J_0 = \begin{pmatrix} J_{11} & 0 & J_{13} \\ 0 & J_{22} & J_{23} \\ 0 & 0 & J_{33} \end{pmatrix},$$

where

$$J_{11} := Df(E^*, L^*, P^*, N_v^*) = \begin{pmatrix} 0 & 0 & 0 & bs_0 \\ s_e(L^*) & s'_e(L^*)E^* & 0 & 0 \\ 0 & (s_l(L^*)L^*)' & 0 & 0 \\ 0 & 0 & s_P & ((s_v(N^{v*}) + \alpha^v)N^{v*})' \end{pmatrix},$$

is the Jacobian matrix of system (6.1.4) at the positive equilibrium (E^*, L^*, P^*, N_v^*) ,

$$J_{13} = \begin{pmatrix} bs_0 & bs_0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\frac{\beta_h r N^{v*}}{S_0^h} \end{pmatrix},$$

$$J_{22} = \begin{pmatrix} \alpha^h & \theta^h \alpha^h \\ 0 & (1 - \theta^h) \alpha^h \end{pmatrix},$$

$$J_{23} = \begin{pmatrix} 0 & -\beta^v r \alpha^h & 0 & 0 \\ 0 & 0 & 0 & \eta^h \alpha^h \end{pmatrix},$$

$$J_{33} = \begin{pmatrix} (1 - \gamma^v)\alpha^v & 0 & 0 & \frac{\alpha^v \beta^h r N^{v*}}{S_0^h} \\ \alpha^v \gamma^v & \alpha^v & 0 & 0 \\ 0 & \alpha^h \beta^v r & (1 - \gamma^h)\alpha^h & 0 \\ 0 & 0 & \alpha^h I \gamma^h & (1 - \eta^h)\alpha^{hI} \end{pmatrix} := F + T,$$

with

$$F = \begin{pmatrix} 0 & 0 & 0 & \frac{\alpha^v \beta^h r N^{v*}}{S_0^h} \\ 0 & 0 & 0 & 0 \\ 0 & \alpha^h \beta^v r & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$T = \begin{pmatrix} (1 - \gamma^v)\alpha^v & 0 & 0 & 0 \\ \alpha^v \gamma^v & \alpha^v & 0 & 0 \\ 0 & 0 & (1 - \gamma^h)\alpha^h & 0 \\ 0 & 0 & \alpha^h I \gamma^h & (1 - \eta^h)\alpha^{hI} \end{pmatrix}.$$

Hence, the reproductive number is the positive, simple, and strictly dominant eigenvalue of $F(I - T)^{-1}$, denoted by R_0 . With tedious algebra calculation, which is omitted, we derive

$$R_0 = \left(\frac{\alpha^h \alpha^{hI} (\alpha^v)^2 \beta^h \beta^v r^2 \gamma^h \gamma^v N^{v*}}{(1 - (1 - \gamma^v)\alpha^v)(1 - \alpha^v)(1 - (1 - \gamma^h)\alpha^h)(1 - (1 - \eta^h)\alpha^{hI})S_0^h} \right)^{\frac{1}{2}}, \quad (6.1.8)$$

and have the following results.

Theorem 6.1.2. *Assume $r_0 > 1$. The infection-free equilibrium \mathcal{E}_0 is locally asymptotically stable if $R_0 < 1$, and is unstable if $R_0 > 1$.*

We have not been able to determine existence of endemic equilibrium and its stability.

CHAPTER 7

CONCLUSIONS

The spread of mosquito-borne diseases, such as malaria, transmitted between human beings by blood-feeding mosquitoes, has always been a big concern and a threat to public health in the world. It has caused serious problems for the survival of human beings and other species, and for economic and social development of human society. Malaria is by far the world's most important tropical parasitic disease. It is the 5th cause of death from infectious diseases worldwide (after respiratory infections, HIV/AIDS, diarrheal diseases, and tuberculosis), and the 2nd leading cause of death from infectious diseases in Africa, after HIV/AIDS. It is a public health problem today in more than 109 countries and territories inhabited by some 3.3 billion people, and approximately half of the world's population is at risk of malaria, particularly those living in lower-income countries.

The life cycle of the mosquito-borne diseases is complicated. No vaccines are available for these mosquito-borne diseases. To prevent and to control these infectious diseases more effectively, it is important to first fully understand the mechanism of the

spread and the transmission dynamics of the diseases, and then provide useful predictions and guidance so that better strategies can be established.

Mathematical models of mosquito-borne diseases have been proven useful in providing a logical structure within which to incorporate knowledge and test assumptions about the complex dynamics. While there is considerable work on modeling of these diseases, in particular, malaria transmission in the literature, few of them have included the structure of mosquitoes metamorphic stages, and most of the work is focused on continuous-time models.

We formulated, in this dissertation, mosquito-stage-structured malaria models of both continuous- and discrete-time. We started with a continuous-time model (2.2.1) for stage-structured mosquitoes, including the four distinct metamorphic stages as separate compartments in Chapter 2. We included the density-dependence for the birth and survival rates such that the model became nonlinear. To keep our mathematical analysis tractable and due to the fact that interspecific competition, among the first three aquatic stages, could represent a major density dependent source for them, and hence the effect of crowding could be an important factor in the population dynamics of mosquitoes, we assume that density-dependence is only based on the larvae size, and it affects both of the survival rates of larvae and pupae with linear density functions αL and βL , respectively, where $\alpha > 0$ and $\beta > 0$.

