GLOBAL DYNAMICS OF SOME MALARIA MODELS IN HETEROGENEOUS ENVIRONMENTS

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Global Dynamics of Some Malaria Models in Heterogeneous Environments

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Abstract

Malaria is one of the most important parasitic infections in humans and more than two billion people are at risk every year. There were an estimated 247 million malaria cases in 2006, causing nearly a million deaths. Currently, malaria is still endemic in 109 countries. Human malaria is caused by protozoan parasites of the genus Plasmodium, transmitted from human-to-human by the female Anopheles mosquito. Over the past century, considerable work has been invested in the study of malaria transmission. However, only a few studies with malaria consider the spatial and temporal heterogeneities of this disease. Hence, there is an essential need for more information on the spatial and temporal patterns of disease burden, distribution and control strategies. The aim of this thesis is to study the malaria transmission in heterogeneous environments.

We begin with a brief introduction of mathematical background for this thesis in chapter 1. We shall provide some mathematical terminologies and theorems related to the theories of monotone dynamical systems, uniform persistence, basic reproduction ratio, spreading speeds and traveling waves.

Chapter 2 is devoted to the study of global dynamics of a periodic susceptible-infected-susceptible compartmental model with maturation delay. We first obtain sufficient conditions for the single population growth equation to admit a globally

attractive positive periodic solution. Then we introduce the basic reproduction ratio $\mathcal{R}_0$ for the epidemic model, and show that the disease dies out when $\mathcal{R}_0 < 1$, and the disease remains endemic when $\mathcal{R}_0 > 1$. Numerical simulations are also provided to confirm our analytic results. The study in this chapter also enables us to consider time-delayed and periodic malaria models.

In chapter 3, we present a malaria transmission model with periodic birth rate and age structure for the vector population. We first introduce the basic reproduction ratio for this model and then show that there exists at least one positive periodic state and that the disease persists when $\mathcal{R}_0 > 1$. It is also shown that the disease will die out if $\mathcal{R}_0 < 1$, provided that the invasion intensity is not strong. We further use these analytic results to study the malaria transmission cases in KwaZulu-Natal Province, South Africa. Some sensitivity analysis of $\mathcal{R}_0$ is performed, and in particular, the potential impact of climate change on seasonal transmission and populations at risk of the disease is analyzed.

Based on the classical Ross-Macdonald model, we propose in chapter 4 a periodic model with diffusion and advection to study the possible impact of the mobility of humans and mosquitoes on malaria transmission. We establish the existence of the leftward and rightward spreading speeds and their coincidence with the minimum wave speeds in the left and right directions, respectively. For the model in a bounded domain, we obtain a threshold result on the global attractivity of either zero or a positive periodic solution.

To understand how the spatial heterogeneity and extrinsic incubation period (EIP) of the parasite within the mosquito affect the dynamics of malaria epidemiology, we formulate a nonlocal and time-delayed reaction-diffusion model in chapter 5. We then define the basic reproduction ratio $\mathcal{R}_0$ and show that $\mathcal{R}_0$ serves as a threshold param-

eter that predicts whether malaria will spread. Furthermore, a sufficient condition is obtained to guarantee that the disease will stabilize at a positive steady state eventually in the case where all the parameters are spatially independent. Numerically, we show that the use of the spatially averaged system may highly underestimate the malaria risk. The spatially heterogeneous framework in this chapter can be used to design the spatial allocation of control resources.

At last, we summarize the results in this thesis, and also point out some problems for future research in chapter 6.

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Chapter 1

Preliminaries

In this chapter, we present some terminologies and known results which are going to be used in the rest of this thesis. They are involved in monotone dynamical systems, uniform persistence and coexistence states, basic reproduction ratios for compartmental epidemic models in periodic environments, and the theory of spreading speeds and traveling waves for monotone periodic semiflows.

1.1 Monotone dynamics

Let E be an ordered Banach space with an order cone P having nonempty interior $int(P)$. For $x, y \in E$, we write $x \geq y$ if $x - y \in P$, $x > y$ if $x - y \in P \setminus \{0\}$ and $x \gg y$ if $x - y \in int(P)$. If $a < b$, we define the order interval $[a, b]:=\{x \in E : a \leq x \leq b\}$.

Definition 1.1.1 *Let U be a subset of E, and $f : U \to U$ a continuous map. The map f is said to be monotone if $x \geq y$ implies that $f(x) \geq f(y)$; strictly monotone if $x > y$ implies that $f(x) > f(y)$; strongly monotone if $x > y$ implies that $f(x) \gg f(y)$.*

Theorem 1.1.1 *(Dancer-Hess connecting orbit theorem) [22, Proposition 1] Let* $u_1 < u_2$ *be fixed points of the strictly monotone continuous mapping* $f : U \to U$*, let* $I := [u_1, u_2] \subset U$*, and assume that* $f(I)$ *is precompact and that* f *has no fixed point distinct from* u_1 *and* u_2 *in* I*. Then either*

(a) there exists an entire orbit $\{x_n\}_{n=-\infty}^{\infty}$ *of* f *in* I *such that* $x_{n+1} > x_n$, $\forall n \in \mathbb{Z}$*, and* $\lim_{n\to-\infty} x_n = u_1$ *and* $\lim_{n\to\infty} x_n = u_2$*; or*

(b) there exists an entire orbit $\{y_n\}_{n=-\infty}^{\infty}$ *of* f *in* I *such that* $y_{n+1} < y_n$, $\forall n \in \mathbb{Z}$*, and* $\lim_{n\to-\infty} y_n = u_2$ *and* $\lim_{n\to\infty} y_n = u_1$*.*

Recall that a subset K of E is said to be order convex if $[u, v] \in K$ whenever $u, v \in K$ satisfy $u < v$.

Definition 1.1.2 *Let* $U \in P$ *be a nonempty, closed and order convex set. A continuous map* $f : U \to U$ *is said to be subhomogeneous if* $f(\lambda x) \geq \lambda f(x)$ *for any* $x \in U$ *and* $\lambda \in [0, 1]$*; strictly subhomogeneous if* $f(\lambda x) > \lambda f(x)$ *for any* $x \in U$ *with* $x \gg 0$ *and* $\lambda \in (0, 1)$*; strongly subhomogeneous if* $f(\lambda x) \gg \lambda f(x)$ *for any* $x \in U$ *with* $x \gg 0$ *and* $\lambda \in (0, 1)$*.*

Theorem 1.1.2 *[105, Theorem 2.3.2] Assume that* $f : U \to U$ *satisfies either*

(i) f *is monotone and strongly subhomogeneous; or*

(ii) f *is strongly monotone and strictly subhomogeneous.*

If $f : U \to U$ *admits a nonempty compact invariant set* $K \subset int(P)$*, then* f *has a fixed point* $e \gg 0$ *such that every nonempty compact invariant set of* f *in* $int(P)$ *consists of* e*.*

Recall that a continuous mapping $f : X \to X$ is said to be asymptotically smooth if for any nonempty closed bounded set $B \subset X$ for which $f(B) \subset B$, there is a compact set $J \subset B$ such that J attracts B. Denote the Fréchet derivative of f at $u = a$ by $Df(a)$ if it exists, and let $r(Df(a))$ be the spectral radius of the linear operator $Df(a) : E \to E$.

Theorem 1.1.3 *(Threshold dynamics) [105, Theorem 2.3.4] Let* $V = [0, b]$ *with* $b \gg 0$*, and* $f : V \to V$ *be a continuous map. Assume that*

(1) $f : V \to V$ *satisfies either*

  (i) f *is monotone and strongly subhomogeneous; or*

  (ii) f *is strongly monotone and strictly subhomogeneous;*

(2) $f : V \to V$ *is asymptotically smooth, and every positive orbit of* f *in* V *is bounded;*

(3) $f(0) = 0$*, and* $Df(0)$ *is compact and strongly positive.*

Then there exists threshold dynamics:

(a) If $r(Df(0)) \leq 1$*, then every positive orbit in* V *converges to* 0*;*

(b) If $r(Df(0)) > 1$*, then there exists a unique fixed point* $u^* \gg 0$ *in* V *such that every positive orbit in* $V \setminus \{0\}$ *converges to* u^**.*

1.2 Uniform persistence and coexistence states

Suppose X is a metric space with metric d. Let $f : X \to X$ be a continuous map and $X_0 \subset X$ an open set. Define $\partial X_0 := X \setminus X_0$, and $M_\partial := \{x \in \partial X_0 : f^n(x) \in \partial X_0, \forall n \geq 0\}$, which may be empty.

Definition 1.2.1 *A bounded set* A *is said to attract a bounded set* B *in* X *if*

$$\limsup_{n\to\infty,\ x\in B} \{d(f^n(x), A)\} = 0.$$

A subset $A \subset X$ *is said to be an attractor for* f *if* A *is nonempty, compact and invariant* ($f(A) = A$)*, and* A *attracts some open neighborhood of itself. A global attractor for* $f : X \to X$ *is an attractor that attracts every point in* X*. For a nonempty invariant set* M*, the set* $W^s(M) := \{x \in X : \lim_{n\to\infty} d(f^n(x), M) = 0\}$ *is called the stable set of* M*.*

Recall that a continuous mapping $f : X \to X$ is said to be point dissipative if there is a bounded set B_0 in X such that B_0 attracts each point in X.

Theorem 1.2.1 *[105, Theorem 1.1.3] If* $f : X \to X$ *is compact and point dissipative, then there is a connected global attractor* A *that attracts each bounded set in* X*.*

Definition 1.2.2 f *is said to be uniformly persistent with respect to* $(X_0, \partial X_0)$ *if there exists an* $\eta > 0$ *such that* $\liminf_{n\to\infty} d(f^n(x), \partial X_0) \geq \eta$ *for all* $x \in X_0$*.*

Definition 1.2.3 *Let* $A \subset X$ *be a nonempty invariant set for* f*. We say* A *is internally chain-transitive if for any* $a, b \in A$ *and any* $\epsilon > 0$*, there is a finite sequence* $x_1, \dots, x_m$ *in* A *with* $x_1 = a$*,* $x_m = b$ *such that* $d(f(x_i), x_{i+1}) < \epsilon$*,* $1 \leq i \leq m-1$*. The sequence* $\{x_1, \dots, x_m\}$ *is called an* ϵ*-chain in* A *connecting* a *and* b*.*

Definition 1.2.4 *A lower semicontinuous function* $p : X \to \mathbb{R}_+$ *is called a generalized distance function for* $f : X \to X$ *if for every* $x \in (X_0 \cap p^{-1}(0)) \cup p^{-1}(0, \infty)$*, we have* $p(f^n(x)) > 0$*,* $\forall n \geq 1$*.*

Theorem 1.2.2 *[83, Theorem 3] (or [105, Theorem 1.3.2]) Let p be a generalized distance function for continuous map $f : X \to X$. Assume that*

(P1) f has a global attractor;

(P2) There exists a finite sequence $M = \{M_1, \dots, M_k\}$ of disjoint, compact, and isolated invariant sets in ∂X_0 with the following properties:

(a) $\cup_{x \in M_\partial} \omega(x) \subset \cup_{i=1}^{k} M_i$, where $\omega(x)$ represents the omega limit set of x;

(b) no subset of M forms a cycle in ∂X_0;

(c) M_i is isolated in X;

(d) $W^s(M_i) \cap p^{-1}(0, \infty) = \emptyset$ for each $1 \leq i \leq k$, where $W^s(M_i)$ is the stable set of M_i.

Then there exists a $\delta > 0$ such that for any compact chain transitive set L with $L \not\subset M_i$, for all $1 \leq i \leq k$, we have $\min_{x \in L} p(x) > \delta$. In particular, f is uniformly persistent in the sense that there exists an $\eta > 0$ such that $\liminf_{n \to \infty} d(f^n(x), \partial X_0) \geq \eta$ for all $x \in X_0$.

Suppose $T > 0$, a family of mappings $\Phi(t) : X \to X$, $t \geq 0$, is called a T-periodic semiflow on X if it possesses the following properties:

(1) $\Phi(0) = I$, where I is the identity map on X;

(2) $\Phi(t + T) = \Phi(t) \circ \Phi(T)$, $\forall t \geq 0$;

(3) $\Phi(t)x$ is continuous in $(t, x) \in [0, \infty) \times X$.

The mapping $\Phi(T)$ is called the Poincaré map (or period map) associated with this periodic semiflow. In particular, if (2) holds for any $T > 0$, $\Phi(t)$ is called an autonomous semiflow.

Theorem 1.2.3 *[105, Theorem 3.1.1] Let $\Phi(t)$ be a T-periodic semiflow on X with $\Phi(t)X_0 \subset X_0$, $\forall t \geq 0$. Assume that $S := \Phi(T)$ is point dissipative in X and compact. Then the uniform persistence of S with respect to $(X_0, \partial X_0)$ implies that of $\Phi(t) : X \to X$.*

Recall that the Kuratowski measure of noncompactness, α, is defined by

$$\alpha(B) := \inf\{r : B \text{ has a finite cover of diameter} < r\}$$

for any bounded set B of X. It is not hard to see that B is precompact if and only if $\alpha(B) = 0$. Let (X, d) be a complete space, and let $\rho : X \to \mathbb{R}_+$ be a continuous function. We define $M_0 := \{x \in X : \rho(x) > 0\}$ and $\partial M_0 := \{x \in X : \rho(x) = 0\}$.

Definition 1.2.5 *A continuous map $f : X \to X$ is said to be ρ uniformly persistent if there exists $\varepsilon > 0$ such that $\liminf_{n\to\infty} \rho(f^n(x)) \geq \varepsilon$, $\forall x \in M_0$. The map is said to be α-condensing (α-contraction of order k, $0 \leq k < 1$) if f takes bounded sets to bounded set and $\alpha(f(B)) < \alpha(B)$ ($\alpha(f(B)) < k\alpha(B)$) for any nonempty closed bounded set $B \subset X$ with $\alpha(B) > 0$.*

Theorem 1.2.4 *[60, Theorem 3.7 and Remark 3.10] Let $f : X \to X$ be a continuous map with $f(M_0) \subset M_0$. Assume that $f : X \to X$ is asymptotically smooth and ρ-uniformly persistent, and that f has a global attractor A. Then $f : M_0 \to M_0$ has a global attractor A_0. Analogously, this result still holds for an autonomous semiflow $\Phi(t)$ on X with $\Phi(t)X_0 \subset X_0$, $\forall t \geq 0$.*

Let $\{f^n\}_{n=1}^{\infty}$ be the discrete semidynamical system defined by a continuous map $f : X \to X$ with $f(M_0) \subset M_0$. A pointed $x_0 \in X$ is called a coexistence state of $\{f^n\}_{n=1}^{\infty}$ if x_0 is a fixed point of f in M_0, i.e., $x_0 \in M_0$ and $f(x_0) = x_0$. Assume that X is a closed and convex subset of a Banach space $(E, \|\cdot\|)$, that $\rho : X \to \mathbb{R}_+$ is a continuous function such that $M_0 := \{x \in X : \rho(x) > 0\}$ is nonempty and convex, and that $f : X \to X$ is a continuous map with $f(M_0) \subset M_0$. Then, we have the following two results on the existence of a coexistence steady state.

Theorem 1.2.5 *[60, Theorem 4.1 and Theorem 4.7] Assume that $f : X \to X$ is α-condensing. If $f : M_0 \to M_0$ has a global attractor $A_0 \subset M_0$, then f has a fixed point $x_0 \in A_0$. The analogous result holds for an autonomous semiflow $\Phi(t)$: let $\Phi(t)$ be an autonomous semiflow on X with $\Phi(t)(M_0) \subset M_0$, $\forall t \geq 0$. Assume that $\Phi(t)$ is α-condensing for each $t > 0$, and that $\Phi(t) : M_0 \to M_0$ has a global attractor A_0. Then $\Phi(t)$ has an equilibrium $x_0 \in A_0$, i.e., $\Phi(t)x_0 = x_0$, $\forall t \geq 0$.*

Theorem 1.2.6 *[60, Theorem 4.5] Assume that*

(1) $f : X \to X$ is point dissipative and ρ-uniformly persistent.

(2) f^{n_0} is compact for some integer $n_0 \geq 1$.

(3) Either f is α-condensing or f is convex k-contracting.

Then $f : M_0 \to M_0$ admits a global attractor A_0, and f has a fixed point in A_0.

1.3 Basic reproduction ratios in periodic environments

A central concept in the study of the spread of communicable diseases is the basic reproduction number, denoted by $\mathcal{R}_0$, which is defined as the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual (see, e.g., [3, 24]). In many cases, one may expect that such a disease can invade the susceptible population if $\mathcal{R}_0 > 1$. Thus, we need to reduce $\mathcal{R}_0$ to be less than 1 in order to eradicate a disease. For a large class of autonomous compartmental epidemic models, the explicit formula for $\mathcal{R}_0$ was obtained in [91]. This work has been extended recently to the periodic case in [95].

In this section, we will introduce the theory of basic reproduction ratios for compartmental epidemic models in periodic environments developed in [95]. We consider a heterogeneous population whose individuals can be grouped into n homogeneous compartments. Suppose that the compartments can be divided into two types: infected compartments, labeled by $i = 1, 2, \ldots, m$, and uninfected compartments, labeled by $i = m + 1, \ldots, n$. Define X_s to be the set of all disease-free states

$$X_s := \{x \geq 0 : x_i = 0, \ \forall i = 1, 2, \ldots, m\}.$$

Let $\mathcal{F}_i(t, x)$ be the input rate of newly infected individuals in the i-th compartment, $\mathcal{V}_i^+(t, x)$ be the input rate of individuals by other means (for example, births, immigrations), and $\mathcal{V}_i^-(t, x)$ be the rate of transfer of individuals out of compartment i (for example, deaths, recovery and emigrations). Thus, the disease transmission model in a periodic environment is governed by a periodic ordinary differential system:

$$\frac{dx_i}{dt} = \mathcal{F}_i(t, x) - \mathcal{V}_i(t, x) := f_i(t, x), \ i = 1, \ldots, n, \tag{1.1}$$

where $\mathcal{V}(t, x) = \mathcal{V}_i^-(t, x) - \mathcal{V}_i^+(t, x)$. Assume that the model (1.1) has an infection-free periodic solution $x^0(t) = (0, \ldots, 0, x^0_{m+1}(t), \ldots, x^0_n(t))^T$ with $x^0_i(t) > 0$, $m + 1 \leq i \leq n$ for all t. Let $f = (f_1, \ldots, f_n)^T$, and define the following matrices

$$M(t) := \left(\frac{\partial f_i(t, x^0(t))}{\partial x_j}\right)_{m+1 \leq i,j \leq n}, \quad F(t) := \left(\frac{\partial \mathcal{F}_i(t, x^0(t))}{\partial x_j}\right)_{1 \leq i,j \leq m},$$

$$\text{and } V(t) := \left(\frac{\partial \mathcal{V}_i(t, x^0(t))}{\partial x_j}\right)_{1 \leq i,j \leq m}.$$

Then

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

where $J(t)$ is an $(n-m)\times n$ matrix.

Denote $\Upsilon_P(t)$ be the monodromy matrix for the periodic system $\frac{dz}{dt} = P(t)z$. Assume that

(B1) For each $1 \le i \le n$, the functions $\mathcal{F}_i(t,x)$, $\mathcal{V}_i^+(t,x)$ and $\mathcal{V}_i^-(t,x)$ are nonnegative and continuous on $\mathbb{R}\times\mathbb{R}_+^n$ and continuously differential with respect to x.

(B2) There is a real number $T > 0$ such that for each $1 \le i \le n$, the functions $\mathcal{F}_i(t,x)$, $\mathcal{V}_i^+(t,x)$ and $\mathcal{V}_i^-(t,x)$ are T-periodic in t.

(B3) If $x_i = 0$, then $\mathcal{V}_i^- = 0$. In particular, if $x \in X_s$, then $\mathcal{V}_i^- = 0$ for $i = 1,\dots,m$.

(B4) $\mathcal{F}_i = 0$ for $i > m$.

(B5) If $x \in X_s$, then $\mathcal{F}_i(t,x) = \mathcal{V}_i(t,x) = 0$ for $i = 1,\dots,m$.

(B6) $\rho(\Upsilon_M(T)) < 1$, where $\rho(\Upsilon_M(T))$ is the spectral radius of $\Upsilon_M(T)$.

(B7) $\rho(\Upsilon_{-V}(T)) < 1$.

Let $Y(t,s)$, $t > s$, be the evolution operator of the linear T-periodic system

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

That is, for each $s \in \mathbb{R}$, the $m\times m$ matrix $Y(t,s)$ satisfies

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

where I is the $m \times m$ identity matrix. Set C_T be the ordered Banach space of all T-periodic functions from $\mathbb{R}$ to $\mathbb{R}^m$, which is equipped with the maximum norm and the positive cone $C_T^+ := \{\phi \in C_T : \phi(t) \geq 0, \ \forall t \geq 0\}$. Then we can define a linear operator $L : C_T \to C_T$ by

$$(L\phi)(t) = \int_0^\infty Y(t, t-a)F(t-a)\phi(t-a)da, \ \forall t \in \mathbb{R}, \ \phi \in C_T.$$

We call L the next infection operator, and define the spectral radius of L as the basic reproduction ratio

$$R_0 := \rho(L)$$

for the periodic epidemic model (1.1).

The following result shows that R_0 is a threshold parameter for the local stability of a disease-free periodic solution $x^0(t)$.

Theorem 1.3.1 *[95, Theorem 2.2] Assume that (B1)-(B7) hold. Then the following statements are valid:*

(1) $R_0 = 1$ *if and only if* $\rho(\Upsilon_{F-V}(T)) = 1$.

(2) $R_0 > 1$ *if and only if* $\rho(\Upsilon_{F-V}(T)) > 1$.

(3) $R_0 < 1$ *if and only if* $\rho(\Upsilon_{F-V}(T)) < 1$.

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

Let $U(t, s, \lambda)$, $t \geq s$, $s \in \mathbb{R}$, be the evolution operator of the following linear system

$$\frac{du}{dt} = \left[-V(t) + \frac{F(t)}{\lambda}\right] u, \ t \in \mathbb{R}.$$

Then the following theorem is useful to numerically compute the basic reproduction ratio R_0.

Theorem 1.3.2 *[95, Theorem 2.1] Let (B1)-(B7) hold. Then the following statements are valid:*

(1) If $\rho(U(T,0,\lambda)) = 1$ has a positive solution λ_0, then λ_0 is an eigenvalue of L, and hence $R_0 > 0$.

(2) If $R_0 > 0$, then $\lambda_0 = R_0$ is the unique solution of $\rho(U(T,0,\lambda)) = 1$.

(3) $R_0 = 0$ if and only if $\rho(U(T,0,\lambda)) < 1$ for all $\lambda > 0$.

For a continuous periodic function $g(t)$ with period T, we define its average as

$$[g] := \frac{1}{T}\int_0^T g(t)dt.$$

The following result gives explicit formulae for $\mathcal{R}_0$ in two special cases.

Theorem 1.3.3 *[95, Lemma 2.2] Let (B1)-(B7) hold. Then the following statements are valid:*

(1) If $V(t) = diag(V_1(t), \ldots, V_m(t))$ and $F(t) = diag(F_1(t), \ldots, F_m(t))$, then $\mathcal{R}_0 = \max_{1\le i\le m}\{\frac{[F_i]}{[V_i]}\}$.

(2) If $V(t) = V$ and $F(t) = F$ are two constant matrices, then $\mathcal{R}_0 = \rho(V^{-1}F) = \rho(FV^{-1})$.

1.4 Spreading speeds and traveling waves

Let $\mathbb{C}$ be the set of all bounded and continuous functions from $\mathbb{H}$ to $\mathbb{R}^k$, where $\mathbb{H} = \mathbb{R}$ or $\mathbb{Z}$. Clearly, every vector in $\mathbb{R}^k$ can be regarded as a function in $\mathbb{C}$. We equip $\mathbb{R}^k$ with the positive cone $\mathbb{R}^k_+$, so that $\mathbb{R}^k$ is an ordered space. For $u = (u_1, \ldots, u_k)$, $w =$

$(w_1, \dots, w_k) \in \mathbb{C}$, we write $u \geq w$ ($u \gg w$) provided $u_i(x) \geq w_i(x)$ ($u_i(x) > w_i(x)$), $\forall i = 1, \dots, k$, $\forall x \in \mathbb{H}$, and $u > v$ provided $u \geq w$ but $u \neq w$. For any $r \gg 0$, we define

$$[0, r] := \{u \in \mathbb{R}^k : 0 \leq u \leq r\} \text{ and } \mathbb{C}_r := \{u \in \mathbb{C} : 0 \leq u \leq r\}.$$

We equip $\mathbb{C}$ with the compact open topology, i.e., $u^m \to u$ in $\mathbb{C}$ means that the sequence of $u^m(x)$ converges to $u(x)$ uniformly for x in any compact set in H. If we define

$$d(u, w) := \sum_{k=1}^{\infty} \frac{\max_{|x| \leq k} |u(x) - w(x)|}{2^k}, \ \forall u, \ w \in \mathbb{C},$$

where $|\cdot|$ denotes the usual norm in $\mathbb{R}^k$, then $(\mathbb{C}, d)$ is a metric space.

Define the reflection operator $\mathcal{R}$ by $\mathcal{R}[u](x) = u(-x)$. Given any $y \in \mathbb{H}$, define the translation operator T_y by $T_y[u](x) := u(x - y)$. Let $Q : \mathbb{C}_\beta \to \mathbb{C}_\beta$ be a map, where $\beta \gg 0$ in $\mathbb{R}^k$. Assume that

(A1) $Q[\mathcal{R}[u]] = \mathcal{R}[Q[u]]$, $T_y[Q[u]] = Q[T_y[u]]$, $\forall y \in \mathbb{H}$.

(A2) $Q : \mathbb{C}_\beta \to \mathbb{C}_\beta$ is continuous with respect to the compact open topology.

(A3) $Q[\mathbb{C}_\beta]$ is precompact in $\mathbb{X}_\beta$.

(A4) $Q : \mathbb{C}_\beta \to \mathbb{C}_\beta$ is monotone (order-preserving) in the sense that $Q[u] \geq Q[v]$ whenever $u \geq v$ in $\mathbb{C}_\beta$.

(A5) Q admits exactly two fixed points 0 and β, and for any positive number ε, there is an $\alpha \in [0, \beta]$ with $\|\alpha\| < \varepsilon$ such that $Q[\alpha] \gg \alpha$.

Then the following theorem guarantee that the discrete-time semiflow $\{Q^n\}_{n=0}^{\infty}$ (in short, the map Q) on $\mathbb{C}_\beta$ admits an asymptotic speed of spread c^*.

Theorem 1.4.1 *[57, Theorem 2.11, Theorem 2.15 and Corollary 2.16] (or [56, Theorem A]) Suppose that Q satisfies (A1)-(A5). Let $u_0 \in \mathbb{C}_\beta$ and $u_n = Q[u_{n-1}]$ for $n \geq 1$. Then there is a real number c^* such that the following statements are valid:*

(i) For any $c > c^*$, if $0 \leq u_0 \ll \beta$ and $u_0(x) = 0$ for x outside a bounded interval, then $\lim_{n\to\infty, |x|\geq nc} u_n(x) = 0$.

(ii) For any $c < c^*$ and any $\sigma \in [0, r]$ with $\sigma \gg 0$, there exists $r_\sigma > 0$ such that if $u_0(x) \geq \sigma$ for x on an interval of length $2r_\sigma$, then $\lim_{n\to\infty, |x|\leq nc} u_n(x) = \beta$. If, in addition, Q is subhomogeneous on $\mathbb{C}_\beta$, then r_σ can be chosen to be independent of $\sigma \gg 0$.

We call c^* in the above theorem the asymptotic speed of spread (in short, spreading speed) of the map Q on $\mathbb{C}_\beta$. In order to estimate the spreading speed c^*, a linear operator approach was developed in [57]. Let $M := \mathbb{C} \to \mathbb{C}$ be a linear operator with the following properties:

(C1) M is continuous with respect to the compact open topology.

(C2) M is a positive operator, that is, $M[u] \geq 0$ whenever $u > 0$.

(C3) M satisfies (A3) with $\mathbb{C}_\beta$ replaced by any subset of $\mathbb{C}$ consisting of uniformly bounded functions.

(C4) $M[\mathcal{R}[u]] = \mathcal{R}[M[u]]$, $T_y[M[u]] = M[T_y[u]]$, $\forall u \in \mathbb{C}$, $y \in \mathbb{H}$.

(C5) M can be extended to a linear operator on the linear space $\tilde{C}$ of all of functions $u \in C(\mathbb{H}, \mathbb{R}^k)$ having the form

$$u(x) = v_1(x)e^{\mu_1 x} + v_2(x)e^{\mu_2 x},\ v_1,\ v_2 \in \mathbb{C},\ \mu_1,\ \mu_2 \in \mathbb{R},\ x \in \mathbb{H},$$

such that if u_n, $u \in \mathbb{C}$ and $u_n(x) \to u(x)$ uniformly on any bounded set, then $M[u_n](x) \to M[u](x)$ uniformly on any bounded set.

Note that hypothesis (C4) implies that M is also a linear operator on $\mathbb{R}^k$. Define the linear map $B_\mu : \mathbb{R}^k \to \mathbb{R}^k$ by

$$B_\mu[\sigma] = M[\sigma e^{-\mu x}](0), \ \forall \sigma \in \mathbb{R}^k.$$

In particular, $B_0 = M$ on $\mathbb{R}^k$. If σ_n, $\sigma \in \mathbb{R}^k$ and $\sigma_n \to \sigma$ as $n \to \infty$, then $\sigma_n e^{-\mu x} \to \sigma e^{-\mu x}$ uniformly on any bounded subset of $\mathbb{H}$. Thus, $B_\mu[\sigma_n] = M[\sigma_n e^{-\mu x}](0) \to M[\sigma e^{-\mu x}](0) = B_\mu[\sigma]$, and hence B_μ is continuous. Moreover, B_μ is a positive operator on $\mathbb{R}^k$. Assume that

(C6) For any $\mu \geq 0$, B_μ is positive, and there is an n_0 such that $B_\mu^{n_0} = \underbrace{B_\mu B_\mu \dots B_\mu}_{n_0}$ is a compact and strongly positive linear operator on $\mathbb{R}^k$.

It then follows from [57, Lemma 3.1] that B_μ has a principal eigenvalue $\lambda(\mu)$ with a strongly positive eigenfunction. Moreover, we have the following property for $\lambda(\mu)$.

Lemma 1.4.1 *[57, Lemma 3.7] $\lambda(\mu)$ is log convex on $\mathbb{R}$.*

The following condition is needed for the estimate of the spreading speed c^*.

(C7) The principal eigenvalue $\lambda(0)$ of B_0 is larger than 1.

Define $\Psi(\mu) := \frac{\ln \lambda(\mu)}{\mu}$, $\forall \mu > 0$. Then, we can use the following result to estimate the spreading speed of map Q.

Theorem 1.4.2 *[57, Theorem 3.10] Let Q be an operator on $\mathbb{C}_\beta$ satisfying (A1)-(A5) and c^* be the asymptotic speed of spread of Q. Assume that the linear operator M satisfies (C1)-(C7), and that the infimum of $\Psi(\mu)$ is attained at some finite value μ^* and $\Psi(+\infty) > \Psi(\mu^*)$. Then the following statements are valid:*

(1) If $Q[u] \leq M[u]$ *for all* $u \in \mathbb{C}_\beta$*, then* $c^* \leq \inf_{\mu>0} \Psi(\mu)$.

(2) If there is some $\eta \in \mathbb{R}^k$*, with* $\eta \gg 0$*, such that* $Q[u] \geq M[u]$ *for any* $u \in \mathbb{C}_\eta$*, then* $c^* \geq \inf_{\mu>0} \Psi(\mu)$.

Based on the theory of spreading speeds and traveling waves for periodic semiflows in the monostable case [56], we have the following result on the existence of spreading speeds for periodic semiflows.

Theorem 1.4.3 *[56, Theorem 2.1] Let* $\{Q_t\}_{t\geq 0}$ *be a* T*-periodic semiflow on* $\mathbb{C}_r$ *with two* x*-independent* T*-periodic orbits* $0 \ll u^*(t)$*. Suppose that the Poincaré map* $Q = Q_T$ *satisfies all hypotheses (A1)-(A5) with* $\beta = u^*(0)$*, and* Q_t *satisfies (A1) for any* $t > 0$*. Let* c^* *be the asymptotic speed of spread for* Q_T*. Then the following statements are valid:*

(1) For any $c > \frac{c^*}{T}$*, if* $v \in \mathbb{C}_\beta$ *with* $0 \leq v \ll \beta$*, and* $v(x) = 0$ *for* x *outside a bounded interval, then* $\lim_{t\to\infty, |x|\geq tc} Q_t[v](x) = 0$.

(2) For any $c < \frac{c^*}{T}$ *and any* $\sigma \in [0, r]$ *with* $\sigma \gg 0$*, there exists a positive number* $r_\sigma > 0$ *such that if* $v \in \mathbb{C}_\beta$ *and* $v(x) \gg \sigma$ *for* x *on an interval of length* $2r_\sigma$*, then* $\lim_{t\to\infty, |x|\leq tc}(Q_t[v](x) - u^*(t)) = 0$*. If, in addition,* Q_T *is subhomogeneous on* $\mathbb{C}_\beta$*, then* r_σ *can be chosen to be independent of* $\sigma \gg 0$.

We say that $W(t, x - ct)$ is a periodic traveling wave of the T-periodic semiflow $\{Q_t\}_{t\geq 0}$ if the vector-valued function $W(t, z)$ is T-periodic in t and $Q_t[W(0, \cdot)](x) = W(t, x - ct)$, and that $W(t, x - ct)$ connects $u^*(t)$ to 0 if $W(t, -\infty) = u^*(t)$ and $W(t, +\infty) = 0$ uniformly for $t \in [0, T]$.

Theorem 1.4.4 *[56, Theorem 2.2 and Theorem 2.3] Let* $\{Q_t\}_{t\geq 0}$ *be an* T*-periodic semiflow on* $\mathbb{C}_\tau$ *with two* x*-independent* T*-periodic orbits* $0 \ll u^*(t)$*. Suppose that the Poincaré map* $Q = Q_T$ *satisfies all hypotheses (A1)-(A5) with* $\beta = u^*(0)$*. Let* c^* *be the asymptotic speed of spread for* Q_T*. Then the following statements are valid:*

(1) For any $0 < c < \frac{c^*}{T}$*,* $\{Q_t\}_{t\geq 0}$ *has no* T*-periodic traveling wave* $W(t, x - ct)$ *connecting* $u^*(t)$ *to 0.*

(2) If, in addition, Q_t *satisfies (A1) and (A4) for each* $t > 0$*, then for any* $c \geq \frac{c^*}{T}$*,* $\{Q_t\}_{t\geq 0}$ *has an* T*-periodic traveling wave* $W(t, x - ct)$ *connecting* $u^*(t)$ *to* 0 *such that* $W(t, z)$ *is continuous, and nonincreasing in* $z \in \mathbb{R}$*.*

Remark: If the reflection invariance, i.e., $Q[\mathcal{R}[u]] = \mathcal{R}[Q[u]]$, is not assumed in (A1), then we have the existence of the rightward spreading speed c_+^* and the leftward spreading speed c_-^*, see [97]. These spreading speeds can also be estimated by the linear operators approach. Further, both c_+^* and c_-^* are the minimum wave speeds for monotone traveling waves in the right and left directions, respectively.

Chapter 2

Threshold Dynamics in A Time-Delayed Periodic SIS Epidemic Model

2.1 Introduction

Many mathematical models for the spread of infectious diseases are described by autonomous systems of differential equations (see, e.g., [3,24]). However, certain diseases admit seasonal behavior and it is now well understood that seasonal fluctuations are often the primary factors responsible for recurrent epidemic cycles. Periodic changes in social interactions can alter the contact rate for some directly transmitted contagious infections. For example, in the case of childhood infectious disease, the contact rates vary seasonally according to the school schedule [26]. Fluctuations of birth rates are also evidenced in the works of population dynamics [58,105]. Periodic vaccination strategies are often used to control diseases [27]. We further refer to two surveys [2,34] and references therein for seasonal fluctuations in epidemic models. It thus becomes natural to model these diseases by periodically forced nonlinear systems.

The purpose of this chapter is to obtain a threshold type result on the global dynamics for a periodic SIS epidemic model with maturation delay. Moreover, we will find conditions to ensure that a periodic single population growth model admit an attractive positive periodic solution, which will be used in the study of mosquito population in the next chapter. The model is presented in the next section and a single species growth model is analyzed with three types of birth rate functions. In section 2.4, we introduce the basic reproduction ratio and show that it acts as a threshold parameter for the uniform persistence and global extinction of the disease. The last two sections in this chapter give some numerical simulations and concluding remarks.

2.2 The model

Many epidemiological models are formulated so that the infectious disease spreads in a population which either is a fixed closed population or has a fixed size with balancing inflows and outflows due to births and deaths or migration. However, it is generally accepted in ecology that the sizes of plant and animal populations are influenced and constrained by foraging, predation, competition and limited resources. In [19], Cooke *et al.* considered the variable population size and derived a time-delayed SIS epidemic model:

$$\left\{\begin{array}{rcl} S'(t) & = & B(N(t-\tau))N(t-\tau)e^{-d_1\tau} - dS(t) - \frac{\beta S(t)I(t)}{N(t)} + \gamma I(t), \\ I'(t) & = & \frac{\beta S(t)I(t)}{N(t)} - (d+d_2+\gamma)I(t), \end{array}\right.$$

where I is the number of the infective population, S is the number of the susceptible population and $N(t) = S(t) + I(t)$. Here $d > 0$ is the death rate constant at the adult stage, $B(N)$ is a birth rate function, τ is the maturation time, $d_2 \geq 0$ is the disease induced death rate, $\gamma > 0$ is the recovery rate ($\frac{1}{\gamma}$ is the average infective time), and d_1 is the death rate constant for the juvenile stage. The standard incidence function is used with $\beta \frac{I}{N}$ giving the average number of adequate contacts with infectives of one susceptible per unit time. Typical examples of birth rate functions $B(N)$ in the biological literature are:

(B1) $B_1(N) = \frac{p}{q+N^n}$, with $p, q, n > 0$ and $\frac{p}{q} > d$.

(B2) $B_2(N) = \frac{A}{N} + c$, with $A > 0$, $d > c > 0$.

(B3) $B_3(N) = be^{-aN}$, with $a > 0$, $b > d$.

Functions B_1 with $n = 1$ and B_3 are known as Beverton-Holt function and Ricker function, respectively.

Their model was obtained under the following assumptions:

(1) Transmission of disease is assumed to occur due to contact between susceptibles and infectives.

(2) There is no vertical transmission.

(3) The disease confers no immunity, thus upon recovery an infective individual returns to the susceptible class (hence the name SIS model).

This type of model is appropriate for some bacterial infections. If the population does not recover from the disease, the recovery rate constant is set to zero, giving an SI model.

Let $B(t,N)$ and $d(t)$, respectively, be the time-dependent birth and death rates of the population at the adult state, and $d_1(t)$ be the death rate of the population at the juvenile stage. Assume that the maturation delay is $\tau > 0$. It then follows that the rate of entry into the adult stage is

$$B(t-\tau, N(t-\tau))N(t-\tau)e^{-\int_{t-\tau}^{t} d_1(s)ds}.$$

Thus, we obtain the following nonautonomous SIS model:

$$\begin{cases} S'(t) = B(t-\tau, N(t-\tau))N(t-\tau)e^{-\int_{t-\tau}^{t} d_1(s)ds} - d(t)S(t) - \dfrac{\beta(t)S(t)I(t)}{N(t)} \\ \qquad + \gamma(t)I(t), \\ I'(t) = \dfrac{\beta(t)S(t)I(t)}{N(t)} - (d(t) + d_2(t) + \gamma(t))I(t), \end{cases} \tag{2.1}$$

where $N(t) = S(t) + I(t)$, $B(t,N)$, $\beta(t)$, $d(t)$, $d_1(t)$, $d_2(t)$ and $\gamma(t)$ are nonnegative. To incorporate seasonal effects, we further assume that all these functions are T-periodic in t for some $T > 0$. It is easy to see that the function

$$\alpha(t) := e^{-\int_{t-\tau}^{t} d_1(s)ds}$$

is also T-periodic in t. Thus, model (2.1) is a periodic time-delayed differential system. We should point out that the model (2.1) with $B(t,N) = \frac{a}{N} + c$ and $d(t)$, $d_1(t)$, $d_2(t)$ and $\gamma(t)$ being constants was studied in [106]. Here we investigate the global dynamics of (2.1) with the general forms of birth rate functions.

We assume that $B(\cdot,\cdot) \in C^1(\mathbb{R} \times (0,+\infty), \mathbb{R}_+)$ and $B(t,N)N$ admits a continuous extension $G(t,N)$ from $\mathbb{R} \times (0,+\infty)$ to $\mathbb{R} \times \mathbb{R}_+$. It then follows that for any $\phi \in C([-\tau,0], \mathbb{R}_+^2)$, there is a unique local solution $(S(t,\phi), I(t,\phi))$ of system (2.1) with $(S(\theta,\phi), I(\theta,\phi)) = \phi(\theta)$, $\forall \theta \in [-\tau, 0]$ (see, e.g., [38, Theorem 2.3]). Further, we have $(S(t,\phi), I(t,\phi)) \geq 0$ in its maximal interval of existence according to [80, Theorem

5.2.1]. It is also easy to see that if $\phi = (\phi_1, \phi_2) \in C([-\tau, 0], \mathbb{R}^2_+)$ with $\phi_2(0) > 0$, then $I(t, \phi) > 0$ and $S(t, \phi) > 0$ for all $t > 0$ in its maximal interval of existence. For any function $x : [-\tau, \sigma) \to \mathbb{R}^m$, $\sigma > 0$, we define $x_t \in C([-\tau, 0], \mathbb{R}^m)$ by $x_t(\theta) = x(t + \theta)$, $\forall \theta \in [-\tau, 0]$. In what follows, we write $\hat{x}$ for the element of $C([-\tau, 0], \mathbb{R}^m)$ satisfying $\hat{x}(\theta) = x$ for all $\theta \in [-\tau, 0]$.

2.3 A single population growth model

In this section, we consider the single-species population growth model:

$$N'(t) = \alpha(t)B(t - \tau, N(t - \tau))N(t - \tau) - d(t)N(t) \triangleq F(t, N(t), N(t - \tau)), \quad \boxed{2.2}$$

where $\alpha(t) = e^{-\int_{t-\tau}^{t} d_1(s)ds}$. We will establish four sets of sufficient conditions under which system (2.2) admits a globally attractive positive T-periodic solution, and hence, the single population stabilizes eventually at an oscillating state.

For any $\phi \in C([-\tau, 0], \mathbb{R}_+)$, there is a unique local solution $N(t, \phi)$ of (2.2) with $N(\theta, \phi) = \phi(\theta)$, $\forall \theta \in [-\tau, 0]$ (see, e.g., [38, Theorem 2.3]). Moreover, we have $N(t, \phi) \geq 0$ in its maximal interval of existence according to [80, Theorem 5.2.1].

Consider the linear equation with time delay τ:

$$u'(t) = a(t)u(t) + b(t)u(t - \tau), \quad \boxed{2.3}$$

where $a(t)$, $b(t)$ are T-periodic and continuous, $b(t) > 0, \forall t \geq 0$.

For any $\phi \in C([-\tau, 0], \mathbb{R})$, let $u(t, \phi)$ be the unique solution of (2.3) satisfying $u_0 = \phi$. Let $\tilde{P}$ be the Poincaré map associated with (2.3) on $C([-\tau, 0], \mathbb{R})$, that is, $\tilde{P}(\phi) = u_T(\phi)$. The following result comes from [101, Proposition 2.1].

Lemma 2.3.1 *Let $r(\tilde{P})$ be the spectral radius of $\tilde{P}$. Then $r = r(\tilde{P})$ is a positive eigenvalue of $\tilde{P}$ with a positive eigenfunction. Moreover, $u(t) = v_0(t)e^{\frac{t}{T}ln(r)}$ is a solution of (2.3), where $v_0(t)$ is T-periodic and $v_0(t) > 0$, $\forall t \geq 0$. If $\tau = kT$ for some integer $k \geq 0$, then $r - 1$ has the same sign as $\int_0^T (a(t) + b(t))dt$.*

Note that the condition $r(\tilde{P}) < 1$ ($r(\tilde{P}) > 1$) implies that the zero solution of (2.3) is stable (unstable). Thus, Lemma 2.3.1 implies that in the case where the time delay is an integer multiple of the time period, the stability of zero solution of (2.3) is equivalent to that of zero solution of the linear periodic ordinary differential equation $u'(t) = (a(t) + b(t))u(t)$.

2.3.1 A general periodic form of $B_1(N)$

Assume that

(H1) $B(\cdot,\cdot) \in C^1(\mathbb{R} \times (0,+\infty), \mathbb{R}_+)$ with $\frac{\partial B(t,N)}{\partial N} < 0$, $\forall N \in (0,+\infty)$, $\frac{d(t)}{\alpha(t)} > B(t-\tau,\infty)$; and there exists $G(\cdot,\cdot) \in C(\mathbb{R} \times \mathbb{R}_+, \mathbb{R}_+)$ such that $G(t,N) = B(t,N)N$, $\forall t \in \mathbb{R}$, $N > 0$.

(H2) $G(t,0) = 0$ and r_1=r(P_1) > 1, where r(P_1) is the spectral radius of P_1, and P_1 is the Poincaré map of the following linear equation

$$N'(t) = \alpha(t)B(t-\tau,0)N(t-\tau) - d(t)N(t). \tag{2.4}$$

(H3) $\frac{\partial G(t,N)}{\partial N} > 0$, $\forall N \in \mathbb{R}_+$, $t \in \mathbb{R}$.

It then follows that the periodic function $F(t, v_1, v_2)$ has the following properties:

(1) $F(t,0,0) = 0$, $F(t,0,v_2) \geq 0$, $\frac{\partial F(t,v_1,v_2)}{\partial v_2} > 0$, $\forall v_1, v_2 \geq 0$.

(2) F is strictly subhomogeneous, i.e., for any $\lambda \in (0,1)$, $\forall v_1, v_2 > 0$, $F(t, \lambda v_1, \lambda v_2) > \lambda F(t, v_1, v_2)$.

(3) There exists a positive number $h_0 > 0$ such that $F(t, h_0, h_0) \leq 0$.

The following result is a straightforward consequence of [101, Theorem 2.1].

Theorem 2.3.1 *Assume (H1)-(H3) hold. Then equation (2.2) admits a globally attractive positive T-periodic solution* $N^*(t)$ *in* $C([-\tau, 0], \mathbb{R}_+) \setminus \{\hat{0}\}$.

2.3.2 A general periodic form of $B_2(N)$

Assume that

(A1) $B(\cdot,\cdot) \in C^1(\mathbb{R} \times (0, +\infty), \mathbb{R}_+)$ with $\frac{\partial B(t,N)}{\partial N} < 0$, $\forall N > 0$, $t \in \mathbb{R}$, and $\frac{d(t)}{\alpha(t)} > B(t-\tau, \infty)$ for all $t \in \mathbb{R}$.

(A2) There exists $G(\cdot,\cdot) \in C(\mathbb{R} \times \mathbb{R}_+, \mathbb{R}_+)$ such that $G(t, N) = B(t, N)N$, $\forall t \in \mathbb{R}$, $N > 0$, and $G(t, 0) > 0$, $\forall t \in \mathbb{R}$.

(A3) $\frac{\partial G(t,N)}{\partial N} > 0$, $\forall N \in \mathbb{R}_+$, $t \in \mathbb{R}$.

Theorem 2.3.2 *Assume (A1)-(A3) hold. Then equation (2.2) admits a globally attractive positive T-periodic solution* $N^*(t)$ *in* $C([-\tau, 0], \mathbb{R}_+) \setminus \{\hat{0}\}$.

Proof. From (A2), we have $F(t, 0, 0) > 0$ and there is $h_0 > 0$ such that $F(t, h, h) \leq 0$ for all $h > h_0$. It then follows from [80, Remark 5.2.1] that $[\hat{0}, \hat{h}]$ is positively invariant. Thus, for any $\phi \geq \hat{0}$, we can find some $h_\phi > h_0$ such that $\phi \leq \hat{h}_\phi$, and hence $N(t, \phi)$ exists for all $t \geq 0$. Define the Poincaré map $P_2 : C([-\tau, 0], \mathbb{R}_+) \to C([-\tau, 0], \mathbb{R}_+)$ by $P_2(\phi) = N_T(\phi)$. Thus, [80, Theorem 5.1.1 and Corollary 5.3.5] imply that P_2 is monotone and $P_2^{n_0}$ is strongly monotone when $n_0T \geq 2\tau$. By the theory of delay differential equation (see, e.g., [38, Theorem 3.6.1]), $P_2^{n_0}$ is compact. Moreover, we note that $F(t, u, v)$ is strictly subhomogeneous in (u, v). Using the similar arguments as in [104, Theorem 3.3], we can deduce that P_2 is strictly subhomogeneous in the sense $P_2(\alpha\phi) > \alpha P_2(\phi)$ for $\phi \gg \hat{0}$ and $0 < \alpha < 1$. Thus, $P_2^{n_0}$ is also strictly subhomogeneous.

Note that $\hat{0} \leq P_2(\hat{0})$. We claim $\hat{0} < P_2(\hat{0})$. Suppose not, then $P_2(\hat{0}) = \hat{0}$. hence, $N(T+\theta, \hat{0}) = 0$ for all $\theta \in [-\tau, 0]$ and $N'(T, \hat{0}) = 0$. However, $N'(T, \hat{0}){=}G(T-\tau, 0)\alpha(t) > 0$, a contradiction. Consequently, $\hat{0} < P_2(\hat{0})$. Thus,

$$\hat{0} < P_2(\hat{0}) \leq P_2^2(\hat{0}) \leq \cdots \leq P_2^{n_0}(\hat{0}) \ll P_2^{n_0+1}(\hat{0}) \leq \cdots .$$

Therefore, for any $\phi_1 \in \omega_{n_0}(\hat{0})$, we have $\phi_1 \geq P_2^{n_0+1}(\hat{0}) \gg 0$, where $\omega_{n_0}(\phi)$ denotes the omega-limit set of ϕ under $P_2^{n_0}$. Moreover, $\forall \phi \geq \hat{0}$ and $\forall \psi \in \omega_{n_0}(\phi)$, we have $\psi \geq P_2^{n_0+1}(\hat{0}) \gg 0$ from the monotonicity of $P_2^{n_0}$.

By Theorem 1.1.2 as applied to $P_2^{n_0}$, there exists a $\phi_0 \gg \hat{0}$ with $P_2^{n_0}(\varphi_0) = \phi_0$ such that $\phi_0 = \omega_{n_0}(\varphi)$ for all of $\varphi \geq \hat{0}$. Regarding (2.2) as an n_0T-periodic system, we then see that (2.2) admits a globally attractive positive n_0T-periodic solution $N(t, \phi_0)$. It remains to prove that $N(t, \phi_0)$ is T-periodic, that is, ϕ_0 is a fixed point of P_2. Since

$$\hat{0} < P_2(\hat{0}) \leq P_2^2(\hat{0}) \leq \cdots \leq P_2^{n_0}(\hat{0}) \ll P_2^{n_0+1}(\hat{0}) \leq \cdots$$

and $P_2^{nn_0}(\hat{0}) \to \phi_0$ as $n \to \infty$, it easily follows that $P_2^n(\hat{0}) \to \phi_0$ as $n \to \infty$, and hence, ϕ_0 is the fixed point of P_2. Therefore, $N(t, \phi_0)$ is a globally attractive T-periodic solution for (2.2) in $C([-\tau, 0], \mathbb{R}_+) \setminus \{\hat{0}\}$. ■

2.3.3 A general periodic form of $B_3(N)$

In this subsection, we take $B(t, N) = p(t)e^{-q(t)N}$ and assume that

(S1) $p(t)$, $q(t)$, $d(t)$, $d_1(t)$ are nonnegative and T-periodic in t, and $p(t) > 0$, $q(t) > 0$ for all $t \in \mathbb{R}$;

(S2) r=r(P_3) > 1, where r(P_3) is the spectral radius of P_3, and P_3 is the Poincaré map of the following linear equation

$$N'(t) = \alpha(t)p(t-\tau)N(t-\tau) - d(t)N(t). \tag*{\boxed{2.5}}$$

Note that

$$\begin{aligned} N'(t) &= \alpha(t)p(t-\tau)e^{-q(t-\tau)N(t-\tau)}N(t-\tau) - d(t)N(t) \\ &\leq \alpha(t)\frac{p(t-\tau)}{q(t-\tau)}e^{-1} - d(t)N(t). \end{aligned}$$

Consider the periodic ordinary differential equation

$$\bar{U}'(t) = \alpha(t)\frac{p(t-\tau)}{q(t-\tau)}e^{-1} - d(t)\bar{U}(t). \tag*{\boxed{2.6}}$$

It then follows that equation (2.6) has a unique periodic solution

$$\begin{aligned} &\bar{U}^*(t) = e^{-\int_0^t d(s)ds} \times \\ &\left[\int_0^t \alpha(w)\frac{p(w-\tau)}{q(w-\tau)}e^{-1}e^{\int_0^w d(s)ds}dw + \frac{\int_0^T \alpha(w)\frac{p(w-\tau)}{q(w-\tau)}e^{-1}e^{\int_0^w d(s)ds}dw}{e^{\int_0^T d(s)ds} - 1}\right] \end{aligned}$$

and $\bar{U}^*(t)$ is globally asymptotically attractive for (2.6) with $\bar{U}(0) \geq 0$. By the comparison theorem, we have $N(t,\phi) \leq \bar{U}(t,\phi(0))$ for all t in its maximal interval of existence, where $\bar{U}(t,\phi(0))$ is the solution of (2.6) with $\bar{U}(0) = \phi(0)$. Since $\lim_{t\to\infty}(\bar{U}(t,\phi(0)) - \bar{U}^*(t)) = 0$, the solution for (2.2) exists globally, and the periodic solution semiflow for (2.2) is point dissipative.

In addition to (S1)-(S2), we further assume that

(S3) $\bar{U}^*(t) \leq \frac{1}{q(t)}$.

Then the following result holds.

Theorem 2.3.3 *Assume (S1)-(S3) hold. Then (2.2) admits a globally attractive positive T-periodic solution* $N^*(t)$ *in* $C([-\tau,0],\mathbb{R}_+)\setminus\{\hat{0}\}$.

Proof. Let P_4 is the Poincaré map associated with (2.2). It then follows that $\omega(\psi)\subseteq[\hat{0},\bar{U}_0^*]$ for any $\psi\in C([-\tau,0],\mathbb{R}_+)$, where $\omega(\psi)$ is the omega limit set of $\psi\geq\hat{0}$ for P_4 and $\bar{U}_0^*\in C([-\tau,0],\mathbb{R}_+)$ with $\bar{U}_0^*(\theta)=\bar{U}^*(\theta)$, $\forall\theta\in[-\tau,0]$. Furthermore, for each $\phi\in[\hat{0},\bar{U}_0^*]$, we have $\phi(0)\leq\bar{U}^*(0)$, and hence, $N(t,\phi)\leq\bar{U}^*(t)$ for all $t\geq0$, which implies that $[\hat{0},\bar{U}_0^*]$ is positively invariant for P_4.

For a positive $\varepsilon>0$, let r_ε be the spectral radius of

$$v'(t)=(\alpha(t)p(t-\tau)-\varepsilon_0)v(t-\tau)-d(t)v(t). \tag*{\boxed{2.7}}$$

Since $r(P_3)>1$, we can choose ε_0 small enough such that $r_{\varepsilon_0}>1$ and $\alpha(t)p(t-\tau)-\varepsilon_0>0$. From Lemma 2.3.1, (2.7) admits a solution $v^*(t)=e^{\frac{t}{T}ln r_{\varepsilon_0}}u_0(t)$, where $u_0(t)$ is positive and T-periodic. Hence, $v^*(t)\to\infty$.

For $\varepsilon_0>0$, we choose a sufficiently small positive number δ_0, such that

$$\alpha(t)p(t-\tau)e^{-q(t-\tau)N}\geq\alpha(t)p(t-\tau)-\varepsilon_0,\ \forall t\geq0,\ 0\leq N<\delta_0.$$

Since $\lim\limits_{\phi\to0}N_t(\phi)\to0$ uniformly for $t\in[0,T]$, there exists $\delta_1>0$ such that

$$\|N_t(\phi)\|\leq\delta_0,\ \forall t\in[0,T],\ \ \|\phi\|\leq\delta_1.$$

We first claim that $\limsup\limits_{n\to\infty}\|P_4^n\psi\|\geq\delta_1$ for all of $\psi\in[\hat{0},\bar{U}_0^*]\setminus\{\hat{0}\}$. Suppose not, and $\limsup\limits_{n\to\infty}\|P_4^n\phi\|<\delta_1$ for some $\phi\in[\hat{0},\bar{U}_0^*]\setminus\{\hat{0}\}$, then there exists an integer $N_1\geq1$ such that $\|P_4^n\phi\|<\delta_1,\forall n\geq N_1$. For any $t-\tau\geq N_1T$, we have $t=nT+t'$ with $n\geq N_1$, $t'\in[0,T]$ and $\|N_t(\phi)\|=\|N_{t'}(P_4^n\phi)\|\leq\delta_0$. Then

$$\begin{aligned}N'(t,\phi)&\geq\alpha(t)p(t-\tau)e^{-q(t-\tau)N(t-\tau,\phi)}N(t-\tau,\phi)-d(t)N(t,\phi)\\&\geq(\alpha(t)p(t-\tau)-\varepsilon_0)N(t-\tau,\phi)-d(t)N(t,\phi).\end{aligned}$$

Since $N(t,\phi) > 0$, $\forall t > \tau$, we can choose a small number $k > 0$ such that $N(t) > kv^*(t)$, $\forall t \in [N_2T, N_2T+\tau]$, where $N_2 > N_1$ and $N_2T > \tau$. By the comparison theorem (see e.g. [80, Theorem 5.1.1]), we have $N(t,\phi) > kN^*(t)$, $\forall t \geq N_2T+\tau$. Thus, $\lim\limits_{t\to\infty} N(t,\phi) = \infty$, a contradiction.

Let $X = [\hat{0}, \bar{U}_0^*]$ and $X_0 = \{\phi \in X : \phi(0) > 0\}$, define $\partial X_0 = X \setminus X_0$. Note that P_4 is point dissipative, asymptotically smooth and the orbits of bounded sets are bounded. It then follows from Theorem 1.2.1 that P_4 admits a global attractor $A \in X$. It is clear that $M_\partial := \{\phi \in \partial X_0 : P_4^n(\phi) \in \partial X_0, \forall n \geq 0\} = \{\hat{0}\}$ and $\Omega(M_\partial) := \cup_{\phi \in M_\partial} \omega(\phi) = \{\hat{0}\}$, where $\omega(\phi)$ is the ω-limit set of ϕ with respect to P_4. In view of the above claim, $\{\hat{0}\}$ is isolated in X and $W^s(\hat{0}) \cap X_0 = \varnothing$ where $W^s(\hat{0})$ is the stable set of $\hat{0}$ for P_4. Moreover, for each $\psi \in \partial X_0$ and $\psi \neq \hat{0}$, there exists a $t_0 \in [0,\tau]$ such that $N(t_0,\psi) > 0$, where $N(t,\psi)$ is the solution of equation (2.2) through ψ. Hence, $N(t,\psi) > 0$ for all $t \geq t_0$, which implies that $P_4^n(\psi) \in X_0$ for $nT > \tau$. Therefore, $\omega(\phi) \neq \{\hat{0}\}$ and there is no cycle in ∂X_0 from $\hat{0}$ to $\hat{0}$. By the acyclicity theorem on uniform persistence for maps (see Theorem 1.2.2 or [105, Theorem 1.3.1 and Lemma 1.3.1]), it follows that $P_4 : C([-\tau,0],\mathbb{R}_+) \to C([-\tau,0],\mathbb{R}_+)$ is uniformly persistent with respect to X_0. Note that P_4 is an α-contraction for an equivalent norm in $C([-\tau,0],\mathbb{R}_+)$ (see [37, Theorem 4.1.1]). Moreover, P_4 is point dissipative and P_4^n is compact for $nT > \tau$. Thus, Theorem 1.2.6 implies that $P_4 : X_0 \to X_0$ admits a global attractor A_0 in X_0. Since for every $\phi \in A_0$, $N(t,\phi) > 0$ for all $t \geq 0$, it follows from the invariance of A_0 for P_4 that $A_0 \subset int(C([-\tau,0],\mathbb{R}_+))$. Consequently, for any $\psi \in X \setminus \{\hat{0}\}$, we have $\omega(\psi) \subset A_0 \subset int(C([-\tau,0],\mathbb{R}_+))$.

Define

$$E(t,u,v) := \alpha(t)p(t-\tau)ve^{-q(t-\tau)v} - d(t)u.$$

For any $\phi \in [\hat{0}, \bar{U}_0^*]$, we have

$$\begin{aligned}
&\frac{\partial E}{\partial v}(t, N(t), N(t-\tau,\phi)) \\
&= (1 - q(t-\tau)N(t-\tau,\phi))\alpha(t)p(t-\tau)e^{-q(t-\tau)N(t-\tau,\phi)} \\
&> (1 - q(t-\tau)U^*(t-\tau))\alpha(t)p(t-\tau)e^{-q(t-\tau)N(t-\tau,\phi)} \geq 0.
\end{aligned}$$

It then follows that $P_4^{n_0}$ is strongly monotone in $[\hat{0}, \bar{U}_0^*]$ when $n_0 T \geq 2\tau$. Note that $E(t, N(t), N(t-\tau))$ is strictly subhomogeneous. Using the same argument as in [104, Theorem 3.3], we can deduce that P_4 is strictly subhomogeneous. Thus, $P_4^{n_0}$ is also strictly subhomogeneous. It then follows from Theorem 1.1.2, as applied to $P_4^{n_0} : U = [\hat{0}, \bar{U}_0^*] \to U$, that $P_4^{n_0}$ has a fixed point $\phi_0 \gg 0$ in $[\hat{0}, \bar{U}_0^*]$ such that every nonempty compact invariant set of $P_4^{n_0}$ is in $int(C([-\tau, 0], \mathbb{R}_+))$. Since for each $\psi \in C([-\tau, 0], \mathbb{R}_+) \setminus \{\hat{0}\}$, $\omega(\psi)$ is a nonempty compact invariant set of $P_4^{n_0}$ in $[\hat{0}, \bar{U}_0^*]$ and $\omega(\psi) \subset int(C([-\tau, 0], \mathbb{R}_+))$, it follows that $\omega(\psi) = \phi_0$, and hence, $P_4(\phi_0) = \phi_0$. Therefore, $N(t, \phi_0)$ is a globally attractive T-periodic solution for (2.2) in $C([-\tau, 0], \mathbb{R}_+) \setminus \{\hat{0}\}$. ∎

Assume that

(S3)$'$ $\max\limits_{0 \leq t \leq T}\{\alpha(t)p(t-\tau)e^{-2}\} < \min\limits_{0 \leq t \leq T}\{\frac{1}{\tau e^{1+\tau d(t)}}\}$.

Then, we have the following result.

Theorem 2.3.4 *Assume that (S1),(S2) and (S3)$'$ hold. Then (2.2) admits a globally attractive positive T-periodic solution in $C([-\tau, 0], \mathbb{R}_+) \setminus \{\hat{0}\}$.*

Proof. Note that

$$E(t, u_2, v_2) - E(t, u_1, v_1) \geq -d(t)(u_2 - u_1) - p(t-\tau)e^{-2}\alpha(t)(v_2 - v_1).$$

We use the exponential ordering introduced in [81] to prove this theorem. For some $\mu \geq 0$, we define

$$\tilde{K_\mu} = \{\phi \in C([-\tau, 0], \mathbb{R}_+) : \phi \geq 0 \text{ and } \phi(s)e^{\mu s} \text{ is nondecreasing on } [-\tau, 0]\},$$

and $K_\mu = \tilde{K_\mu} \cap C_L$ where C_L is the Banach space of Lipschitz functions on $[-\tau, 0]$ with the norm $\|\phi\|_{Lip} := |\phi| + \sup\{|\frac{\phi(s)-\phi(t)}{s-t}| : s \neq t, s, t \in [-\tau, 0]\}$.

Denote the exponential ordering defined by K_μ as $\leq_\mu$. Then if $\phi <_\mu \psi$, we have

$$e^{-\mu\tau}[\psi(-\tau) - \varphi(-\tau)] \leq \psi(0) - \phi(0), \quad i.e., \quad \psi(-\tau) - \phi(-\tau) \leq e^{\mu\tau}[\psi(0) - \phi(0)].$$

Therefore,

$$\begin{aligned}
&\mu(\psi(0) - \phi(0)) + E(t, N(t, \psi), N(t-\tau, \psi)) - E(t, N(t, \phi), N(t-\tau, \phi)) \\
&= \mu(\psi(0) - \phi(0)) + E(t, \psi(0), \psi(-\tau)) - E(t, \phi(0), \phi(-\tau)) \\
&\geq \mu(\psi(0) - \phi(0)) - d(t)(\psi(0) - \phi(0)) - \alpha(t)p(t-\tau)e^{-2}(\psi(-\tau) - \phi(-\tau)) \\
&\geq [\mu - d(t) - \alpha(t)p(t-\tau)e^{-2}e^{\mu\tau}](\psi(0) - \phi(0)).
\end{aligned}$$

Since

$$\max_{0 \leq t \leq T}\{\alpha(t)p(t-\tau)e^{-2}\} < \min_{0 \leq t \leq T}\{\frac{1}{\tau e^{1+\tau d(t)}}\} \quad \text{and} \quad \psi(0) - \phi(0) > 0,$$

there is some $\mu > 0$ such that

$$\mu - d(t) - \alpha(t)p(t-\tau)e^{-2}e^{\mu\tau} > 0,$$

and hence,

$$\mu(\psi(0) - \phi(0)) + E(t, \psi(0), \psi(-\tau)) - E(t, \phi(0), \phi(-\tau)) > 0.$$

For every $\phi \geq \hat{0}$, we have $N(t, \phi) \geq 0$ and there exists $M_\phi > 0$ such that $\phi \ll_\mu \hat{M}_\phi$ and $E(t, M_\phi, M_\phi) < 0$. Thus $N(t, \phi) \leq M_\phi$, $N(t, \phi)$ exists for all $t \geq 0$. By [80, Theorem

6.2.3], $P_5^{n_0}$ is strongly monotone in the ordered space (C_L, K_μ) for $n_0T \geq \tau$, where P_5 is the Poincaré map of (2.2).

If $\phi \gg_\mu 0$ in K_μ, then $N(t,\phi) > 0$ for all $t > -\tau$. For $0 < \lambda < 1$, let $W(t) = N(t,\lambda\phi) - \lambda N(t,\phi)$, then W(0)=0. Since

$$\begin{aligned} W'(0) &= N'(0,\lambda\phi) - \lambda N'(0,\phi) \\ &= \alpha(0)p(-\tau)e^{-q(-\tau)\lambda\phi(-\tau)}\lambda\phi(-\tau) - \lambda\alpha(0)p(-\tau)e^{-q(-\tau)\phi(-\tau)}\phi(-\tau) > 0, \end{aligned}$$

we have $W(t) > 0$ for all sufficiently small $t > 0$.

We further claim $W(t) > 0$ for all $t > 0$. Suppose not. Then there is $t_0 > 0$ such that $W(t_0) = 0$, $W(t) > 0$ for $t < t_0$, and $\frac{dW(t)}{dt}\Big|_{t_0} \leq 0$. Since $\lambda\phi \ll_\mu \phi$, $N(t_0-\tau,\lambda\phi) < N(t_0-\tau,\phi)$. Then we have

$$\begin{aligned} \frac{dW(t)}{dt}\Big|_{t_0} &= E(t_0, N(t_0,\lambda\phi), N(t_0-\tau,\lambda\phi)) - \lambda E(t_0, N(t_0,\phi), N(t_0-\tau,\phi)) \\ &= \alpha(t_0)p(t_0-\tau)e^{-q(t_0-\tau)N(t_0-\tau,\lambda\phi)}N(t_0-\tau,\lambda\phi) - d(t_0)N(t_0,\lambda\phi) \\ &\quad -[\alpha(t_0)p(t_0-\tau)e^{-q(t_0-\tau)N(t_0-\tau,\phi)}\lambda N(t_0-\tau,\phi) - \lambda d(t_0)N(t_0,\phi)] \\ &> \alpha(t_0)p(t_0-\tau)e^{-q(t_0-\tau)N(t_0-\tau,\lambda\phi)}\lambda N(t_0-\tau,\phi) \\ &\quad -\alpha(t_0)p(t_0-\tau)e^{-q(t_0-\tau)N(t_0-\tau,\phi)}\lambda N(t_0-\tau,\phi) \\ &= \alpha(t_0)p(t_0-\tau)[e^{-q(t_0-\tau)N(t_0-\tau,\lambda\phi)} - e^{-q(t_0-\tau)N(t_0-\tau,\phi)}]\lambda N(t_0-\tau,\phi) > 0, \end{aligned}$$

a contradiction. This proves that $W(t) > 0$ for all $t > 0$.

For every $\phi \gg_\mu 0$, let $Z(t)$=$[N(t,\lambda\phi) - \lambda N(t,\phi)]' + \mu[N(t,\lambda\phi) - \lambda N(t,\phi)]$. Then $Z(0) = W'(0) > 0$, hence for sufficiently small $t > 0$, $Z(t) > 0$. We claim that $Z(t) > 0$ for all $t > 0$. Suppose not, then there is a $t_0 > 0$ such that $Z(t_0) = 0$ and

$Z(t) > 0$ for $t < t_0$. It then follows that

$$
\begin{aligned}
Z(t_0) &= \alpha(t_0)p(t_0-\tau)e^{-q(t_0-\tau)N(t_0-\tau,\lambda\phi)}N(t_0-\tau,\lambda\phi) + \mu[N(t_0,\lambda\phi)-\lambda N(t_0,\phi)] \\
&\quad -[\lambda\alpha(t_0)p(t_0-\tau)e^{-q(t_0-\tau)N(t_0-\tau,\phi)}N(t_0-\tau,\phi) - \lambda d(t_0)N(t_0,\phi)] - d(t_0)N(t_0,\lambda\phi) \\
&> \alpha(t_0)p(t_0-\tau)e^{-q(t_0-\tau)N(t_0-\tau,\lambda\phi)}N(t_0-\tau,\lambda\phi) + [\mu - d(t_0)][N(t_0,\lambda\phi)-\lambda N(t_0,\phi)] \\
&\quad -\alpha(t_0)p(t_0-\tau)e^{-q(t_0-\tau)\lambda N(t_0-\tau,\phi)}\lambda N(t_0-\tau,\phi) \\
&\geq -\alpha(t_0)p(t_0-\tau)e^{-2}[N(t_0-\tau,\lambda\phi)-\lambda N(t_0-\tau,\phi)] \\
&\quad +[\mu - d(t_0)][N(t_0,\lambda\phi)-\lambda N(t_0,\phi)].
\end{aligned}
$$

Since $Z(t) > 0$ for all $t < t_0$, we have $N(t_0-\tau,\lambda\phi) - \lambda N(t_0-\tau,\phi) \leq e^{\mu\tau}$ $[N(t_0,\lambda\phi) - \lambda N(t_0,\phi)]$, and hence

$$Z(t_0) > [-\alpha(t_0)p(t_0-\tau)e^{-2}e^{\mu t} + \mu - d(t_0)][N(t_0,\lambda\phi) - \lambda N(t_0,\phi)] > 0,$$

a contradiction. Thus, $Z(t) > 0$ for all $t > 0$. It then follows from [80, Theorem 6.2.3] that $N_t(\lambda\phi) \gg_\mu \lambda N_t(\phi)$ for $t > \tau$ and $P_5^{n_0}(\lambda\phi) \gg_\mu \lambda P_5^{n_0}(\phi)$ in K_μ for $n_0 T > \tau$.

Since for every $\phi \in C([-\tau,0],\mathbb{R}_+) \setminus \{\hat{0}\}$ and $t > 0$, we have

$$
\begin{aligned}
&[N(t,\phi)]' + \mu N(t,\phi) \\
&= \alpha(t)p(t-\tau)e^{-q(t-\tau)N(t-\tau,\phi)}N(t-\tau,\phi) - d(t)N(t,\phi) + \mu N(t,\phi) \\
&> [\mu - d(t)]N(t,\phi) \geq 0,
\end{aligned}
$$

and hence, $P_5^{n_0}(\phi) \in int(K_\mu)$ for $n_0 T > \tau$. By using $P_5^{n_0}(\phi)$ if necessary, we may therefore assume that $\phi \in int(K_\mu)$ to study the asymptotic behavior of $\phi > 0$ under $P_5^{n_0}$.

For any $\beta \geq 1$, choose $V_\beta = [\hat{0}, \beta\hat{h_0}]_{K_\mu}$ where h_0 is determined such that $p(t-\tau)$ $e^{-q(t-\tau)h}$ $\alpha(t) < d(t)$ always holds for all $t \geq 0$ and $h > h_0$. Then V_β is positively invariant. First note that when $n_0 T > \tau$, $P_5^{n_0}$ is order-compact in the sense that $P_5^{n_0}([u,v]_{K_\mu})$ is precompact for all of $u <_{K_\mu} v$. Moreover, $P_5^{n_0}$ is strictly subhomogeneous and strongly monotone with respect to the exponential ordering.

By the continuity and differentiability of solutions with respect to initial values, it follows that the P_5 is differentiable at zero, and $DP_5(0) = P_3$, where P_3 is the Poincaré map of the linear equation of (2.5). Clearly, $P_3^{n_0}$ is compact. Moreover, $P_3^{n_0}$ is strongly positive for the exponential ordering K_μ. Furthermore, $D(P_5^{n_0}(\hat{0})) = (DP_5(\hat{0}))^{n_0}$ and $r\{D(P_5^{n_0}(\hat{0}))\} = r\{(DP_5(\hat{0}))\}^{n_0} = [r(P_3)]^{n_0}$. By Theorem 1.1.3, $P_5^{n_0}$ has a unique positive fixed point ϕ_0 in V_β, and ϕ_0 is globally asymptotically stable with respect to $V_\beta \setminus \{\hat{0}\}$. This implies that $\omega_{n_0}(\phi) = \phi_0$ for all $\phi \in V_\beta$, where $\omega_{n_0}(\phi)$ is the ω-limit set of ϕ associated with $P_5^{n_0}$.

By the arbitrariness of β, it then follows that (2.2) admits a globally attractive, positive n_0T-periodic solution $N(t, \phi_0)$ in $C([-\tau, 0], \mathbb{R}_+) \setminus \{\hat{0}\}$. It remains to prove that $N(t, \phi_0)$ is also T-periodic. For $\phi > \hat{0}$, since $P_5^{nn_0}(\phi) \to \phi_0$ as $n \to \infty$, it then follows that $P_5(P_5^{nn_0}(\phi)) \to P_5(\varphi_0)$ as $n \to \infty$. On the other hand, $P_5(P_5^{nn_0}(\phi)) = P_5^{nn_0}(P_5(\phi)) \to \phi_0$ as $n \to \infty$. Thus, $P_5(\phi_0) = \phi_0$, and $N(t, \phi_0)$ is a globally attractive T-periodic solution for (2.2) in $C([-\tau, 0], \mathbb{R}_+) \setminus \{\hat{0}\}$. ■

2.4 Threshold dynamics

We now assume that a disease is invading the population, and the population is divided into susceptible and infective classes. The disease transmission is modeled by system (2.1). In this section, we will study the global dynamics of system (2.1). Let

$$M := C([-\tau, 0], \mathbb{R}_+^2),\ M_0 := \{(\phi_1, \phi_2) \in M : \phi_2(0) > 0\} \text{ and } \partial M_0 := M \backslash M_0.$$

Clearly, M_0 is an open set relative to M. Note that $(N^*(t), 0)$ is the disease-free periodic solution of (2.1). By linearizing (2.1) at $(N^*(t), 0)$, we obtain the following linearized equation for the infective population variable I:

$$I'(t) = \beta(t)I(t) - (d(t) + d_2(t) + \gamma(t))I(t). \tag{2.8}$$

Let C_T be the ordered Banach space of all T-periodic functions from $\mathbb{R}$ to $\mathbb{R}$, which is equipped with the maximum norm $\|\cdot\|$ and the positive cone $C_T^+ := \{\phi \in C_T : \phi(t) \geq 0, \ \forall t \in \mathbb{R}\}$. According to the theory developed in [95] (see also section 1.3) with $F(t) = \beta(t)$ and $V(t) = d(t) + d_2(t) + \gamma(t)$, we define the next infection operator $L : C_T \to C_T$ by

$$(L\phi)(t) = \int_0^\infty Y(t, t-a)\beta(t-a)\phi(t-a)da, \quad \forall t \in \mathbb{R}, \quad \phi \in C_T,$$

where $Y(t,s) = e^{-\int_s^t V(u)du} = e^{-\int_s^t (d(u)+d_2(u)+\gamma(u))du}$, $t \geq s$. Then the basic reproduction ratio is defined as $\mathcal{R}_0 := \rho(L)$, the spectral radius of L. By Theorem 1.3.3, it follows that

$$\mathcal{R}_0 = \frac{\int_0^T \beta(t)dt}{\int_0^T (d(t) + d_2(t) + \gamma(t))dt}.$$

Note that in the previous section, we have obtained four sets of sufficient conditions for system (2.2) to have a globally attractive positive T-periodic solution $N^*(t)$ (see Theorems 2.3.1–2.3.4). We are now in a position to prove the threshold type result on the global dynamics of (2.1) in terms of $\mathcal{R}_0$.

Theorem 2.4.1 *Assume that (2.2) has a globally attractive positive T-periodic solution $N^*(t)$ in $C([-\tau, 0], R_+) \setminus \{\hat{0}\}$, and that there is an L such that $B(t-\tau, N)\alpha(t) < d(t)$, $\forall N > L$, $t > 0$. Let $G(t,N) = B(t,N)N$ satisfy one of the following conditions:*

(C1) $G(t,0) \equiv 0$ and $r = r(\check{P}) > 1$, where $r(\check{P})$ is the spectral radius of $\check{P}$ and $\check{P}$ is the Poincaré map of the following linear equation:

$$N'(t) = \alpha(t)B(t-\tau, 0)N(t-\tau) - (d(t) + d_2(t))N(t).$$

(C2) $G(t, 0) > 0$ for all $t \geq 0$.

Then the following statements are valid:

(a) If $\mathcal{R}_0 < 1$*, then any solution* $(S(t,\phi), I(t,\phi))$ *of system (2.1) with* $\phi \in M_0$ *satisfies* $\lim_{t\to\infty}(S(t,\phi) - N^*(t)) = 0$ *and* $\lim_{t\to\infty} I(t,\phi) = 0$.

(b) If $\mathcal{R}_0 > 1$*, system (2.1) has a positive* T*-periodic solution in* M_0*, and there is an* $\eta > 0$ *such that any solution* $(S(t,\phi), I(t,\phi))$ *of system (2.1) with* $\phi \in M_0$ *satisfies* $\liminf_{t\to\infty} S(t,\phi) \geq \eta$ *and* $\liminf_{t\to\infty} I(t,\phi) \geq \eta$.

Proof. Let $(S(t,\phi), I(t,\phi))$ be the unique solution of (2.1) with $(S(\theta,\phi), I(\theta,\phi)) = \phi(\theta)$, $\forall \theta \in [-\tau, 0]$. Since $N(t,\phi) = S(t,\phi) + I(t,\phi) \geq 0$ in the maximal interval of existence, N(t) satisfies the differential inequality

$$N'(t) \leq \alpha(t)B(t-\tau, N(t-\tau))N(t-\tau) - d(t)N(t).$$

For $\phi \in M$, there is a $M_\phi > L$ and $\hat{M}_\phi > \phi$ such that $B(t-\tau, M_\phi)\alpha(t) \leq d(t)$. By [80, Theorem 5.2.1], $N(t,\phi)$ is uniformly bounded. Since $S(t,\phi) \leq N(t,\phi)$ and $I(t,\phi) \leq N(t,\phi)$, it follows that each solution $(S(t,\phi), I(t,\phi))$ exists globally on $[0,\infty)$, and solutions of (2.1) is uniformly bounded in M. Define $\Phi(t)\phi = (S_t(\phi), I_t(\phi))$, $t \geq 0$, $\phi \in M$. Then $\Phi(t)$ is a T-periodic semiflow on M. We have following claims:

Claim 1. There is some $\delta_1 > 0$ such that $\limsup_{n\to\infty} \|\Phi(nT)\phi\| \geq \delta_1$ for all $\phi \in M_0$.

In the case where (C1) holds, for a positive $\varepsilon > 0$, let r_ε be the spectral radius of

$$u'(t) = (\alpha(t)B(t-\tau, 0^+) - \varepsilon)u(t-\tau) - (d(t) + d_2(t))u(t). \qquad \boxed{2.9}$$

Since $\mathrm{r}(\check{P}) > 1$, we can choose ε small enough such that $r_\varepsilon > 1$ and $B(t, 0^+) - \varepsilon > 0$ for all $t \geq 0$. From Lemma 2.3.1, (2.9) admits a solution $u^*(t) = e^{\frac{t}{T} ln r_\varepsilon} u_0(t)$, where $u_0(t)$ is positive and T-periodic. Hence $u^*(t) \to \infty$.

For $\varepsilon > 0$, we can choose a sufficiently small positive number δ_0, such that

$$\alpha(t)B(t-\tau, N) \geq \alpha(t)B(t-\tau, 0^+) - \varepsilon,\ \forall t \geq 0,\ 0 \leq N < \delta_0.$$

Since $\lim\limits_{\phi\to 0} N_t(\phi) \to 0$ uniformly for $t \in [0, T]$, there exists $\delta_1 > 0$ such that

$$\|N_t(\phi)\| \leq \delta_0,\ \forall t \in [0, T],\ \|\phi\| \leq \delta_1.$$

Suppose, by contradiction, that $\limsup\limits_{n\to\infty} \|\Phi(nT)\phi\| < \delta_1$ for some $\phi \in M_0$. Then there exists an integer $N_1 \geq 1$ such that $\|\Phi(nT)\phi\| < \delta_1$, $\forall n \geq N_1$. For any $t - \tau \geq N_1T$, we have $t = nT + t'$ with $n \geq N_1$, $t' \in [0, T]$ and $\|\Phi(t)\phi\| = \|\Phi(t')\Phi(nT)\phi\| \leq \delta_0$. Then,

$$\begin{aligned} N'(t) &\geq \alpha(t)B(t-\tau, N(t-\tau))N(t-\tau) - (d(t) + d_2(t))N(t) \\ &\geq (\alpha(t)B(t-\tau, 0^+) - \varepsilon)N(t-\tau) - (d(t) + d_2(t))N(t). \end{aligned}$$

Since $N(t,\phi) = S(t,\phi) + I(t,\phi) > 0$, $\forall t > 0$, $\forall \phi \in M_0$, we can choose a small number $k > 0$ such that $N(t,\phi) > ku^*(t), \forall t \in [N_1T, N_1T + \tau]$. By the comparison theorem [80, Theorem 5.1.1], we have $N(t,\phi) > ku^*(t), \forall t \geq N_1T$, and hence, $\lim\limits_{t\to\infty} N(t,\phi) = \infty$, a contradiction to the uniform boundedness of $N(t,\phi)$.

In the case where (C2) holds, we can choose ε small enough such that

$$\min_{t\geq 0}\{\alpha(t)B(t-\tau, 0^+) - \varepsilon\} > \max_{t\geq 0}\{d(t) + d_2(t)\}.$$

For $\varepsilon > 0$, we can choose a sufficiently small positive number δ_0, such that

$$\alpha(t)B(t-\tau, N) \geq \alpha(t)B(t-\tau, 0^+) - \varepsilon,\ \forall t \geq 0,\ 0 \leq N < \delta_0.$$

Since $\lim\limits_{\phi\to 0} N_t(\phi) \to 0$ uniformly for $t \in [0, T]$, there exists $\delta_1 > 0$ such that

$$\|N_t(\phi)\| \leq \delta_0,\ \forall t \in [0, T],\ \|\phi\| \leq \delta_1.$$

Suppose, by contradiction, that $\limsup_{n\to\infty} \|\Phi(nT)\phi\| < \delta_1$ for some $\phi \in M_0$. Then there exists an integer $N_1 \geq 1$ such that $\|\Phi(nT)\phi\| < \delta_1$, $\forall n \geq N_1$. For any $t-\tau \geq N_1 T$, we have $t = nT + t'$ with $n \geq N_1$, $t' \in [0,T]$ and $\|\Phi(t)\phi\| = \|\Phi(t')\Phi(nT)\phi\| \leq \delta_0$. Thus

$$\begin{aligned} N'(t) &\geq \alpha(t)B(t-\tau, N(t-\tau))N(t-\tau) - (d(t)+d_2(t))N(t) \\ &\geq (\alpha(t)B(t-\tau, 0^+) - \varepsilon)N(t-\tau) - (d(t)+d_2(t))N(t) \\ &> \min_{t\geq 0}\{\alpha(t)B(t-\tau,0^+) - \varepsilon\}N(t-\tau) - \max_{t\geq 0}\{d(t)+d_2(t)\}N(t). \end{aligned}$$

Since

$$\min_{t\geq 0}\{\alpha(t)B(t-\tau,0^+) - \varepsilon\} > \max_{t\geq 0}\{d(t)+d_2(t)\},$$

it follows from [80, Theorem 5.1.1] that there is a solution $u^*(t) = e^{st}u$ with $s > 0$ and $u > 0$ for the following equation:

$$u(t) = \min_{t\geq 0}\{\alpha(t)B(t-\tau,0^+) - \varepsilon\}u(t-\tau) - \max_{t\geq 0}\{d(t)+d_2(t)\}u(t).$$

Hence, $u^*(t) \to \infty$ as $t \to \infty$. Since $N(t,\phi) = S(t,\phi) + I(t,\phi) > 0$, $\forall t > 0$, $\phi \in M_0$, we can choose a small number $k > 0$ such that $N(t,\phi) > ku^*(t)$, $\forall t \in [N_1 T, N_1 T + \tau]$. By the comparison theorem [80, Theorem 5.1.1], we have $N(t,\phi) > ku^*(t)$, $\forall t \geq N_1 T + \tau$. Thus $\lim_{t\to\infty} N(t,\phi) = \infty$, also a contradiction. This completes the proof of claim 1.

In the case where $\mathcal{R}_0 < 1$, we have $\int_0^T \beta(t)dt < \int_0^T (d(t) + d_2(t) + \gamma(t))dt$. If $I(0) > 0$, then $N(t) \geq I(t) > 0$, $\forall t \geq 0$ and hence, we have

$$I'(t) \leq (\beta(t) - (d(t) + d_2(t) + \gamma(t)))I(t), \ \forall t \geq 0.$$

Then

$$I(t) \leq I(0)e^{\int_0^t \beta(s)-(d(s)+d_2(s)+\gamma(s))ds} \quad \forall t \geq 0,$$

and hence, $\lim_{t\to\infty} I(t) = 0$. Therefore, the equation for the whole population is asymptotic to the following periodic time-delayed equation:

$$N'(t) = B(t-\tau, N(t-\tau))N(t-\tau)\alpha(t) - d(t)N(t), \tag{2.10}$$

which is the same as (2.2). Note that $N^*(t)$ is a global attractive solution of (2.2). Next, we use the theory of internally chain transitive sets (see e.g., [43, 105]) to prove $\lim_{t\to\infty}(S(t) - N^*(t)) = 0$.

In fact, if we denote the Poincaré map $P := \Phi(T) : M \to M$, then $P^n(\phi) = \Phi(nT)\phi, \forall n \geq 0, \phi \in M$. Let $\phi = (\phi_1, \phi_2) \in M \setminus \{\hat{0}\}$ and $\omega = \omega(\phi)$ be the omega limit set of $\{P^n(\phi)\}$. Since $I(t, \phi) \to 0$ as $t \to \infty$, there holds $\omega = \bar{\omega} \times \{\hat{0}\}$. We first claim that $\bar{\omega} \neq \{\hat{0}\}$. Assume not, i.e., $\bar{\omega} = \{\hat{0}\}$, then $\lim_{n\to\infty}(S_{nT}(\phi), I_{nT}(\phi)) = \lim_{n\to\infty} \Phi(nT)\phi = (\hat{0}, \hat{0})$, which contradicts claim 1. It is easy to see that $P^n|_\omega(\phi, \hat{0}) = (\bar{P}^n(\phi), \hat{0})$ where $\bar{P}$ is the periodic solution semiflow of (2.2). By [105, Lemma 1.2.1], ω is an internally chain transitive set for P, and hence, $\bar{\omega}$ is an internally chain transitive set for $\bar{P}$. Define $N_0^* \in C([-\tau, 0], \mathbb{R}_+)$ by $N_0^*(\theta) = N^*(\theta), \forall \theta \in [-\tau, 0]$. Since $\bar{\omega} \neq \{\hat{0}\}$ and N_0^* is a globally stable fixed point for $\bar{P}$ in $C([-\tau, 0], \mathbb{R}_+) \setminus \{\hat{0}\}$, we have $\bar{\omega} \cap W^s(N_0^*) \neq \varnothing$, where $W^s(N_0^*)$ is the stable set of N_0^*. By [105, Theorem 1.2.1], we then get $\bar{\omega} = N_0^*$. This proves $\omega = (N_0^*, \hat{0})$, and hence, $\lim_{t\to\infty}((S(t, \phi), I(t, \phi)) - (N^*(t), 0)) = 0$.