For the stage-structured mosquito population model (2.2.1), we derived the inherent net reproductive number, r_0 , of mosquitoes and showed, in Theorem 2.5.1, that

if $r_0 < 1$, the unique trivial equilibrium is globally asymptotically stable which implies the mosquito population goes to extinct regardless of its initial value. If $r_0 > 1$, the trivial equilibrium is unstable and a unique positive equilibrium exists which is globally asymptotically stable such that the mosquito population survives.

Using the malaria disease model in [66] as our baseline model, we incorporated the stage-structured mosquito population into the disease model and formulated a mosquito-stage-structured malaria model (3.2.2) in Chapter 3. After showing the well-posedness of the model biologically and mathematically, we derived a formula for the reproductive number of infection, R_0 , and investigated the existence of the endemic equilibria. As in any epidemiological studies, the infection-free equilibrium is locally asymptotically stable if $R_0 < 1$, and is unstable if $R_0 > 1$. Meanwhile there exists an endemic equilibrium if $R_0 > 1$.

Under the assumption of the inherent net reproductive number of mosquitoes $r_0 > 1$ such that the mosquito population is stabilized in the absence of infection, we further determined a quantity $0 < R_c \leq 1$ and showed that the infection-free equilibrium is globally asymptotically stable if $R_0 < R_c$. Hence, if, in particular, the disease-induced death rate $\delta_h = 0$, the infection-free equilibrium is globally asymptotically stable if $R_0 < 1$. Moreover, if $\delta_h = 0$, we show that the endemic equilibrium is also globally asymptotically stable if $R_0 > 1$. We notice that it may not be appropriate to assume the disease-induced death rate $\delta_h = 0$ for malaria. However, there are other mosquito-borne diseases, such as Chikungunya or Chikungunya fever [46, 51, 52], transmitted by *Aedes*

mosquitoes, that fatalities related to the disease are rare. Our global analysis can be applied to those diseases.

There have been epidemic models in the literature where an unstable positive endemic equilibrium bifurcates through a transcritical bifurcation when the reproductive number is less than one, which is referred to as backward bifurcation [40,45,53,56,59,78]. It has been shown in [66] that a backward bifurcation can occur for our baseline model but the analysis is incomplete. We obtained a more thorough analysis in Chapter 3, derived a formula for the quantity R_b , and gave a complete determination whether a forward or backward bifurcation occurs in Theorem 3.5.3. We then provided numerical simulations in Example (3.5.1) which demonstrates that as the model undergoes a backward bifurcation with the given set of parameters, even with $R_0 < 1$, the disease may die out or spread, depending on the initial infection values. This gives another evidence, as those in the literature with backward bifurcation, that we need to be very cautious in making predictions or any policy guidance based on reducing the reproductive number. Nevertheless, as the existence of backward bifurcation can make disease control more difficult, if the critical value R_b is very close to one, such a backward bifurcation may not be a serious concern for disease control. However, as we showed in Theorem 3.5.1, using δ_h as a determining variable, R_b is a monotone decreasing function of δ_h and approaching R_b^{\min} in (3.5.17), as $\delta_h \rightarrow \infty$. If R_b^{\min} is significantly less than one, it could cause a serious concern as shown in Example (3.5.1) that with different initial infection stages in the population, the disease may die out or spread.

Since the time scales of the lifespan and development of human beings and mosquitoes are significantly different, we formulated discrete-time model (4.2.1) for the mosquito population, including the four distinct stages in Chapter 4. We assume density-dependent vital rates with either the Beverton-Holt form or the Ricker-type form. We also derived the formula for the inherent net reproductive number of mosquitoes, r_0 , for the discrete-time mosquito population model, and determined the global stability of the trivial fixed point as $r_0 < 1$. We showed that if $r_0 > 1$, the trivial equilibrium becomes unstable, is a uniform repeller, and system (4.2.1) is uniformly persistent. In the mean time, there exists a unique positive equilibrium. We also established conditions for the stability of the positive equilibrium. While we are only able to show the local stability of the positive equilibrium for the models with the Beverton-Holt form survival functions, the stability seems global. The models with the Ricker-type nonlinearity, nevertheless, have much more complex dynamics. Using numerical examples, we demonstrated that period-doubling bifurcation and chaotic behavior occur.

As is well known, discrete-time models can have very rich dynamics and can exhibit chaotic behavior. To build a theoretical framework and a fundamental analytic basis for further studies, we formulated a discrete-time malaria model, given by (5.2.1) and (5.2.2), in Chapter 5. We derived a formula for the reproductive number R_0 by using the next generation matrix method for the special case where the birth rate and survival rates of mosquitoes are constant. The infection-free equilibrium is locally asymptotically

stable if $R_0 < 1$, and is unstable if $R_0 > 1$. Under certain assumptions, we showed the existence of a positive equilibrium.

Combining the discrete-time stage-structured mosquito population model and the malaria transmission model, we formulated a discrete-time malaria model with stage-structured mosquitoes (6.1.1) in Chapter 6. Not surprisingly, mathematical analysis for system (6.1.1) is difficult. We were only able to show the positive invariance of the system and to derive a formula for the reproductive number R_0 .

There are many unsolved open problems from this dissertation. For the continuous-time malaria model in Chapter 3, we have not been able to show the global stability of the infection-free equilibrium for $R_0 \geq R_c$, in the case of existence of backward bifurcation and $R_c < R_b$, or the stability of the endemic equilibrium if $\delta_h > 0$. For the discrete-time mosquito-stage-structured malaria models, we only obtain special results under assumption (A1) and the assumption of constant $\alpha^v(t)$. We were unable to show the stability of the endemic equilibrium. The mathematical analysis for the stage-structured malaria model in Chapter 6 is only preliminary. All of these will be projects for our future studies.

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