In the case where $\mathcal{R}_0 > 1$, we have $\int_0^T \beta(t)dt > \int_0^T (d(t) + d_2(t) + \gamma(t))dt$. Fix a number $\eta_0 \in (\frac{1}{\mathcal{R}_0}, 1)$, since

$$\lim_{(I(t), N(t)) \to (0, N^*(t))} \frac{N(t) - I(t)}{N(t)} = 1 > \eta_0,$$

there exists $\eta_1 > 0$, such that

$$\frac{N(t) - I(t)}{N(t)} > \eta_0, \ \forall 0 \leq I(t) \leq \eta_1, \ |N(t) - N^*(t)| \leq 2\eta_1.$$

Since $\lim\limits_{\phi \to (N_0^*,\hat{0})} \Phi(t)\phi = (N_0^*,\hat{0})$ uniformly for $t \in [0,T]$, there exists $\eta_2 > 0$ such that $\|\Phi(t)\phi - (N_0^*,0)\| \leq \eta_1, \forall t \in [0,T]$, $\|\phi - (N_0^*,0)\| \leq \eta_2$. Then we have the following claim:

Claim 2. $\limsup\limits_{n\to\infty} \|\Phi(nT)\phi - (N_0^*,\hat{0})\| \geq \eta_2$ for all $\phi \in M_0$.

Suppose, by contradiction, that $\limsup\limits_{n\to\infty} \|\Phi(nT)\phi - (N_0^*,\hat{0})\| < \eta_2$ for some $\phi \in M_0$. Then there exists an integer $N_2 \geq 1$ such that $\|\Phi(nT)\phi - (N_0^*,0)\| < \eta_2, \forall n \geq N_2$. For any $t \geq N_2T$, we have $t = nT + t'$ with $n \geq N_2$ and $t' \in [0,T]$. Thus, we have

$$\|\Phi(t)\phi - (N_0^*,0)\| = \|\Phi(t')(\Phi(nT)\phi) - (N_0^*,\hat{0})\| \leq \eta_1, \ \forall t \geq N_2T.$$

Therefore, $I(t)$ satisfies the following differential inequality

$$I'(t) \geq (\beta(t)\eta_0 - (d(t) + d_2(t) + \gamma(t)))I(t), \ \forall t \geq N_2T.$$

By the comparison theorem, it follows that

$$I(t) \geq I(N_2T)e^{\int_{N_2T}^{t}(\beta(s)\eta_0 - (d(s)+d_2(s)+\gamma(s))ds}.$$

Since $\mathcal{R}_0 > 1$ and $\eta_0 \in (\frac{1}{\mathcal{R}_0}, 1)$, we have $\lim\limits_{t\to\infty} I(t) = \infty$, a contradiction.

In the case where $G(t,0) \equiv 0$, we choose

$$M_1 = (\hat{0},\hat{0}) \quad \text{and} \quad M_2 = (N_0^*,\hat{0}).$$

It then follows that M_1 and M_2 are disjoint, compact and isolated invariant set for P in ∂M_0, and $\tilde{A}_\partial := \bigcup_{\phi\in\partial M_0} \omega(\phi) = \{M_1, M_2\}$. Further, no subset of M_1, M_2 forms a cycle in ∂M_0. In view of two claims above, we see that M_1 and M_2 are isolated invariant sets for P in M, and $W^s(M_i) \cap M_0 = \emptyset$, $i = 1,2$, where $W^s(M_i)$ is the stable sets of M_i for P.

In the case where $G(t,0) > 0$ for all $t \geq 0$, M_2 is the only compact invariant set for P in ∂M_0, and hence we only choose $i = 2$ in the above argument.

By the acyclicity theorem on uniform persistence for maps (see Theorem 1.2.2 or [105, Theorem 1.3.1 and Remark 1.3.1]), it follows that $P : M \to M$ is uniformly persistent with respect to M_0. Thus, Theorem 1.2.3 implies that the periodic semiflow $\Phi(t) : M \to M$ is also uniformly persistent with respect to M_0. According to [106, Theorem 3.1], system (2.1) has a T-periodic solution $(S^*(t), I^*(t))$ with $(S_t^*, I_t^*) \in M_0$ for all $t \geq 0$. Clearly, $S_t^* > 0$ and $I_t^* > 0$ for all $t > 0$.

It follows from Theorem 1.2.6, with $\rho(x) = d(x, \partial M_0)$, that P: $M_0 \to M_0$ has a compact global attractor A_0. Since $A_0 = P(A_0) = \Phi(T)A_0$, it follows that $\phi_1(0) > 0$ and $\phi_2(0) > 0$ for all $\phi \in A_0$. Let $B_0 := \bigcup_{t\in[0,T]} \Phi(t)A_0$. We have $B_0 \subset M_0$ and $\lim\limits_{t\to\infty} d(\Phi(t)\phi, B_0) = 0$ for all $\phi \in M_0$. Define a continuous function $p : M \to \mathbb{R}_+$ by

$$p(\phi) = \min(\phi_1(0), \phi_2(0)), \quad \forall\phi = (\phi_1, \phi_2) \in M.$$

Since B_0 is a compact subset of M_0, we have $\inf_{\phi\in B_0} p(\phi) = \min_{\phi\in B_0} p(\phi) > 0$. Consequently, there exists $\eta > 0$ such that

$$\liminf_{t\to\infty} \min(S(t,\phi), I(t,\phi)) = \liminf_{t\to\infty} p(\Phi(t)\phi) \geq \eta, \quad \forall\phi \in M_0.$$

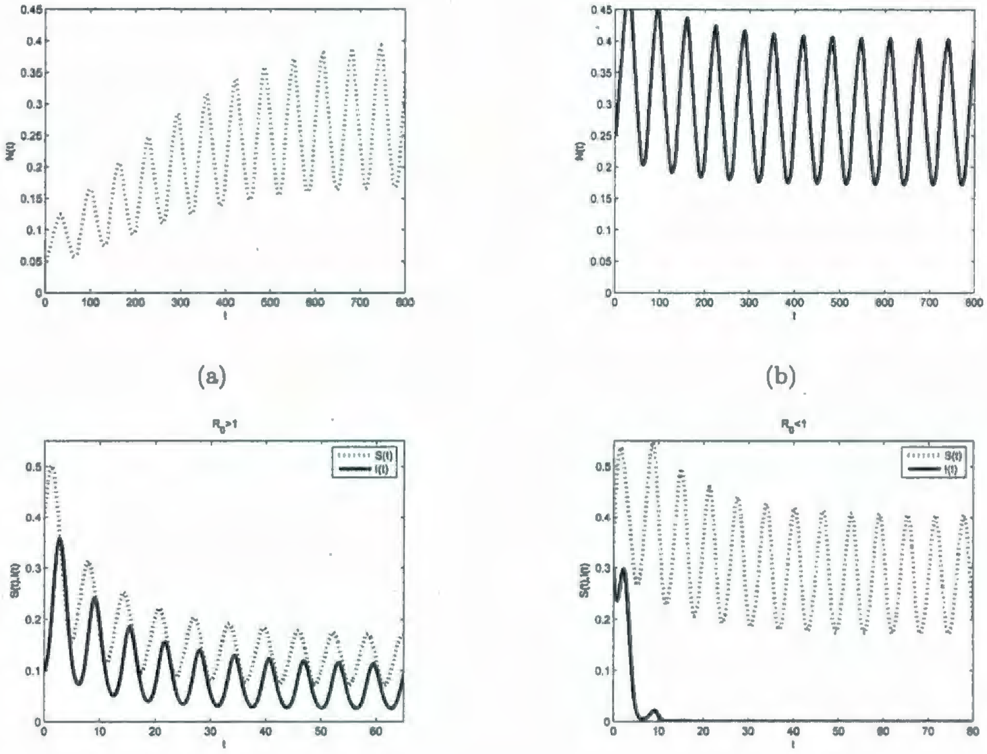
This completes the proof. ■

2.5 Numerical simulations

In this section, we use specific birth functions to verify our results in the previous two sections by numerical simulations.

Example 1. In this example, we choose $B(t,N)N = N\frac{2(1+\cos(t))}{1+N}$, $d(t) = 0.5$, $d_1(t) = 1$, $\tau = 1$. Then $\alpha(t) = e^{-1}$ and the equation (2.2) becomes

$$N'(t) = N(t-1)\frac{2(1+\cos(t-1))}{1+N(t-1)}e^{-1} - \frac{1}{2}N(t).$$



(a) (b)

(c) (d)

Figure 2.1: Time series for each compartment with $B(t, N)$ taking a general periodic form of $B_1(N)$.

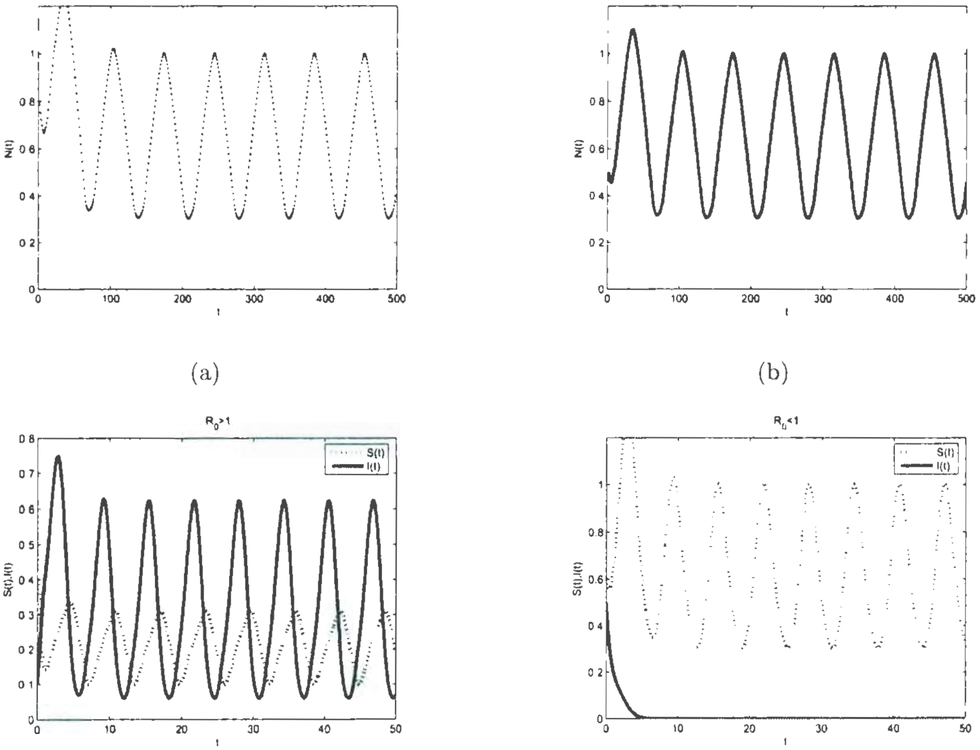
It is easy to see that (H1)-(H3) in Theorem 2.3.1 hold for this equation, our numerical simulations in Fig. 2.1(a) and Fig. 2.1(b) show that there is a globally asymptotically attractive positive periodic solution $N^*(t)$. Moreover, if we choose $d_2(t) = \frac{1}{10}$, $\beta(t) = 1 + \sin(t)$ and $\gamma(t) = \frac{1}{10}$, then $\mathcal{R}_0 = \frac{10}{7} > 1$. Thus, we have Fig. 2.1(c), which shows that the disease is uniform persistence and there is a positive periodic solution when $\mathcal{R}_0 > 1$. On the contrary, if we choose $d_2(t) = \frac{1}{5}(1 + \sin(t))$, $\beta(t) = \frac{1}{2}(1 + 3\sin(t))$ and $\gamma(t) = \frac{1}{5}$, then $\mathcal{R}_0 = \frac{5}{9} < 1$. We have Fig. 2.1(d) for this case. For other initial data, we have similar simulations, which may suggest that every solution converges to the disease-free periodic solution.

Example 2. In this example, we choose $B(t, N)N = 0.8 + N$, $d(t) = 1$, $d_1(t) = 1 + \sin(t)$, $\tau = 1$. Then $\alpha(t) = e^{-1+\cos(t)-\cos(t-1)}$ and the equation (2.2) becomes

$$N'(t) = (0.8 + N(t-1))e^{-1+\cos(t)-\cos(t-1)} - N(t).$$

It is easy to see that (A1)-(A3) in Theorem 2.3.2 hold for this equation, our numerical simulations in Fig. 2.2(a) and Fig. 2.2(b) show that there is a globally asymptotically attractive positive periodic solution $N^*(t)$. Moreover, if we choose $d_2(t) = \frac{1}{5}$, $\beta(t) = 4(1 + \sin(t))$ and $\gamma(t) = \frac{1}{5}$, then $\mathcal{R}_0 = \frac{20}{7} > 1$. Thus, we have Fig. 2.2(c), which shows that the disease is uniform persistence and there is a positive periodic solution when $\mathcal{R}_0 > 1$. On the other hand, if we choose $d_2(t) = \frac{1}{5}$, $\beta(t) = \frac{1}{2}(1 + \sin(t))$ and $\gamma(t) = \frac{1}{5}$, then $\mathcal{R}_0 = \frac{5}{14} < 1$. We have Fig. 2.2(d) for this case. For other initial data, we have similar simulations, which may suggest every solution converges to the disease-free periodic solution.

Example 3. In this example, we choose $B(t, N)N = 1.2N(1 + \sin(t))e^{-\frac{1}{2}N}$, $d(t) = \frac{1}{5}$, $d_1(t) = 1 + \sin(t)$, $\tau = 4$. Then $\alpha(t) = e^{-4+\cos(t)-\cos(t-4)}$ and, the equation (2.2)



(a)

(b)

(c)

(d)

Figure 2.2: Time series for each compartment with $B(t,N)$ taking a general periodic form of $B_2(N)$.

becomes

$$N'(t) = \frac{6}{5}N(t-4)e^{-4+\cos(t)-\cos(t-4)}(1+\sin(t-4))e^{-\frac{1}{2}N(t-4)} - \frac{1}{5}N(t).$$

It is easy to see that (S1) and (S2) hold for this equation. In this case, $\frac{1}{q(t)} = 2$ and (2.6) becomes

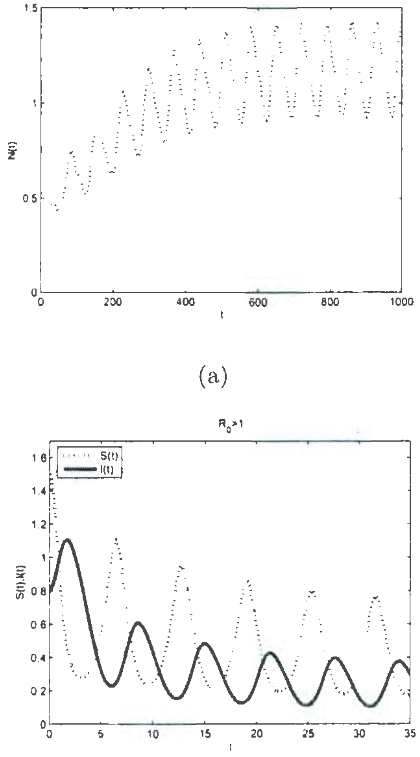
$$\begin{aligned}
\bar{U}'(t) &= \alpha(t)\frac{p(t-\tau)}{q(t-\tau)}e^{-1} - d(t)\bar{U}(t) \\
&= e^{-4+\cos(t)-\cos(t-4)}\frac{1.2(1+\sin(t-4))}{\frac{1}{2}}e^{-1} - \frac{1}{5}\bar{U}(t)(t) \\
&\leq e^{-3} \times 4.8 - \frac{1}{5}\bar{U}(t).
\end{aligned}$$

Hence, $\bar{U}^*(t) \leq \frac{5\times 4.8}{e^3} \leq 2$, and (S3) holds. Our numerical simulations in Fig. 2.3(a) and Fig. 2.3(b) show that there is a globally asymptotically attractive positive periodic solution $N^*(t)$. Moreover, if we choose $d_2(t) = \frac{1}{5}$, $\beta(t) = 1 + \sin(t)$ and $\gamma(t) = \frac{1}{5}$, then $\mathcal{R}_0 = \frac{5}{3} > 1$. Then, we have Fig. 2.3(c), which shows that the disease is uniform persistence and there is a positive periodic solution when $\mathcal{R}_0 > 1$. On the other hand, if we choose $d_2(t) = \frac{1}{5}$, $\beta(t) = 0.2(1 + \sin(t))$ and $\gamma(t) = \frac{1}{5}$, then $\mathcal{R}_0 = \frac{1}{3} < 1$. We have Fig. 2.3(d) for this case. For other initial data, we have similar simulations, which may imply that every solution converges to the disease-free periodic state.

Example 4. In this example, we choose $d(t) = 0.2$, $d_1(t) = 1 + 0.2\sin(t)$, $\tau = 0.1$ and $B(t, N)N = N(1 + \cos(t))e^{-2N}$, then $\alpha(t) = e^{-0.1+0.2(\cos(t)-\cos(t-0.1))}$ and the equation (2.2) becomes

$$N'(t) = N(t-0.1)(1+\cos(t-0.1))e^{-2N(t-0.1)}e^{-\frac{1}{10}+\frac{1}{5}(\cos(t)-\cos(t-0.1))} - \frac{1}{5}N(t).$$

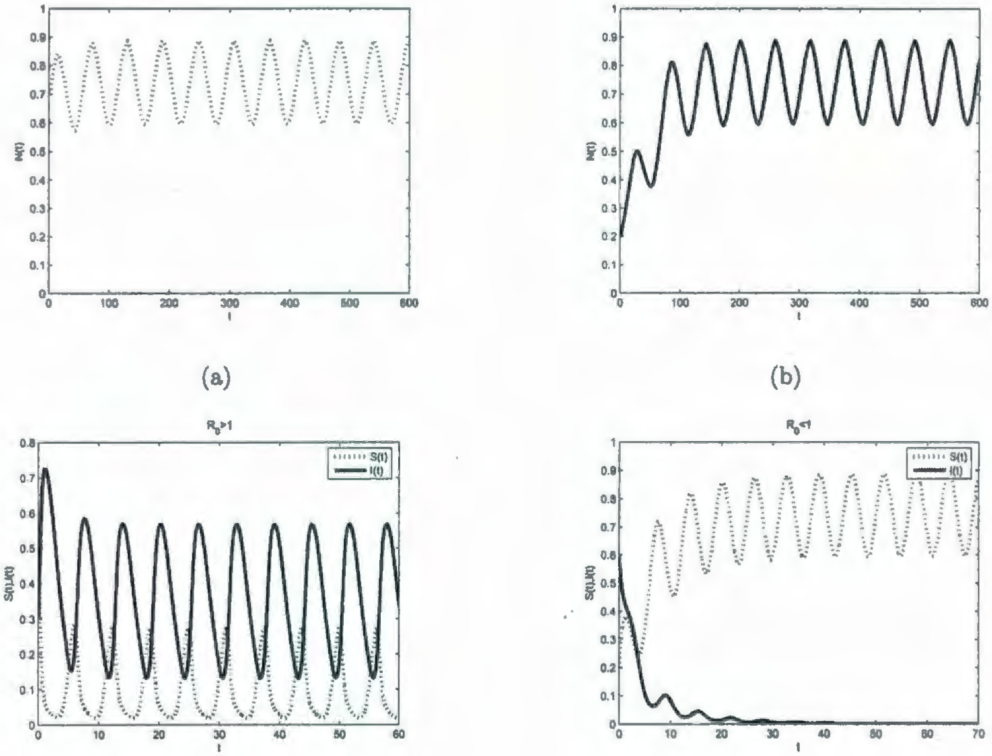
It is easy to see that (S1), (S2) and (S3)$'$ hold for this equation, our numerical simulations in Fig. 2.4(a) and Fig. 2.4(b) show that there is a globally asymptotically



(a) (b)

(c) (d)

Figure 2.3: Time series for each compartment with $B(t,N)$ taking a general periodic form of $B_3(N)$: Case 1.



(a) (b)

(c) (d)

Figure 2.4: Time series for each compartment with $B(t, N)$ taking a general periodic form of $B_3(N)$: Case 2.

attractive positive periodic solution $N^*(t)$. Moreover, if we choose $d_2(t) = \frac{1}{5}$, $\beta(t) = 4(1 + \sin(t))$ and $\gamma(t) = \frac{1}{5}$, then $\mathcal{R}_0 = \frac{20}{3} > 1$. Thus, we have Fig. 2.4(c), which shows that the disease is uniform persistence and there is a positive periodic solution when $\mathcal{R}_0 > 1$. On the other hand, if we choose $d_2(t) = \frac{1}{5}$, $\beta(t) = \frac{1}{2}(1 + \sin(t))$ and $\gamma(t) = \frac{1}{5}$, then $\mathcal{R}_0 = \frac{5}{6} < 1$. We have Fig. 2.4(d) for this case. For other initial data, we have similar simulations, which may suggest that every solution converges to the disease-free periodic solution.

2.6 Concluding remarks

As discussed in [106], we remark that in the case $d_2(t) \equiv 0$, $N(t)$ satisfies equation (2.2), and hence

$$\lim_{t \to \infty} (N(t) - N^*(t)) = 0.$$

Note that I(t) satisfies the following nonautonomous equation

$$I'(t) = \frac{\beta(t)(N(t) - I(t))I(t)}{N(t)} - (d(t) + \gamma(t))I(t), \tag{2.11}$$

which is asymptotic to the following periodic equation

$$I'(t) = \frac{\beta(t)(N^*(t) - I(t))I(t)}{N^*(t)} - (d(t) + \gamma(t))I(t). \tag{2.12}$$

If $\mathcal{R}_0 > 1$, i.e., $\int_0^T (\beta(t) - d(t) - \gamma(t))dt > 0$, and $\beta(t) > 0$, $\forall t \in [0, T]$, then it follows from [105, Theorem 5.2.1] that equation (2.12) admits a unique positive T-periodic solution $I^*(t)$, which is globally asymptotically stable in $\mathbb{R}_+ \setminus \{0\}$. It then follows from the theory of asymptotically periodic system (see [105, Section 3.2]) that $\lim_{t \to \infty} (I(t) - I^*(t)) = 0$. This implies that system (2.1) has a globally attractive positive T-periodic solution $(N^*(t) - I^*(t), I^*(t))$.

By applying the perturbation theory of a globally stable fixed point (see [82, Theorem 2.2]) and the theorem on uniform persistence uniform in parameters (see [105, Theorem 1.4.2]) to the Poincaré map of system (2.1), we can further show that if $\mathcal{R}_0 > 1$, $\beta(t) > 0$, $\forall t \in [0, T]$, and $\|d_2(\cdot)\| := \max_{0 \le t \le T} |d_2(t)|$ is sufficiently small, system (2.1) has a globally attractive positive T-periodic solution $(\bar{S}(t), \bar{I}(t))$. On the other side, our numerical results (for example, see Figs.(2.1(c)), (2.2(c)), (2.3(c)) and (2.4(c))) suggest that in the case where $\mathcal{R}_0 > 1$, every solution with nontrivial initial data is asymptotic to a periodic solution, while these periodic solutions may be different. This implies that there may be no uniqueness of positive T-periodic solution for some $d_2(t) \ge 0$.

Chapter 3

A Climate-Based Malaria Transmission Model with Structured Vector Population

3.1 Introduction

The first model of malaria transmission was developed by Ross [73] and later reformulated by Macdonald [59]. In [59], Macdonald figured out that there exists a threshold density, the basic reproduction number $\mathcal{R}_0$, defined as the average number of secondary cases produced by an index case during its infectious period. The threshold theorem states that malaria can persist in a population only if the number of mosquitoes is greater than a given threshold. Moreover, Macdonald [59] performed a sensitivity analysis of the basic reproduction number on the parameters. The sensitivity analysis consists of calculating the effect of small changes in each of the parameters on the basic reproduction number, and comparing the effects with each other.

His analysis showed the potential use of the basic reproduction number for malaria intervention. Much further work has been done to model the malaria transmission dynamics, see, e.g., Chitnis, Cushing and Hyman [15], Ngwa and Shu [69], Ngwa [68], Chiyaka and coworkers [17], Gumel and collaborators [28,66,70], Li [53], Ruan, Xiao and Beier [74] and references therein.

The standard technique for developing mathematical descriptions of mosquito - plasmodium interactions is to model the system as a set of autonomous ordinary differential equations (ODEs). This is an immensely powerful approach, and has led to many insights into the factors that affect malaria prevalence and control. However, the following two important biological aspects seem to have received little attention.

The first aspect is the stage structure of the vector (mosquitoes). The biological cycle of a mosquito goes through four separate and distinct stages: egg, larva, pupa and adult mosquito. The first three stages are also known as immature stage or aquatic form. The life cycle of a mosquito begins as an egg, it hatch into larvae, which turns into pupa. After about 2 to 4 days of pupation, the mosquito emerges as an adult. The maturity of mosquitoes is defined as the time of the first flight, which is shortly followed by the first bite [44]. As noted in [44], the developmental stages of vector have a profound impact on the transmission dynamics of vector borne diseases. First, the immature mosquitoes do not fly and bite humans, so they do not participate in the infection cycle and are, basically in a waiting period, which limits rapid vector population growth. Second, matured mosquitoes are quite different from immature mosquitoes from biological and epidemiological perspectives, and a realistic model needs to take these different stages into account. Although, there is auite a bit of research on epidemic models with structured host population (see [19, 32, 54, 94] and the references therein), it is also important to consider the age structure of the vector population in the study of vector-borne diseases.

The second aspect is the climate effect on the dynamics of vector population and the biting rate from mosquitoes to humans. Transmission and distribution of vector-borne diseases are greatly influenced by environmental and climatic factors. Seasonality and circadian rhythm of mosquito populations, as well as other ecological and behavioral features, are strongly influenced by climatic factors such as temperature, rainfall, humidity, wind, and duration of daylight [44, 71]. It is believed that malaria epidemics caused by meteorological factors can be predicted from climatic indicators and climate forecasts. Moreover, the malaria cases may significantly increase due to climate change [62, 71, 108], since it will induce the change of the population dynamics and biting pattern of its mosquito vector. Therefore, it is important to understand the climate-based dynamics of malaria transmission well enough to predict the malaria burden and manage control programs efficiently.

In this chapter, by taking the key feature of climate/seasonality into account, we derive a periodic model to describe the dynamics of malaria transmission. We calculate the basic reproduction ratio $\mathcal{R}_0$ and prove a threshold dynamics result in terms of $\mathcal{R}_0$. Using the monthly mean temperature for KwaZulu-Natal Province, South Africa, we estimate the periodic coefficients for the model and carry out some sensitivity analysis on $\mathcal{R}_0$ in order to to study the effect of control strategy, vector immature duration, and global warming on the basic reproduction ratio. Numerical simulations are carried out to illustrate the obtained results.

3.2 The model

Motivated by the compartmental malaria models in [15, 68, 69], we derive an age-structured malaria model with seasonality to account for the cross-infection between mosquitoes and humans. The human population is divided into four epidemiological categories representing the state variables: the susceptible class S_h, exposed class E_h, infective class I_h, and recovered class R_h (immune and asymptomatic, but slightly infectious humans) [68]. The adult mosquito population is divided into three epidemiological classes: the susceptible class S_v, exposed class E_v, and infectious class I_v. If a susceptible human is bitten by an infectious mosquitoe, then the human progresses through the exposed, infectious, and recovered classes before reentering the susceptible class. Susceptible mosquitoes can become infected when they bite infectious or recovered humans, and once infected they move through the exposed and infectious classes. Since mosquitoes never recover from infection after they are infected, (their infective period ends with their death due to their relatively short life-cycle), the vector population does not include an immune class. It is assumed throughout this chapter that all vector population measures refer to densities of female mosquitoes unless specifically stated. We divide the mosquitoes into two stages: immature and mature, and we assume that the average mature period is τ. For the aquatic stage, we suppose that the egg, larva, and pupa have the same development rate with death rate $d_J(t)$ at time t, where $d_J(t)$ is determined by the climate profile. It then follows that $b(t-\tau, N_v(t-\tau))e^{-\int_{t-\tau}^{t} d_J(\eta)d\eta}$ is the mature rate at time t, which is produced by the mature mosquitoes at time $t-\tau$. Here, $b(t, N_v(t))$ is the egg reproduction function, which is a function of the total number of mature mosquitoes $N_v(t)$.

For the infection term, we assume reservoir frequency-dependent disease transmission [98] for our model. The infection rate for each species depends on the biting rate of mosquitoes and the transmission probabilities, as well as on the number of infectives and susceptibles of each species. The biting rate $\beta(t)$ of mosquitoes is the average number of bites per mosquito per unit time at time t. This rate depends on a number of factors, and in particular, climatic ones, but for simplicity in this chapter we assume $\beta(t)$ to be periodic. Based on the fact that the total number of bites made by mosquitoes is equal to the total number of bites received by humans, the average number of bites per human per unit time at time t is $\frac{\beta(t)N_v(t)}{N_h(t)}$, where $N_h(t)$ is the total human population at time t. The transmission probability is the probability that an infectious bite produces a new case in a susceptible member of the other species. Suppose the transmission probabilities from humans to vectors and from vectors to humans are denoted by c and d, respectively. Then, the infection rates per susceptible vector and per susceptible human are given by

$$c\beta(t)\frac{I_h(t)+\sigma R_h(t)}{N_h(t)} \quad \text{and} \quad d\beta(t)\frac{N_v(t)}{N_h(t)}\frac{I_v(t)}{N_v(t)} = \frac{d\beta(t)}{N_h(t)}I_v,$$

respectively.

Following the above assumptions, we get the schematic diagram (see Fig. 3.1) for malaria transmission, and Table 3.1 shows the model coefficients. Considering climate effects on mosquito development, we further assume that $\beta(t)$, $d_v(t)$, and $d_J(t)$ are positive and periodic functions with the same period T=12 months.

From the schematic diagram for malaria transmission (Fig. 3.1), we obtain the following model:

c	Probability of transmission of infection from an infectious human to a susceptible mosquito given that a contact between the two occurs. Dimensionless.
$\beta(t)$	Biting rate of the mosquitoes to the humans. Time^{-1}.
σ	Ratio between the probability of transmission from recovered humans to susceptible mosquitoes and the probability of transmission from infectious humans. Dimensionless.
$d_v(t)$	Death rate for adult vectors. Time^{-1}.
$d_J(t)$	Mortality rate for immature vectors. Time^{-1}.
α	Transmission rate of mosquitoes from the exposed state to the infectious state, with $1/\alpha$ the average duration of the latent period. Time^{-1}.
ρ_E	Transmission rate of mosquitoes from the exposed state to the infectious state, with $1/\rho_E$ the average duration of the latent period. Time^{-1}.
ρ_I	Recovery rate of humans, with $1/\rho_I$ the average duration of the infectious period. Time^{-1}.
ρ_R	Per capita rate of loss of immunity for humans, with $1/\rho_R$ the average duration of the immune period. Time^{-1}.
Λ_h	Constant recruitment rate for humans. Humans × Time^{-1}.
d_h	Human death rate. Time^{-1}.
δ_h	Disease-induced death rate for humans. Time^{-1}.
d	Probability of transmission of infection from an infectious mosquito to a susceptible human given that a contact between the two occurs. Dimensionless.
τ	Maturation period. Time.

Table 3.1: The model parameters and their dimensions.

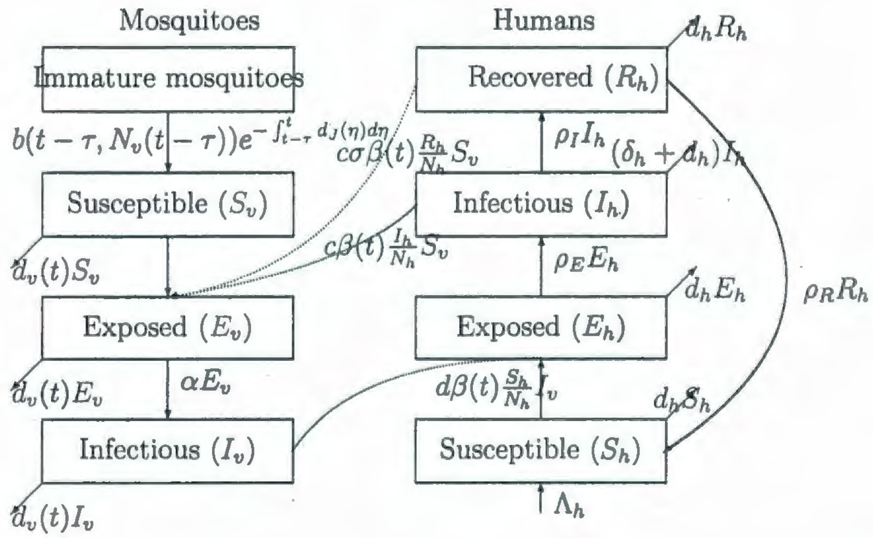


Figure 3.1: Compartmental model for malaria. See Table 3.1 for parameter descriptions.

$$\frac{dS_v(t)}{dt} = b(t-\tau, N_v(t-\tau))e^{-\int_{t-\tau}^{t} d_J(\eta)d\eta} - d_v(t)S_v(t) - c\beta(t)\frac{H(t)}{N_h(t)}S_v(t), \tag{3.1a}$$

$$\frac{dE_v(t)}{dt} = c\beta(t)\frac{H(t)}{N_h(t)}S_v(t) - (d_v(t)+\alpha)E_v(t), \tag{3.1b}$$

$$\frac{dI_v(t)}{dt} = \alpha E_v(t) - d_v(t)I_v(t), \tag{3.1c}$$

$$\frac{dS_h(t)}{dt} = \Lambda_h + \rho_R R_h(t) - d\beta(t)\frac{S_h(t)}{N_h(t)}I_v(t) - d_hS_h(t), \tag{3.1d}$$

$$\frac{dE_h(t)}{dt} = d\beta(t)\frac{S_h(t)}{N_h(t)}I_v(t) - (\rho_E + d_h)E_h(t), \tag{3.1e}$$

$$\frac{dI_h(t)}{dt} = \rho_E E_h(t) - (\rho_I + \delta_h + d_h)I_h(t), \tag{3.1f}$$

$$\frac{dR_h(t)}{dt} = \rho_I I_h(t) - (\rho_R + d_h)R_h(t), \tag{3.1g}$$

where $N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t)$, and $H(t) = I_h(t) + \sigma R_h(t)$. It is a time-delayed periodic differential system, allowing us to study the effect of seasonal fluactuations on malaria transmission.

Note that the whole adult mosquito population $N_v(t) = S_v(t) + E_v(t) + I_v(t)$ satisfies the following time-delayed equation:

$$N_v'(t) = b(t-\tau, N_v(t-\tau)) \exp\left[-\int_{t-\tau}^{t} d_J(\eta)d\eta\right] - d_v(t)N_v(t). \tag{3.2}$$

In the biological literature, there are three types of time T-periodic birth functions (see, e.g., [17, 19, 84] for the autonomous case):

(B1) $b_1(t, N) = \frac{p(t)N}{q(t)+N^n}$, with $p(t) > 0$, $q(t) > 0$ and $n > 0$.

(B2) $b_2(t, N) = a(t) + c(t)N$, with $a(t) > 0$, $c(t) \geq 0$.

(B3) $b_3(t, N) = b(t)e^{-a(t)N}N$, with $a(t) > 0$, $b(t) > 0$.

Using the theory of monotone dynamical systems, we obtained in chapter 2 and [101] four sets of sufficient conditions for system (3.2) to have a globally asymptotically stable positive T-periodic solution $N_v^*(t)$ (see [101, Theorem 2.1] and Theorems 2.3.1 - 2.3.4 in chapter 2). In the case where $b(t, N) = b(t) > 0$ for all $t \geq 0$, equation (3.2) reduces to a periodic ordinary differential equation, and the dynamics of the mosquito population is governed by the following equation:

$$N_v'(t) = b(t-\tau) \exp\left[-\int_{t-\tau}^{t} d_J(\eta)d\eta\right] - d_v(t)N_v(t). \tag{3.3}$$

It is easy to see that (3.3) has a globally asymptotically periodic solution

$$N_v^*(t) = e^{-\int_0^t d_v(s)ds} \times \left[\int_0^t b(s-\tau) \exp\left[-\int_{s-\tau}^{s} d_J(\eta)d\eta\right] e^{\int_0^s d_v(w)dw} ds \right.$$
$$\left. + \frac{\int_0^T b(w-\tau) \exp[-\int_{w-\tau}^{w} d_J(\eta)d\eta] e^{\int_0^w d_v(s)ds} dw}{e^{\int_0^T d_v(s)ds} - 1}\right].$$

In order to study the malaria transmission in a periodic environment, we assume that the vector (mosquito) population stabilizes at a periodic state. Accordingly, we make the following assumption throughout this chapter:

(A) For the time T-periodic function $b(t, N) \in C^1(\mathbb{R} \times \mathbb{R}_+, \mathbb{R}_+)$, there is a positive number h_0 such that $b(t-\tau_1, L)\exp[-\int_{t-\tau_1}^{t} d_J(\eta)d\eta] - d_v(t)L < 0$, $\forall L \geq h_0$. Moreover, system (3.2) has a globally asymptotically stable positive T-periodic solution $N_v^*(t)$ in $C([-\tau, 0], \mathbb{R}_+) \setminus \{0\}$.

Then we have the following result.

Lemma 3.2.1 *For any $\phi \in C([-\tau, 0], \mathbb{R}_+^7)$, system (3.1) has a unique nonnegative solution through ϕ, and all solutions are ultimately bounded and uniformly bounded.*

Proof. For all of $\phi \in C([-\tau, 0], \mathbb{R}_+^7)$, define $G(t, \phi) :=$

$$\begin{bmatrix} b\left(t-\tau, \sum\limits_{i=1}^{3} \phi_i(-\tau)\right) e^{-\int_{t-\tau}^{t} d_J(\eta)d\eta} - d_v(t)\phi_1(0) - c\beta(t)\frac{\phi_6(0)+\sigma\phi_7(0)}{\sum\limits_{i=4}^{7}\phi_i(0)}\phi_1(0) \\ c\beta(t)\frac{\phi_6(0)+\sigma\phi_7(0)}{\sum\limits_{i=4}^{7}\phi_i(0)}\phi_1(0) - (d_v(t)+\alpha)\phi_2(0) \\ \alpha\phi_2(0) - d_v(t)\phi_3(0) \\ \Lambda_h + \rho_R\phi_7(0) - d\beta(t)\frac{\phi_4(0)}{\sum\limits_{i=4}^{7}\phi_i(0)}\phi_3(0) - d_h\phi_4(0) \\ d\beta(t)\frac{\phi_4(0)}{\sum\limits_{i=4}^{7}\phi_i(0)}\phi_3(0) - (\rho_E + d_h)\phi_5(0) \\ \rho_E\phi_5(0) - (\rho_I + \delta_h + d_h)\phi_6(0) \\ \rho_I\phi_6(0) - (\rho_R + d_h)\phi_7(0) \end{bmatrix}.$$

Since for all $\phi \in C([-\tau, 0], \mathbb{R}_+^7)$, $G(t, \phi)$ is continuous, and $G(t, \phi)$ is Lipschitzian in ϕ in each compact set in $\mathbb{R} \times C([-\tau, 0], \mathbb{R}_+^7)$. Hence, there is a unique solution of system through $(0, \phi)$. Note that $G_i(t, \psi) \geq 0$ whenever $\psi \geq 0$ and $\psi_i(0) = 0$. It then follows from [80, Remark 5.2.1] that $C([-\tau, 0], \mathbb{R}_+^7)$ is positively invariant.

For the whole host population $N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t)$ and vector population $N_v(t)$, we have

$$\begin{aligned} \tfrac{dN_h(t)}{dt} &= \Lambda_h - d_h N_h(t) - \delta_h I_h(t) \leq \Lambda_h - d_h N_h(t), \\ \tfrac{dN_v(t)}{dt} &= b(t-\tau, N_v(t-\tau)) \exp\left[-\int_{t-\tau}^{t} d_J(\eta) d\eta\right] - d_v(t) N_v(t). \end{aligned}$$

By the comparison principle, it follows that the solution exists for all $t \geq 0$. Moreover, we have

$$\limsup_{t\to\infty} (S_h(t) + E_h(t) + I_h(t) + R_h(t)) \leq \frac{\Lambda_h}{d_h}$$

and

$$\limsup_{t\to\infty} (S_v(t) + E_v(t) + I_v(t) - N_v^*(t)) \leq 0,$$

where $N_v^*(t)$ is the unique positive periodic solution to (3.2). This implies that all solutions are ultimately bounded. Moreover, when $N_h(t) > \max\{h_0, \frac{\Lambda_h}{d_h}\}$ and $N_v(t) > \max\{h_0, \frac{\Lambda_h}{d_h}\}$, we have

$$\frac{dN_h(t)}{dt} < 0 \quad \text{and} \quad \frac{dN_v(t)}{dt} < 0.$$

This implies that all solutions are uniformly bounded. ■

3.3 Threshold dynamics

We define the "diseased" classes as the human or mosquito populations that are either exposed, infectious, or recovered but slightly infectious, i. e., E_v, I_v, E_h, I_h and R_h.

To find the disease-free state, letting $E_v = I_v = E_h = I_h = R_h = 0$, we then get

$$\frac{dS_v(t)}{dt} = -d_v(t)S_v(t) + b(t-\tau, S_v(t-\tau)) \exp\left[-\int_{t-\tau}^{t} d_J(\eta)d\eta\right], \tag{3.4}$$

$$\frac{dS_h(t)}{dt} = \Lambda_h - d_h S_h. \tag{3.5}$$

Hence, there is only one disease-free state, $(N_v^*(t), 0, 0, N_h^*, 0, 0, 0)$, in the case where 0 is not an equilibrium of (3.2), where $N_v^*(t)$ is the positive periodic solution of (3.4) and $N_h^* = \frac{\Lambda_h}{d_h}$. In the case where 0 is an equilibrium of (3.2), there exists another trivial equilibrium, $(0, 0, 0, N_h^*, 0, 0, 0)$.

In what follows, we introduce the basic reproduction ratio for the malaria transmission system according to the theory developed in [95] (see also section 1.3), which is a generalization of the work in [91] to the periodic case. Linearizing the system at the disease-free periodic state $(N_v^*(t), 0, 0, N_h^*, 0, 0, 0)$, we obtain the following system (here we write down only the equations for the "diseased" classes):

$$\begin{cases} \frac{dE_v(t)}{dt} = -(d_v(t) + \alpha)E_v(t) + c\beta(t)\frac{N_v^*(t)}{N_h^*}I_h(t) + c\sigma\beta(t)\frac{N_v^*(t)}{N_h^*}R_h(t), \\ \frac{dI_v(t)}{dt} = \alpha E_v(t) - d_v(t)I_v(t), \\ \frac{dE_h(t)}{dt} = d\beta(t)I_v(t) - (\rho_E + d_h)E_h(t), \\ \frac{dI_h(t)}{dt} = \rho_E E_h(t) - (\rho_I + \delta_h + d_h)I_h(t), \\ \frac{dR_h(t)}{dt} = \rho_I I_h(t) - (\rho_R + d_h)R_h(t). \end{cases} \tag{3.6}$$

Let

$$F(t) = \begin{bmatrix} 0 & 0 & 0 & c\beta(t)\frac{N_v^*(t)}{N_h^*} & c\sigma\beta(t)\frac{N_v^*(t)}{N_h^*} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & d\beta(t) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

and

$$V(t)=\begin{bmatrix} d_v(t)+\alpha & 0 & 0 & 0 & 0 \\ -\alpha & d_v(t) & 0 & 0 & 0 \\ 0 & 0 & \rho_E+d_h & 0 & 0 \\ 0 & 0 & -\rho_E & \rho_I+\delta_h+d_h & 0 \\ 0 & 0 & 0 & -\rho_I & \rho_R+d_h \end{bmatrix}.$$

Then we can rewrite (3.6) as

$$\frac{dx(t)}{dt}=(F(t)-V(t))x(t),$$

where $x(t)=(E_v(t),I_v(t),E_h(t),I_h(t),R_h(t))^T$.

Assume $Y(t,s)$, $t\geq s$, is the evolution operator of the linear-periodic system

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

That is, for each $s\in\mathbb{R}$, the 5 × 5 matrix Y(t,s) satisfies

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

where I is the 5×5 identity matrix.

Let C_T be the Banach space of all T-periodic functions from $\mathbb{R}$ to $\mathbb{R}^5$, equipped with the maximum norm. Suppose $\phi\in C_T$ is the initial distribution of infectious individuals in this periodic environment, then $F(s)\phi(s)$ is the rate of new infections produced by the infected individuals who were introduced at time s, and $Y(t,s)F(s)\phi(s)$ represent the distribution of those infected individuals who were newly infected at time s and remain in the infected compartments at time t for $t\geq s$. Hence,

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

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

We define the linear operator $L : C_T \to C_T$ by

$$(L\phi)(t) = \int_0^\infty Y(t, t-a)F(t-a)\phi(t-a)da, \quad \forall t \in \mathbb{R}, \quad \phi \in C_T.$$

It then follows from section 1.3 (see also [95]) that L is the next infection operator, and the basic reproduction ratio is $\mathcal{R}_0 := \rho(L)$, the spectral radius of L.

Let $W(t, \lambda)$ be the monodromy matrix of the following linear T-periodic system

$$\frac{dW(t)}{dt} = \left(-V(t) + \frac{1}{\lambda}F(t)\right) W(t), \ t \in \mathbb{R},$$

with parameter $\lambda \in (0, \infty)$. Since $F(t)$ is nonnegative and $-V(t)$ is cooperative, it follows that $\rho(W(T, \lambda))$ is continuous and non-increasing for $\lambda \in (0, \infty)$, and $\lim\limits_{\lambda \to \infty} \rho(W(T, \lambda)) < 1$.

Thanks to Theorem 1.3.2, we have the following argument, which implies that $\mathcal{R}_0$ is in scale with $\beta(t)$. That is, if $\hat{\beta}(t)$=$a\beta(t)$ is another biting rate for some $a > 0$, then $\hat{\mathcal{R}}_0 = a\mathcal{R}_0$. In fact, when $\hat{\beta}(t)$=$a\beta(t)$, then $\hat{F}(t) = aF(t)$, and $\hat{V}(t) = V(t)$ and the monodromy matrix $\hat{W}(t, \lambda)$ satisfies

$$\frac{d\hat{W}}{dt} = \left(-\hat{V}(t) + \frac{1}{\lambda}\hat{F}(t)\right) \hat{W}(t) = \left(-V(t) + \frac{1}{\lambda}aF(t)\right) \hat{W}(t).$$

Hence, $\hat{W}(t, \lambda) = W(t, \frac{\lambda}{a})$ and $\hat{W}(T, \lambda) = W(T, \frac{\lambda}{a})$. Therefore, $\rho(\hat{W}(T, \hat{\mathcal{R}}_0)) = 1$, which implies that $\rho(W(T, \frac{\hat{\mathcal{R}}_0}{a})) = 1$. This implies that $\hat{\mathcal{R}}_0 = a\mathcal{R}_0$.

Our first result shows the uniform persistence of the disease if $\mathcal{R}_0 > 1$.

Theorem 3.3.1 *Let (A) hold. If $\mathcal{R}_0 > 1$, then system (3.1) admits at least one positive periodic solution and there is an $\eta > 0$ such that any solution* $(S_v(t)$, $E_v(t)$, $I_v(t)$,

$S_h(t)$, $E_h(t)$, $I_h(t)$, $R_h(t)$) of the system in $C([-\tau,0],\mathbb{R}^7_+)$ with $E_v(0) > 0, I_v(0) > 0, E_h(0) > 0, I_h(0) > 0, R_h(0) > 0$ satisfies

$$\liminf_{t\to\infty}(E_v(t), I_v(t), E_h(t), I_h(t), R_h(t)) \geq (\eta,\eta,\eta,\eta,\eta).$$

Proof. Let

$$X = C([-\tau,0],\mathbb{R}^7_+),$$

$$X_0 := \{\phi = (\phi_1,\phi_2,\phi_3,\phi_4,\varphi_5,\phi_6,\phi_7) \in X : \phi_i(0) > 0,\ \forall i \in \{2,3,5,6,7\}\},$$

$$\text{and}\quad \partial X_0 := X\backslash X_0 = \{\phi \in X : \varphi_i(0) = 0 \text{ for some } i \in \{2,3,5,6,7\}\}.$$

Clearly, X_0 is an open set relative to X. Let $u(t,\phi)$ be the unique solution of the system (3.1) with $u_0(\phi) = \phi$. Let $\Phi(t)\psi = u_t(\psi)$ and $P : X \to X$ be the Poincaré map associated with system (3.1), that is, $P(\phi) = u_T(\phi)$, $\forall \phi \in X$. It is easy to see that $\Phi(t)(X_0) \subset X_0$, $\forall t \geq 0$. Note that Lemma 3.2.1 implies that the discrete-time system $P : X \to X$ is point dissipative and P^{n_0} is compact whenever $n_0T > \tau$. It then follows from Theorem 1.2.1 that P admits a global attractor A in X. We first prove that P is uniformly persistent with respect to $(X_0, \partial X_0)$.

Let $M_1 := \{(0,0,0,N_h^*,0,0,0)\}$ and $M_2 := \{(N_{v0}^*,0,0,N_h^*,0,0,0)\}$, where $N_{v0}^*(\theta) = N_v^*(\theta)$, $\forall\theta \in [-\tau,0]$. Since $N_v^*(t)$ is a positive periodic solution, we can choose a small positive number δ_0 such that

$$3\delta_0 < \inf_{t\geq 0} N_v^*(t).$$

Since $\lim\limits_{\phi\to M_1}(\Phi(t)\phi - M_1) = 0$ uniformly for $t \in [0,T]$, there exists δ_1 such that

$$\|\Phi(t)\phi - M_1\| \leq \delta_0,\quad \forall t \in [0,T],\quad \|\phi - M_1\| \leq \delta_1.$$

We have the following claims:

Claim 1. $\limsup\limits_{n\to\infty}\|\Phi(nT)\phi - M_1\| \geq \delta_1$ for all $\phi \in X_0$.

Suppose, by contradiction, that $\limsup_{n\to\infty} \|\Phi(nT)\psi - M_1\| < \delta_1$ for some $\psi \in X_0$. Then there exists an integer $N_1 \geq 1$ such that $\|\Phi(nT)\psi - M_1\| < \delta_1, \forall n \geq N_1$. For any $t - \tau \geq N_1 T$, we have $t = nT + t'$ with $n \geq N_1$, $t' \in [0, T]$ and $\|\Phi(t)\psi - M_1\| = \|\Phi(t')\Phi(nT)\psi - M_1\| \leq \delta_0$. Hence $S_v(t) \leq \delta_0$, $E_v(t) \leq \delta_0$, $I_v(t) \leq \delta_0$ and $N_v(t) \leq 3\delta_0$ when $t - \tau \geq N_1 T$. Since $N_v(0) = \psi_1(0) + \psi_2(0) + \psi_3(0) > 0$, we have $\lim_{t\to\infty}(N_v(t) - N_v^*(t)) = 0$, a contradiction.

Let $M_\epsilon(t)$=

$$\begin{bmatrix} -(d_v(t)+\alpha) & 0 & 0 & c\beta(t)(\frac{N_v^*(t)}{N_h^*} - \epsilon) & c\sigma\beta(t)(\frac{N_v^*(t)}{N_h^*} - \epsilon) \\ \alpha & -d_v & 0 & 0 & 0 \\ 0 & d\beta(t)(1-\epsilon) & -(\rho_E + d_h) & 0 & 0 \\ 0 & 0 & \rho_E & -(\rho_I + \delta_h + d_h) & 0 \\ 0 & 0 & 0 & \rho_I & -(\rho_R + d_h) \end{bmatrix}.$$

It then follows from Theorem 1.3.1 that $\mathcal{R}_0 > 1$ if and only if $\rho(\Phi_{F-V}(T)) > 1$. By the continuity of solutions with respect to parameter ϵ, we see that $\lim_{\epsilon\to 0^+} \Phi_{M_\epsilon}(T) = \Phi_{F-V}(T)$. Moreover, we have $\lim_{\epsilon\to 0^+} \rho(\Phi_{M_\epsilon}(T)) = \rho(\Phi_{F-V}(T))$ by the continuity of the spectrum for matrices [46, Section II.5.8]. Thus, there exists an $\epsilon_1 > 0$ such that $\rho(\Phi_{M_\epsilon}(T)) > 1$, $\forall \epsilon \in [0, \epsilon_1]$. Since $\lim_{\phi\to M_2} \Phi(t)\phi - \Phi(t)M_2 = 0$ uniformly for $t \in [0, T]$, there exists η_1 such that

$$\frac{S_v(t,\phi)}{N_h(t,\phi)} \geq \frac{N_v^*(t)}{N_h^*} - \epsilon_1 \quad \text{and} \quad \frac{S_h(t,\phi)}{N_h(t,\phi)} \geq 1 - \epsilon_1, \quad \forall t \in [0,T], \quad \|\phi - M_2\| \leq \eta_1.$$

Claim 2. $\limsup_{n\to\infty} \|\Phi(nT)\phi - M_2\| \geq \eta_1$ for all $\phi \in X_0$.

Assume, by contradiction, that $\limsup_{n\to\infty} \|\Phi(nT)\psi - M_2\| < \eta_1$ for some $\psi \in X_0$. Then there exists an integer $N_2 \geq 1$ such that $\|\Phi(nT)\psi - M_2\| < \eta_1, \forall n \geq N_2$. For any $t - \tau \geq N_2 T$, we have $t = nT + t'$ with $n \geq N_2$, $t' \in [0, T]$ such that $\|\Phi(t)\psi - \Phi(t)M_2\| = \|\Phi(t')\Phi(nT)\psi - \Phi(t')\Phi(nT)M_2\| = \|\Phi(t')\Phi(nT)\psi - \Phi(t')M_2\|$,

and

$$\begin{cases} \frac{dE_v(t)}{dt} \geq -(d_v(t)+\alpha)E_v(t) + c\beta(t)(I_h(t)+\sigma R_h(t))\left(\frac{N_v^*(t)}{N_h^*} - \epsilon_1\right), \\ \frac{dI_v(t)}{dt} = \alpha E_v(t) - d_v(t)I_v(t), \\ \frac{dE_h(t)}{dt} \geq d\beta(t)(1-\epsilon_1)I_v(t) - (\rho_E + d_h)E_h(t), \\ \frac{dI_h(t)}{dt} = \rho_E E_h(t) - (\rho_I + \delta_h + d_h)I_h(t), \\ \frac{dR_h(t)}{dt} = \rho_I I_h(t) - (\rho_R + d_h)R_h(t). \end{cases}$$

Consider the linear system

$$\frac{dw(t)}{dt} = M_{\epsilon_1}(t)w(t). \tag{3.7}$$

By [102, Lemma 2.1], it follows that there exists a positive, T-periodic function $v(t)$ such that $w(t) = e^{\theta t}v(t)$ is a solution of system (3.7), where $\theta = \frac{1}{T}\ln\rho(\Phi_{M_\epsilon}(T))$. Since $\rho(\Phi_{M_{\epsilon_1}}(T)) > 1$, θ is a positive constant. We have $w(t) \to +\infty$ as $t \to \infty$. On the other hand, since $\Phi(t)\psi \in X_0$, $\forall t \geq 0$, there exists an integer $N_0 \geq N_2$ and a real number $\bar{\eta} > 0$ such that

$$(E_v(N_0T), I_v(N_0T), E_h(N_0T), I_h(N_0T), R_h(N_0T)) \geq \bar{\eta}w(0) = \bar{\eta}v(0).$$

By the standard comparison theorem [80, Proposition 1.1 and Remark 1.2], we have

$$(E_v(N_0T+t), I_v(N_0T+t), E_h(N_0T+t), I_h(N_0T+t), R_h(N_0T+t)) \geq \bar{\eta}w(t), \ \forall t \geq 0.$$

This implies that

$$\lim_{t\to\infty} |(E_v(t), I_v(t), E_h(t), I_h(t), R_h(t))| = \infty,$$

a contradiction.

Define

$$M_\partial := \{\phi \in \partial X_0 : P^n(\phi) \in \partial X_0, n \geq 0\},$$
$$D_1 := \{\phi \in X : \phi_i(0) = 0, \forall i \in \{2,3,5,6,7\}\},$$
$$D_2 := \{\phi \in X : \phi_i = 0, \forall i = 1,2,3\}.$$

In the case where 0 is an equilibrium of (3.2), we claim that $M_\partial = D_1 \cup D_2$. We first prove that $D_1 \cup D_2 \subset M_\partial$. For any $\psi \in D_2$, it is easy to see that $u_i(t, \psi) = 0$ for $i = 1, 2, 3$. Hence, $D_2 \subset M_\partial$. For any $\psi \in D_1$, we can define $V(t) \in C(\mathbb{R}_+, \mathbb{R}^7_+)$ such that $V_i(t) \equiv 0$, $\forall t \geq 0$ for $i = 2, 3, 5, 6, 7$. Let $V_1(t)$ satisfy the following equations:

$$\frac{dV_1(t)}{dt} = b\left(t - \tau, \sum_{j=1}^{3} \psi_j(t-\tau)\right) \exp\left[-\int_{t-\tau}^{t} d_J(\eta)d\eta\right] - d_v(t)V_1(t) \text{ for } 0 \leq t \leq \tau,$$
$$\frac{dV_1(t)}{dt} = b(t-\tau, V_1(t-\tau)) \exp\left[-\int_{t-\tau}^{t} d_J(\eta)d\eta\right] - d_v(t)V_1(t) \text{ for t} \geq \tau,$$

with $V_1(0) = \psi_1(0)$. Letting $V_4(t)$ be the solution of the equation:

$$\tfrac{dV_4(t)}{dt} = \Lambda_h - d_h V_4(t) \text{ for t} \geq 0 \text{ with } \mathrm{V}_4(0) = \psi_4(0).$$

Then $V(t)$ is a solution of system (3.1) through ψ. By the uniqueness of the solution, we have $u(t, \psi) = V(t)$, $\forall t \geq 0$, and hence $D_1 \subset M_\partial$. To prove this claim, it then suffices to show $M_\partial \subset D_1 \cup D_2$. For any $\psi \in \partial X_0 \setminus (D_1 \cup D_2)$, we have $\sum\limits_{j=1}^{3} \psi_j(0) > 0$, and hence $\lim\limits_{t\to\infty} |\sum\limits_{j=1}^{3} u_j(t,\psi) - N_v^*(t)| = 0$. From (3.1a), there exists a $t_0 > 0$ such that $u_1(t, \psi) > 0$ for all $t > t_0$. It is easy to see that $u_4(t, \psi) > 0$ for all $t > 0$ from (3.1d). It then follows from (3.1b–3.1c) that if $\psi_2(0) > 0$, then $u_2(t, \psi) > 0$ and $u_3(t, \psi) > 0$, $\forall t > 0$. In view of (3.1c,3.1e–3.1g), we see that if $\psi_3(0) > 0$, then $u_j(t, \psi) > 0$, $\forall j \in \{3, 5, 6, 7\}$, $\forall t > 0$. Moreover, if $\psi_5(0) > 0$ or $\psi_6(0) > 0$, then $u_j(t, \psi) > 0$, $\forall j \in \{6, 7\}$ and $\forall t > 0$, which can be deduced from (3.1e–3.1g). If $\psi_7(0) > 0$, then (3.1b) and (3.1c) imply that $u_2(t, \psi) > 0$ and $u_3(t, \psi) > 0$ for all $t > t_0$. Therefore, we have $u(t, \psi) \in X_0$, $\forall t > t_0$. This implies that for any $\psi \in \partial X_0 \setminus (D_1 \cup D_2)$, we have some n with $nT > t_0$ such that $P^n(\psi) \notin \partial X_0$, and hence $M_\partial \subset D_1 \cup D_2$. It then follows that M_1 and M_2 are disjoint, compact and isolated invariant sets for P in M_∂, and $\tilde{A}_\partial := \bigcup_{\phi \in M_\partial} \omega(\phi) = \{M_1, M_2\}$. Further, no subset of $\{M_1, M_2\}$ forms a cycle in

M_∂ (and hence in ∂X_0). In view of the two claims above, we see that M_1 and M_2 are isolated invariant sets for P in X, and $W^s(M_i) \cap X_0 = \emptyset$, $\forall i = 1, 2$, where $W^s(M_i)$ is the stable set of M_i for P.

In the case where 0 is not an equilibrium of (3.2), we can show that $M_\partial = D_1$ in a similar manner. It then follows that $\{M_2\}$ is the only compact invariant set for P in M_∂, and hence we need only choose $i = 2$ in the above argument.

By the acyclicity theorem on uniform persistence for maps (see Theorem 1.2.2 or [105, Theorem 1.3.1 and Remark 1.3.1]), it follows that $P : X \to X$ is uniformly persistent with respect to X_0. Thus, Theorem 1.2.3 implies that the periodic semiflow $\Phi(t) : X \to X$ is also uniformly persistent with respect to X_0. It then follows from Theorem 1.2.6 (see also [106, Theorem 3.1]) that system (3.1) admits a T-periodic solution $\Phi(t)\phi^*$ with $\phi^* \in X_0$.

By Theorem 1.2.6, with $\rho(x) = d(x, \partial X_0)$, it then follows that P: $X_0 \to X_0$ has a compact global attractor A_0. Since $A_0 = P(A_0) = \Phi(T)A_0$, we see that $\phi_i(0) > 0$ for all $i = 2, 3, 5, 6, 7$. This implies that $\phi_i(0) > 0$ for $i = 1, 4$ from the invariance of A_0. Let $B_0 := \bigcup_{t\in[0,T]} \Phi(t)A_0$, then $\psi_i(0) > 0$ for all $\psi \in B_0$, $i \in [1, 7]$. Moreover, $B_0 \subset X_0$ and $\lim_{t\to\infty} d(\Phi(t)\phi, B_0) = 0$ for all $\phi \in X_0$. Define a continuous function $p : X \to \mathbb{R}_+$ by

$$p(\phi) = \min_{1\le i\le 7} \{\phi_i(0)\}, \quad \forall \phi \in X.$$

Since B_0 is a compact subset of X_0, we have $\inf_{\phi\in B_0} p(\phi) = \min_{\phi\in B_0} p(\phi) > 0$. Consequently, there exists $\eta > 0$ such that

$$\begin{aligned}
&\liminf_{t\to\infty} \min(S_v(t,\phi), E_v(t,\phi), I_v(t,\phi), S_h(t,\phi), E_h(t,\phi), I_h(t,\phi), R_h(t,\phi)) \\
&= \liminf_{t\to\infty} p(\Phi(t)\phi) \ge \eta, \quad \forall \phi \in X_0.
\end{aligned}$$

In particular, $\liminf_{t\to\infty} \min(\Phi(t)\phi^*) \ge \eta$, and hence $u_i(t, \phi^*) > 0$, $1 \le i \le 7$, for all

$t \geq 0$. This implies that $u(t, \phi^*)$ is a positive T-periodic solution. ∎

Applying Theorem 1.3.1, we know that the disease-free periodic state is locally stable when $\mathcal{R}_0 < 1$ and is unstable when $\mathcal{R}_0 > 1$. Next we show that the disease dies out if $\mathcal{R}_0 < 1$, provided that there is only a small invasion. For every $K > 0$, denote $X_K = C([-\tau, 0], [0, K]^7)$, then we have the following result.

Theorem 3.3.2 *Let (A) hold. If $\mathcal{R}_0 < 1$, then for every $K > \max\{h_0, \frac{\Lambda_h}{d_h}\}$, there exists a $\zeta = \zeta(K) > 0$ such that for any $\phi \in X_K \backslash M_1$ with $(\phi_2(0), \phi_3(0), \phi_5(0), \phi_6(0), \phi_7(0)) \in [0, \zeta]^5$, the solution of system (3.1) through ϕ, $u(t, \phi)$, satisfies*

$$\lim_{t \to \infty} \|u(t, \phi) - (N_v^*(t), 0, 0, N_h^*, 0, 0, 0)\| = 0.$$

Proof. Let $K > \max\{h_0, \frac{\Lambda_h}{d_h}\}$ be given. By Lemma 3.2.1 and its proof, X_K is positively invariant for the periodic solution semiflow of (3.1). We then have

$$\Phi(t, \phi) \in [0, K]^7, \quad \forall t \geq 0, \phi \in X_L.$$

Let $\tilde{M}_\epsilon(t)$=

$$\begin{bmatrix} -(d_v(t) + \alpha) & 0 & 0 & c\beta(t)\frac{N_v^*(t)+\epsilon}{N_h^*-\epsilon} & c\sigma\beta(t)\frac{N_v^*(t)+\epsilon}{N_h^*-\epsilon} \\ \alpha & -d_v & 0 & 0 & 0 \\ 0 & d\beta(t) & -(\rho_E + d_h) & 0 & 0 \\ 0 & 0 & \rho_E & -(\rho_I + \delta_h + d_h) & 0 \\ 0 & 0 & 0 & \rho_I & -(\rho_R + d_h) \end{bmatrix}.$$

It follows from Theorem 1.3.1 that $\mathcal{R}_0 < 1$ if and only if $\rho(\Phi_{F-V}(T)) < 1$. By the continuity of solutions with respect to parameter ϵ, we see that $\lim\limits_{\epsilon \to 0^+} \Phi_{\tilde{M}_\epsilon}(T) = \Phi_{F-V}(T)$. Moreover, we have $\lim\limits_{\epsilon \to 0^+} \rho(\Phi_{\tilde{M}_\epsilon}(T)) = \rho(\Phi_{F-V}(T))$ from the continuity of the spectrum for matrices [46, Section II.5.8]. Thus, there exists an $\epsilon > 0$ such that $\rho(\Phi_{\tilde{M}_\epsilon}(T)) < 1$.

Now consider the following equations:

$$\begin{aligned}\tfrac{dw_1(t)}{dt} &= b(t-\tau, w_1(t-\tau))\exp\left[-\int_{t-\tau}^{t} d_J(\eta)d\eta\right] - d_v(t)w_1(t),\\ \tfrac{dw_2(t)}{dt} &= \Lambda_h - d_h w_2(t) - \delta_h \xi_1.\end{aligned}$$

We can choose small $\xi_1 > 0$ and large $T_1 = T_1(K) > 0$ such that for any solution $(w_1(t), w_2(t))$ with $(w_1(0), w_2(0)) \in [0, K]^2$, we have

$$w_1(t) < N_v^*(t) + \epsilon \quad \text{and} \quad w_2(t) > N_h^* - \epsilon, \quad \forall t \geq T_1.$$

Without loss of generality, we can set $T_1 = nT$ for some positive integer n.

Let $\mu = \frac{1}{T}\ln \rho(\Phi_{\tilde{M}_\epsilon}(T))$, it then follows from Lemma 2.1 in [102] that there exists a positive, T-periodic function $v(t)$ such that $e^{\mu t}v(t)$ is a solution of $x'(t) = \tilde{M}_\epsilon(t)x(t)$. Choose $\xi_2 > 0$ such that $\xi_2 v_i(t) < \xi_1$ for all $t \geq 0$, $i \in \{1, 2, 3, 4, 5\}$. For every solution $u(t, \phi)$ of the system (3.1) through ϕ, if we denote $\bar{u}(t, \phi) = (u_2(t, \phi), u_3(t, \phi), u_5(t, \phi), u_6(t, \phi), u_7(t, \phi))^T$, then there exists a $\zeta = \zeta(K) > 0$ such that

$$\bar{u}_i(t, \phi) < \xi_2 v_i(t), \quad i \in [1, 5], \quad t \in [0, T_1] \tag{3.8}$$

provided that $\phi_i(0) < \zeta$ for $i = 2, 3, 5, 6, 7$.

We further claim that (3.8) holds for all $t \geq 0$. If this claim is not true , then there exists a $T_2 = T_2(\phi) > T_1$ such that $\bar{u}_i(t, \phi) < \xi_2 v_i(t)$ for $i \in [1, 5]$, $0 \leq t < T_2$ and $\bar{u}_j(T_2, \phi) = \xi_2 v_j(t)$ for some $j \in [1, 5]$. Then for $T_1 \leq t \leq T_2$, we have $\frac{d\bar{u}(t)}{dt} \leq \tilde{M}_\epsilon(t)\bar{u}(t)$. By the standard comparison principle, we have $\bar{u}(t, \phi) \leq e^{\mu(t-T_1)}\xi_2 v(t - T_1) = e^{\mu(t-T_1)}\xi_2 v(t - nT) = e^{\mu(t-T_1)}\xi_2 v(t)$ for $T_1 < t \leq T_2$. Since $\mu < 0$ and $t > T_1$, we have $\bar{u}_i(t, \phi) < \xi_2 v_i(t)$ for $i \in [1, 5]$, a contradiction. This implies that (3.8) holds for all $t \geq 0$, and $u(t, \phi) \leq e^{\mu(t-T_1)}\xi_2 v(t)$ for all $t \geq T_1$, which implies that $\lim_{t\to\infty} \bar{u}(t, \phi) = 0$. By the theory of chain transitive sets (see, e.g., [105, Theorem 1.2.1]), as argued in

Theorem 2.4.1, we further obtain that $\lim_{t\to\infty}(S_v(t) - N_v^*(t)) = 0$ and $\lim_{t\to\infty} S_h(t) = N_h^*$.
■

The following theorem shows that when the disease-induced death rate is equal to zero, the infection will be cleared from the population if $\mathcal{R}_0 < 1$.

Theorem 3.3.3 *Let (A) hold. If $\mathcal{R}_0 < 1$ and $\delta_h = 0$, then the disease-free periodic state of the system (3.1) is globally asymptotically stable with respect to $C([-\tau, 0], \mathbb{R}_+^7)\setminus \{(0,0,0,N_h^*,0,0,0)\}$.*

Proof. As argued in Theorem 3.3.2, there exists an $\epsilon > 0$ such that $\rho(\Phi_{\tilde{M}_\epsilon}(T)) < 1$.

If $\delta_h = 0$, the whole human and mosquito populations admit the following two equations:

$$\begin{aligned} \tfrac{dN_h(t)}{dt} &= \Lambda_h - d_h N_h(t), \\ \tfrac{dN_v(t)}{dt} &= b(t-\tau, N_v(t-\tau)) \exp\left[-\int_{t-\tau}^{t} d_J(\eta)d\eta\right] - d_v(t)N_v(t). \end{aligned}$$

Therefore, there exists $T_3 = T(\epsilon) > 0$ such that

$$N_v(t) \le N_v^*(t) + \epsilon, \quad N_h(t) \ge N_h^* - \epsilon, \quad \forall t \ge T_3.$$

Thus, when $t \ge T_3$, we have

$$\begin{cases} \frac{dE_v(t)}{dt} \le -d_v(t)E_v(t) + c\beta(t)\frac{N_v^*(t)+\epsilon}{N_h^*-\epsilon} I_h(t) + c\beta(t)\sigma\frac{N_v^*(t)+\epsilon}{N_h^*-\epsilon} R_h(t), \\ \frac{dI_v(t)}{dt} = \alpha E_v(t) - d_v(t)I_v(t), \\ \frac{dE_h(t)}{dt} \le d\beta(t)I_v(t) - \rho_E E_h - d_h E_h, \\ \frac{dI_h(t)}{dt} = \rho_E E_h - \rho_I I_h - d_h I_h, \\ \frac{dR_h(t)}{dt} = \rho_I I_h - \rho_R R_h - d_h R_h. \end{cases} \tag{3.9}$$

By [102, Lemma 2.1], there exists a positive, T-periodic function $v(t)$ such that $\bar{w}(t) = e^{\theta t}v(t)$ is a solution of $\bar{w}'(t) = \tilde{M}_\epsilon(t)\bar{w}(t)$, where $\theta = \frac{1}{T}\ln \rho(\Phi_{\tilde{M}_\epsilon}(T))$. Clearly,

$\theta < 0$. Since the positive, T-periodic function $v(t)$ is bounded, we see that $\bar{w}(t) \to 0$ as $t \to \infty$. Using a comparison argument similar to that in the proof of claim 2 of Theorem 3.3.1, as applied to (3.8), we have

$$\lim_{t\to\infty}(E_v(t), I_v(t), E_h(t), I_h(t), R_h(t)) = (0,0,0,0,0).$$

It then follows from the theory of asymptotically periodic semiflow [105, Theorem 3.2.1] that

$$\lim_{t\to\infty}(S_v(t) - N_v^*(t)) = 0 \quad \text{and} \quad \lim_{t\to\infty} S_h(t) = N_h^*.$$

This completes the proof. ■

Remark 3.3.1 *We can further show, using the perturbation theory of a globally stable fixed point (see [82, Theorem 2.2]) to the Poincaré map of the system (3.1), the above result still holds for* $\mathcal{R}_0 < 1$ *and* $\delta_h > 0$, *but is sufficiently small.*

3.4 A case study

In this section, we first validate the model against the malaria transmission cases in KwaZulu-Natal Province, South Africa. Epidemic malaria in South Africa is mainly caused by *Plasmodium falciparum* species and transmitted by the *Anopheles arabiensis* and *Anopheles funestus.* The transmission of malaria occurs in three northeastern provinces of the country with low altitude, including Mpumalanga, KwaZulu-Natal and Limpopo [30]. In the highlands, climatic conditions, such as temperature, affect the development of mosquitoes and malaria parasites. Since temperatures during the preceding summer and current spring are significantly associated with malaria transmission in South Africa [21], we focus on the discussion of the temperature effects on the malaria transmission. To do this, we should evaluate the temperature-dependent coefficients ($b(t, N_v(t))$, $d_v(t)$, $\beta(t)$ and $d_J(t)$) and the temperature-independent (constant) coefficients for our mathematical model.

3.4.1 Parameter estimates

First, we estimate the temperature-independent parameters. Note that Chitnis et.al. [16] determined some realistically feasible constant parameters for the malaria transmission model, we refer the reader to their work and references therein and list values of some constant parameters for the malaria model (3.1) in Table 3.2.

	Dimension	Value	Reference
τ	Month	12/30.4	[31]
d_h	Month^{-1}	1/49.1/12	Estimated
α	Month^{-1}	2.523	[16]
ρ_E	Month^{-1}	3.04	[16]
ρ_I	Month^{-1}	0.0159	[16]
ρ_R	Month^{-1}	0.01672	[16]
c	Dimensionless	0.2	[16]
d	Dimensionless	0.011	[16]
σ	Dimensionless	$\frac{1}{10}$	[16,69]
Λ_h	Huamns × Month^{-1}	15997.99	Estimated
δ_h	Month^{-1}	2.8×10^{-3}	[16]

Table 3.2: Values for constant parameters for the malaria model (3.1).

Estimate of d_h and Λ_h: According to the 2002 World Health Report [99], we suppose that the life expectancy for South Africa is 49.1 years, and we choose

$$d_h = \frac{1}{49.1 \times 12} = 1.697\% \quad \text{Month}^{-1}.$$

In the South Africa census for 2001, the total human population for KwaZulu-Natal Province is 9,426,017. Hence, the recruitment rate Λ_h for KwaZulu-Natal Province can be calculated by

$$\Lambda_h = d_h \times 9426017 = 15997.99 \quad \text{Humans} \times \text{Month}^{-1}.$$

Next, we use the monthly mean temperatures and relationship between temperature and death rate, and biting pattern to determine the temperature-dependent parameters $d_J(t)$, $d_v(t)$, $\beta(t)$ and $b(t, N_v(t))$. In this case study, we take July 1 as the starting point.

The monthly mean temperature for KwaZulu-Natal Province: Using the reported monthly mean temperature [67] for Durban International Airport in KwaZulu-Natal Province, from July 1999 to April 2007, we can calculate the average monthly temperature for KwaZulu-Natal Province, as shown in Table 3.3.

Month	Jul	Aug	Sep	Oct	Nov	Dec
Temperature	16.66	18.34	17.22	20.8	22.1	23.46
Month	Jan	Feb	Mar	Apr	May	June
Temperature	23.82	25.32	23.52	20.24	19.1	16.84

Table 3.3: Monthly mean temperature for KwaZulu-Natal Province (in °C).

Estimation of $\beta(t)$: It follows from [51] that the temperature dependence of the duration of the gonotrophic cycle (i.e, the duration period for oviposition) can be expressed as shown in Table 3.4.

Using Mathematica software, the best fitted curve for the duration of the mosquito

Temp.	15°C	20°C	23°C	25°C	27°C	29°C	31°C	33°C	35°C
Time	12.8	6.4	5.1	3.5	3.3	2.7	2.1	2.4	2.3

Table 3.4: Mean times to oviposition (in days) in the corresponding temperature.

gonotrophic cycle is given by

$$\begin{aligned} &107.204 - 13.3523 * C + 0.677509 * C^2 - 0.0159732 * C^3 + 0.000144876 * C^4 \text{ day} \\ &= \tfrac{107.204-13.3523*C+0.677509*C^2-0.0159732*C^3+0.000144876*C^4}{30.4} \text{ Month.} \end{aligned}$$

Here, C is the temperature in Celsius. Hence, the temperature-dependent contact rate per unit time can be expressed as the reciprocal of this period, that is

$$\bar{k}(C) = \frac{30.4}{107.204 - 13.3523C + 0.677509C^2 - 0.0159732C^3 + 0.000144876C^4} \text{ Month}^{-1}.$$

Using the corresponding mean temperature of each month, we can fit the biting rate in KwaZulu-Natal Province by

$$\begin{aligned} \beta(t) &= 5.1492 - 1.83692\cos(0.523599t) - 0.175817\cos(1.0472t) \\ &-0.166233\cos(1.5708t) - 0.16485\cos(2.0944t) - 0.17681\cos(2.61799t) \\ &-1.37079\sin(0.523599t) + 0.296267\sin(1.0472t) + 0.2134\sin(1.5708t) \\ &-0.295228\sin(2.0944t) - 0.201712\sin(2.61799t) \quad \text{Month}^{-1}. \end{aligned}$$

Estimation of $d_v(t)$*:* The temperature-dependent adult mortality rate for mosquitoes $d_v(t)$ can be approximated by [75, 86]:

$$\bar{d}_v(\bar{C}) = 3.04 + 29.564\exp\left(-\frac{\bar{C} - 278^\circ K}{2.7035}\right) \quad \text{Month}^{-1},$$

where $\bar{C}$ is the temperature in absolute degrees (Kelvin, equal to 273.15 plus °C) in the range $278^\circ K \leq \bar{C} \leq 303^\circ K$. Hence, the mortality rate for adult mosquitoes $d_v(t)$

in KwaZulu-Natal Province can be approximated by

$$\begin{aligned}d_v(t) \quad &= 3.18293 + 0.135362\cos(0.523599t) + 0.02495\cos(1.0472t)\\ &+0.01925\cos(1.5708t) + 0.0358\cos(2.0944t) + 0.00548754\cos(2.61799t)\\ &+0.0904893\sin(0.523599t) + 0.0338905\sin(1.0472t) - 0.00476667\sin(1.5708t)\\ &+0.0235848\sin(2.0944t) + 0.042194\sin(2.61799t) \quad \text{Month}^{-1}.\end{aligned}$$

Estimation of $d_J(t)$: The larvae mortality rate for mosquitoes $d_J(t)$ per month (Month^{-1}) can be expressed as an empirically function of temperature [61, 86]:

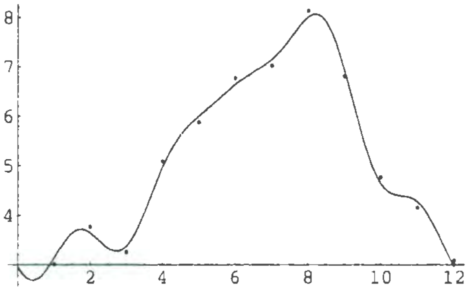
$$\bar{d}_J(C) = \frac{30.4}{-4.4 + 1.31C - 0.03C^2} \quad \text{Month}^{-1}.$$

Here, C is the temperature in Celsius. Therefore, the immature mosquito mortality rate in KwaZulu-Natal Province $d_J(t)$ can be approximated by

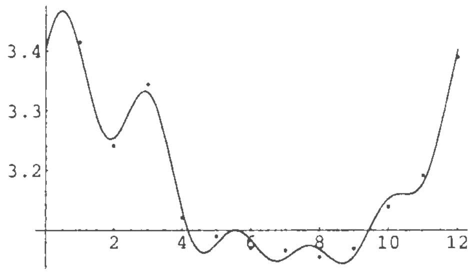
$$\begin{aligned}d_J(t) \quad &= 3.16738 + 0.0827969\cos(0.523599t) + 0.0154833\cos(1.0472t)\\ &+0.0353\cos(1.5708t) + 0.0316\cos(2.0944t) - 0.00504691\cos(2.61799t)\\ &+0.0424931\sin(0.523599t) + 0.063191\sin(1.0472t) - 0.00361667\sin(1.5708t)\\ &+0.00502294\sin(2.0944t) + 0.0463902\sin(2.61799t) \quad \text{Month}^{-1}.\end{aligned}$$

The discrete data and its corresponding fitted curves for $\beta(t)$, $d_v(t)$ and $d_J(t)$ are shown in Fig. 3.2.

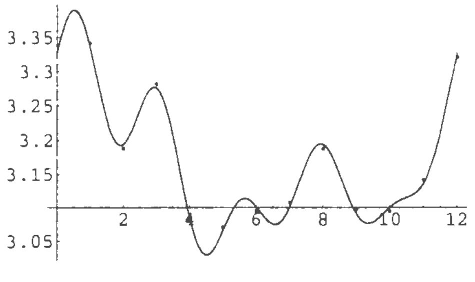
Estimation of the mosquito birth function: We suppose that the egg-deposition rate is a linear function of the biting rate (scaled reciprocal of the gonotrophic cycle), i. e., $b(t, N) = b(t) = \mu \times \beta(t)$ Mosquitoes × Month^{-1}, where μ is a positive constant number. We estimate $\mu = 5 \times 9426017$ to make sure that when there is no disease, the stable mosquito population remains about 2.5 times more than that of the human population.



(a) Fitting curve for β(t).



(b) Fitting curve for d_v(t).

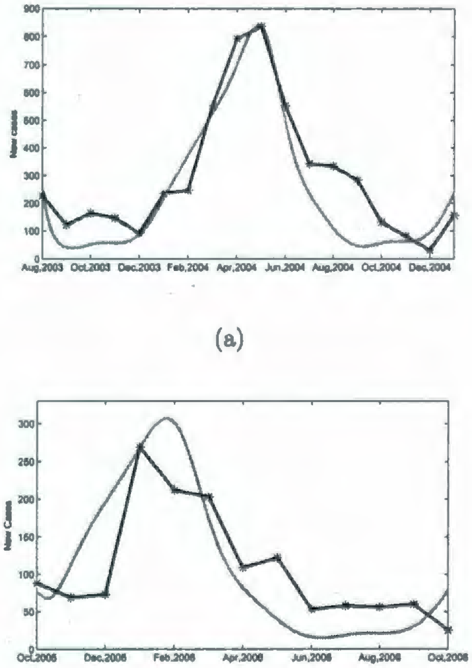


(c) Fitting curve for d_J(t).

Figure 3.2: Fitting curves for β(t), d_v(t) and d_J(t).

3.4.2 Model validation

The model was simulated in MATLAB software using the fourth–order Runge–Kutta method. For the period from August 2003 to January 2005, we use the following initial values: $S_v(0) = 11277924$, $E_v(0) = 443$, $I_v(0) = 1452$, $S_h(0) = 9384291$, $E_h(0) = 82$, $I_h(0) = 12000$ and $R_h(0) = 450$.



(a)

(b)

Figure 3.3: The monthly reported cases against the model predicting cases.

For the period from October 2005 to October 2006, people became more conscious about the malaria disease in response to the severity of malaria. Humans can implement some personal protection methods to reduce vector-host contacts, e.g., by using bed nets. To account for this prevention, we use $\hat{\beta}(t) = (1-q)\beta(t)$ to replace $\beta(t)$ in our malaria system (3.1). Here, q denotes the efficiency of intervention measures. Suppose in 2005-2006, q=30%. Setting the initial value as $S_v(0) = 13530844$, $E_v(0) = 450$, $I_v(0) = 1500$, $S_h(0) = 9313894$, $E_h(0) = 25$, $I_h(0) = 9000$ and $R_h(0) = 300$, we get Fig. 3.3, which shows the comparison between the monthly reported malaria cases [23] and model predicting cases for KwaZulu-Natal Province.

3.4.3 Basic reproduction ratio $\mathcal{R}_0$

Using Lemma 1.3.2, we can numerically compute the basic reproduction ratio $\mathcal{R}_0$. For the endemic period from August 2003–January 2005, with less intervention measure, we get $\mathcal{R}_0 = 1.1713$. For the October 2005–October 2006 epidemic period, some personal protection measures were introduced and the contact rate $\beta(t)$ became $\hat{\beta}(t) = (1-30\%)\beta(t)$. Then, $\mathcal{R}_0 = 0.8199$ for this period. Fig. 3.4 shows the long-term behavior of the infectious human population when $\mathcal{R}_0 > 1$ and $\mathcal{R}_0 < 1$. These simulations are consistent with our theoretical results in the previous section.

3.4.4 Sensitivity analysis of $\mathcal{R}_0$

In order to reduce the malaria induced human mortality and morbidity, it is necessary to know the relative importance of the different factors responsible for its transmission. Initial disease transmission is directly related to $\mathcal{R}_0$. In this subsection, we will analyze the relationship between $\mathcal{R}_0$ and some coefficients in our model (3.1).

Prolonging the duration of the immature state: Our numerical analysis (Fig. 3.5) shows that the larger τ is (the longer the immature stage is), the smaller the reproduction ratio becomes. Hence, we can prolong immature duration (via medical drugs

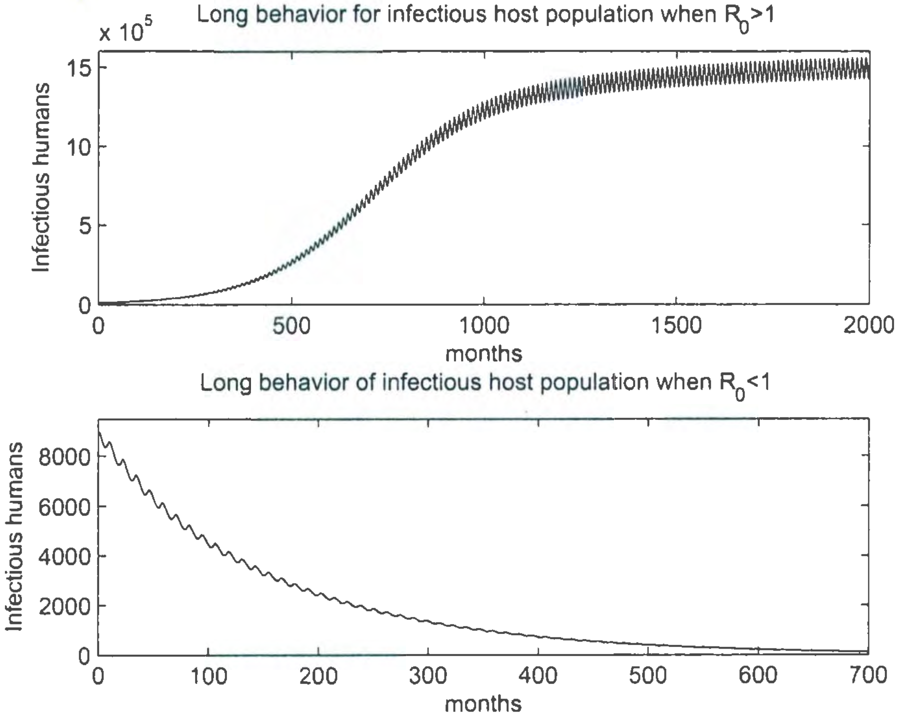


Figure 3.4: Time series of infectious host population when $\mathcal{R}_0 > 1$ and $\mathcal{R}_0 < 1$.

or control measures) to control malaria. For example, to eradicate disease for the epidemic period August 2003–January 2005, we should keep $\tau > \tau_0 = 14.96$ days.

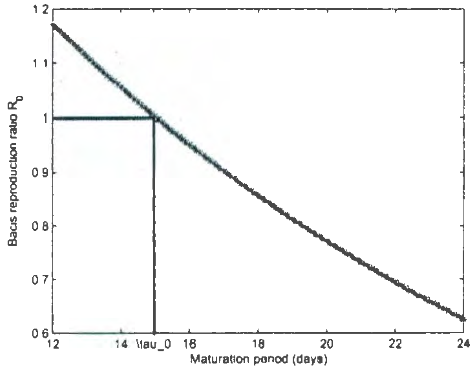


Figure 3.5: Relationship between $\mathcal{R}_0$ and τ.

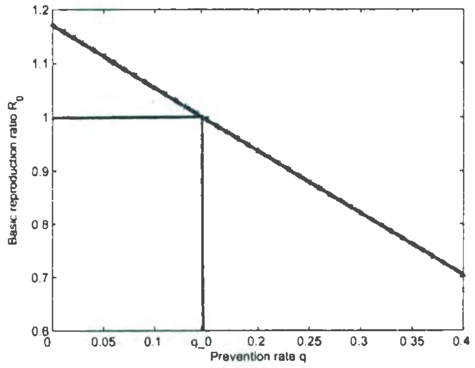


Figure 3.6: Relationship between $\mathcal{R}_0$ and q.

Prevention of host-vector contact: To simulate the effect of keeping humans from mosquito bites causing the disease transmission, we replace $\beta(t)$ with $\hat{\beta}(t) = (1 - q)\beta(t)$ in our model. Then Figure 3.6 shows the relationship between intervention efficiency q and basic reproduction ratio, $\mathcal{R}_0$. It admits our analytic result that $\mathcal{R}_0$ is in scale with $(1-q)$. Moreover, this figure shows that we should keep $q > q_0 = 14.5\%$ to control malaria transmission for August 2003–January 2005 epidemic period.

Global warming effects on $\mathcal{R}_0$*:* To simulate the effect of global warming, by the increasing temperatures, we change the corresponding periodic temperature-dependent coefficients $\beta(t)$, $d_v(t)$, $d_J(t)$ and $b(t, N_v(t))$. Using Lemma 1.3.2, we can calculate the correspondence $\mathcal{R}_0$ for each increasing temperature. Fig. 3.7 shows the effects of increasing temperature, δ, on $\mathcal{R}_0$.

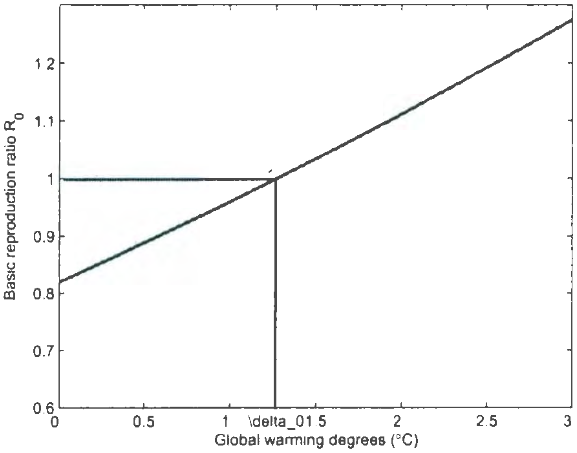


Figure 3.7: Relationship between $\mathcal{R}_0$ and δ.

For the malaria epidemic period October 2005–October 2006, if the temperatures have risen by 1°C, then $\mathcal{R}_0$ will grow to 0.9596. If the temperatures have risen by $\delta > \delta_0 = 1.3°C$, then $\mathcal{R}_0$ will larger than 1, which means that malaria resurgence happens.

3.5 Discussion

In this chapter, we have presented and analyzed a mathematical malaria model, which was motivated by the compartmental models in [15,68,69]. The modifications essentially address the age-structure of mosquitoes and the seasonal climate effects on malaria transmission. Such a model provides a baseline against which climate change scenarios (e.g., global warming) can be evaluated in the long term. From the theoretical point of view, we have figured out the basic reproduction ratio and showed that the infection will be cleared from the population provided there is only a small invasion. Moreover, the disease free periodic state is globally asymptotically stable if the disease induced death rate is sufficiently small and $\mathcal{R}_0 < 1$, which is very important for epidemiologists (and even for entomologists) to control a disease.

Although, $\mathcal{R}_0$ has been evaluated for some autonomous malarial models (in homogeneous environments) using the next generation matrix/operator approach presented in [25,91] (see also [16,53,70] for some examples), there is little work on estimating the basic reproduction ratio for malaria in the periodic time-dependent environment. Our work shows that $\mathcal{R}_0$ provides an index of transmission intensity, and good estimates of malaria transmission intensity are necessary to compare and interpret malaria interventions conducted in different places to objectively evaluate options for malaria control. The prospects for the success of malaria control depend, in part, on the basic reproductive number for malaria, $\mathcal{R}_0$ [79].

For our model, we picked feasible temperature-dependent coefficients for modeling malaria cases in KwaZulu-Natal Province, South Africa. The basic reproduction ratios of the model are computed numerically for two disease periods. For the October 2005–October 2006 period, since $\mathcal{R}_0 = 0.8199 < 1$, the disease will be contained eventually in KwaZulu-Natal Province if people keep human-mosquito contact with efficiency $q = 30\%$ while all other coefficients stay the same. This trend is consistent with the field data, since the total cases are 4193, 1999, 1389 and 491 for July 2003–June 2004, July 2004–June 2005, July 2005-June 2006 and July 2006–March 2007, respectively.

In this chapter, we numerically simulated the effect of personal protection measures on the basic reproduction ratio (Fig. 3.6). The result predicts that if people in KwaZulu-Natal Province keep intervention efficiency $q > 14.5\%$, the disease will eventually be controlled and eliminated from the population. Our numerical simulation in Fig. 3.5 indicates that an increase of the preadult duration (via medical drugs or control measures) could reduce the basic reproduction ratio $\mathcal{R}_0$. It is a vector-based idea for combating malaria transmission to prolong the immature duration of mosquitoes. Moreover, our model can be used to simulate the effects of other malaria control methods. For example, to analyze the effect of lowering the adult mosquito lifespan on $\mathcal{R}_0$, we just need to simulate $\mathcal{R}_0$ against the increased $d_v(t)$. Our mathematical modeling and the threshold parameter $\mathcal{R}_0$ can provide a quantitative framework for strategic planning, as noted in [35].

Global atmospheric temperatures are presently in a warming phase that began 250-300 years ago and rising temperatures are likely to continue. It is predicted that the average global surface temperature could rise 0.6–2.5°C in the next 50 years, and 1.4°C to 5.8°C by the year 2100 [18]. The climate-induced changes in the potential distribution of malaria were simulated in Fig. 3.7, which shows that if the temperatures have risen by $\delta > \delta_0 = 1.3°C$, the basic reproduction ratio will grow from 0.8199 to be greater than 1 and malaria will reenter KwaZulu-Natal even if people protect themselves from biting with efficiency $q = 30\%$.

Since the temperature scenarios can be derived from global climate models (GCMs) (e.g., the modeling experiments completed by the Hadley Center [45]), our model in this chapter may provide an early warning system for malaria risk.

Chapter 4

The Periodic Ross-Macdonald Model with Diffusion and Advection

4.1 Introduction

Mathematical models have long provided important insight into the malaria dynamics and control [5]. The earliest model of malaria transmission is the Ross-Macdonald model, which captures the essentials of the transmission process. Much has been done based on this classical model (see, e.g., [6,53,74] and references therein). The classical Ross-Macdonald model is highly simplified. One omission is the temporal heterogeneity in the distribution of mosquito populations and human biting rate. Transmission and distribution of vector-borne diseases are greatly influenced by environmental and climatic factors. Seasonality and circadian rhythm of mosquito populations, as well as other ecological and behavioral features, are strongly influenced by climatic factors such as temperature, rainfall, humidity, wind, and duration of daylight [44, 71, 78]. Since the climate change induces the change of the population dynamics and biting pattern of the mosquito vector, the malaria cases may significantly increase due to climate change [62, 71, 108]. Another omission is the spatial movements of reservoirs and vectors. Spatial dispersal of mosquitoes and reservoirs has also contributed to the spread of mosquito-borne diseases [52, 63, 87]. Moreover, modern transport facilitates the movement of human and disease vectors, which may play a role in the global dissemination of malaria [76, 87]. To plan and implement effective control measures, we should understand the spatial-temporal distribution of risk for malaria infections [78]. To address these two omissions, we propose a reaction-diffusion-advection malaria model in a periodic environment.

As in the classical Ross-Macdonald model, the adult female mosquito and human populations are divided into two epidemiological categories: the susceptible class and infectious class. We assume the total density of human and mosquito population at any point x and time t are H and $M(t)$, respectively. Let the spatial density of infectious humans and vectors be $h(t,x)$ and $v(t,x)$, respectively, then the density of susceptible humans and susceptible mosquitoes are $H - h(t,x)$ and $M(t) - v(t,x)$. Suppose the mortality rate of the humans and mosquitoes are d_h and $d_v(t)$, respectively. Assume $a(t)$ is the mosquito biting rate, that is, $a(t)$ is the average number of bites per mosquito per unit time at time t. Based on the fact that the total number of bites made by mosquitoes is equal to the total number of bites received by humans, the average number of bites per human receives per unit time at time t is $\frac{a(t)M(t)}{H}$. Suppose the transmission probabilities from infectious vectors to humans and from infectious humans to vectors are denoted by b and c, respectively. Thus, the infection rates per susceptible human and susceptible vector are given by

$$b\frac{a(t)M(t)}{H}\frac{v(t,x)}{M(t)} = \frac{a(t)b}{H}v(t,x) \text{ and } a(t)c\frac{h(t,x)}{H}, \text{ respectively.}$$

To take into account climate effects on mosquito development, we further assume that $M(t)$, $d_v(t)$ and $a(t)$ are positive and periodic functions with the same period being $\omega = 365$ days.

To describe the random movement of humans and mosquitoes, we use Fick's law to model the diffusion for simplicity. The diffusion coefficients for humans and mosquitoes are D_h and D_v, respectively. To account for the wind advection to the mosquito dispersal, we use g to denote the constant velocity flux. We will always assume that the advection points to the right.

Combining the viral dynamics and dispersal process together, we then have the following mathematical model on malaria dispersal:

$$\begin{cases} \frac{\partial h(t,x)}{\partial t} = a(t)b\frac{H-h(t,x)}{H}v(t,x) - d_h h(t,x) + D_h\frac{\partial^2 h(t,x)}{\partial x^2}, \\ \frac{\partial v(t,x)}{\partial t} = a(t)c\frac{h(t,x)}{H}(M(t) - v(t,x)) - d_v(t)v(t,x) + D_v\frac{\partial^2 v(t,x)}{\partial x^2} - g\frac{\partial}{\partial x}v(t,x). \end{cases} \tag{4.1}$$

This chapter is devoted to the study of the asymptotic behavior of system (4.1) in both unbounded and bounded spatial domains. In section 4.2, we prove the existence of the rightward and leftward spreading speeds c_+^* and c_-^*, and their coincidence with the minimal wave speeds for monotone periodic traveling waves in the right and left directions. In section 4.3, we establish a threshold result on the global dynamics of system (4.1) in a bounded domain $\Omega \subset \mathbb{R}^n$. Section 4.4 presents some numerical simulations to illustrate our analytic results. The chapter concludes with a brief discussion in section 4.5.

4.2 Spreading speeds and traveling waves

In this section, we study the spatial dynamics of system (4.1) in terms of spreading speeds and traveling waves.

4.2.1 The periodic Ross-Macdonald model

We first study the global dynamics of the following periodic version of Ross-Macdonald model:

$$\begin{cases} \frac{dh(t)}{dt} = a(t)b\frac{H-h(t)}{H}v(t) - d_h h(t), \\ \frac{dv(t)}{dt} = a(t)c\frac{h(t)}{H}(M(t)-v(t)) - d_v(t)v(t). \end{cases} \tag{4.2}$$

We can rewrite system (4.2) as

$$\frac{dy}{dt} = G(t,y) \tag{4.3}$$

with $y = \begin{pmatrix} h(t) \\ v(t) \end{pmatrix}$, $G(t,y) = \begin{pmatrix} a(t)b\frac{H-y_1}{H}y_2 - d_h y_1 \\ a(t)c\frac{y_1}{H}(M(t)-y_2) - d_v(t)y_2 \end{pmatrix}$. Denote $\mathbb{D} := \{(t,y) : 0 \le y \le \bar{y}(t), t \ge 0\}$ with $\bar{y}(t) = \begin{pmatrix} H \\ M(t) \end{pmatrix}$ and $L_0 = \max\{H, \max_{t\ge 0} M(t)\}$. Let $\mathbb{D}_t := \{y : 0 \le y \le \bar{y}(t)\}$. Clearly, $\mathbb{D}_0 = \{(h,v) : 0 \le h \le H, 0 \le v \le M(0)\}$.

Lemma 4.2.1 *For any $(h(0), v(0)) \in [0,l] \times [0,l]$ with $l \ge L_0$, system (4.3) has a unique solution $(h(t), v(t)) \in [0,l] \times [0,l]$ through $(h(0), v(0))$, $\forall t \ge 0$. Furthermore, $(h(t), v(t)) \in \mathbb{D}_t$, $\forall t \ge 0$, whenever $(h(0), v(0)) \in \mathbb{D}_0$.*

Proof. Since for all $y \ge 0$, $G(t,y)$ is continuous and locally Lipschitzian in y in any bounded set, there is a unique solution for system (4.3) through $(h(0), v(0)) \in [0,l] \times [0,l]$. It then follows from [80, Remark 5.2.1] that for any initial value $(h(0), v(0)) \in [0,l] \times [0,l]$, the unique solution $(h(t), v(t))$ admits $0 \le h(t) \le l$, $0 \le v(t) \le l$ on its maximal interval of existence. Hence, all solutions exist globally. Using a similar argument, we can further get the second statement. ■

Note that $(0,0)$ is an ω-periodic solution of (4.3), and the corresponding linearized system for (4.3) is

$$\frac{dz}{dt} = D_yG(t,0)z = \begin{bmatrix} -d_h & a(t)b \\ \frac{c}{H}a(t)M(t) & -d_v(t) \end{bmatrix} z. \tag{4.4}$$

Using the notations in section 1.3, we set $F(t) = \begin{bmatrix} 0 & a(t)b \\ \frac{c}{H}a(t)M(t) & 0 \end{bmatrix}$ and $V(t) = \begin{bmatrix} d_h & 0 \\ 0 & d_v(t) \end{bmatrix}$. Then we can rewrite system (4.4) as

$$\frac{dz(t)}{dt} = (F(t) - V(t))z(t).$$

Assume Y(t,s), $t \geq s$, is the evolution operator of the linear-periodic system

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

That is, for each $s \in \mathbb{R}$, the 2×2 matrix $Y(t,s)$ satisfies

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

where I is the 2×2 identity matrix.

Let C_ω be the Banach space of all ω-periodic functions from $\mathbb{R}$ to $\mathbb{R}^2$, equipped with the maximum norm. Suppose $\phi \in C_\omega$ is the initial distribution of infectious individuals in this periodic environment, then $F(s)\phi(s)$ is the rate of new infections produced by the infected individuals who were introduced at time s, and $Y(t,s)F(s)\phi(s)$ represent the distribution of those infected individuals who were newly infected at time

s and remain in the infected compartments at time t for $t \geq s$. Hence,

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

gives the distribution of accumulative new infections at time t produced by all those infected individuals $\phi(s)$ introduced at previous time. As in section 1.3, we define the next infection operator $L : C_\omega \to C_\omega$ by

$$(L\phi)(t) = \int_{0}^{\infty} Y(t,t-a)F(t-a)\phi(t-a)da, \quad \forall t \in \mathbb{R}, \quad \phi \in C_T.$$

Then the basic reproduction ratio is $\mathcal{R}_0 := \rho(L)$, the spectral radius of L.

Let ρ be the principal Floquet multiplier of the linear system (4.4). According to Theorem 1.3.1, $\mathcal{R}_0 > 1$ (< 1) if and only if $\rho > 1$ (< 1). We further have the following result on the global dynamics of system (4.2).

Lemma 4.2.2 *The following statements are valid:*

- *(i) If $\mathcal{R}_0 > 1$, then system (4.2) admits a unique positive ω-periodic solution $(h^*(t), v^*(t))$, and it is globally asymptotically stable for (4.2) with initial values in $\mathbb{D}_0 \setminus \{0\}$;*

- *(ii) If $\mathcal{R}_0 \leq 1$, then $(0,0)$ is globally asymptotically stable for system (4.2) in $\mathbb{D}_0$.*

Proof. Let $y_t(y_0) = y(t, y_0)$ be the solution map of system (4.2) through y_0. Denote $X(t) = \frac{\partial y_t}{\partial y_0}(y_0)$ and $A(t) = D_y(G(t, y(t, y_0)))$. Then, $X(t) = (x_{ij}(t))_{2\times 2}$ satisfies

$$X'(t) = A(t)X(t), \quad X(0) = I.$$

Since $\frac{\partial G_i}{\partial y_j} \geq 0$, $i \neq j$, $\forall (t,y) \in \mathbb{D}$, then $x'_{ik}(t) \geq a_{ii}(t)x_{ik}(t)$, $\forall t \geq 0$ and $i, k \in \{1, 2\}$. If $t_0 \geq 0$ and $x_{ik}(t_0) > 0$, it then follows that $x_{ik}(t) > 0$ for all $t \geq t_0$. Since $x_{ii}(0) = 1$, we have $x_{ii}(t) > 0$, $\forall t \geq 0$, $i = 1, 2$. We further prove that $x_{ij}(t_{ij}) > 0$ for some $t_{ij} \in [0, \omega]$, $\forall i \neq j$, and hence $x_{ij}(t) > 0$, $\forall t \geq \omega$, $i \neq j$. Assume, by contradiction, that there is an element $x_{ij}(t) = 0$ for all $t \in [0, \omega]$ with $i, j \in \{1, 2\}$ and $i \neq j$. Then

$$0 = x'_{ij}(t) = \sum_{l=1}^{2} a_{il}(t)x_{lj}(t) = a_{ij}(t)x_{jj}(t), \quad \forall t \in [0, \omega].$$

Since $x_{jj}(t) > 0$, it then follows from the above equality that $a_{ij}(t) \equiv 0$, $\forall t \in [0, \omega]$. Note that

$$A(t) = \begin{pmatrix} -\frac{a(t)b}{H}y_2(t, y_0) - d_h & \frac{a(t)b}{H}(1 - y_1(t, y_0)) \\ \frac{a(t)c}{H}(M(t) - y_2(t, y_0)) & -\frac{a(t)c}{H}y_1(t, y_0) - d_v(t) \end{pmatrix}.$$

If $a_{12}(t) = 0$, $\forall t \in [0, \omega]$, then $y_1(t, y_0) = H$ and $\frac{dy_1(t,y_0)}{dt} = -d_h y_1(t, y_0)$. Since $\frac{dy_1(t,y_0)}{dt} = 0$ while $-d_h y_1(t, y_0) = -d_h H$, we get a contradiction. If $a_{21}(t) \equiv 0$, $\forall t \in [0, \omega]$, then $y_2(t, y_0) = M(t)$ and $\frac{dy_2(t,y_0)}{dt} = -d_v(t)y_2(t, y_0)$, which contradicts the periodicity of $M(t)$. Thus, we get $\frac{\partial y_t}{\partial y_0}(y_0) \gg 0$, $t \geq \omega$. Furthermore, if $y_2, y_3 \in \mathbb{D}_0$ satisfy $y_2 < y_3$, then for all $t \geq \omega$, we have

$$y_t(y_2) - y_t(y_3) = \int_0^1 \frac{\partial y_t}{\partial y_0}(y_2 + r(y_3 - y_2))(y_3 - y_2)dr \gg 0.$$

Hence, we have $y_t(y_2) \ll y_t(y_3)$, $\forall t \geq \omega$, and in particular, y_ω is strongly monotone. It is easy to check that the following two conditions hold for system (4.3):

(B1) $G(t, y) \geq 0$ for every $(t, y) \in \mathbb{D}$ with $y_i = 0$, $i = 1, 2$;

(B2) For each $t \geq 0$, $y \in \mathbb{D}_t$, $G(t, y)$ is strictly subhomogeneous on y in the sense that $G(t, \alpha y) > \alpha G(t, y)$, $\forall y \in \mathbb{D}_t$ and $y \gg 0$, $\alpha \in (0, 1)$.

Using the same proof as in [105, Theorem 2.3.4], as applied to the Poincaré map associated with system (4.2) on $\mathbb{D}_0$ (see, e.g., [105, Theorem 3.1.2]), we see that two statements are valid. ■

4.2.2 Spatial dynamics

In the rest of this section, we always assume that $\mathcal{R}_0 > 1$. According to Lemma 4.2.2, there exist two periodic solution, $(0,0)$ and $u^*(t) = (h^*(t), v^*(t))$, for the spatially homogeneous system (4.2). We will consider system (4.1) with initial conditions

$$0 \leq h(0,x) = \phi_1(x) \leq H,\ 0 \leq v(0,x) = \phi_2(x) \leq M(0),\ \forall x \in \mathbb{R}. \tag{4.5}$$

Let $\mathbb{X}$ be the set of all bounded and continuous functions from $\mathbb{R}$ to $\mathbb{R}^2$ and $\mathbb{X}_+ = \{\phi \in \mathbb{X} : \phi(x) \geq 0, \forall x \in \mathbb{R}\}$. Clearly, any vector in $\mathbb{R}^2$ can be regarded as a function in $\mathbb{X}$. For $u = (u_1, u_2)$, $w = (w_1, w_2)$, we write $u \geq v$ ($u \gg v$) provided $u_i(x) \geq v_i(x)$ ($u_i(x) > v_i(x)$), $\forall i = 1, 2$, $x \in \mathbb{R}$, and $u > v$ provided $u \geq v$ but $u \neq v$. For any $r \gg 0$, we define $[0, r] := \{u \in \mathbb{R}^2 : 0 \leq u \leq r\}$ and $\mathbb{X}_r := \{u \in \mathbb{X} : 0 \leq u \leq r\}$. We equip $\mathbb{X}$ with the compact open topology, i.e., $u^m \to u$ in $\mathbb{X}$ means that the sequence of $u^m(x)$ converges to $u(x)$ as $m \to \infty$ uniformly for x in any compact set in $\mathbb{R}$. Define

$$\|u\|_{\mathbb{X}} = \sum_{k=1}^{\infty} \frac{\max_{|x| \leq k} |u(x)|}{2^k}, \quad \forall u \in \mathbb{X},$$

where $|\cdot|$ denotes the usual norm in $\mathbb{R}^2$. Then $(\mathbb{X}, \|\cdot\|)$ is a normed space. Let $d(\cdot,\cdot)$ be the distance induced by the norm $\|\cdot\|$. It follows that the topology in the metric space $(\mathbb{X}_r, d)$ is the same as the compact open topology in $\mathbb{X}_r$. Moreover, $\mathbb{X}_r$ is a complete metric space.

Let $\mathbb{E} := \{(t, \phi) \in [0, \infty) \times \mathbb{X}_+ : \phi \leq \bar{y}(t)\}$ be the subset of $[0, \infty) \times \mathbb{X}_+$ and $\mathbb{E}_t := \{\phi \in \mathbb{X}_+ : (t, \phi) \in \mathbb{E}\} = \mathbb{X}_{\bar{y}(t)}$, where $\bar{y}(t) = \begin{pmatrix} H \\ M(t) \end{pmatrix}$. Assume $\mathbb{Y}$ is the set of all bounded and continuous functions from $\mathbb{R}$ to $\mathbb{R}$. Let $S_1(t)$ and $S_2(t)$ be the solution semigroups on $\mathbb{Y}$ generated by two equations

$$\frac{\partial u_1}{\partial t} = D_h \frac{\partial^2 u_1}{\partial x^2}, \quad \text{and} \quad \frac{\partial u_2}{\partial t} = D_v \frac{\partial^2 u_2}{\partial x^2} - g\frac{\partial u_2}{\partial x},$$

respectively. Then

$$S_1(t)\phi_1(x) = \int_{\mathbb{R}} \frac{e^{-\frac{(x-y)^2}{4D_h t}}}{\sqrt{4\pi D_h t}} \phi_1(y)dy, \ t > 0,$$
$$S_2(t)\phi_2(x) = \int_{\mathbb{R}} \frac{e^{-\frac{(x-gt-y)^2}{4D_v t}}}{\sqrt{4\pi D_v t}} \phi_2(y)dy, \ t > 0.$$

Note that the equations

$$\frac{\partial u_1}{\partial t} = D_h \frac{\partial^2 u_1}{\partial x^2} - d_h u_1, \quad \text{and} \quad \frac{\partial u_2}{\partial t} = D_v \frac{\partial^2 u_2}{\partial x^2} - g \cdot \frac{\partial u_2}{\partial x} - d_v(t)u_2,$$

admit evolution operators $T_1(t,s)$ and $T_2(t,s)$ on $\mathbb{Y}$, respectively. Indeed, $T_1(t,s)$ and $T_2(t,s)$ can be defined as follows:

$$T_1(t,s)\phi_1 = e^{-d_h(t-s)} S_1(t-s)\phi_1,$$
$$T_2(t,s)\phi_2 = e^{-\int_s^t d_v(\tau)d\tau} S_2(t-s)\phi_2.$$

Define $B : \mathbb{E} \to \mathbb{X}$ by

$$B(t,\phi)(x) := \begin{pmatrix} a(t)b^{\frac{H-\phi_1(x)}{H}}\phi_2(x) \\ a(t)c^{\frac{\phi_1(x)}{H}}(M(t) - \phi_2(x)) \end{pmatrix}, \ \forall (t,\phi) \in \mathbb{E}, \ x \in \mathbb{R}. \tag{4.6}$$

Let $u_1(t,x) = h(t,x)$ and $u_2(t,x) = v(t,x)$. Then (4.1) becomes

$$\begin{cases} \partial_t u(t,x) = \begin{pmatrix} D_h \frac{\partial^2}{\partial x^2} u_1 - d_h u_1 \\ D_v \frac{\partial^2}{\partial x^2} u_2 - g \cdot \frac{\partial}{\partial x} u_2 - d_v(t) u_2 \end{pmatrix} + B(t,u), \ t > 0, \\ u(0,x) = \phi(x), \ x \in \mathbb{R}. \end{cases} \tag{4.7}$$

Integrating two equations of system (4.7) together with (4.5), we have

$$\begin{cases} u_1(t,\cdot,\phi) = T_1(t,0)\phi_1 + \int_0^t T_1(t,s)B_1(s,u(s))ds, \\ u_2(t,\cdot,\phi) = T_2(t,0)\phi_2 + \int_0^t T_2(t,s)B_2(s,u(s))ds. \end{cases} \tag{4.8}$$

It follows that system (4.7) can be written as an integral equation

$$u(t,\cdot,\phi) = T(t,0)\phi + \int_0^t T(t,s)B(s,u(s))ds, \tag{4.9}$$

whose solutions are called mild solutions to system (4.7).

Definition 4.2.1 *A function $u(t,x)$ is said to be an upper (a lower) solution of (4.7) if it satisfies*

$$u(t) \geq (\leq) T(t,0)u(0) + \int_0^t T(t,s)B(s,u(s))ds. \tag{4.10}$$

Theorem 4.2.1 *For any $\phi \in \mathbb{X}_{\bar{y}(0)}$, system (4.7) has a unique mild solution $u(t,\cdot,\phi)$ $= (u_1(t,\cdot,\phi),\ u_2(t,\cdot,\phi)) \in \mathbb{X}_{\bar{y}(t)}$ with $u(0,\cdot,\phi) = \phi \in \mathbb{X}_{\bar{y}(0)}$, $\forall t \geq 0$, and $u(t,x,\phi)$ is a classical solution when $t > 0$. Moreover, if $\underline{u}(t,x)$ and $\bar{u}(t,x)$ are a pair of lower and upper solutions of system (4.7), respectively, with $\underline{u}(0,\cdot) \leq \bar{u}(0,\cdot)$, then $\underline{u}(t,\cdot) \leq \bar{u}(t,\cdot)$, $\forall t \geq 0$.*

Proof. We first show that B is a quasi-monotone map from $\mathbb{E}$ to $\mathbb{X}$ in the sense that

$$\lim_{k\to 0^+} d(\psi - \phi + k[B(t,\psi) - B(t,\phi)]; \mathbb{X}_+) = 0, \tag{4.11}$$

for all $\psi, \phi \in \mathbb{X}_{\bar{y}(t)}$ with $\phi(x) \leq \psi(x)$, $x \in \mathbb{R}$. In fact, for any $\psi, \phi \in \mathbb{X}_{\bar{y}(t)}$ with

$\phi(x) \leq \psi(x)$, we have

$$\begin{aligned}
&B(t,\psi) - B(t,\phi) \\
&= \begin{pmatrix} \frac{a(t)}{H} b[(H-\psi_1)\psi_2 - (H-\phi_1)\phi_2] \\ \frac{a(t)}{H} c[(M(t)-\psi_2)\psi_1 - (M(t)-\phi_2)\phi_1] \end{pmatrix} \\
&\geq \begin{pmatrix} \frac{a(t)}{H} b[(H-\psi_1)\psi_2 - (H-\phi_1)\psi_2] \\ \frac{a(t)}{H} c[(M(t)-\psi_2)\psi_1 - (M(t)-\phi_2)\psi_1] \end{pmatrix} \\
&\geq \begin{pmatrix} \frac{a(t)}{H} b(\phi_1-\psi_1)\psi_2 \\ \frac{a(t)}{H} c(\phi_2-\psi_2)\psi_1 \end{pmatrix} \geq \begin{pmatrix} -\frac{a(t)}{H} bM(t)(\psi_1-\phi_1) \\ -\frac{a(t)}{H} cH(\psi_2-\phi_2) \end{pmatrix}.
\end{aligned}$$

Thus, for any $k \geq 0$ satisfying $\frac{1}{k} > \max\limits_{0\leq t\leq\omega}\{\frac{a(t)}{H} bM(t), a(t)c\}$, we have

$$\psi - \phi + k[B(t,\psi) - B(t,\phi)] \geq 0,$$

and hence, (4.11) holds. By [65, Corollary 5] with $v^+(t,x)$=$u(t,x,\bar{y}(0))$, $v^-(t,x) = 0$, system (4.7) has a unique solution $u(t,\cdot,\phi)$ on $[0,\infty)$ for any $\phi \in \mathbb{E}_0$ and $u(t,\cdot,\phi) \in \mathbb{X}_{\bar{y}(t)}$, $\forall t \geq 0$. It follows from [65, Theorem 1] that $u(t,x,\phi)$ is a classical solution if $t > 0$. Moreover, the comparison principle holds for the lower and upper solutions. ■

To study spreading speeds and traveling waves for system (4.7), we define a family of maps $\{Q_t\}_{t\geq 0}$ from $\mathbb{X}_{\bar{y}(0)}$ to $\mathbb{X}_{\bar{y}(t)}$ by

$$Q_t(\phi)(x) = u(t,x,\phi) = (u_1(t,x,\phi), u_2(t,x,\phi)), \ \forall t \geq 0, \ x \in \mathbb{R},$$

where $u(t,x,\phi)$ is the mild solution of system (4.7) with $u(0,\cdot,\phi) = \phi$. We then have the following observation.

Lemma 4.2.3 *The following two statements hold for the solution map* $Q_t : \mathbb{X}_{\bar{y}(0)} \to \mathbb{X}_{\bar{y}(t)}$*:*

(1) $Q_t[\mathbb{X}_{\bar{y}(0)}]$ *is precompact in* $\mathbb{X}_{\bar{y}(t)}$ *for all* $t > 0$.

(2) $\{Q_t\}_{t\geq 0}$ *is an* ω*-periodic semiflow in the sense that*

(i) $Q_0(v) = v$, $\forall v \in \mathbb{X}_{\bar{y}(0)}$.

(ii) $Q_{t+\omega}[v] = Q_t[Q_\omega(v)]$, $\forall t \geq 0$, $v \in \mathbb{X}_{\bar{y}(0)}$.

(iii) $Q(t,v) = Q_t(v)$ *is continuous in* $(t,v) \in \mathbb{R}_+ \times \mathbb{X}_{\bar{y}(0)}$ *with respect to the compact open topology.*

Proof. It is easy to see that (2)(i) and (ii) are satisfied for the solution map associated with the periodic system. To prove the remaining parts, we just need to show that $T(t,s)$ is compact whenever $t > s \geq 0$, and then use a same argument as in [64, Theorem 8.5.2] to prove that (1) and (2)(iii) hold.

In fact, we can write $T_1(t,s)$ and $T_2(t,s)$ explicitly as follows:

$$T_1(t,s)\phi_1(x) = e^{-d_h(t-s)} \int_{\mathbb{R}} \frac{e^{-\frac{(x-y)^2}{4D_h t}}}{\sqrt{4\pi D_h t}} \phi_1(y)dy,$$

$$T_1(t,s)\phi_2(x) = e^{-\int_s^t d_v(\tau)d\tau} \int_{\mathbb{R}} \frac{e^{-\frac{(x-gt-y)^2}{4D_v t}}}{\sqrt{4\pi D_v t}} \phi_2(y)dy.$$

For any $\mathbb{Y}_M := \{\phi \in \mathbb{Y} : 0 \leq \phi(x) \leq M,\ \forall x \in \mathbb{R}\}$ with $M > 0$, it is easy to see that

$T_1\mathbb{Y}_M \subset \mathbb{Y}_M$. Moreover, for any $\phi \in \mathbb{Y}_M$ and $x_1, x_2 \in \mathbb{R}$, we have

$$
\begin{aligned}
&|T_1(t,s)\phi(x_1) - T_1(t,s)\phi(x_2)| \\
&= \frac{e^{-d_h(t-s)}}{\sqrt{4\pi D_h t}} \Big| \int_{\mathbb{R}} e^{-\frac{(x_1-y)^2}{4D_h t}} \phi(y)dy - \int_{\mathbb{R}} e^{-\frac{(x_2-y)^2}{4D_h t}} \phi(y)dy \Big| \\
&\leq \frac{e^{-d_h(t-s)}}{\sqrt{4\pi D_h t}} \int_{\mathbb{R}} |e^{-\frac{(x_1-y)^2}{4D_h t}} - e^{-\frac{(x_2-y)^2}{4D_h t}}| \cdot |\phi(y)|dy \\
&\leq \frac{e^{-d_h(t-s)}}{\sqrt{4\pi D_h t}} \cdot M \int_{\mathbb{R}} |e^{-\frac{(x_1-y)^2}{4D_h t}} - e^{-\frac{(x_2-y)^2}{4D_h t}}|dy \\
&= \frac{e^{-d_h(t-s)}}{\sqrt{4\pi D_h t}} \cdot M \int_{\mathbb{R}} |e^{-\frac{(x_1-x_2+y)^2}{4D_h t}} - e^{-\frac{y^2}{4D_h t}}|dy \\
&= g(x_1 - x_2),
\end{aligned}
$$

where $g(\xi) = \frac{e^{-d_h(t-s)}}{\sqrt{4\pi D_h t}} \cdot M \int_{\mathbb{R}} |e^{-\frac{(\xi+y)^2}{4D_h t}} - e^{-\frac{y^2}{4D_h t}}|dy$. Clearly, $\lim_{\xi \to 0} g(\xi) = 0$. Therefore, $T_1\mathbb{Y}_M$ is a family of equicontinuous functions. It then follows from Arzelà-Ascoli theorem and a standard diagonal argument that $T_1\mathbb{Y}_M$ is precompact with respect to the compact open topology. Thus, T_1 is compact. Similarly, we can prove T_2 is compact. ■

Lemma 4.2.4 *Q_ω is subhomogeneous and monotone from $\mathbb{X}_{\bar{y}(0)}$ to $\mathbb{X}_{\bar{y}(0)}$. Moreover, for any $\phi \in \mathbb{X}_{\bar{y}(0)}$ with $\phi > 0$, $u(t,x,\phi) \gg 0$ for all $t > 0$, $x \in \mathbb{R}$.*

Proof. For any $\phi \in \mathbb{X}_{\bar{y}(0)}$, let $u(t,x,\phi)$ be the solution of system (4.7) with $u(0,x,\phi) = \phi(x)$ for $x \in \mathbb{R}$. Since $B(t,\phi)$ is strictly subhomogeneous in ϕ, $\forall (t,\phi) \in \mathbb{E}$, then, for any $k \in [0,1]$, we have

$$
\begin{aligned}
ku(t,x,\phi) &= kT(t,0)\phi + k\int_0^t T(t,s)B(s,u(s))ds \\
&= T(t,0)(k\phi) + \int_0^t T(t,s)[kB(s,u(s))]ds \\
&\leq T(t,0)(k\phi) + \int_0^t T(t,s)[B(s,ku(s))]ds.
\end{aligned}
$$

Hence, $ku(t,\cdot,\phi)$ is a lower solution of system (4.7) with initial value $k\phi$. By Theorem 4.2.1, we then have $ku(t,x,\phi) \leq u(t,x,k\phi)$ for $t \geq 0$, i.e., $Q_t(k\phi) \geq kQ_t(\phi)$. Thus, Q_t is subhomogeneous.

By Theorem 4.2.1, $\{Q_t\}_{t\geq 0}$ is a periodic monotone semiflow from $\mathbb{X}_{\bar{y}(0)}$ to $\mathbb{X}_{\bar{y}(t)}$. Since for any $t > 0$, $u(t,x,\phi)$ satisfies

$$\begin{aligned}\frac{\partial u_1(t,x,\phi)}{\partial t} &= a(t)b\frac{H-u_1}{H}u_2 - d_h u_1 + D_h\frac{\partial^2 u_1}{\partial x^2},\\ \frac{\partial u_2(t,x,\phi)}{\partial t} &= a(t)c\frac{u_1}{H}(M(t)-u_2) - d_v(t)u_2 - g\frac{\partial u_2}{\partial x} + D_v\frac{\partial^2 u_2}{\partial x^2}.\end{aligned}$$

It then follows from [92, Theorem 5.5.4] that $u_i(t,x,\phi) > 0$ for all $t > 0$, $x \in \mathbb{R}$ whenever $u_i(0,\cdot,\phi) = \phi_i > 0$. Since $\phi > 0$, we have $\phi_1 > 0$ or $\phi_2 > 0$. Without loss of generality, we assume that $\phi_1 > 0$. Then $u_1(t,x,\phi) > 0$, $\forall x \in \mathbb{R}$, $\forall t > 0$. By contradiction, suppose $u_2(t_0,x_0,\phi) = 0$ for some $t_0 > 0$ and $x_0 \in \mathbb{R}$. It then follows that $u_2(t,x,\phi) = 0$, $\forall t \in [0,t_0]$, $\forall x \in \mathbb{R}$. Since the second equation of system (4.7) implies

$$0 = a(t)c\frac{u_1(t,x,\phi)}{H}M(t), \quad \forall t \in [0,t_0],\ \forall x \in \mathbb{R},$$

we get a contradiction. Therefore, for any $\phi \in \mathbb{X}_{\bar{y}(0)}$ with $\phi > 0$, $u(t,x,\phi) \gg 0$ for all $t > 0$, $x \in \mathbb{R}$. ■

To use the theory of spreading speeds and traveling waves developed in [56, 57] (see section 1.4), we need to verify that hypotheses (A1)-(A5) hold. As noted in the remark of section 1.4, we can replace hypothesis (A1) with the following one without reflection invariance:

(A1)$'$ $T_y[Q[u]] = Q[T_y[u]]$, $\forall y \in \mathbb{H}$.

Then, the following lemma holds.

Lemma 4.2.5 *The Poincaré map Q_ω satisfies all hypotheses (A1)$'$, (A2)-(A5) with $\beta = u^*(0)$ and Q_t satisfies (A1)$'$ and (A4) for any $t > 0$.*

Proof. If $u(t,x)$ is a solution for system (4.7), then $u(t, x+y)$, $\forall y \in \mathbb{R}$, is also a solution, and hence (A1)$'$ holds. (A2) and (A3) come from Lemma 4.2.3. (A4) follows directly from the comparison principle in Theorem 4.2.1.

Let $\hat{Q}_\omega = Q_\omega|_{[0,u^*(0)]_{\mathbb{R}^2}}$. Then $\hat{Q}_\omega : \mathbb{D}_0 \to \mathbb{D}_0$ is the Poincaré map generated by (4.2). Note that (4.2) has a positive ω-periodic solution $u^*(t)$ which is globally asymptotically stable in $\mathbb{D}_0 \setminus \{0\}$. We see that $\hat{Q}_\omega$ has only two fixed points 0 and $u^*(0)$ in $\mathbb{D}_0$. Thus, by the Dancer-Hess connecting orbit lemma (see Theorem 1.1.1), it follows that there exists a strictly monotone full orbit $\{a_n\}_{-\infty}^{\infty} \subset \mathbb{D}_0$ connecting 0 to $u^*(0)$ and $a_i < a_{i+1}$ for all $i \in \mathbb{Z}$. Since $\hat{Q}_\omega$ is strongly monotone from the proof of Lemma 4.2.2, then $a_{i+1} = \hat{Q}_\omega(a_i) \ll \hat{Q}_\omega(a_{i+1}) = a_{i+2}$ for any $i \in \mathbb{Z}$. Therefore $a_i \ll a_{i+1}$ for any $i \in \mathbb{Z}$. This implies that (A5) holds for Q_ω. ∎

According to Theorem 1.4.3 and [97, Theorem 6.1], the map Q_ω admits a rightward spreading speed c_+^* and a leftward spreading speed c_-^*. Let $r_+(\mu)$ and $r_-(\mu)$, respectively, be the spectral radiuses of the Poincaré maps associated with the following two linear ordinary differential systems:

$$\begin{cases} \frac{d\bar{u}_1(t)}{dt} = a(t)b\bar{u}_2(t) - d_h\bar{u}_1(t) + D_h\mu^2\bar{u}_1(t), \\ \frac{d\bar{u}_2(t)}{dt} = a(t)cM(t)\frac{\bar{u}_1(t)}{H} - d_v(t)\bar{u}_2(t) + D_v\mu^2\bar{u}_2(t) + g\mu\bar{u}_2(t), \end{cases} \tag{4.12}$$

and

$$\begin{cases} \frac{d\bar{u}_1(t)}{dt} = a(t)b\bar{u}_2(t) - d_h\bar{u}_1(t) + D_h\mu^2\bar{u}_1(t), \\ \frac{d\bar{u}_2(t)}{dt} = \frac{a(t)}{H}cM(t)\bar{u}_1(t) - d_v(t)\bar{u}_2(t) + D_v\mu^2\bar{u}_2(t) - g\mu\bar{u}_2(t), \end{cases} \tag{4.13}$$

where $\mu \geq 0$ is a parameter. It then follows from the Kreín-Rutman Theorem (see, e.g., [42, Theorem 7.2]) that $r_\pm(\mu) > 0$. We further have the following computation formulas for $c_\pm^*$.

Proposition 4.2.1 $c_{\pm}^{*} = \inf\limits_{\mu>0} \frac{\ln r_{\pm}(\mu)}{\mu}$.

Proof. Let $(\bar{u}_1(t,\bar{u}_0), \bar{u}_2(t,\bar{u}_0))$ be the solution of system (4.12) satisfying $(\bar{u}_1(0,\bar{u}_0), \bar{u}_2(0,\bar{u}_0)) = \bar{u}_0 \in \mathbb{R}^2$. It is easy to see that

$$(u_1(t,x), u_2(t,x)) := e^{-\mu x}(\bar{u}_1(t,\bar{u}_0), \bar{u}_2(t,\bar{u}_0))$$

is a solution of the following linear parabolic system:

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} &= a(t)bu_2(t,x) - d_h u_1(t,x) + D_h \frac{\partial^2 u_1(t,x)}{\partial x^2}, \\ \frac{\partial u_2(t,x)}{\partial t} &= \frac{a(t)}{H} cM(t)u_1(t,x) - d_v(t)u_1(t,x) + D_v \frac{\partial^2 u_2(t,x)}{\partial x^2} - g\frac{\partial}{\partial x}u_2(t,x). \end{cases} \qquad \boxed{4.14}$$

Let $\{M_t\}_{t\geq 0}$ be the solution map associated with the system (4.14). Then we have

$$B_{\mu}^{t}(\phi) := M_t(\phi e^{-\mu x})(0) = (\bar{u}_1(t,\phi), \bar{u}_2(t,\phi)), \ \forall \phi \in \mathbb{R}^2, \ t \geq 0.$$

Therefore, B_{μ}^{t} is also the solution map of the linear differential equations (4.12) on $\mathbb{R}^2$. By [102, Lemma 2.1], there exists a positive ω-periodic function $w(t)$ such that $v(t) = e^{\lambda_+(\mu)t}w(t)$ is a solution of (4.12), where $\lambda_+(\mu) = \frac{1}{\omega}\ln r_+(\mu)$. Thus $B_{\mu}^{t}(w(0)) = e^{\lambda_+(\mu)t}w(t)$, and by the ω-periodicity of $w(t)$, it follows that $B_{\mu}^{\omega}(w(0)) = e^{\lambda_+(\mu)\omega}w(0)$. This implies that $e^{\lambda_+(\mu)\omega}$ is the principal eigenvalue of B_{μ}^{ω} with the positive eigenfunction $w(0)$. Define the function

$$\Phi_+(\mu) := \frac{1}{\mu}\ln(e^{\lambda_+(\mu)\omega}) = \frac{\lambda_+(\mu)\omega}{\mu} = \frac{\ln r_+(\mu)}{\mu}, \ \forall \mu > 0. \qquad \boxed{4.15}$$

When $\mu = 0$, system (4.12) reduces to system (4.4). Since $\mathcal{R}_0 > 1$, we have $r_+(0) > 1$. Hence, condition (C7) in [57] (see also section 1.4) is satisfied. Now we prove that $\Phi_+(\infty) = \infty$. Since $v(t) = e^{\lambda_+(\mu)t}w(t)$ is a solution of (4.12), we have $v_1'(t) \geq (D_h\mu^2 - d_h)v_1(t)$. It then follows that

$$\frac{w_1'(t)}{w_1(t)} \geq (D_h\mu^2 - d_h - \lambda_+(\mu)).$$

Integrating the above inequality from 0 to ω, we obtain

$$0 = \int_0^{\omega} \frac{w_1'(t)}{w_1(t)} dt \geq (D_h\mu^2 - d_h - \lambda_+(\mu))\omega,$$

and hence $\Phi_+(\mu) = \frac{\lambda_+(\mu)\omega}{\mu} \geq \frac{(D_h\mu^2 - d_h)\omega}{\mu}$, which implies that $\Phi_+(\infty) = \infty$. Thus $\Phi_+(\mu)$ attains its minimum at some finite value μ^*. Since the solution of system (4.7) $u(t,x,\phi)$ is a lower solution of the linear system (4.14), we have $Q_t[\phi] \leq M_t[\phi]$, $\forall \phi \in \mathbb{X}_{u^*(0)}$, $t \geq 0$. It then follows from Theorem 1.4.2 that $c_+^* \leq \inf\limits_{\mu>0} \Phi_+(\mu)$. Note that the reflection invariance property is assumed in [57] for M_t and Q_t in (A1), but this property is not needed in the proof of Theorem 1.4.2.

For any $\mu > 0$, let $r_+^{\varepsilon}(\mu)$ be the spectral radius of the Poincaré map associated with the following differential system:

$$\begin{cases} \frac{d\bar{u}_1(t)}{dt} &= (1-\varepsilon)a(t)b\bar{u}_2(t) - d_h\bar{u}_1(t) + D_h\mu^2\bar{u}_1(t), \\ \frac{d\bar{u}_2(t)}{dt} &= (1-\varepsilon)\frac{a(t)}{H}cM(t)\bar{u}_1(t) - d_v(t)\bar{u}_2(t) + D_v\mu^2\bar{u}_2(t) + g\mu\bar{u}_2(t). \end{cases} \tag{4.16}$$

Let $\{M_t^{\varepsilon}\}_{t\geq 0}$ be the solution map associated with

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} = (1-\varepsilon)a(t)bu_2 - d_hu_1 + D_h\frac{\partial^2 u_1}{\partial x^2}, \\ \frac{\partial u_2(t,x)}{\partial t} = (1-\varepsilon)\frac{a(t)}{H}cM(t)u_1 - d_v(t)u_1 + D_v\frac{\partial^2 u_2}{\partial x^2} - g\frac{\partial}{\partial x}u_2. \end{cases} \tag{4.17}$$

By the continuous dependence of solutions on initial conditions, it follows that for any $\varepsilon \in (0,1)$, there is a sufficiently small $\eta \in \mathbb{R}^2$ and $\eta \gg 0$ such that the solution $w(t,\eta)$ of the periodic system (4.3) with $w(0,\eta) = \eta$ satisfies $w(t,\eta) \leq \varepsilon \cdot (H, \min_{0\leq t\leq\omega}\{M(t)\})^T$, $\forall t \in [0,\omega]$. Thus, the comparison principle (Theorem 4.2.1) implies that

$$u(t,x,\phi) \leq w(t,\eta) \leq \varepsilon \cdot (H, \min_{0\leq t\leq\omega}\{M(t)\})^T,\ \forall x \in \mathbb{R},\ \phi \in \mathbb{X}_{\eta},\ t \in [0,\omega]. \tag{4.18}$$

Since $Q_t(\phi)$ is an upper solution of linear system (4.17) for $t \in [0,\omega]$, $\phi \in \mathbb{X}_{\eta}$, we have

$$M_t^{\varepsilon}(\phi) \leq Q_t(\phi),\ \forall \phi \in \mathbb{X}_{\eta},\ t \in [0,\omega]. \tag{4.19}$$

In particular, $M_\omega^\varepsilon(\phi) \leq Q_\omega(\phi)$, $\forall \phi \in \mathbb{X}_\eta$. Define the function

$$\Phi_+^\varepsilon(\mu) := \frac{\ln r_+^\varepsilon(\mu)}{\mu}, \quad \forall \mu > 0. \tag{4.20}$$

By a similar analysis and [57, Theorem 3.10 (ii)], we have $\inf\limits_{\mu>0} \Phi_+^\varepsilon(\mu) \leq c_+^* \leq \inf\limits_{\mu>0} \Phi_+(\mu)$, $\forall \varepsilon \in (0,1)$. Letting $\varepsilon \to 0$, we obtain $c_+^* = \inf\limits_{\mu>0} \Phi_+(\mu)$.

Let $\hat{w}_1(t,x) = h(t,-x)$ and $\hat{w}_2(t,x) = v(t,-x)$, we get

$$\begin{cases} \frac{\partial \hat{w}_1(t,x)}{\partial t} = a(t) b \frac{H-\hat{w}_1}{H} \hat{w}_2 - d_h \hat{w}_1 + D_h \frac{\partial^2 \hat{w}_1}{\partial x^2}, \\ \frac{\partial \hat{w}_2(t,x)}{\partial t} = a(t) c \frac{\hat{w}_1}{H} (M(t) - \hat{w}_2) - d_v(t) \hat{w}_2 + D_v \frac{\partial^2 \hat{w}_2}{\partial x^2} + g \frac{\partial}{\partial x} \hat{w}_2. \end{cases} \tag{4.21}$$

If we denote c_-^* as the leftward spreading speed of system (4.7), then c_-^* is the rightward spreading speed of system (4.21). As argued for (4.7), we then have $c_-^* = \inf\limits_{\mu>0} \frac{\ln r_-(\mu)}{\mu}$. ■

Lemma 4.2.6 $c_+^* + c_-^* > 0$.

Proof. If we define $r(\mu)$, $\mu \in \mathbb{R}$, as the spectral radius of the Poincaré map of (4.12), then $r_+(\mu) = r(\mu)$, $\forall \mu \geq 0$, and $r_-(\mu) = r(-\mu)$, $\forall \mu \geq 0$. It follows from Lemma 1.4.1 (see also [57, Lemma 3.7]) that $r(\mu)$ is log convex on $\mathbb{R}$. Thus, for all μ_1, $\mu_2 \in \mathbb{R}$ and $\theta \in (0,1)$, we have

$$\theta \ln r(\mu_1) + (1-\theta) \ln r(\mu_2) \geq \ln r(\theta\mu + (1-\theta)\mu_2).$$

Let μ_1 and μ_2 be two positive numbers such that $\inf\limits_{\mu>0} \frac{\ln r_+(\mu)}{\mu} = \frac{\ln r_+(\mu_1)}{\mu_1}$ and $\inf\limits_{\mu>0} \frac{\ln r_-(\mu)}{\mu} =$

$\frac{\ln r_-(\mu_2)}{\mu_2}$. Choosing $\theta = \frac{\mu_2}{\mu_1+\mu_2}$, we then obtain

$$\begin{aligned} c_+^* + c_-^* &= \inf_{\mu>0} \frac{\ln r_+(\mu)}{\mu} + \inf_{\mu>0} \frac{\ln r_-(\mu)}{\mu} \\ &= \frac{\ln r_+(\mu_1)}{\mu_1} + \frac{\ln r_-(\mu_2)}{\mu_2} \\ &= \frac{\ln r(\mu_1)}{\mu_1} + \frac{\ln r(-\mu_2)}{\mu_2} \\ &= \frac{\mu_1+\mu_2}{\mu_1\mu_2}[\theta \ln r(\mu_1) + (1-\theta)\ln r(-\mu_2)] \\ &\geq \frac{\mu_1+\mu_2}{\mu_1\mu_2} \ln r(\theta\mu_1 - (1-\theta)\mu_2) = \frac{\mu_1+\mu_2}{\mu_1\mu_2} \ln r(0). \end{aligned}$$

Note that $\mathcal{R}_0 > 1$ implies $r(0) > 1$. Thus, we have $c_+^* + c_-^* > 0$. ■

The following result shows that $\frac{c_+^*}{\omega}$ and $\frac{c_-^*}{\omega}$ are the rightward and leftward spreading speeds for system (4.7), respectively.

Theorem 4.2.2 *Let $c_\pm^*$ be defined as in Proposition 4.2.1. Then the following two statements are valid for system (4.7):*

(i) If $\phi \in \mathbf{X}_{u^*(0)}$ and $\phi(x) = 0$ outside a bounded interval, then $\lim_{t\to\infty, x\geq ct} u(x,t,\phi) = 0$ for all $c > \frac{c_+^*}{\omega}$, and $\lim_{t\to\infty, x\leq -ct} u(x,t,\phi) = 0$ for all $c > \frac{c_-^*}{\omega}$.

(ii) For any c and c' satisfying $\frac{-c_-^*}{\omega} < -c' < c < \frac{c_+^*}{\omega}$, we have $\lim_{t\to\infty, -c't\leq x\leq ct} (u(x,t,\phi) - u^*(t)) = 0$ for all $\phi \in \mathbf{X}_{u^*(0)}$ with $\phi > 0$.

Proof. Statement (i) is a consequence of Lemma 4.2.5, [97, Theorem 6.1] and the proof of [56, Theorem 2.1 (i)]. For the last statement, since Q_t is subhomogeneous, by [56, Theorem 2.1] (see also Theorem 1.4.3), r_σ can be chosen to be independent of $\sigma \gg 0$. Thus, we can write r_σ as $\bar{r}$. For every $\phi \in \mathbf{X}_{u^*(0)}$ with $\phi > 0$, it then follows from Lemma 4.2.4 that $Q_t(\phi)(x) \gg 0$, $\forall x \in \mathbb{R}$, $t > 0$. Fix a $t_0 = \omega > 0$, then there is a vector $\sigma \gg 0$ such that $u(\omega, x, \phi) \geq \sigma$ for x on an interval of length $2\bar{r}$. Taking

$Q_\omega(\phi)$ as a new initial date, it then follows from Lemma 4.2.5, [97, Theorem 6.2] and the proof of [56, Theorem 2.1 (ii)] (see also Theorem 1.4.3) that statement (ii) is also valid for all $\phi \in \mathbb{X}_{u^*(0)}$ with $\phi > 0$. ■

We say that $W(t, x-ct)$ is a rightward periodic traveling wave of the ω-periodic semiflow $\{Q_t\}_{t\geq 0}$ if the vector-valued function $W(t,z)$ is ω-periodic in t and $Q_t[W(0,\cdot)](x) = W(t, x-ct)$, and that $W(t,x-ct)$ connects $\beta(t)$ to 0 if $W(t,-\infty) = \beta(t)$ and $W(t,\infty) = 0$. A leftward periodic traveling wave $V(t, x+ct)$ can be defined for the ω-periodic semiflow $\{Q_t\}_{t\geq 0}$ in a similar way.

The existence and non-existence of periodic traveling wave solutions are consequences of Lemma 4.2.5 and Theorem 1.4.4 (see also [56, Theorem 2.2 and 2.3]).

Theorem 4.2.3 *Let $c^*_\pm$ be defined as in Proposition 4.2.1. Then the following statements are valid:*

(i) For every $c \geq c^*_+/\omega$, system (4.7) has a traveling wave solution $U(t, x-ct)$ connecting $u^*(t)$ to 0 such that $U(t,s)$ is continuous and nonincreasing in $s \in \mathbb{R}$, and for any $c < c^*_+/\omega$, system (4.7) admits no traveling wave solution $U(t,x-ct)$ connecting $u^*(t)$ to 0.

(ii) For every $c \geq c^*_-/\omega$, system (4.7) has a traveling wave solution $V(t, x+ct)$ connecting 0 to $u^*(t)$ such that $V(t,s)$ is continuous and nondecreasing in $s \in \mathbb{R}$, and for any $c < c^*_-/\omega$, system (4.7) admits no traveling wave solution $V(t,x+ct)$ connecting 0 to $u^*(t)$.

4.3 Threshold dynamics in a bounded domain

In this section, we consider system (4.1) on a bounded spatial domain

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} = a(t)b\frac{H-u_1}{H}u_2 - d_h u_1 + D_h\frac{\partial^2 u_1}{\partial x^2}, \\ \frac{\partial u_2(t,x)}{\partial t} = a(t)c\frac{u_1}{H}(M(t)-u_2) - d_v(t)u_2 + D_v\frac{\partial^2 u_2}{\partial x^2} - g\frac{\partial}{\partial x}u_2, \\ B_i u_i = 0 \quad \text{on} \quad (0,\infty)\times\partial\Omega, \quad i=1,2, \\ u_i(0,x) = \phi_i(x), \quad i=1,2, \end{cases} \tag{4.22}$$

where $\Omega \subset \mathbb{R}^N$ ($N \geq 1$) is a bounded domain with boundary $\partial\Omega$ of class $C^{1+\theta}$ ($0 < \theta \leq 1$), either $B_i u_i = u_i$ or $B_i u_i = \frac{\partial u_i}{\partial n} + \alpha_i(x)u$ for some nonnegative function $\alpha_i \in C^{1+\theta}(\partial\Omega, \mathbb{R})$, $\frac{\partial}{\partial n}$ denotes the differentiation in the direction of outward normal n to $\partial\Omega$.

Let $N < p < \infty$ be fixed and $\mathbb{W} = L^p(\Omega)$. For each $\beta \in (\frac{1}{2} + \frac{N}{2p}, 1)$, let $\mathbb{X}_i^\beta$ be the fractional power space of $L^p(\Omega)$ with respect to $(-\Delta, B_i)$ (see, e.g., [41]). Then $\mathbb{W}_\beta := \mathbb{X}_1^\beta \times \mathbb{X}_2^\beta$ is an ordered Banach space with the positive cone $\mathbb{W}_\beta^+$ consisting of all nonnegative functions in $\mathbb{W}_\beta$, and $\mathbb{W}_\beta^+$ has nonempty interior $int(\mathbb{W}_\beta^+)$. Moreover, $\mathbb{W}_\beta \subset C^{1+m}(\bar{\Omega})$ with continuous inclusion for $m \in [0, 2\beta - 1 - \frac{N}{p})$ (see, e.g., [42]). Let $\|\cdot\|_\beta$ be the norm on $\mathbb{W}_\beta$. It then follows that there exists a constant $K_\beta > 0$ such that $\|\phi\|_\infty := \max_{x\in\bar{\Omega}} |(\phi_1(x), \phi_2(x))| \leq K_\beta\|\phi\|_\beta$, for all $\phi \in \mathbb{W}_\beta$.

Denote $\mathbb{W}_{\bar{y}(t)} := \{\phi \in \mathbb{W}_\beta : 0 \leq \phi(x) \leq \bar{y}(t)\}$, by a similar argument as in the previous section, we can write system (4.22) as an integral equation with $u(0,\cdot) = \phi \in \mathbb{W}_{\bar{y}(0)}$. It then follows from [65, Corollary 5] that the system (4.22) has a unique solution $u(t,\phi) \in \mathbb{W}_{\bar{y}(t)}$ on $[0,\infty)$ with $u(0,\phi) = \phi \in \mathbb{W}_{\bar{y}(0)}$, and the comparison principle holds for system (4.22).

Define a family of maps $\{Q_t\}_{t\geq 0}$ from $\mathbb{W}_{\bar{y}(0)}$ to $\mathbb{W}_{\bar{y}(t)}$ by $Q_t(\phi)(x) = u(t,x,\phi)$, $\forall \phi \in \mathbb{W}_{\bar{y}(0)}$, $x \in \bar{\Omega}$, $t \geq 0$. Then $\{Q_t\}_{t\geq 0}$ is a monotone ω-periodic semiflow from

$\mathbb{W}_{\bar{y}(0)}$ to $\mathbb{W}_{\bar{y}(t)}$. Moreover, we can show that $\{Q_t\}_{t\geq 0}$ is strongly monotone for $t \geq \omega$ by similar arguments as in the proof of [80, Theorem 7.4.1 and Corollary 7.4.2]. Since $Q_\omega : \mathbb{W}_{\bar{y}(0)} \to \mathbb{W}_{\bar{y}(0)}$ is compact (see, e.g., [42]), it then follows from Theorem 1.2.1 that the following lemma holds.

Lemma 4.3.1 *The Poincaré map Q_ω admits a global attractor on $\mathbb{W}_{\bar{y}(0)}$.*

Consider the following linearized system of system (4.22)

$$\begin{cases} \frac{\partial \tilde{u}_1(t,x)}{\partial t} = a(t)b\tilde{u}_2 - d_h\tilde{u}_1 + D_h\frac{\partial^2\tilde{u}_1}{\partial x^2}, \\ \frac{\partial \tilde{u}_2(t,x)}{\partial t} = \frac{a(t)}{H}cM(t)\tilde{u}_1 - d_v(t)\tilde{u}_2 + D_v\frac{\partial^2\tilde{u}_2}{\partial x^2} - g\frac{\partial}{\partial x}\tilde{u}_2, \\ B_iu_i = 0 \quad \text{on} \quad (0,\infty)\times\partial\Omega, \quad i = 1,2. \end{cases} \qquad \boxed{4.23}$$

Similarly, we can show that the solution $\tilde{u}(t,x,\phi)$ exists for all $\phi \in \mathbb{W}_\beta$ and the comparison principle holds for (4.23). Define the Poincaré map of system (4.23) $P_1 : \mathbb{W}_\beta \to \mathbb{W}_\beta$ by $P_1(\phi) = \tilde{u}(\omega,\cdot,\phi)$ for all $\phi \in \mathbb{W}_\beta$. Then P_1 is compact. Moreover, P_1 is strongly positive by the standard parabolic maximum principle (see, e.g., [80, Theorem 7.4.1]). Let $r_1 = r(P_1)$ be the spectral radius of P_1. By the Krein-Rutman theorem (see, e.g., [42, Theorem 7.2]), it follows that $r_1 > 0$ and P_1 has an eigenfunction $\tilde{\phi} \in int(\mathbb{W}_\beta^+)$ corresponding to r_1, that is, $P_1(\tilde{\phi}) = r_1\tilde{\phi}$.

Lemma 4.3.2 *Let $\lambda = -\frac{1}{\omega}\ln r_1$. Then there exists a positive ω-periodic function $\tilde{v}(t,x)$ such that $e^{-\lambda t}\tilde{v}(t,x)$ is a solution of system (4.23).*

Proof. Let $\tilde{u}(t,x,\tilde{\phi})$ be the solution of system (4.22) through $\tilde{\phi}$. Denote $\tilde{v}(t,x) = e^{\lambda t}\tilde{u}(t,x,\tilde{\phi})$, then $\tilde{v}(t,x) \gg 0$ for all $(t,x) \in (0,\infty)\times\Omega$. Substituting $\tilde{u}(t,x,\tilde{\phi}) = e^{-\lambda t}\tilde{v}(t,x)$ into (4.23), we obtain the following linear periodic system with parameter

λ:

$$\begin{cases} \frac{\partial \tilde{v}_1(t,x)}{\partial t} = \lambda \tilde{v}_1(t,x) + a(t)b\tilde{v}_2(t,x) - d_h\tilde{v}_1(t,x) + D_h\frac{\partial^2 \tilde{v}_1(t,x)}{\partial x^2}, \\ \frac{\partial \tilde{v}_2(t,x)}{\partial t} = \frac{a(t)}{H}cM(t)\tilde{v}_1(t,x) + (\lambda - d_v(t))\tilde{v}_2(t,x) + D_v\frac{\partial^2 \tilde{v}_2(t,x)}{\partial x^2} - g\frac{\partial}{\partial x}\tilde{v}_2(t,x), \end{cases} \tag{4.24}$$

for all $(t,x) \in (0,\infty) \times \Omega$. Thus, $\tilde{v}(t,x)$ is a solution of the ω-periodic system (4.24) with $B_i\tilde{v}_i = 0$ on $\partial\Omega$ and $\tilde{v}(0,x) = \tilde{\phi}(x)$ for all $x \in \Omega$. Since $P_1(\tilde{\phi}) = r_1\tilde{\phi}$ and $e^{\lambda\omega}r_1 = 1$, we have $\tilde{v}(\omega,x) = e^{\lambda\omega}\tilde{u}(\omega,x,\tilde{\phi}) = e^{\lambda\omega}P_1(\tilde{\phi})(x) = e^{\lambda\omega}r_1\tilde{\phi}(x) = \tilde{\phi}(x) = \tilde{v}(0,x)$. Therefore, the existence and uniqueness of solutions of (4.24) imply that $\tilde{v}(t,x) = \tilde{v}(t+\omega,x)$, $\forall t \geq 0$, $x \in \Omega$, and hence, $\tilde{v}(t,x)$ is an ω-periodic solution of (4.24) and $e^{-\lambda t}\tilde{v}(t,x)$ is a solution of (4.23). ∎

Theorem 4.3.1 *For any $\phi \in \mathbb{W}_{\bar{y}(0)}$, let $u(t,x,\phi)$ be the solution of system (4.22) with $u(0,x,\phi) = \phi(x)$ for all $x \in \Omega$. Then the following two statements are valid:*

(i) If $r_1 < 1$, then $\lim_{t\to\infty} \|u(t,\cdot,\phi)\|_\beta = 0$ for all $\phi \in \mathbb{W}_{\bar{y}(0)}$.

(ii) If $r_1 > 1$, then system (4.22) admits a unique positive ω-periodic solution $u^*(t,x)$ and $\lim_{t\to\infty} \|u(t,\cdot,\phi) - u^*(t,\cdot)\|_\beta = 0$ for all $\phi \in \mathbb{W}_{\bar{y}(0)} \setminus \{0\}$.

Proof. In the case where $r_1 < 1$, we have $\lambda = -\frac{1}{\omega}\ln r_1 > 0$. Then the following inequalities hold:

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} \leq a(t)bu_2(t,x) - d_hu_1(t,x) + D_h\frac{\partial^2 u_1(t,x)}{\partial x^2}, \\ \frac{\partial u_2(t,x)}{\partial t} \leq \frac{a(t)}{H}cM(t)u_1(t,x) - d_v(t)u_2(t,x) + D_v\frac{\partial^2 u_2(t,x)}{\partial x^2} - g\frac{\partial}{\partial x}u_2(t,x). \end{cases} \tag{4.25}$$

Let $\tilde{u}(t,x,\phi)$ be the solution of (4.23) through ϕ. Then the comparison theorem implies that $u(t,x,\phi) \leq \tilde{u}(t,x,\phi)$, $\forall t \geq 0$, $x \in \Omega$. Since for any $\phi \in \mathbb{W}_{\bar{y}(0)}$, we can choose $\zeta > 0$ such that $\phi \leq \zeta\tilde{\phi}$. Hence, $0 \leq u(t,x,\phi) \leq \tilde{u}(t,x,\zeta\tilde{\phi}) = \zeta e^{-\lambda t}\tilde{v}(t,x)$. Since $\lim_{t\to\infty} \|\tilde{u}(t,\cdot,\zeta\tilde{\phi})\|_\infty = 0$, we have $\lim_{t\to\infty} \|u(t,\cdot,\phi)\|_\infty = 0$. Next, we show that

$\lim_{t\to\infty}\|u(t,\cdot,\phi)\|_\beta = 0$. Let $\omega(\phi)$ be the omega-limit set of the orbit $\{Q_{n\omega}(\phi)\}_{n\geq 1}$ with respect to the $\|\cdot\|_\beta$ norm. It suffices to show that $\omega(\phi) = \{0\}$. For any given $\psi \in \omega(\phi)$, there exists a sequence $\{n_i\}$ such that $\lim_{n_i\to\infty}\|Q_{n_i\omega}(\phi) - \psi\|_\beta = 0$, and hence, $\lim_{n_i\to\infty}\|u(n_i\omega,\cdot,\phi) - \psi\|_\infty = 0$. Thus, $\lim_{n_i\to\infty}\|u(n_i\omega,\cdot,\phi)\|_\infty = 0$ implies $\psi = 0$.

In the case where $r_1 > 1$, we have $\lambda < 0$. Let $\mathbb{W}_0 = \{\phi \in \mathbb{W}_{\bar{y}(0)} : \phi \not\equiv 0\}$, $\partial\mathbb{W}_0 = \mathbb{W}_{\bar{y}(0)} \setminus \mathbb{W}_0 = \{0\}$. Note that for all $\phi \in \mathbb{W}_0$, the solution $u(t,x,\phi) \gg 0$ for all $t > 0$, $x \in \Omega$. It follows that $Q_{n\omega}(\mathbb{W}_0) \subset \mathbb{W}_0$ for all $n > 0$. Clearly, $Q_t(0) = 0$ for all $t \geq 0$. We now prove the following claim.

Claim. Zero is a uniform weak repeller for $\mathbb{W}_0$ in the sense that there exists $\delta_0 > 0$ such that $\limsup_{n\to\infty}\|Q_{n\omega}(\phi)\|_\beta \geq \delta_0$ for all $\phi \in \mathbb{W}_0$.

We consider the following linear system:

$$\begin{cases} \frac{\partial u_1^\varepsilon(t,x)}{\partial t} = a(t)b\frac{H-\varepsilon}{H}u_2^\varepsilon(t,x) - d_h u_1^\varepsilon(t,x) + D_h\frac{\partial^2 u_1^\varepsilon(t,x)}{\partial x^2}, \\ \frac{\partial u_2^\varepsilon(t,x)}{\partial t} = a(t)c(M(t)-\varepsilon)\frac{u_1^\varepsilon(t,x)}{H} - d_v(t)u_2^\varepsilon(t,x) + D_v\frac{\partial^2 u_2^\varepsilon(t,x)}{\partial x^2} - g\frac{\partial}{\partial x}u_2^\varepsilon(t,x), \\ B_i u_i^\varepsilon = 0 \quad \text{on} \quad (0,\infty)\times\partial\Omega, \quad i = 1,2, \\ u_i^\varepsilon(0,x) = \phi_i(x), \quad x \in \Omega, \quad i = 1,2. \end{cases} \tag{4.26}$$

Let $u^\varepsilon(t,x,\phi)$ be the solution of system (4.26) with $u^\varepsilon(0,x,\phi) = \phi(x)$. Define the Poincaré map of system (4.26), $P_\varepsilon : \mathbb{W} \to \mathbb{W}$, by $P_\varepsilon(\phi) = u^\varepsilon(\omega,\cdot,\phi)$. Let $r_\varepsilon = r(P_\varepsilon)$ be the spectral radius of P_ε. Since $r_1 = r(P_1) > 1$, there exists a sufficiently small positive number ε_1 such that $r_\varepsilon > 1$ for all $\varepsilon \in [0,\varepsilon_1)$. Fix an $\varepsilon \in [0,\varepsilon_1)$. Then there exists some $\delta > 0$ such that $\|u^\varepsilon(t,\cdot,\phi)\|_\infty < \varepsilon$ for all $t \in [0,\omega]$ whenever $\|\phi\|_\infty < \delta$. Let $\delta_0 = \frac{\delta}{K_\beta}$. Suppose, by contradiction, that $\limsup_{n\to\infty}\|Q_n(\phi_0)\|_\beta < \delta_0$ for some $\phi_0 \in \mathbb{W}_0$. Then there exist $n_0 > 0$ such that $\|Q_{n\omega}(\phi_0)\|_\infty \leq K_\beta\|Q_{n\omega}(\phi_0)\|_\beta < \delta$ for all $n \geq n_0$. For any $t \geq n_0\omega$, we can rewrite $t = n\omega + t'$ with $n \geq n_0\omega$ and $t \in [0,\omega]$.

Therefore, we have

$$\|Q_t(\phi_0)\|_\infty = \|Q_{t'}(Q_{n\omega}(\phi_0))\|_\infty < \varepsilon, \ \forall t \geq n_0\omega,$$

and $u(t, x, \phi_0)$ satisfies the following system

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} \geq a(t)b\frac{H-\epsilon}{H}u_2(t,x) - d_h u_1(t,x) + D_h\frac{\partial^2 u_1(t,x)}{\partial x^2}, \\ \frac{\partial u_2(t,x)}{\partial t} \geq a(t)c(M(t)-\varepsilon)\frac{u_1(t,x)}{H} - d_v(t)u_2(t,x) + D_v\frac{\partial^2 u_2(t,x)}{\partial x^2} - g\frac{\partial}{\partial x}u_2(t,x), \end{cases} \tag{4.27}$$

for all $t \geq n_0\omega$, $x \in \Omega$. Let $\tilde{\phi}_\varepsilon$ be the positive eigenfunction of P_ε associated with r_ε and $\lambda_\varepsilon = -\frac{1}{\omega}\ln r_\varepsilon < 0$. Then by Lemma 4.3.2, there is a solution $u^\varepsilon(t, x,_\varepsilon) = e^{-\lambda_\varepsilon t}v_\varepsilon(t, x)$, with $v_\varepsilon(t, x)$ a periodic positive function. Since $u(t, x, \phi_0) \gg 0$ for all $t > 0$, $x \in \Omega$, there exists $\eta > 0$ such that $u(n_0\omega, x, \phi_0) \geq \eta_\varepsilon$. By (4.27) and the comparison principle, we have

$$u(t, x, \phi_0) \geq \eta u^\varepsilon(t - n_0\omega, x,_\varepsilon) = \eta e^{-\lambda_\varepsilon(t-n_0\omega)}v_\varepsilon(t, x), \ \forall t \geq n_0\omega, \ x \in \bar{\Omega}.$$

Since $\lambda_\varepsilon < 0$, it then follows that $u(t, x, \phi_0)$ is unbounded, a contradiction. This proves the claim.

By the claim above, Q_ω is weakly uniform persistence with respect to $(\mathbb{W}_0, \partial\mathbb{W}_0)$. Since Q_ω admits a global attractor on $\mathbb{W}_{\bar{y}(0)}$, it follows from [105, Theorem 1.3.3] that Q_ω is uniformly persistent with respect to $(\mathbb{W}_0, \partial\mathbb{W}_0)$ in the sense that there exists δ_1 such that $\liminf\limits_{n\to\infty} \|Q_\omega^n(\phi)\|_\beta \geq \delta_1$ for all $\phi \in \mathbb{W}_0$. Note that Q_ω is compact, point dissipative and uniformly persistent. It follows from Theorem 1.2.6 (or [105, Theorem 1.3.6]) that $Q_\omega : \mathbb{W}_0 \to \mathbb{W}_0$ admits a global attractor A_0 and has a fixed point $\hat{\phi}$ in A_0. Since Q_ω is strongly monotone semiflow on $\mathbb{W}_0$, we have $A_0 = Q_\omega(A_0) \gg 0$, and hence $\hat{\phi} \gg 0$.

By a similar argument as in the Lemma 4.2.4, it is easy to see that for each $t > 0$, Q_t is strictly subhomogeneous. Then [103, Lemma 1] implies that Q_ω has at most one fixed point in $\mathbb{W}_0$. Moreover, it follows from Theorem 1.1.2 that $A_0 = \{\hat{\phi}\}$. Thus, $\hat{\phi}$ is globally attractive in $\mathbb{W}_0$ for Q_ω.

Let $u(t, x, \hat{\phi})$ be the solution of system (4.22) with $u(0, x, \hat{\phi}) = \hat{\phi}(x)$ for all $x \in \Omega$. Since $\hat{\phi}$ is a fixed point of Q_ω and is globally attractive in $\mathbb{W}_0$, we see that $u(t, x, \hat{\phi})$ is an ω-periodic solution of system (4.22) which attracts all solution of (4.22) in $\mathbb{W}_0$. That is, $\lim_{t\to\infty} \|u(t, \cdot, \phi) - u(t, \cdot, \hat{\phi})\|_\beta = 0$, $\forall \phi \in \mathbb{W}_0$. Thus, $u^*(t, x) := u(t, x, \hat{\phi})$ is the desired ω-periodic solution. ■

4.4 Numerical simulations

To numerically illustrate our analytic results, we study the malaria cases in KwaZulu-Natal province in South Africa.

4.4.1 Model coefficients and the basic reproduction ratio

We choose $H = 109$ humans/km, $d_h = \frac{1}{49.1 \times 365}$ day^{-1}. As estimated in chapter 3, the mortality rate for adult mosquitoes $d_v(t)$ in KwaZulu-Natal Province can be approximated by

$$\begin{aligned} d_v(t) &= 0.1047 + 0.00445\cos(\frac{2\pi}{365}t) + 0.00082\cos(\frac{4\pi}{365}t) \\ &+0.00063\cos(\frac{6\pi}{365}t) + 0.00118\cos(\frac{8\pi}{365}t) + 0.00018\cos(\frac{10\pi}{365}t) \\ &+0.00298\sin(\frac{2\pi}{365}t) + 0.00112\sin(\frac{4\pi}{365}t) - 0.00016\sin(\frac{6\pi}{365}t) \\ &+0.00078\sin(\frac{8\pi}{365}t) + 0.00139\sin(\frac{10\pi}{365}t) \quad \text{day}^{-1}. \end{aligned}$$

The biting rate per unit time of mosquitoes in KwaZulu-Natal Province can be fitted by

$$\begin{aligned} a(t) &= 0.16938 - 0.06043\cos(\frac{2\pi}{365}t) - 0.00578\cos(\frac{4\pi}{365}t) \\ &+0.00547\cos(\frac{6\pi}{365}t) - 0.00542\cos(\frac{8\pi}{365}t) - 0.00582\cos(\frac{10\pi}{365}t) \\ &-0.04509\sin(\frac{2\pi}{365}t) + 0.00975\sin(\frac{4\pi}{365}t) + 0.00702\sin(\frac{6\pi}{365}t) \\ &-0.00971\sin(\frac{8\pi}{365}t) - 0.00664\sin(\frac{10\pi}{365}t) \quad \text{day}^{-1}. \end{aligned}$$

Suppose the mosquito density $M(t) = 20 \times H \times a(t)$ mosquitoes/km, a linear function of the biting rate, such that the average mosquito density is about three times as that of the human density. The proportions of infected bites on humans and mosquitoes that produce an infection are $b = 0.011$ and $c = 0.2$. For illustration, we choose $D_v = 1.25\times10^{-2}$ km^2/day, $D_h = 1$ km^2/day and $g = 5.0\times10^{-2}$ km/day. Using the method introduced in [95] (see also section 1.3), we can numerically compute the basic reproduction ratio $\mathcal{R}_0 = 7.04$. Fig. 4.1 shows the variation of the basic reproduction ratio $\mathcal{R}_0$ as a function of the mosquito density and mosquito biting rate.

4.4.2 The averaged system

For a continuous periodic function $p(t)$ with the period ω, we define its average as

$$[p] := \frac{1}{\omega}\int_0^\omega p(t)dt.$$

Then, the time averaged autonomous system for (4.1) can be represented as

$$\begin{cases} \frac{\partial h(t,x)}{\partial t} = \frac{[a]}{H}b(H-h)v - d_h h + D_h\frac{\partial^2 h}{\partial x^2}, \\ \frac{\partial v(t,x)}{\partial t} = \frac{[a]}{H}c([M]-v)h - [d_v]v + D_v\frac{\partial^2 v}{\partial x^2} - g\frac{\partial v}{\partial x}, \end{cases}$$

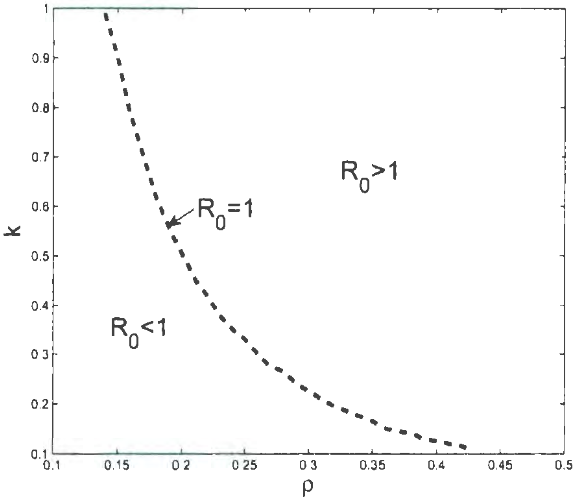


Figure 4.1: Graph for the basic reproduction ratio $\mathcal{R}_0$. Here the biting rate is $\rho a(t)$ and the whole mosquito density is $kM(t)$.

where $[a] = 0.1694$ day^{-1}, $[d_v] = 0.1047$ day^{-1}, and $[M] = 369.292$ mosquitoes/km. Consider the linear autonomous system:

$$\begin{cases} \frac{d\bar{u}_1(t)}{dt} &= [a]b\bar{u}_2(t) - d_h\bar{u}_1(t) + D_h\mu^2\bar{u}_1(t), \\ \frac{d\bar{u}_2(t)}{dt} &= \frac{[a]}{H}c[M]\bar{u}_1(t) - [d_v]\bar{u}_2(t) + D_v\mu^2\bar{u}_2(t) + g\mu\bar{u}_2(t), \end{cases} \tag{4.28}$$

where $\mu \geq 0$ is a parameter. Note that the fundamental solution matrix of system (4.28) is $e^{A(\mu)t}$ with

$$A(\mu) = \begin{pmatrix} -d_h + D_\mu\mu^2 & [a]b \\ \frac{[a]c}{H}[M] & -[d_v] + D_v\mu^2 + g\mu \end{pmatrix}.$$

Thus, the spectral radius of the time one map associated with system (4.28) is $e^{\lambda(\mu)}$, where $\lambda(\mu)$ is the spectral radius of the matrix $A(\mu)$, that is,

$$\lambda(\mu)=\tfrac{1}{2}(D_h\mu^2 - d_h + D_v\mu^2 + g\mu - [d_v]$$
$$+\sqrt{(D_h\mu^2 - d_h + D_v\mu^2 + g\mu - [d_v])^2 - 4[(D_h\mu^2 - d_h)(D_v\mu^2 + g\mu - [d_v]) - \tfrac{[a]^2bc[M]}{H}]}).$$

Hence, $\bar{c}_+^* = \inf\limits_{\mu>0} \frac{\ln e^{\lambda(\mu)}}{\mu} = \inf\limits_{\mu>0} \frac{\lambda(\mu)}{\mu}$. Let μ^* be the positive root of $(\frac{\lambda(\mu)}{\mu})' = 0$. Then the rightward spreading speed for the time-averaged autonomous system is $\bar{c}_+^* = \frac{\lambda(\mu^*)}{\mu^*}$. Similarly, we can obtain the leftward spreading speed $\bar{c}_-^*$. Two spreading speeds can be numerically computed as $\bar{c}_+^* = 0.0884$ km/day and $\bar{c}_-^* = 0.0866$ km/day.

4.4.3 The periodic system

For the periodic system, using Proposition 4.2.1, we can numerically get $c_+^* = 0.1019$ km/day and $c_-^* = 0.0996$ km/day. This implies that the spreading speeds of the time-averaged autonomous system underestimate the real spreading speeds. Fig. 4.2 shows a plot of the spreading speed c_+^* and c_-^* as functions of the advection velocity g. The downstream spreading speed increases with advection velocity, while the upstream spreading speed decreases with advection velocity. Fig. 4.3 indicates that the rightward spreading speed c_+^* and leftward spreading speed c_-^* both increase with human diffusion coefficient D_h.

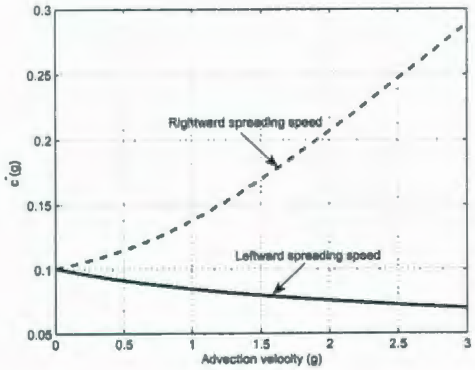


Figure 4.2: Leftward and rightward spreading speeds as functions of the advection velocity g.

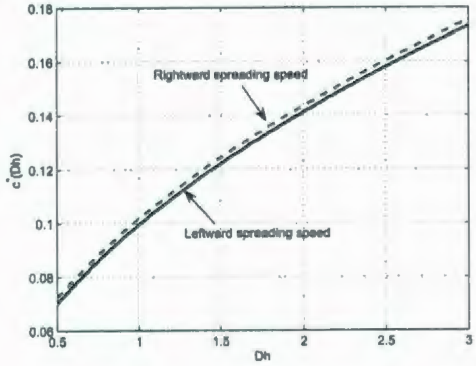


Figure 4.3: Leftward and rightward spreading speeds as functions of D_h.

To simulate the spatial spread of malaria, we discretize system (4.1) by the difference method on a finite spatial interval $[-L, L]$ with the Neumann boundary condition, where L is sufficiently large. Figs. 4.4 and 4.5 show numerical plots of the solution through the initial condition

$$h(0,x) = \begin{cases} 80, & \text{if } |x| \le 50 \\ \frac{8}{5}(100 - |x|), & \text{if } 50 \le |x| \le 100 \\ 0, & \text{if } |x| \ge 100 \end{cases}, \quad v(0,x) = \frac{3}{2} \times h(0,x).$$

The infectious host and vector spread in both directions with a bias towards downstream.

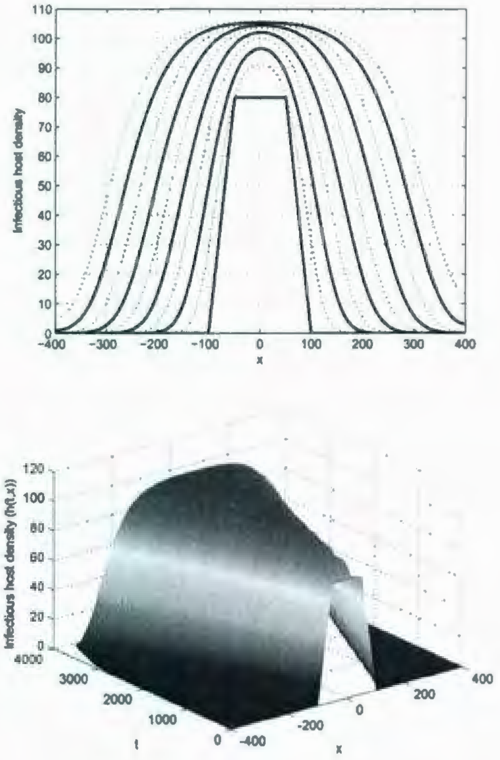


Figure 4.4: The spread of infectious host. The top plot shows the density of infectious host at different times t year, with $t = 1, 2, 3, 4, 5, 6, 7, 8, 9$ respectively.

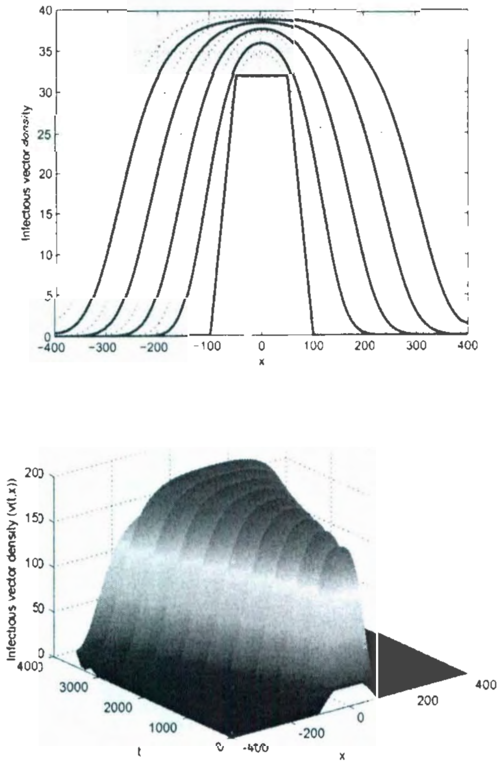


Figure 4.5: The spread of infectious vector. The top plot shows the density of infectious vector at different times t year, with $t = 1, 2, 3, 4, 5, 6, 7, 8, 9$ respectively.

To get rightward traveling waves, we choose the initial condition as

$$h(0,x) = v(0,x) = \begin{cases} \frac{220}{3}, & \text{if } x \leq -\frac{100}{3} \\ \frac{11}{10}(\frac{100}{3} - x), & \text{if } |x| \leq \frac{100}{3} \\ 0, & \text{if } x \geq \frac{100}{3} \end{cases}.$$

The evolution of the solution is shown as in Fig. 4.6.

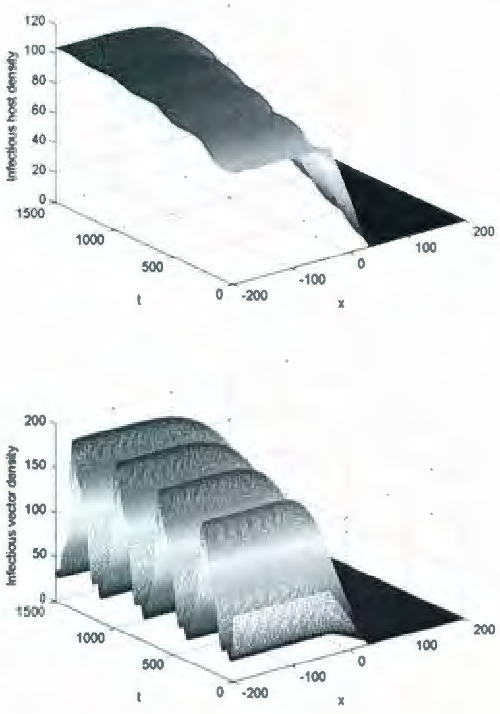


Figure 4.6: The rightward periodic traveling waves observed for two components.

To simulate the global dynamics of system (4.1) on a bounded domain, we choose the following initial condition

$$h(0, x) = v(0, x) = 100 \times \cos(\frac{\pi x}{2L}),$$

and the Dirichlet boundary condition

$$h(t, -L) = h(t, L) = v(t, -L) = v(t, L) = 0.$$

The evolution of the solution is shown in Fig. 4.7 for $L = 50$. It indicates that in this case the disease persists in the host and vector populations.

4.5 Discussion

In this chapter, we analyzed a periodic Ross-Macdonald type model with diffusion and advection to account for the movement of host and vector population and the seasonal fluctuation of mosquito dynamics. For the spatially homogeneous system, we determined the basic reproduction ratio $\mathcal{R}_0$, and proved that $\mathcal{R}_0$ is a threshold value for the malaria transmission in a periodic environment. This implies that the disease dies out when $\mathcal{R}_0 \leq 1$; while the disease can invade the population when $\mathcal{R}_0 > 1$. In order to study the spatial propagation of malaria, we should consider the spatially inhomogeneous system in the case where $\mathcal{R}_0 > 1$.

In the case of the unbounded domain, the risk of invasion can be described in terms of spreading speeds and periodic traveling waves. In this case, we obtained the existence of the leftward and rightward spreading speeds, and showed that they coincide with the minimal wave speeds for monotone traveling waves in the left and right directions, respectively. To control the disease, we should use physical or chemical strategies to reduce the values of the rightward and leftward spreading speeds, $c_{\pm}^*$, as close to zero as possible. As shown in Proposition 4.2.1, the spreading speeds depend

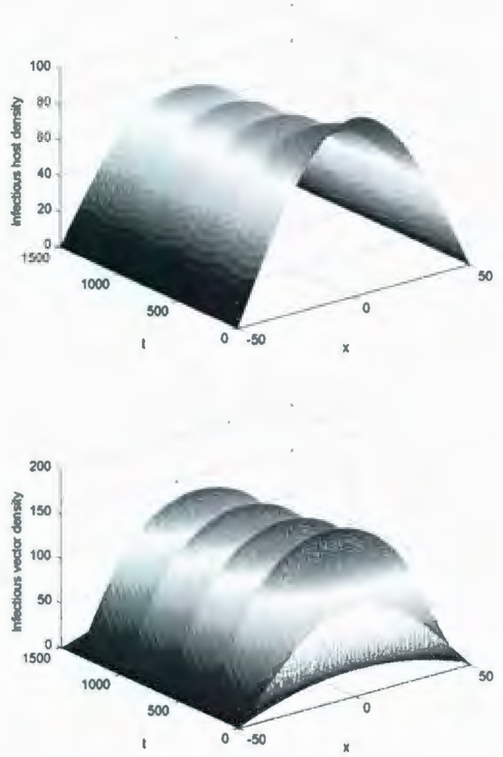


Figure 4.7: The evolution of two components when $L = 50$.

on parameters in the model, which permits the assessment of control strategies. Numerically, we studied how advection increases the rightward spreading speed, whereas decreases the leftward spreading speed. Since human movements are the source of long-distance transmission of malaria, numerical simulations were also performed to investigate the effect of human movements on disease propagation. Both the rightward and leftward spreading speeds increase with diffusion coefficient for humans, which means that global traffic networks may deteriorate malaria situation. In the case of the bounded domain, we established a threshold result on the global attractivity of either zero or a positive periodic solution. Biologically, this result shows that malaria disease stabilizes at a unique positive periodic solution when the zero solution is linearly unstable; while it dies out when the zero solution is linearly stable.

Several authors have used reaction-diffusion systems to study the spatial dynamics of vector-borne diseases (see, e.g., [32, 52]). The authors of [52] proposed a reaction-diffusion system to describe the spatial spread of West Nile virus, and simplified their original model as the following one under some reasonable assumptions:

$$\begin{cases} \frac{\partial I_V}{\partial t} = \alpha_V \beta_R \frac{I_R}{N_R}(A_V - I_V) - d_V I_V + \varepsilon \frac{\partial^2 I_V}{\partial x^2}, \\ \frac{\partial I_R}{\partial t} = \alpha_R \beta_R \frac{N_R - I_R}{N_R} I_V - \gamma_R I_R + D \frac{\partial^2 I_R}{\partial x^2}, \end{cases} \tag{4.29}$$

where A_V, N_R are constant. Further, they proved the existence of traveling waves and calculated the spreading speed for system (4.29), and also showed that the spreading speed for system (4.29) is an upper bound for that of the original model, provided that the spreading speed for the latter exists. We should mention that the techniques in our current chapter can be employed to study spreading speeds and traveling waves for the time-periodic version of system (4.29) and other cooperative type vector-borne diseases models with temporal and spatial heterogeneities.

Chapter 5

A Reaction-Diffusion Malaria Model with Incubation Period in The Vector Population

5.1 Introduction

According to etiological literature, mosquitoes may spend a period of time during which they can not transmit the disease to humans after taking an infected blood meal, which is the extrinsic incubation period (EIP). This incubation period varies from 10 to 14 days [13, 47], which is long compared with the longevity of the adult mosquito (within 12 days [13]). These infected mosquitoes that survive the incubation period will remain infectious for the rest of their lives. Thus, EIP may greatly influence the number of infected mosquitoes that live long enough to become infectious. On the other hand, spatial heterogeneity, spatial movement of human and vector populations may be important for the malaria dynamics (see, for instance, chapter 4 and [20,87]). It is therefore necessary to study the impacts of the EIP and the spatial heterogeneity on the transmission of the malaria parasite [78].

In this chapter, we modify the standard Ross's malaria model [73] to incorporate the extrinsic incubation period and human and vector movements in spatially heterogeneous environments. However, the modeling process is not trivial since mosquitoes may not stay at the same location in space during the incubation period, which involves a delay term with spatial averaging on the whole spatial domain [12,33]. Our analysis suggests that the model admits a basic reproduction ratio $\mathcal{R}_0$ and it serves as a threshold parameter for disease persistence. Moreover, we show that the risk based on the model with spatially averaged parameters may significantly underestimate the transmission intensity.

The rest of this chapter is organized as follows. The next section presents the model, which turns out to be a nonlocal and time-delayed reaction-diffusion system. The basic reproduction ratio and mathematical analysis are established in Sections 3. Section 4 is devoted to the study of the model with spatially independent parameters. Some carefully designed numerical simulations and a discussion section complete the chapter.

5.2 Model formulation

The model is based on monitoring the temporal and spatial dynamics of host (the human) and vector (the adult female mosquito) densities. We develop a spatial model for malaria infection by ignoring superinfection, immunity and clinical death (see, e.g., [5,78]). The human population is divided into two epidemiological classes: susceptible (S_h) and infectious classes (I_h). Assume that the density of total human population

$N_h(t,x) = S_h(t,x) + I_h(t,x)$ is described by a logistic population growth law, and that all populations perform an unbiased random walk. Thus, we have the following reaction-diffusion equation,

$$\frac{\partial N_h(t,x)}{\partial t} = D_h \Delta N_h(t,x) + b_h N_h(t,x)\left[1 - \frac{N_h(t,x)}{K(x)}\right],$$

where Δ is the usual Laplacian operator. The diffusion coefficient D_h and the natural growth rate b_h for humans are supposed to be positive constants while the carrying capacity $K(x)$ is a positive function of location x, allowing for the diversity in habitats. Let Ω be a spatial habitat with smooth boundary $\partial\Omega$. We assume that all populations remain confined to the region Ω for all time, and we supplement the Neumann boundary condition to the above equation

$$\frac{\partial N_h}{\partial n} = 0, \ \forall t > 0, \ x \in \partial\Omega,$$

where $\frac{\partial}{\partial n}$ denotes the differentiation along the outward normal n to $\partial\Omega$. It easily follows that the above reaction-diffusion equation admits a unique positive steady state $H(x)$ such that $\lim_{t\to\infty} N_h(t,x) = H(x)$ for all solutions with nonnegative and nonzero initial data (see, e.g., [105, Theorem 3.1.5 and the proof of Theorem 3.1.6]). Biologically, we may suppose that the total human density at location point x stabilizes at $H(x)$, that is, $N_h(t,x) = H(x)$, $\forall t \geq 0$.

Human acquire malaria through effective contact with infectious mosquitoes. For the disease transmission term, we take into account the conservation of bites, that is, the total number of bites made by mosquitoes equals to the number of bites received by host at a fixed habitat x (see, e.g., [9]). Thus, we suppose the force of infection at location x and time t is given by

$$c\beta(x)\frac{S_h(t,x)}{H(x)}I_m(t,x) = c\beta(x)\frac{H(x) - I_h(t,x)}{H(x)}I_m(t,x),$$

where c is the transmission probability per bite from infectious mosquitoes to susceptible humans, $\beta(x)$ is the habitat dependent biting rate of female mosquitoes, and I_m is the density of infectious female mosquitoes. This cross-infection between hosts and vectors is modeled as mass-action mechanism normalized by host-density, see, e.g., [9, 98]. It then follows that the density of infectious human population can be described by

$$\frac{\partial I_h(t,x)}{\partial t} = D_h \Delta I_h(t,x) + \frac{c\beta(x)}{H(x)}(H(x) - I_h(t,x))I_m(t,x) - (d_h + \rho)I_h(t,x), \tag{5.1}$$

where d_h is the human natural death rate, and ρ is the recovery rate, i.e., $1/\rho$ is the human infectious period.

The susceptible adult mosquito population is increased via the recruitment of aquatic mosquitoes, and diminished by infection and by natural death at a rate d_m. Suppose that $\mu(x)$ denotes the habitat dependent recruitment rate at which adult female mosquitoes emerge from larval. As in [39, 78], here we assume that the emergence of adults is not explicitly linked to the density of adult mosquitoes. Moreover, the force of infection for mosquito population is

$$\frac{b\beta(x)}{H(x)} S_m(t,x) I_h(t,x),$$

where b is the transmission probability per bite from infectious humans to susceptible mosquitoes. Thus, the dynamics of susceptible adult mosquitoes can be described by

$$\frac{\partial S_m(t,x)}{\partial t} = D_m \Delta S_m(t,x) + \mu(x) - \frac{b\beta(x)}{H(x)} S_m(t,x) I_h(t,x) - d_m S_m(t,x). \tag{5.2}$$

To incorporate an extrinsic incubation period (EIP) into Ross's model [73], the infected mosquito population is divided into two epidemiological categories: latent (E_m) and infectious (I_m) classes. Since these latent mosquitoes can fly around during the incubation period, we should carefully formulate this process. To achieve this, we introduce an infection age variable a and let $y(t, a, x)$ be the density of the mosquito population with infection age a at time t and habitat x. Using the standard method on describing age structured population with spatial diffusion (see, e.g., [33] and references therein), we get

$$\frac{\partial y(t,a,x)}{\partial t} + \frac{\partial y(t,a,x)}{\partial a} = D_m \Delta y(t,a,x) - d_m y(t,a,x), \tag{5.3}$$

where D_m is the mosquito diffusion coefficient and d_m is the mosquito death rate. Suppose that τ is the average incubation period, we then have

$$E_m(t,x) = \int_0^{\tau} y(t,a,x)da,$$

and

$$I_m(t,x) = \int_{\tau}^{\infty} y(t,a,x)da.$$

Integrating both sides of equation (5.3) from 0 to τ, and from τ to ∞, we obtain

$$\frac{\partial E_m(t,x)}{\partial t} = D_m \Delta E_m(t,x) - d_m E_m(t,x) - y(t,\tau,x) + y(t,0,x),$$

and

$$\frac{\partial I_m(t,x)}{\partial t} = D_m \Delta I_m(t,x) - d_m I_m(t,x) - y(t,\infty,x) + y(t,\tau,x),$$

respectively. Biologically, we assume that $y(t,\infty,x) = 0$. Since the recruitment of newly infected mosquitoes ($y(t,0,x)$) is due to the contact of susceptible mosquitoes and infectious humans, it follows that

$$y(t,0,x) = \frac{b\beta(x)}{H(x)} S_m(t,x) I_h(t,x).$$

It is then necessary to determine $y(t,\tau,x)$, which can be done by the integration along characteristics. Let $v(r,a,x) = y(a+r,a,x)$, with $r \geq 0$. Then we have

$$\begin{cases} \frac{\partial v(r,a,x)}{\partial a} &= [\frac{\partial y(t,a,x)}{\partial t} + \frac{\partial y(t,a,x)}{\partial a}]_{t=a+r} \\ &= D_m\Delta y(a+r,a,x) - d_m y(a+r,a,x) \\ &= D_m\Delta v(r,a,x) - d_m v(r,a,x), \\ v(r,0,x) &= \frac{b\beta(x)}{H(x)}S_m(r,x)I_h(r,x). \end{cases}$$

Regarding r as a parameter and integrating the last equation, we obtain

$$v(r,a,x) = e^{-d_m a}\int_\Omega \Gamma(D_m a,x,y)\frac{b\beta(y)}{H(y)}S_m(r,y)I_h(r,y)dy,$$

where Γ is the Green function associated with Δ and the Neumann boundary condition. Since $y(t,\tau,x) = v(t-\tau,\tau,x)$, $\forall t \geq \tau$, we can derive the formula for $y(t,\tau,x)$:

$$y(t,\tau,x) = e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau,x,y)\frac{b\beta(y)}{H(y)}S_m(t-\tau,y)I_h(t-\tau,y)dy,\ \forall t \geq \tau.$$

It then follows that

$$\begin{aligned} \frac{\partial E_m(t,x)}{\partial t} &= D_m\Delta E_m(t,x) - d_m E_m(t,x) + \frac{b\beta(x)}{H(x)}S_m(t,x)I_h(t,x) - \\ &\quad e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau,x,y)\frac{b\beta(y)}{H(y)}S_m(t-\tau,y)I_h(t-\tau,y)dy,\ t \geq \tau, \end{aligned} \tag{5.4}$$

and

$$\begin{aligned} \frac{\partial I_m(t,x)}{\partial t} &= D_m\Delta I_m(t,x) - d_m I_m(t,x) + \\ &\quad e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau,x,y)\frac{b\beta(y)}{H(y)}S_m(t-\tau,y)I_h(t-\tau,y)dy,\ t \geq \tau. \end{aligned} \tag{5.5}$$

Consequently, we have a full model (5.1), (5.2), (5.4) and (5.5) subject to the Neumann boundary condition. Since system (5.1), (5.2), (5.4) and (5.5) is an autonomous system, we may assume that the starting time is 0 and the initial data is in

$C([-\tau,0],\mathbb{R}^4_+)$. Note that E_m can be determined if I_h, S_m, and I_m are known. It then suffices to study the following nonlocal and time-delayed reaction-diffusion system

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} = D_h\Delta u_1(t,x) + \frac{c\beta(x)}{H(x)}(H(x)-u_1(t,x))u_3(t,x) - (d_h+\rho)u_1(t,x), \\ \frac{\partial u_2(t,x)}{\partial t} = D_m\Delta u_2(t,x) + \mu(x) - \frac{b\beta(x)}{H(x)}u_2(t,x)u_1(t,x) - d_m u_2(t,x), \\ \frac{\partial u_3(t,x)}{\partial t} = D_m\Delta u_3(t,x) - d_m u_3(t,x) \\ \qquad +e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta(y)}{H(y)}u_2(t-\tau,y)u_1(t-\tau,y)dy, \\ \frac{\partial u_i}{\partial n} = 0,\ \forall x\in\partial\Omega,\ t>0,\ i=1,2,3, \end{cases} \tag{5.6}$$

where $u(t,x) = (u_1(t,x),u_2(t,x),u_3(t,x))^T = (I_h(t,x),S_m(t,x),I_m(t,x))^T$.

5.3 Threshold dynamics

In this section, we define the basic reproduction ratio $\mathcal{R}_0$ and show that $\mathcal{R}_0$ is a threshold index to determine the disease invasion. We start with some basic properties for system (5.6).

Let $\mathbb{X} := C(\bar{\Omega},\mathbb{R}^3)$ be the Banach space with the supremum norm $\|\cdot\|_{\mathbb{X}}$. For $\tau\geq 0$, define $C = C([-\tau,0],\mathbb{X})$ with the norm $\|\phi\| = \max_{\theta\in[-\tau,0]}\|\phi(\theta)\|_{\mathbb{X}}$. Then, C is a Banach space. Define $\mathbb{X}^+ := C(\bar{\Omega},\mathbb{R}^3_+)$ and $C^+ := C([-\tau,0],\mathbb{X}^+)$, then both $(\mathbb{X},\mathbb{X}^+)$ and (C,C^+) are strongly ordered spaces. Given a function $u:[-\tau,\sigma)\to\mathbb{X}$ for $\sigma>0$, define $u_t\in C$ by $u_t(\theta)=u(t+\theta)$, $\theta\in[-\tau,0]$. Let $\mathbb{X}_H$ and C_H be the subsets in $\mathbb{X}$ and C defined by

$$\mathbb{X}_H := \{\phi = (\phi_1,\phi_2,\phi_3)^T\in\mathbb{X}^+ : 0\leq\phi_1(x)\leq H(x),\ \forall x\in\bar{\Omega}\}$$

and

$$C_H := C([-\tau,0],\mathbb{X}_H),$$

respectively.

Let $\mathbb{Y} := C(\bar{\Omega}, \mathbb{R})$ and $\mathbb{Y}^+ := C(\bar{\Omega}, \mathbb{R}_+)$. Suppose that $T_1(t)$, $T_2(t)$: $\mathbb{Y} \to \mathbb{Y}$, $t \geq 0$, are the strongly continuous semigroups associated with $D_h\Delta - (d_h + \rho)$ and $D_m\Delta - d_m$ subject to the Neumann boundary condition, respectively. It then follows that for each $t > 0$, $T_i(t) : \mathbb{Y} \to \mathbb{Y}$, $i = 1, 2$, is compact and strongly positive (see, e.g., [80, Section 7.1 and Corollary 7.2.3]). Clearly, for any $\varphi \in \mathbb{Y}$, $t \geq 0$,

$$T_1(t)\varphi(x) = e^{-(d_h+\rho)t} \int_\Omega \Gamma(D_h t, x, y)\varphi(y)dy,$$

and

$$T_2(t)\varphi(x) = e^{-d_m t} \int_\Omega \Gamma(D_m t, x, y)\varphi(y)dy.$$

Moreover, $T(t) = (T_1(t), T_2(t), T_2(t))$: $\mathbb{X} \to \mathbb{X}$, $t \geq 0$, is a strongly continuous semigroup. Let $A_i : D(A_i) \to \mathbb{Y}$ be the generator of T_i, $i = 1, 2$. Then $T(t) : \mathbb{X} \to \mathbb{X}$ is a semigroup generated by the operator $A = (A_1, A_2, A_2)$ defined on $D(A) = D(A_1) \times D(A_2) \times D(A_2)$.

Define $F = (F_1, F_2, F_3)$: $C_H \to \mathbb{X}$ by

$$\begin{aligned} F_1(\phi)(x) &= \frac{c\beta(x)}{H(x)}(H(x) - \phi_1(0,x))\phi_3(0,x), \\ F_2(\phi)(x) &= \mu(x) - \frac{b\beta(x)}{H(x)}\phi_2(0,x)\phi_1(0,x), \\ F_3(\phi)(x) &= e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta(y)}{H(y)}\phi_2(-\tau,y)\phi_1(-\tau,y)dy, \end{aligned} \tag{5.7}$$

$\forall x \in \bar{\Omega}$, $\phi = (\phi_1, \phi_2, \phi_3)^T \in C_H$. Then system (5.6) can be rewritten as the following abstract functional differential equation:

$$\begin{cases} \frac{du}{dt} = Au + F(u_t), & t > 0, \\ u_0 = \phi \in C_H. \end{cases} \tag{5.8}$$

Let $\bar{\beta} = \max_{x \in \bar{\Omega}} \beta(x)$ and $\tilde{H} = \min_{x \in \bar{\Omega}} H(x)$. For any $\phi \in C_H$ and $k \geq 0$, we then have

$$\begin{aligned} &\phi(0,x) + kF(\phi)(x) \\ = &\begin{pmatrix} \phi_1(0,x) + k\frac{c\beta(x)}{H(x)}(H(x) - \phi_1(0,x))\phi_3(0,x) \\ \phi_2(0,x) + k(\mu - \frac{b\beta(x)}{H(x)}\phi_2(0,x)\phi_1(0,x)) \\ \phi_3(0,x) + k(e^{-d_m\tau} \int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta(y)}{H(y)}\phi_2(-\tau,y)\phi_1(-\tau,y)dy) \end{pmatrix} \\ \geq &\begin{pmatrix} \phi_1(0,x)[1 - k\frac{c\bar{\beta}}{\tilde{H}}\phi_3(0,x)] \\ \phi_2(0,x)[1 - k\frac{b\bar{\beta}}{\tilde{H}}\phi_1(0,x)] \\ \phi_3(0,x) \end{pmatrix}, \end{aligned}$$

and

$$H(x) - (\phi_1(0,x) + kF_1(\phi)(x)) = (H(x) - \phi_1(0,x))\left[1 - k\frac{c\beta(x)}{H(x)}\phi_3(0,x)\right].$$

This implies that

$$\lim_{k \to 0^+} \frac{1}{k} dist(\phi(0) + kF(\phi), \mathbb{X}_H) = 0, \ \forall \phi \in C_H.$$

It then follows from [65, Corollary 4] (see also [100, Corollary 8.1.3]) that for each $\phi \in C_H$, there exists a unique non-continuable mild solution $u(t,\phi)$ on $(0, \sigma_\phi)$ with $u_0 = \phi$. Moreover, $u(t,\phi) \in \mathbb{X}_H$ for all $t \in (0, \sigma_\phi)$ and $u(t,\phi)$ is a classical solution of (5.6) for $t > \tau$.

For the scalar reaction-diffusion equation

$$\begin{aligned} &\frac{\partial w(t,x)}{\partial t} = D\Delta w(t,x) + g(x) - dw(t,x), \ t > 0, \ x \in \Omega, \\ &\frac{\partial w}{\partial n} = 0, \ x \in \partial\Omega, \end{aligned} \tag{5.9}$$

where $D > 0$, $d > 0$, and $g(x)$ is a continuous and positive function on $\bar{\Omega}$, we have the following observation.

Lemma 5.3.1 *Equation (5.9) admits a unique positive steady state w^* which is globally attractive in $\mathbb{Y}$. Moreover, if $g(x) \equiv g$, $\forall x \in \bar{\Omega}$, then $w^* = \frac{g}{d}$.*

Proof. Denote $\tilde{g} = \min_{x\in\bar{\Omega}} g(x)$ and $\bar{g} = \max_{x\in\bar{\Omega}} g(x)$. It is easy to see that for any $\psi \in C(\bar{\Omega}, \mathbb{R}_+)$, (5.9) has a unique solution $w(t,\psi)$ on $[0,\infty)$ with $w(0,\psi) = \psi$. Let $P(t)$ be the solution semiflow associated with (5.9), that is, $P(t)\psi = w(t,\psi)$. By the standard comparison arguments, it then follows that for any $\psi \in \mathbb{Y}$, the omega limit set $\omega(\psi)$ satisfies

$$\omega(\psi) \subset \left\{\varphi : \frac{\tilde{g}}{d} \le \varphi \le \frac{\bar{g}}{d}\right\}.$$

Again, by the comparison principle, we have $P(t)\varphi \gg P(t)\psi$, $\forall t > 0$, whenever $\varphi > \psi$. Note that $f(x,w) := g(x) - dw$ is strictly subhomogeneous in the sense that $f(x,\alpha w) > \alpha f(x,w)$ for any $\alpha \in (0,1)$ and $w \gg 0$. By a similar argument as in [29, Theorem 2.2], we see that $P(t)\psi$ is strictly subhomogeneous, i.e., $P(t)\alpha\psi > \alpha P(t)\psi$ for any $\alpha \in (0,1)$ and $\psi \gg 0$. It then follows from Theorem 1.1.2 that $P(t)$ has a positive equilibrium $w^*(x)$ such that $\omega(\psi) = w^* \in \mathbb{Y}$, $\forall \psi \in \mathbb{Y}$. In particular, if $g(x) \equiv g$, $\forall x \in \bar{\Omega}$, then $w^* = \frac{g}{d}$. ∎

The following result shows that solutions of system (5.6) exist globally on $[0,\infty)$ and converge to a compact attractor in C_H.

Theorem 5.3.1 *For any $\phi \in C_H$, system (5.6) has a unique solution $u(t,\phi)$ on $[0,\infty)$, and the solution semiflow $\Phi(t) = u_t(\cdot) : C_H \to C_H$, $t \ge 0$, has a global compact attractor.*

Proof. Let $\bar{\mu} = \max_{x\in\bar{\Omega}} \mu(x)$. By Lemma 5.3.1, $\frac{\bar{\mu}}{d_m}$ is globally attractive in $\mathbb{Y}$ for the scalar parabolic equation

$$\begin{cases} \frac{\partial w(t,x)}{\partial t} = D_m \Delta w(t,x) + \bar{\mu} - d_m w(t,x), \ x \in \Omega, \ t > 0, \\ \frac{\partial w}{\partial n} = 0, \ x \in \partial\Omega, \ t > 0. \end{cases} \tag{5.10}$$

Since the second equation of system (5.6) is dominated by equation (5.10), the standard parabolic comparison theorem (see, e.g., [80, Theorem 7.3.4]) implies that $u_2(t, \phi)$ is bounded on $[0, \sigma_\phi)$. Thus, there exists a positive number Q such that the third equation of system (5.6) is dominated by the equation

$$\begin{cases} \frac{\partial w(t,x)}{\partial t} = D_m \Delta w(t,x) - d_m w(t,x) + Q, \ x \in \Omega, \ t > 0, \\ \frac{\partial w}{\partial n} = 0, \ x \in \partial\Omega, \ t > 0. \end{cases} \tag{5.11}$$

Again, from Lemma 5.3.1 and the comparison principle, $u_3(t, \phi)$ is bounded on $[0, \sigma_\phi)$. It then follows that $u(t, \phi) = (u_1(t, \phi), u_2(t, \phi), u_3(t, \phi))^T$ is bounded on $[0, \sigma_\phi)$, and hence $\sigma_\phi = +\infty$ for each $\phi \in C_H$. Therefore, system (5.6) defines a semiflow $\Phi(t)$: $C_H \to C_H$ by

$$(\Phi(t)\phi)(\theta, x) = u(t + \theta, x, \phi), \ \forall \theta \in [-\tau, 0], \ x \in \bar{\Omega}.$$

For any fixed $\phi \in C_H$, we have some $t_1(\phi)$ such that $u_2(t, \phi) \leq 2\frac{\bar{\mu}}{d_m}$ when $t > t_1$, and

$$\begin{cases} \frac{\partial u_3(t,x)}{\partial t} \leq D_m \Delta u_3(t,x) - d_m u_3(t,x) + 2e^{-d_m \tau} \frac{\bar{\mu}}{d_m} b\bar{\beta}, \ x \in \Omega, \ t > t_1, \\ \frac{\partial u_3}{\partial n} = 0, \ x \in \partial\Omega, \ t > t_1. \end{cases}$$

It then follows from Lemma 5.3.1 that there is a $t_2(\phi) > t_1$ such that $u_3(t, \phi) \leq 4e^{-d_m \tau} \frac{\bar{\mu}}{d_m^2} b\bar{\beta}$, $\forall t > t_2$. Therefore, the solution semiflow $\Phi(t)$: $C_H \to C_H$ is point dissipative. Moreover, $\Phi(t)$: $C_H \to C_H$ is compact for each $t > \tau$ by [100, Theorem 2.1.8]. Thus, [37, Theorem 3.4.8] implies that $\Phi(t)$: $C_H \to C_H$, $t \geq 0$, has a global compact attractor. ■

The following result is a consequence of the comparison principle for scalar parabolic equations.

Lemma 5.3.2 *Let $u(t,x,\phi)$ be the solution of system (5.6) with $u_0 = \phi \in C_H$. If there exists some $t_0 \geq 0$ such that $u_i(t_0,\cdot,\phi) \not\equiv 0$, for some $i \in \{1,3\}$, then $u_i(t,x,\phi) > 0$, $\forall t > t_0$, $x \in \bar{\Omega}$. Moreover, for any $\phi \in C_H$, we have $u_2(t,x,\phi) > 0$, $\forall t > 0$, $x \in \bar{\Omega}$ and $\liminf\limits_{t\to\infty} u_2(t,x) \geq \frac{\tilde{\mu}}{d_m + b\bar{\beta}}$ uniformly for $x \in \bar{\Omega}$, where $\bar{\beta} = \max\limits_{x\in\bar{\Omega}} \beta(x)$ and $\tilde{\mu} = \min\limits_{x\in\bar{\Omega}} \mu(x)$.*

Proof. It is easy to see that $u_1(t,x,\phi)$ and $u_3(t,x,\phi)$ satisfy

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} \geq D_m \Delta u_1(t,x) - (d_h + \rho) u_1(t,x), \\ \frac{\partial u_3(t,x)}{\partial t} \geq D_m \Delta u_3(t,x) - d_m u_3(t,x), \\ \frac{\partial u_1}{\partial n} = \frac{\partial u_3}{\partial n} = 0, \ x \in \partial\Omega. \end{cases}$$

If $u_i(t_0,\cdot,\phi) \not\equiv 0$ for some $t_0 \geq 0$, $i \in \{1,3\}$, it then follows from the comparison principle that $u_i(t,x,\phi) > 0$ for all $t > t_0$, $x \in \bar{\Omega}$.

Let $v(t,x,\phi)$ be the solution of

$$\begin{cases} \frac{\partial v(t,x)}{\partial t} = D_m \Delta v(t,x) + \tilde{\mu} - (b\bar{\beta} + d_m) v(t,x), \\ \frac{\partial v}{\partial n} = 0, \ x \in \partial\Omega, \\ v(0,x) = \phi(0,x). \end{cases}$$

Then we have $u_2(t,x,\phi) \geq v(t,x,\phi) > 0$, $\forall t > 0$, $x \in \bar{\Omega}$. Furthermore, by Lemma 5.3.1 and the comparison principle, $\liminf_{t\to\infty} u_2(t,x,\phi) \geq \frac{\tilde{\mu}}{b\bar{\beta} + d_m}$ uniformly for $x \in \bar{\Omega}$.

■

In order to define the basic reproduction ratio, we should first find the disease-free equilibrium (infection-free steady state). By letting the densities of the diseased compartments (u_1 and u_3) be zero, we get the following equation for the density of susceptible mosquitoes,

$$\begin{cases} \frac{\partial w(t,x)}{\partial t} = D_m \Delta w(t,x) + \mu(x) - d_m w(t,x), \ t > 0, \ x \in \Omega, \\ \frac{\partial w}{\partial n} = 0, \quad x \in \partial\Omega. \end{cases} \tag{5.12}$$

By Lemma 5.3.1, it is easy to see that equation (5.12) has a positive steady state m^*, which is globally asymptotically stable. Linearizing system (5.6) at the disease-free equilibrium $(0, m^*, 0)^T$, we get the following time-delayed nonlocal and cooperative system for the infectious compartments:

$$\left\{\begin{array}{rcl} \frac{\partial w_1}{\partial t} & = & D_h \Delta w_1(t,x) + c\frac{\beta(x)}{H(x)} h(x) w_2(t,x) - (d_h + \rho) w_1(t,x), \\ \frac{\partial w_2}{\partial t} & = & D_m \Delta w_2(t,x) - d_m w_2(t,x) \\ & & + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} m(y) w_1(t-\tau, y) dy, \\ \frac{\partial w_1}{\partial n} & = & \frac{\partial w_2}{\partial n} = 0, \ \forall x \in \partial\Omega, \end{array}\right. \tag{5.13}$$

with $h(x) = H(x)$ and $m(x) = m^*(x)$.

Before defining the basic reproduction ratio, we need to study the following linear nonlocal and cooperative system

$$\left\{\begin{array}{rcl} \frac{\partial w_1}{\partial t} & = & D_h \Delta w_1(t,x) + \frac{c\beta(x)}{H(x)} h(x) w_2(t,x) - (d_h + \rho) w_1(t,x), \\ \frac{\partial w_2}{\partial t} & = & D_m \Delta w_2(t,x) - d_m w_2(t,x) \\ & & + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} m(y) w_1(t, y) dy, \\ \frac{\partial w_1}{\partial n} & = & \frac{\partial w_2}{\partial n} = 0, \ \forall x \in \partial\Omega, \end{array}\right. \tag{5.14}$$

with $h(x) > 0$, $m(x) > 0$, $\forall x \in \bar{\Omega}$.

Substituting $w_1(t,x) = e^{\lambda t}\psi_1(x)$ and $w_2(t,x) = e^{\lambda t}\psi_2(x)$ into (5.14), we obtain the following nonlocal eigenvalue problem

$$\left\{\begin{array}{rcl} \lambda\psi_1(x) & = & D_h \Delta \psi_1(x) + \frac{c\beta(x)}{H(x)} h(x) \psi_2(x) - (d_h + \rho) \psi_1(x), \ x \in \Omega, \\ \lambda\psi_2(x) & = & D_m \Delta \psi_2(x) - d_m \psi_2(x) \\ & & + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} m(y) \psi_1(y) dy, \ x \in \Omega, \\ \frac{\partial \psi_1}{\partial n} & = & \frac{\partial \psi_2}{\partial n} = 0, \ x \in \partial\Omega. \end{array}\right. \tag{5.15}$$

By a similar argument as in [80, Theorem 7.6.1], it follows that (5.15) has a principal eigenvalue $\lambda(h, m)$ with a positive eigenfunction.

Define $\mathbb{E} := C([-\tau, 0], \mathbb{Y}) \times \mathbb{Y}$ and $\mathbb{E}^+ := C([-\tau, 0], \mathbb{Y}^+) \times \mathbb{Y}^+$. For any $\psi \in \mathbb{E}^+ \setminus \{0\}$, let $w(t, \psi)$, $t \geq 0$, be the solution of the system (5.13). We claim that $w_i(t, \psi)(x) > 0$ for all $x \in \bar{\Omega}$ and $t > \tau$, $i = 1, 2$. Indeed, if $\psi_1(0, \cdot) \not\equiv 0$ or $\psi_2 \not\equiv 0$, then the parabolic maximum principle implies that $w_1(t, \psi)(x) > 0$ and $w_2(t, \psi)(x) > 0$ for all $x \in \partial\bar{\Omega}$, $t > \tau$. If there is a $\theta_0 \in (0, \tau)$ such that $\psi_1(-\theta_0, \cdot) \not\equiv 0$, then we can show that $w_2(\tau - \theta_0, \psi) \not\equiv 0$ as follows. Suppose, by contradiction, that $w_2(\tau - \theta_0, \psi) \equiv 0$, then

$$\frac{\partial w_2(\tau-\theta_0,x)}{\partial t} = e^{-d_m\tau} \int_\Omega \Gamma(D_m\tau, x, y) \frac{b\beta(y)}{H(y)} m(y) \psi_1(-\theta_0, y) dy > 0, \ \forall x \in \Omega.$$

Since $w_2(t, \psi) \geq 0$, $t \geq 0$, and $w_2(\tau - \theta_0, \psi)(x) = 0$, $\forall x \in \bar{\Omega}$, then $\frac{\partial w_2(\tau-\theta_0,x)}{\partial t} \leq 0$, which is a contradiction. Thus, we have $w_2(t, \psi)(x) > 0$, $\forall t > \tau - \theta_0$, $x \in \bar{\Omega}$. It then follows that $w_1(t, \psi)(x) > 0$, $\forall t > \tau - \theta_0$, $x \in \bar{\Omega}$.

By similar arguments as in [90, Theorem 2.2], we have the following result for the nonlocal eigenvalue problem corresponding to (5.13):

$$\begin{cases} \lambda\psi_1(x) &= D_h\Delta\psi_1(x) + \frac{c\beta(x)}{H(x)} h(x)\psi_2(x) - (d_h + \rho)\psi_1(x), \ x \in \Omega, \\ \lambda\psi_2(x) &= D_m\Delta\psi_2(x) - d_m\psi_2(x) \\ & \quad + e^{-d_m\tau} e^{-\lambda\tau} \int_\Omega \Gamma(D_m\tau, x, y) \frac{b\beta(y)}{H(y)} m(y)\psi_1(y) dy, \ x \in \Omega, \\ \frac{\partial\psi_1}{\partial n} &= \frac{\partial\psi_2}{\partial n} = 0, \quad x \in \partial\Omega. \end{cases} \tag{5.16}$$

Lemma 5.3.3 *There exists a principal eigenvalue $\bar{\lambda}(h, m, \tau)$ of (5.16) associated with a strongly positive eigenvector, and for any $\tau \geq 0$, $\bar{\lambda}(h, m, \tau)$ has the same sign as $\lambda(h, m)$.*

Next, we use the same idea as in [96] to define the basic reproduction ratio for system (5.6). Assume that both human and mosquito populations are near the disease free equilibrium $(0, m^*, 0)^T$. Let $(\psi_1(x), \psi_2(x))^T$ be the spatial distribution of initial infective humans and mosquitoes, and assume that the temporal distribution of this initial data is homogeneous. From system (5.14), with $h(x) = H(x)$, $m(x) = m^*(x)$, we then see that $S(t)\psi := (T_1(t)\psi_1, T_2(t)\psi_2)^T$ represents the remaining distribution of infective humans and mosquitoes at time $t > 0$. Let V be the positive linear operator on $\mathbb{Y} \times \mathbb{Y}$ defined by

$$V(\psi)(x) = (V_1(\psi)(x), V_2(\psi)(x)),\ \forall \psi \in \mathbb{Y} \times \mathbb{Y},\ x \in \bar{\Omega},$$

where

$$V_1(\psi)(x) = c\beta(x)\psi_2(x),$$

and

$$V_2(\psi)(x) = e^{-d_m\tau} \int_\Omega \Gamma(D_m\tau, x, y)m^*(y)\frac{b\beta(y)}{H(y)}\psi_1(y)dy.$$

Then, $V(S(t)\psi)$ is the distribution of newly infected humans and mosquitoes at time t. It follows that

$$L(\psi) := \int_0^\infty V(S(t)\psi)dt = V\left(\int_0^\infty S(t)\psi dt\right)$$

represents the distribution of the total infective humans and mosquitoes produced during the infection period, and hence, L is the next infection operator. We define the spectral radius of L as the basic reproduction ratio, that is,

$$\mathcal{R}_0 := r(L)$$

for model (5.6).

By the general results in [89] and the same arguments as in [96, Lemma 2.2], we have the following observation.

Lemma 5.3.4 $\mathcal{R}_0 - 1$ *has the same sign as* $\lambda(H, m^*)$.

By this lemma, combined with Lemma 5.3.3, we see that $\mathcal{R}_0$ is a threshold parameter for the stability of the the zero solution for system (5.13) with $h(x) = H(x)$ and $m(x) = m^*(x)$.

Now we are in a position to prove the main result of this section, which indicates that $\mathcal{R}_0$ is also a threshold index for disease persistence.

Theorem 5.3.2 *Let $u(t, x, \phi)$ be the solution of (5.6) with $u_0 = \phi \in C_H$. Then the following two statements are valid:*

(i) *If $\mathcal{R}_0 < 1$, then the disease free equilibrium $(0, m^*, 0)^T$ is globally attractive.*

(ii) *If $\mathcal{R}_0 > 1$, then system (5.6) admits at least one positive steady state $u^*(x)$, and there exists an $\eta > 0$ such that for any $\phi \in C_H$ with $\phi_i(0, \cdot) \not\equiv 0$ for $i = 1, 3$, we have*

$$\liminf_{t\to\infty} u_i(t, x) \geq \eta, \ \forall i = 1, 2, 3,$$

uniformly for all $x \in \bar{\Omega}$.

Proof. (i) In the case where $\mathcal{R}_0 < 1$, we have $\lambda(H, m^*) < 0$. Since

$$\lim_{\epsilon\to 0} \lambda(H, m^* + \epsilon) = \lambda(H, m^*) < 0,$$

there is an $\epsilon_0 > 0$ such that $\lambda(H, m^* + \epsilon_0) < 0$. For fixed $\epsilon_0 > 0$, by Lemma 5.3.1, there exists $t_0 = t_0(\phi)$ such that $u_2(t, x) \leq m^*(x) + \epsilon_0$, $\forall t \geq t_0$, $x \in \bar{\Omega}$. Therefore, for all $t \geq t_0$, we have

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} \leq & D_h \Delta u_1(t, x) + c\beta(x) u_3(t, x) - (d_h + \rho) u_1(t, x), \\ \frac{\partial u_3(t,x)}{\partial t} \leq & D_m \Delta u_3(t, x) - d_m u_3(t, x) \\ & + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} (m^*(y) + \epsilon_0) u_1(t - \tau, y) dy. \end{cases}$$

By Lemma 5.3.3, $\bar{\lambda}(H, m^* + \epsilon_0, \tau) < 0$ and there is a strongly positive eigenfunction ψ_0 corresponding to $\bar{\lambda}(H, m^* + \epsilon_0, \tau)$. It then follows that the linear system

$$\begin{cases} \frac{\partial v_1(t,x)}{\partial t} &= D_h \Delta v_1 + c\beta(x) v_2 - (d_h + \rho) v_1, \ t > 0, \ x \in \Omega, \\ \frac{\partial v_2(t,x)}{\partial t} &= D_m \Delta v_2 + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} (m^*(y) + \epsilon_0) v_1(t - \tau, y) dy \\ & \quad -d_m v_2, \ t > 0, \ x \in \Omega, \\ \frac{\partial v_1}{\partial n} &= \frac{\partial v_2}{\partial n} = 0, \ x \in \partial\Omega, \end{cases}$$

admits a solution $v(t, x) = e^{\bar{\lambda}(H, m^* + \epsilon_0, \tau)t} \psi_0(x)$. Since for any given $\phi \in C_H$, there exists some $\alpha > 0$ such that $(u_1(t, \cdot, \phi), u_3(t, \cdot, \phi))^T \leq \alpha v(t, \cdot)$, $\forall t \in [t_0 - \tau, t_0]$. By the comparison principle, it follows that

$$(u_1(t, x, \phi), u_3(t, x, \phi))^T \leq \alpha e^{\bar{\lambda}(H, m^* + \epsilon_0, \tau)t} \psi_0(x), \ \forall t \geq t_0.$$

Thus, $\lim_{t \to \infty} (u_1(t, x, \phi), u_3(t, x, \phi))^T = 0$ uniformly for $x \in \bar{\Omega}$. Then, the equation for u_2 is asymptotic to the following reaction-diffusion equation

$$\begin{cases} \frac{\partial w(t,x)}{\partial t} = D_m \Delta w(t, x) + \mu(x) - d_m w(t, x), \\ \frac{w(t,x)}{\partial n} = 0. \end{cases}$$

By the theory for asymptotically autonomous semiflows (see [88, Corollary 4.3]), we have

$$\lim_{t \to \infty} u_2(t, x, \phi) = m^*(x)$$

uniformly for $x \in \bar{\Omega}$.

(ii) In the case where $\mathcal{R}_0 > 1$, we have $\lambda(H, m^*) > 0$. It then follows from Lemma 5.3.3 that $\bar{\lambda}(H, m^*, \tau) > 0$. Let

$$\mathbb{W}_0 = \{\phi \in C_H : \phi_1(0, \cdot) \not\equiv 0 \text{ and } \phi_3(0, \cdot) \not\equiv 0\},$$

and

$$\partial\mathbb{W}_0 := C_H \setminus \mathbb{W}_0 = \{\phi \in C_H : \phi_1(0, \cdot) \equiv 0 \text{ or } \phi_3(0, \cdot) \equiv 0\}.$$

Note that for any $\phi \in \mathbb{W}_0$, Lemma 5.3.2 implies that $u_i(t, \cdot, \phi) > 0$, $i = 1, 3$, $\forall x \in \bar{\Omega}$, $t > 0$, that is, $\Phi(t)\mathbb{W}_0 \subset \mathbb{W}_0$. Define

$$M_\partial := \{\phi \in \partial\mathbb{W}_0 : \Phi(t)\phi \in \partial\mathbb{W}_0,\ t \geq 0\}.$$

Let $\omega(\phi)$ be the omega limit set of the orbit $\gamma^+(\phi) := \{\Phi(t)\phi : \forall t \geq 0\}$, and set $M = (0, m^*, 0)^T$. For any given $\psi \in M_\partial$, we have $\Phi(t)\psi \in \partial\mathbb{W}_0$, $\forall t \geq 0$. It then follows that for each $t \geq 0$, either $u_1(t, \cdot, \psi) \equiv 0$ or $u_3(t, \cdot, \psi) \equiv 0$. In the case where $u_1(t, \cdot, \psi) \equiv 0$ for all $t \geq 0$, we see from Lemma 5.3.1 that $\lim_{t \to \infty} u_2(t, x, \psi) = m^*(x)$ uniformly for $x \in \bar{\Omega}$. In view of the u_3 equation in (5.6), we see that $\lim_{t \to \infty} u_3(t, x, \psi) = 0$ uniformly for $x \in \bar{\Omega}$. In the case where $u_1(t_0, \cdot, \psi) \not\equiv 0$ for some $t_0 \geq 0$, Lemma 5.3.2 implies that $u_1(t, x, \psi) > 0$, $\forall t > t_0$, $x \in \bar{\Omega}$. Thus, we have $u_3(t, \cdot, \psi) \equiv 0$, $\forall t \geq t_0$. In view of the u_1 equation in (5.6), we see that $\lim_{t \to \infty} u_1(t, x, \psi) = 0$ uniformly for $x \in \bar{\Omega}$. By the u_2 equation and the theory of asymptotically autonomous semiflows (see [88, Corollary 4.3]), it then follows that $\lim_{t \to \infty} u_2(t, x, \psi) = m^*(x)$ uniformly for $x \in \bar{\Omega}$. Thus, we have $\omega(\psi) = \{M\}$, $\forall \psi \in M_\partial$.

Since $\bar{\lambda}(H, m^*, \tau) > 0$, there exists a sufficiently small positive number δ_0 such that $\bar{\lambda}(H - \delta_0, m^* - \delta_0, \tau) > 0$. We now prove the following claim.

Claim. M is a uniform weak repeller for $\mathbb{W}_0$ in the sense that

$$\limsup_{t \to \infty} \|\Phi(t)(\phi) - M\| \geq \delta_0 \text{ for all } \phi \in \mathbb{W}_0.$$

Suppose, by contradiction, that $\limsup_{t \to \infty} \|\Phi(t)(\phi_0) - M\| < \delta_0$ for some $\phi_0 \in \mathbb{W}_0$. Then, there exists $t_1 > 0$ such that $u_1(t, x, \phi_0) < \delta_0$ and $u_2(t, x, \phi_0) > m^*(x) - \delta_0$, $\forall t \geq t_1$, $x \in \bar{\Omega}$. Hence, $u(t, x, \phi_0)$ satisfies

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} \geq D_h \Delta u_1(t, x) + \frac{c\beta(x)}{H(x)}(H(x) - \delta_0)u_3(t, x) - (d_h + \rho)u_1(t, x), \\ \frac{\partial u_3(t,x)}{\partial t} \geq D_m \Delta u_3(t, x) - d_m u_3(t, x) \\ \qquad + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)}(m^*(y) - \delta_0)u_1(t - \tau, y)dy, \end{cases} \tag{5.17}$$

for all $t > t_1$, $x \in \Omega$. Let φ_0 be the positive eigenfunction associated with $\bar{\lambda}(H - \delta_0, m^* - \delta_0, \tau)$. Then the linear system

$$\begin{cases} \frac{\partial v_1(t,x)}{\partial t} &= D_h \Delta v_1 + \frac{c\beta(x)}{H(x)}(H(x) - \delta_0)v_2 - (d_h + \rho)v_1, \\ \frac{\partial v_2(t,x)}{\partial t} &= D_m \Delta v_2 - d_m v_2 + \\ & \quad e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)}(m^*(y) - \delta_0) v_1(t-\tau, y) dy, \\ \frac{\partial v_1}{\partial n} &= \frac{\partial v_2}{\partial n} = 0, \ x \in \partial\Omega. \end{cases}$$

admits a solution $v(t,x) = e^{\bar{\lambda}(H-\delta_0, m^*-\delta_0, \tau)t}\varphi_0(x)$. Since $u(t,x,\phi_0) \gg 0$ for all $t > 0$ and $x \in \bar{\Omega}$, there exists $\xi > 0$ such that $(u_1(t_1,x,\phi_0), u_3(t_1,x,\phi_0))^T \geq \xi v(t,x)$, $\forall t \in [t_1 - \tau, t_1]$, $x \in \bar{\Omega}$. According to (5.17) and the comparison principle, we have

$$(u_1(t,x,\phi_0), u_3(t,x,\phi_0))^T \geq \xi e^{\bar{\lambda}(H-\delta_0, m^*-\delta_0, \tau)t}\varphi_0(x), \ \forall t > t_1, \ x \in \bar{\Omega}.$$

Since $\bar{\lambda}(H - \delta_0, m^* - \delta_0, \tau) > 0$, it follows that $u(t,x,\phi_0)$ is unbounded, a contradiction. This proves the claim.

Define a continuous function $p : C_H \to \mathbb{R}_+$ by

$$p(\phi) = \min\{\min_{x \in \bar{\Omega}} \phi_1(0,x), \min_{x \in \bar{\Omega}} \phi_3(0,x)\}, \ \forall \phi \in C_H.$$

Clearly, $p^{-1}(0,\infty) \subset \mathbb{W}_0$. By Lemma 5.3.2, it then follows that p has the property that if $p(\phi) = 0$ and $\phi \in \mathbb{W}_0$ or $p(\phi) > 0$, then $p(\Phi(t)\phi) > 0$ for all $t > 0$. Thus, p is a generalized distance function for the semiflow $\Phi(t) : C_H \to C_H$ (see Theorem 1.2.4 or [83]). Note that any forward orbit of $\Phi(t)$ in M_∂ converges to M. Moreover, the claim above implies that M is isolated in C_H and $W^s(M) \cap \mathbb{W}_0 = \emptyset$, where $W^s(M)$ is the stable set of M. Further, there is no cycle in M_∂ from M to M. It then follows from Theorem 1.2.2 (see also [83, Theorem 3]) that there exists an $\eta > 0$ such that $\min\{p(\psi) : \psi \in \omega(\phi)\} > \eta$ for any $\phi \in \mathbb{W}_0$. Hence,

$$\liminf_{t \to \infty} u_i(t,x) \geq \eta, \ i = 1, 3,$$

uniformly for all $x \in \bar{\Omega}$. Further, it follows from Lemma 5.3.2 that we can choose η small enough such that $\liminf\limits_{t\to\infty} u_2(t,x) \geq \eta$ uniformly for all $x \in \bar{\Omega}$. Thus, the uniform persistence stated in the conclusion (ii) holds. By Theorem 1.2.4, $\Phi(t) : \mathbb{W}_0 \to \mathbb{W}_0$ has a global attractor A_0. It then follows from Theorem 1.2.5 that $\Phi(t)$ has an equilibrium $u^* \in \mathbb{W}_0$. Clearly, Lemma 5.3.2 implies that $u^*(x)$ is a positive steady state of (5.6). ■

5.4 Global attractivity

In this section, we consider the reaction-diffusion system (5.6) in the case where $\beta(x)$, $H(x)$ and $\mu(x)$ are positive constants, that is,

$$\left\{\begin{aligned} \frac{\partial u_1(t,x)}{\partial t} &= D_h\Delta u_1(t,x) + \frac{c\beta}{H}(H - u_1(t,x))u_3(t,x) - (d_h+\rho)u_1(t,x),\\ \frac{\partial u_2(t,x)}{\partial t} &= D_m\Delta u_2(t,x) + \mu - \frac{b\beta}{H}u_2(t,x)u_1(t,x) - d_m u_2(t,x),\\ \frac{\partial u_3(t,x)}{\partial t} &= D_m\Delta u_3(t,x) - d_m u_3(t,x)\\ &\quad + e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)\frac{b\beta}{H}u_2(t-\tau, y)u_1(t-\tau, y)dy,\\ \frac{\partial u_i}{\partial n} &= 0,\ \forall t > 0,\ x \in \partial\Omega,\ i = 1,2,3. \end{aligned}\right. \tag{5.18}$$

By a similar argument as in [96, Theorem 2.1], we can show that the basic reproduction ratio $\mathcal{R}_0$ equals the spectral radius of the following 2×2 matrix

$$M_0 = \begin{pmatrix} 0 & c\beta\frac{1}{d_m} \\ e^{-d_m\tau}\frac{\mu}{d_m}\frac{b\beta}{H}\frac{1}{(d_h+\rho)} & 0 \end{pmatrix},$$

and hence, we have the following formula for $\mathcal{R}_0$ (see also Appendix in this chapter).

Lemma 5.4.1 *For system (5.18), the basic reproduction ratio*

$$\mathcal{R}_0 = \sqrt{c\beta\frac{1}{d_m} \times e^{-d_m\tau}\frac{\mu}{d_m}\frac{b\beta}{H}\frac{1}{(d_h+\rho)}}.$$

In addition to the threshold result in Theorem 5.3.2, we are able to prove the global attractivity of the positive steady state under some appropriate conditions.

Theorem 5.4.1 *Let $u(t,x,\phi)$ be the solution of (5.18) with $u_0 = \phi \in C_H$. Then the following three statements are valid:*

(i) If $\mathcal{R}_0 < 1$, then the disease free equilibrium $(0, \frac{\mu}{d_m}, 0)^T$ is globally attractive.

(ii) If $\mathcal{R}_0 > 1$, then system (5.18) admits at least one positive steady state u^*, and there exists an $\eta > 0$ such that for any $\phi \in C_H$ with $\phi_i(0,\cdot) \not\equiv 0$ for $i = 1,3$, we have $\liminf\limits_{t\to\infty} u_i(t,x) \geq \eta$, $\forall i = 1,2,3$, uniformly for $x \in \bar{\Omega}$.

(iii) If $\mathcal{R}_0 > \max\{1, \sqrt{\frac{b\beta}{d_m}}\}$, then the system (5.18) has a unique constant steady state $u^* = (u_1^*, u_2^*, u_3^*)^T$ such that for any $\phi \in C_H$ with $\phi_1(0,\cdot) \not\equiv 0$ and $\phi_3(0,\cdot) \not\equiv 0$, $\lim\limits_{t\to\infty} u(t,x,\phi) = u^*$ uniformly for $x \in \bar{\Omega}$.

Proof. It is easy to see from the proof of Theorem 5.3.1 that the set

$$A := \left\{ u \in C_H : u_2(\theta, x) \leq \frac{2\mu}{d_m},\ u_3(\theta,x) \leq 4e^{-d_m\tau}\frac{\mu}{d_m^2} b\beta, \forall\theta \in [-\tau, 0], x \in \bar{\Omega} \right\}$$

is positively invariant for the solution semiflow $\Phi(t)$ and every forward orbit enters into A eventually. Therefore, we will study the dynamics of (5.18) on A. Conclusions (i) and (ii) follow directly from Theorem 5.3.2. To prove (iii), we use a fluctuation method, which was developed in [90] for a nonlocal, delayed and diffusive predator-prey model (see also [107] for this method).

Since $\mathcal{R}_0 > 1$, there is a unique constant endemic equilibrium $u^* = (u_1^*, u_2^*, u_3^*)^T$ with

$$u_1^* = \frac{d_m^2 (d_h + \rho) H^2 (\mathcal{R}_0^2 - 1)}{b\beta(\mu c\beta e^{-d_m\tau} + (d_h + \rho) d_m H)}, \quad u_2^* = \frac{1}{b\beta + d_m}\left(\mu + \frac{H(d_h + \rho) d_m}{c\beta e^{-d_m\tau}}\right),$$

$$\text{and } u_3^* = \frac{e^{-d_m\tau}}{d_m}\frac{b\beta}{H}u_1^*u_2^*.$$

For notational simplicity, we denote $\gamma = \frac{c\beta}{H}$ and $\gamma' = \frac{b\beta}{H}$. We choose a sufficiently large number $k > 0$ such that the function $ku_1 - (d_h+\rho)u_1 + \gamma(H-u_1)u_3$ is monotone increasing in u_1 for all $(u_1, u_3)^T \in [0, H] \times [0, 4e^{-d_m\tau}\frac{\mu}{d_m^2}b\beta]$. It then follows that

$$\begin{aligned} u_1(t,x) = e^{-kt}\int_\Omega \Gamma(D_h t, x, y)u_1(0,y)dy + \int_0^t e^{-ks}\int_\Omega \Gamma(D_h s, x, y) \\ [ku_1(t-s,y) - (d_h+\rho)u_1(t-s,y) + \gamma(H - u_1(t-s,y))u_3(t-s,y)]dyds. \end{aligned}$$

Let

$$u_i^\infty(x) := \limsup_{t\to\infty} u_i(t,x),\ \ u_{i\infty}(x) := \liminf_{t\to\infty} u_i(t,x),\ \ i = 1,2,3.$$

By the uniform persistence of (5.18), there exists an $\eta > 0$ such that

$$u_i^\infty \ge u_{i\infty} \ge \eta,\ \forall x \in \bar{\Omega},\ i = 1,2,3.$$

Using Fatou's lemma, we then get

$$\begin{aligned} u_1^\infty(x) \ &\le \int_0^\infty e^{-ks}\int_\Omega \Gamma(D_h s, x, y)[ku_1^\infty(y) - \\ &\quad (d_h+\rho)u_1^\infty(y) + \gamma(H - u_1^\infty(y))u_3^\infty(y)]dyds. \end{aligned}$$

Let

$$\alpha_i^\infty := \sup_{x\in\bar{\Omega}} u_i^\infty(x) \text{ and } \alpha_{i\infty} := \inf_{x\in\bar{\Omega}} u_{i\infty}(x).$$

Clearly, $\alpha_i^\infty \ge \alpha_{i\infty} \ge \eta$ and $\alpha_{1\infty} \le \alpha_1^\infty \le H$. Since $\int_\Omega \Gamma(D_h s, x, y)dy = 1$ for all $x \in \Omega$, $s > 0$, we have

$$\begin{aligned} \alpha_1^\infty \ &\le \int_0^\infty e^{-ks}[k\alpha_1^\infty - (d_h+\rho)\alpha_1^\infty + \gamma(H-\alpha_1^\infty)\alpha_3^\infty]ds \\ &= \frac{1}{k}[k\alpha_1^\infty - (d_h+\rho)\alpha_1^\infty + \gamma(H-\alpha_1^\infty)\alpha_3^\infty], \end{aligned}$$

and hence,

$$0 \leq -(d_h + \rho)\alpha_1^\infty + \gamma(H - \alpha_1^\infty)\alpha_3^\infty. \qquad \boxed{5.19}$$

Similarly, we have the following inequality,

$$0 \geq -(d_h + \rho)\alpha_{1\infty} + \gamma(H - \alpha_{1\infty})\alpha_{3\infty}. \qquad \boxed{5.20}$$

Using the second and third equations of (5.18), with arguments similar to those above, we further obtain

$$\begin{aligned}
0 &\leq \mu - \gamma'\alpha_{1\infty}\alpha_2^\infty - d_m\alpha_2^\infty, && \boxed{5.21}\\
0 &\geq \mu - \gamma'\alpha_1^\infty\alpha_{2\infty} - d_m\alpha_{2\infty}, && \boxed{5.22}\\
0 &\leq e^{-d_m\tau}\gamma'\alpha_1^\infty\alpha_2^\infty - d_m\alpha_3^\infty, && \boxed{5.23}\\
0 &\geq e^{-d_m\tau}\gamma'\alpha_{1\infty}\alpha_{2\infty} - d_m\alpha_{3\infty}. && \boxed{5.24}
\end{aligned}$$

Inserting (5.23) into (5.19), we have

$$0 \leq -(d_h + \rho) + \gamma(H - \alpha_1^\infty)\frac{e^{-d_m\tau}}{d_m}\gamma'\alpha_2^\infty. \qquad \boxed{5.25}$$

Similarly, combining (5.24) with (5.20), we obtain

$$0 \geq -(d_h + \rho) + \gamma(H - \alpha_{1\infty})\frac{e^{-d_m\tau}}{d_m}\gamma'\alpha_{2\infty}. \qquad \boxed{5.26}$$

Inserting (5.21) and (5.22) into (5.25) and (5.26), respectively, we get

$$0 \leq -(d_h + \rho) + \gamma(H - \alpha_1^\infty)\frac{e^{-d_m\tau}}{d_m}\gamma'\frac{\mu}{\gamma'\alpha_{1\infty} + d_m}, \qquad \boxed{5.27}$$

and

$$0 \geq -(d_h + \rho) + \gamma(H - \alpha_{1\infty})\frac{e^{-d_m\tau}}{d_m}\gamma'\frac{\mu}{\gamma'\alpha_1^\infty + d_m}. \qquad \boxed{5.28}$$

It then follows that

$$(H - \alpha_1^\infty)\gamma\gamma' e^{-d_m\tau}\mu - (\gamma'\alpha_{1\infty} + d_m)(d_h + \rho)d_m \geq 0,$$

and

$$(H - \alpha_{1\infty})\gamma\gamma' e^{-d_m\tau}\mu - (\gamma'\alpha_1^\infty + d_m)(d_h + \rho)d_m \leq 0.$$

Thus, we have

$$\gamma\gamma' e^{-d_m\tau}\mu\alpha_1^\infty + \gamma'\alpha_{1\infty}(d_h + \rho)d_m \leq \gamma\gamma' e^{-d_m\tau}\mu\alpha_{1\infty} + \gamma'\alpha_1^\infty(d_h + \rho)d_m,$$

and hence,

$$(\gamma\gamma' e^{-d_m\tau}\mu - \gamma'(d_h + \rho)d_m)(\alpha_1^\infty - \alpha_{1\infty}) \leq 0.$$

Since $\mathcal{R}_0 > \sqrt{\frac{b3}{d_m}}$, that is, $\gamma\gamma' e^{-d_m\tau}\mu - \gamma'(d_h + \rho)d_m > 0$, we must have $\alpha_1^\infty = \alpha_{1\infty}$. Moreover, we see from (5.21-5.24) that $\alpha_2^\infty = \alpha_{2\infty}$ and $\alpha_3^\infty = \alpha_{3\infty}$. It then follows that

$$\lim_{t\to\infty} u(t, x, \phi) = (\alpha_1^\infty, \alpha_2^\infty, \alpha_3^\infty)^T, \ \forall x \in \bar{\Omega}. \qquad \boxed{5.29}$$

Now we prove $\lim\limits_{t\to\infty} u(t, x, \phi) = (\alpha_1^\infty, \alpha_2^\infty, \alpha_3^\infty)^T$ uniformly for all $x \in \bar{\Omega}$. For any $\psi \in \omega(\phi)$, there exists a sequence $t_n \to \infty$ such that $\Phi(t_n)\phi \to \psi$ in C_H as $n \to \infty$, and hence,

$$\lim_{t\to\infty} u(t_n + \theta, x, \phi) = \psi(\theta, x)$$

uniformly for $(\theta, x) \in [-\tau, 0] \times \bar{\Omega}$. In view of (5.29), we have $\psi(\theta, x) = (\alpha_1^\infty, \alpha_2^\infty, \alpha_3^\infty)^T$, $\forall \theta \in [-\tau, 0]$, $x \in \bar{\Omega}$. This implies that $\omega(\phi) = (\alpha_1^\infty, \alpha_2^\infty, \alpha_3^\infty)^T$. Since $\omega(\phi)$ is invariant for $\Phi(t)$, it follows that $(\alpha_1^\infty, \alpha_2^\infty, \alpha_3^\infty)^T$ is a positive constant equilibrium of system (5.18), and hence, $(\alpha_1^\infty, \alpha_2^\infty, \alpha_3^\infty)^T = u^*$. ■

To finish this section, we remark that every solution of the time-delayed differential system

$$
\begin{aligned}
\frac{du_1(t)}{dt} &= \frac{c\beta}{H}(H - u_1(t))u_3(t) - (d_h + \rho)u_1(t), \\
\frac{du_2(t)}{dt} &= \mu - \frac{b\beta}{H}u_2(t)u_1(t) - d_m u_2(t), \\
\frac{du_3(t)}{dt} &= -d_m u_3(t) + e^{-d_m\tau}\frac{b\beta}{H}u_2(t-\tau)u_1(t-\tau),
\end{aligned}
\tag{5.30}
$$

is a spatially homogeneous solution of the time-delayed reaction-diffusion system (5.18). Thus, three statements in Theorem 5.4.1 are also valid for system (5.30).

5.5 Numerical simulations

In this section, we implement numerical simulations in order to show how to derive some epidemiological insights from our analytic results.

For the sake of convenience, we concentrate on one dimensional domain Ω, which can be taken, without loss of generality, to be $(0, \pi)$. Here, we adapt some parameter values from [78] by choosing the transmission probabilities $b = c = 0.5$. Moreover, we suppose that the life expectancy of adult mosquitoes and the incubation period are 10 days. Then we have $d_m = 0.1$ day^{-1}, and $\tau = 10$ days. Further, we set $\rho = 0.01$ day^{-1} by assuming the average human infectious period is 100 days. As pointed out in [78], these values are roughly consistent with *Anopheles gambiae*. For illustration, we choose $d_h = \frac{1}{365 \times 70}$ day^{-1}, $D_m = 1.25 \times 10^{-2}$ km$^2 \cdot$ day^{-1}, $D_h = 1$ km$^2 \cdot$ day^{-1} and allow other coefficients vary spatially. To describe the spatial heterogeneity on domain Ω, we suppose two ends are rural areas and the middle point of Ω is the urban area. Biologically, the human population density is higher in urban area while the anopheline species density and the likelihood of malaria transmission are lower in urban than rural areas with transmission lowest in central urban areas [72]. Hence, we choose the following location-dependent parameters $\beta(x) = 0.1(1.1 + cos(2x))$, $H(x) = 100(1.1 - cos(2x))$ and $\mu(x) = 20(1.1 + cos(2x))$ day^{-1} as an example.

To compute the basic reproduction ratio $\mathcal{R}_0$, we use the orthogonal projection method in the computation of eigenvalues for compact linear operators (see, e.g., [14, Section 3.1]). Our numerical scheme is shown in the appendix section of this chapter. For this set of parameters, the basic reproduction ratio can be computed numerically and $\mathcal{R}_0 = 3.0611$. If we consider system (5.18) by setting $\tilde{\beta}(x) \equiv 0.3$, $\tilde{H}(x) \equiv 100$ and $\tilde{\mu}(x) \equiv 20$, then Lemma 5.4.1 implies $\tilde{\mathcal{R}}_0 = 1.4890$, which is significantly less than $\mathcal{R}_0$. This means that the spatially averaged system may be highly underestimating the disease burden.

In order to simulate the long-time behavior of system (5.6), we discretize it by the difference method on $(0, \pi)$. Our numerical scheme for the nonlocal and time-delayed reaction-diffusion model (5.6) was motivated by that given in [55, Appendix]. Figure 5.1 shows numerical plots of two diseased compartments, $u_1(t, x)$ and $u_3(t, x)$, with the initial data

$$u(\theta, x) = \begin{pmatrix} 20 - cos2x \\ 140 - 5cos2x \\ 19 - 2cos2x \end{pmatrix}, \quad \forall \theta \in [-\tau, 0], \ \ x \in [0, \pi].$$

It indicates that the disease persists in host and vector populations in this case.

To investigate the sensitivity of $\mathcal{R}_0$ on model parameters, we have the following two graphs (Figure 5.2) indicating the plots of $\mathcal{R}_0$ as functions of D_h and τ. It seems the disease cannot be contained solely by extending the incubation period with chemical measures.

To estimate the spatial heterogeneity effect on the disease risk $\mathcal{R}_0$, we take the

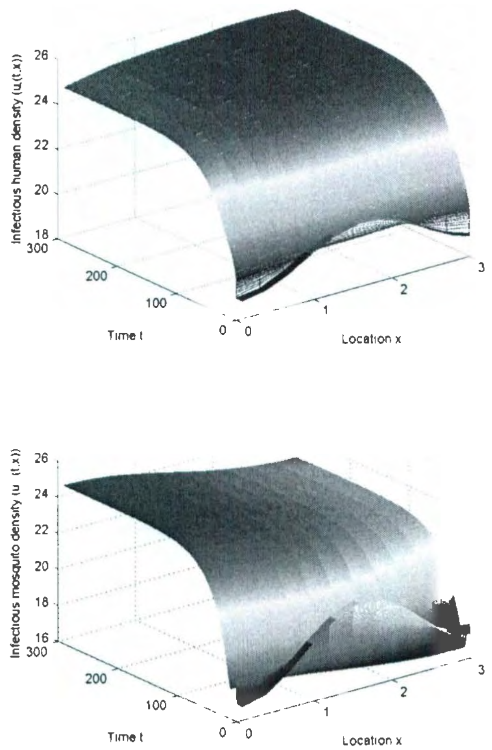


Figure 5.1: Long term behavior of the diseased compartments.

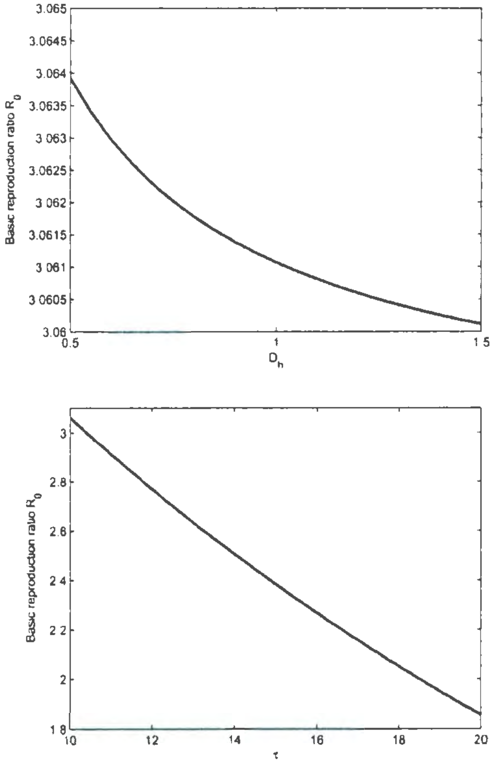


Figure 5.2: $\mathcal{R}_0$ as functions of D_h and τ.

variation of human distribution $H(x)$ for example. As more and more people leave villages and farms to live in cities, the distribution of whole human density will change, and urbanization may have impact on malaria risk. Set $H(x) = 100(1.1 - \delta\cos(2x))$, with $\delta \in [0,1]$ being a parameter. Note that when $\delta = 0$, humans distribute evenly in space ($H(x) \equiv 110$, $\forall x \in \bar{\Omega}$), as δ changing from 0 to 1, more and more people leave the rural areas (near $x = 0$ or $x = \pi$) and accumulate at the urban area (around the middle point of Ω, i.e., $x = \frac{\pi}{2}$). However, the total human density on Ω remains unchanged since the spatial average of $H(x)$ does not change for all $\delta \in [0,1]$. Thus, we can use $\delta \in [0,1]$ to describe the urbanizing process. Figure 5.3 shows the relationship between $\mathcal{R}_0$ and δ.

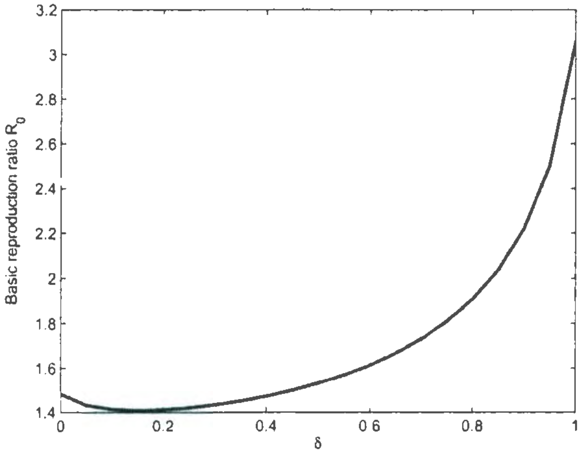


Figure 5.3: Relationship between $\mathcal{R}_0$ and δ.

It indicates that urbanization may increase or decrease malaria risk depending on other model parameters. However, rapid urbanization may deteriorate the disease burden.

To simulate the efficiency of spatial control strategies, we take vaccination programs for example. Suppose that the unvaccinated population distribution for a vaccination program is $h(x)$, then the model with the vaccination program can be modified from our earlier model (5.6) as follows:

$$\begin{cases} \frac{\partial u_1(t,x)}{\partial t} = D_h \Delta u_1(t,x) + \frac{c\beta(x)}{H(x)}(h(x) - u_1(t,x))u_3(t,x) - (d_h + \rho)u_1(t,x), \\ \frac{\partial u_2(t,x)}{\partial t} = D_m \Delta u_2(t,x) + \mu(x) - \frac{b\beta(x)}{H(x)} u_2(t,x)u_1(t,x) - d_m u_2(t,x), \\ \frac{\partial u_3(t,x)}{\partial t} = D_m \Delta u_3(t,x) - d_m u_3(t,x) \\ \qquad + e^{-d_m \tau} \int_\Omega \Gamma(D_m \tau, x, y) \frac{b\beta(y)}{H(y)} u_2(t-\tau, y)u_1(t-\tau, y)dy, \\ \frac{\partial u_i}{\partial n} = 0, \ \forall x \in \partial\Omega, \ t > 0, \ i = 1, 2, 3. \end{cases} \tag{5.31}$$

Using the same idea as in section 3, we can define the basic reproduction ratio for system (5.31). Assume that we have two vaccination programs, program 1 and program 2, which are shown in Figure 5.4.

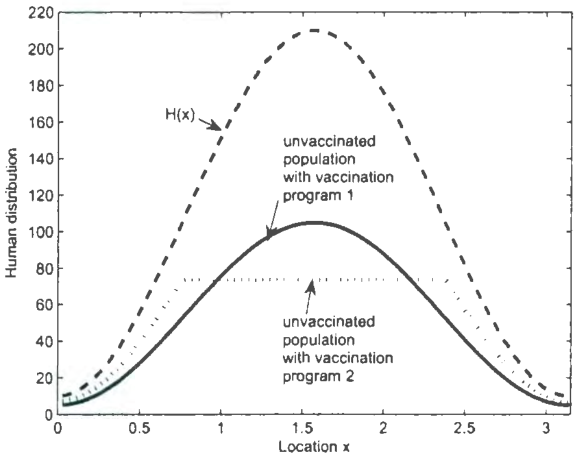


Figure 5.4: Two vaccination programs.

The unvaccinated population distribution for program 1 is

$$h_1(x) = \frac{1}{2} \times 100 \times (1.1 - cos2x),$$

while that for program 2 is

$$h_2(x) = \begin{cases} 0.7036 \times 100, & \text{if } \frac{\pi}{4} \leq x \leq \frac{3\pi}{4}, \\ 0.7036 \times (100 - cos2x), & \text{if } x \geq \frac{3\pi}{4} \text{ or } x \leq \frac{\pi}{4}. \end{cases}$$

In program 1, people living in the rural areas have the same opportunity to get vaccinated (half of the rural and urban populations is vaccinated). In program 2, people in urban area are easier to get access to the vaccination than those in rural areas. Note that the spatial average of $h_1(x)$ and $h_2(x)$ are same, being 55. This implies that the numbers of vaccinated population in these two vaccination programs are same. Numerical computation shows that the basic reproduction ratio corresponding to the first vaccination program is 2.1645 and that to the second program is 2.4979. Thus, the first spatial vaccination strategy seems to be more efficient.

5.6 Discussion

As pointed out in [40], the magnitude of $\mathcal{R}_0$ can be used to gauge the risk of an epidemic or pandemic in emerging infectious disease. Our result shows that this risk may be highly underestimated if we do just consider the model with spatially averaged parameters. By numerically calculating the basic reproduction ratio, our work suggests that spatial heterogeneity does strongly affect $\mathcal{R}_0$. As shown in Fig. 5.3, if δ, an index describing urbanization process, varies from 0 to 1, then the corresponding basic reproduction ratio changes from around 1.5 to 3.0, about two folds. It is worth for the field workers to determine those habitat-dependent parameters in the model.

With regard to application, the threshold result suggests that we should use chemical or physical strategies to reduce the value of $\mathcal{R}_0$ to be less than unity. As shown in the definition of the basic reproduction ratio, $\mathcal{R}_0$ also depends on spatial parameters in this model, which permits the assessment of spatial control strategies. Perhaps the most useful part of this framework would be to design an efficient spatial allocation of financial resources for malaria control. For example, Figure 5.4 shows two vaccination programs, and the numerical computation of $\mathcal{R}_0$ suggests that the first vaccination program is more efficient than the second one. In field work, with accurate spatial-dependent parameters, appropriate spatial vaccination strategies should be designed in the most efficient way. Analogously, we can study the effects of spatial insecticide treated nets (ITN) distribution and spatial indoor residual spraying (IRS) on the basic reproduction ratio.

5.7 Appendix: Numerical computation of $\mathcal{R}_0$

In order to compute the basic reproduction ratio $\mathcal{R}_0$, we use the orthogonal projection method in the computation of eigenvalues for compact linear operators (see, e.g., [14, Section 3.1]).

From the definition of $\mathcal{R}_0$, we have $\mathcal{R}_0 = r(L)$, where L is define as

$$L(\phi) := \int_0^\infty V(S(t)\phi)dt = V\int_0^\infty S(t)\phi dt$$

where $S(t)$ is the positive linear operator on $\mathbb{Y} \times \mathbb{Y}$ given by

$$S(t)\phi := (T_1(t)\phi_1, T_2(t)\phi_2),\ \forall \phi = (\phi_1, \phi_2) \in \mathbb{Y} \times \mathbb{Y},\ x \in \bar{\Omega},\ t \geq 0$$

with

$$T_1(t)\phi_1(x) = e^{-(d_h+\rho)t}\int_\Omega \Gamma(D_h t, x, y)\phi_1(y)dy,$$

and

$$T_2(t)\phi_2(x) = e^{-d_m t}\int_\Omega \Gamma(D_m t, x, y)\phi_2(y)dy.$$

V is the positive linear operator on $\mathbb{Y} \times \mathbb{Y}$ defined by

$$V(\phi)(x) = (V_1(\phi)(x), V_2(\phi)(x)), \ \forall \phi \in \mathbb{Y} \times \mathbb{Y}, \ x \in \bar{\Omega},$$

with

$$V_1(\phi)(x) = c\beta(x)\phi_2(x),$$

and

$$V_2(\phi)(x) = e^{-d_m\tau}\int_\Omega \Gamma(D_m\tau, x, y)m^*(y)\frac{b\beta(y)}{H}\phi_1(y)dy.$$

To compute $\mathcal{R}_0$, we need to determine all of λ and φ^* such that $L\varphi^* = \lambda\varphi^*$. Since L is compact, we have $\mathcal{R}_0 = \sup\{|\lambda|\}$. For convenience, we concentrate on a one dimensional domain Ω, which can be taken, without loss of generality, to be $(0, \pi)$. It then follows that

$$\Gamma(t, x, y) = \frac{1}{\pi} + \frac{2}{\pi}\sum_{n=1}^{\infty} e^{-n^2 t} cosnxcosny.$$

For every $f \in C([0, \pi], \mathbb{R})$, f has the Fourier cosine series

$$f(x) = \frac{a_0}{2} + \sum_{n=1}^{\infty} a_n cosnx,$$

with $a_n = \frac{2}{\pi}\int_0^\pi f(x)cos(nx)dx, n = 0, 1, 2, ...$ Therefore, for any $\varphi^* = (\varphi_1^*, \varphi_2^*)^T$, φ_1^* and φ_2^* can be expanded as Forier cosine serieses,

$$\varphi_1^* = \frac{a_0}{2} + \sum_{n=1}^{\infty} a_n cosnx,$$

and

$$\varphi_2^* = \frac{A_0}{2} + \sum_{n=1}^{\infty} A_n cosnx.$$

We first compute

$$L\begin{pmatrix} a_n cosnx \\ A_m cosmx \end{pmatrix}.$$

Since

$$S(t)\begin{pmatrix} a_n cosnx \\ A_m cosmx \end{pmatrix} = \begin{pmatrix} a_n e^{-(d_h+\rho)t} \int_0^{\pi}(\frac{1}{\pi}+\frac{2}{\pi}\sum\limits_{k=1}^{\infty} e^{-k^2 D_h t} coskxcosky)cosnydy \\ A_m e^{-d_m t} \int_0^{\pi}(\frac{1}{\pi}+\frac{2}{\pi}\sum\limits_{k=1}^{\infty} e^{-k^2 D_m t} coskxcosky)cosmydy \end{pmatrix},$$

by the orthogonality of the sine and cosine functions (see page 549 in [10]), we have the following formulae.

If $n = 0$ and $m = 0$, then

$$S(t)\begin{pmatrix} a_0 \\ A_0 \end{pmatrix} = \begin{pmatrix} a_0 e^{-(d_h+\rho)t} \\ A_0 e^{-d_m t} \end{pmatrix}.$$

If $m \neq 0$ and $n \neq 0$, then

$$S(t)\begin{pmatrix} a_n cosnx \\ A_m cosmx \end{pmatrix} = \begin{pmatrix} a_n e^{-((d_h+\rho)+n^2 D_h)t} cosnx \\ A_m e^{-(d_m+m^2 D_m)t} cosmx \end{pmatrix}.$$

Thus, for all $m, n \in \mathbb{N}$, we obtain

$$S(t)\begin{pmatrix} a_n cosnx \\ A_m cosmx \end{pmatrix} = \begin{pmatrix} a_n e^{-((d_h+\rho)+n^2 D_h)t} cosnx \\ A_m e^{-(d_m t+m^2 D_m)t} cosmx \end{pmatrix},$$

and therefore

$$\int_0^{\infty} S(t)\begin{pmatrix} a_n cosnx \\ A_m cosmx \end{pmatrix} dt = \begin{pmatrix} \frac{a_n cosnx}{(d_h+\rho)+n^2 D_h} \\ \frac{A_m cosmx}{d_m+m^2 D_m} \end{pmatrix}.$$

Consequently, we get

$$L\begin{pmatrix} a_n cosnx \\ A_m cosmx \end{pmatrix} = \begin{pmatrix} c\beta(x)\frac{A_m}{d_m+m^2D_m}cosmx \\ e^{-d_m\tau}\frac{a_n}{(d_h+\rho)+n^2D_h}\int_0^\pi \frac{b\beta(y)}{H(y)}m^*(y)[\frac{1}{\pi}+\frac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjy]cosnydy \end{pmatrix}. \tag{5.32}$$

In view of

$$L\begin{pmatrix} \varphi_1^* \\ \varphi_2^* \end{pmatrix} = L\begin{pmatrix} \frac{a_0}{2}+\sum_{n=1}^{\infty}a_n cosnx \\ \frac{A_0}{2}+\sum_{n=1}^{\infty}A_n cosnx \end{pmatrix} = L\begin{pmatrix} \frac{a_0}{2} \\ \frac{A_0}{2} \end{pmatrix} + \sum_{n=1}^{\infty} L\begin{pmatrix} a_n cosnx \\ A_n cosnx \end{pmatrix},$$

we proceed in two steps.

First step: Compute $L\begin{pmatrix} \frac{a_0}{2} \\ \frac{A_0}{2} \end{pmatrix}$.

It follows from (5.32) that

$$L\begin{pmatrix} \frac{a_0}{2} \\ \frac{A_0}{2} \end{pmatrix} = \begin{pmatrix} c\beta(x)\frac{A_0}{2d_m} \\ e^{-d_m\tau}\frac{a_0}{2(d_h+\rho)}\int_0^\pi \frac{b\beta(y)}{H(y)}m^*(y)[\frac{1}{\pi}+\frac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjy]dy \end{pmatrix}.$$

Suppose we can express the following functions into Fourier Cosine serieses such that

$$\begin{aligned} c\beta(y) &= \frac{\beta_0}{2}+\sum_{i=1}^{\infty}\beta_i cosiy, \\ \text{and } e^{-d_m\tau}\frac{b\beta(y)}{H(y)}m^*(y) &= \frac{b_0}{2}+\sum_{i=1}^{\infty}b_i cosiy. \end{aligned}$$

Then we have

$$L\begin{pmatrix} \frac{a_0}{2} \\ \frac{A_0}{2} \end{pmatrix} = \begin{pmatrix} \frac{A_0}{2d_m}(\frac{\beta_0}{2}+\sum_{i=1}^{\infty}\beta_i cosix) \\ \frac{a_0}{2(d_h+\rho)}\int_0^{\pi}(\frac{b_0}{2}+\sum_{i=1}^{\infty}b_i cosiy)[\frac{1}{\pi}+\frac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjy]dy \end{pmatrix}$$

$$= \begin{pmatrix} \frac{A_0}{2d_m}(\frac{\beta_0}{2}+\sum_{i=1}^{\infty}\beta_i cosix) \\ \frac{a_0}{2(d_h+\rho)}\frac{b_0}{2}+\frac{a_0}{2(d_h+\rho)}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}b_j cosjx \end{pmatrix}.$$

Second step: Compute $L\begin{pmatrix} a_n cosnx \\ A_n cosnx \end{pmatrix}$.

According to (5.32), we have

$$L\begin{pmatrix} a_n cosnx \\ A_n cosnx \end{pmatrix}$$

$$= \begin{pmatrix} (\frac{\beta_0}{2}+\sum_{i=1}^{\infty}\beta_i cosix)\frac{A_n}{d_m+n^2D_m}cosnx \\ \frac{a_n}{(d_h+\rho)+n^2D_h}\int_0^{\pi}(\frac{b_0}{2}+\sum_{i=1}^{\infty}b_i cosiy)[\frac{1}{\pi}+\frac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjy]cosnydy \end{pmatrix}. \tag{5.33}$$

The first element of (5.33) can be expressed as

$$\begin{aligned} & (\frac{\beta_0}{2}+\sum_{i=1}^{\infty}\beta_i cosix)\frac{A_n}{d_m+n^2D_m}cosnx \\ = & \frac{\beta_0}{2}\frac{A_n cosnx}{d_m+n^2D_m}+\frac{A_n}{d_m+n^2D_m}\sum_{i=1}^{\infty}\beta_i cosixcosnx \\ = & \frac{\beta_0}{2}\frac{A_n cosnx}{d_m+n^2D_m}+\frac{1}{2}\frac{A_n}{d_m+n^2D_m}(\sum_{i=1}^{\infty}\beta_i cos(i+n)x \\ & +\sum_{i=1}^{n-1}\beta_i cos(n-i)x+\sum_{i=1+n}^{\infty}\beta_i cos(i-n)x+\beta_n). \end{aligned}$$

The second element of (5.33) turns out to be

$$\begin{aligned}
&\tfrac{a_n}{(d_h+\rho)+n^2D_h}\int_0^{\pi}(\tfrac{b_0}{2}+\sum_{i=1}^{\infty}b_icosiy)[\tfrac{1}{\pi}+\tfrac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjy]cosnydy\\
=\ &\tfrac{a_n}{(d_h+\rho)+n^2D_h}(\int_0^{\pi}\tfrac{b_0}{2}\tfrac{1}{\pi}cosnydy+\int_0^{\pi}\tfrac{b_0}{2}\tfrac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjycosnydy\\
&+\int_0^{\pi}\tfrac{1}{\pi}\sum_{i=1}^{\infty}b_icosiycosnydy+\int_0^{\pi}(\tfrac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjy)(\sum_{i=1}^{\infty}b_icosiy)cosnydy)\\
=\ &\tfrac{a_n}{(d_h+\rho)+n^2D_h}(0+\tfrac{b_0}{2}e^{-n^2D_m\tau}cosnx+\tfrac{b_n}{2}\\
&+\int_0^{\pi}(\tfrac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjy)(\sum_{i=1}^{\infty}b_icosiy)cosnydy).
\end{aligned}$$

Since

$$\begin{aligned}
&\tfrac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjy)(\sum_{i=1}^{\infty}b_icosiy)\\
=\ &\tfrac{2}{\pi}\sum_{j=1}^{\infty}(\sum_{i=1}^{\infty}b_icosiycosjy)e^{-j^2D_m\tau}cosjx\\
=\ &\tfrac{2}{\pi}\sum_{j=1}^{\infty}(\sum_{i=1}^{\infty}\tfrac{b_i}{2}cos(i+j)y+\sum_{i=1}^{j-1}\tfrac{b_i}{2}cos(j-i)y\\
&+\sum_{i=j+1}^{\infty}\tfrac{b_i}{2}cos(i-j)y+\tfrac{b_j}{2})e^{-j^2D_m\tau}cosjx,
\end{aligned}$$

it follows that

$$\begin{aligned}
&\int_0^{\pi}(\tfrac{2}{\pi}\sum_{j=1}^{\infty}e^{-j^2D_m\tau}cosjxcosjy)(\sum_{i=1}^{\infty}b_icosiy)cosnydy\\
=\ &\sum_{i=1}^{n-1}\tfrac{b_i}{2}\tfrac{2}{\pi}\tfrac{\pi}{2}e^{-j^2D_m\tau}cos(jx)\ (i+j=n)\\
&+\sum_{i=1}^{\infty}\tfrac{b_i}{2}\tfrac{2}{\pi}\tfrac{\pi}{2}e^{-j^2D_m\tau}cos(jx)\ (j-i=n)\\
&+\sum_{j=1}^{\infty}\tfrac{b_i}{2}\tfrac{2}{\pi}\tfrac{\pi}{2}e^{-j^2D_m\tau}cos(jx)\ (i-j=n).
\end{aligned}$$

Thus, the second element becomes

$$\begin{aligned}
&\tfrac{a_n}{(d_h+\rho)+n^2D_h}(\tfrac{b_0}{2}e^{-n^2D_m\tau}cosnx+\tfrac{b_n}{2}+\sum_{i=1}^{n-1}\tfrac{b_i}{2}e^{-(n-i)^2D_m\tau}cos((n-i)x)\\
&+\sum_{i=1}^{\infty}\tfrac{b_i}{2}e^{-(n+i)^2D_m\tau}cos((n+i)x)+\sum_{j=1}^{\infty}\tfrac{b_{n+j}}{2}e^{-j^2D_m\tau}cos(jx)).
\end{aligned}$$

Therefore, we obtain

$$
\begin{aligned}
& L\begin{pmatrix} \varphi_1^* \\ \varphi_2^* \end{pmatrix} = L\begin{pmatrix} \frac{a_0}{2} \\ \frac{A_0}{2} \end{pmatrix} + \sum_{n=1}^{\infty} L\begin{pmatrix} a_n cosnx \\ A_n cosnx \end{pmatrix} \\
= & \begin{pmatrix} \frac{A_0}{2d_m}\left(\frac{\beta_0}{2} + \sum_{i=1}^{\infty} \beta_i cosix\right) \\ \frac{a_0}{2(d_h+\rho)}\frac{b_0}{2} + \frac{a_0}{2(d_h+\rho)} \sum_{j=1}^{\infty} e^{-j^2 D_m \tau} b_j cosjx \end{pmatrix} \\
+ & \sum_{n=1}^{\infty} \begin{pmatrix} \frac{\beta_0}{2}\frac{A_n cosnx}{d_m+n^2 D_m} + \frac{1}{2}\frac{A_n}{d_m+n^2 D_m}\left(\sum_{i=1}^{\infty} \beta_i cos(i+n)x + \sum_{i=1}^{n-1} \beta_i cos(n-i)x \right. \\ \left. + \sum_{i=1+n}^{\infty} \beta_i cos(i-n)x + \beta_n\right) \\ \\ \frac{a_n}{(d_h+\rho)+n^2 D_h}\left(\frac{b_0}{2} e^{-n^2 D_m \tau} cosnx + \frac{b_n}{2} + \sum_{i=1}^{n-1} \frac{b_i}{2} e^{-(n-i)^2 D_m \tau} cos((n-i)x) \right. \\ \left. + \sum_{i=1}^{\infty} \frac{b_i}{2} e^{-(n+i)^2 D_m \tau} cos((n+i)x) + \sum_{j=1}^{\infty} \frac{b_{n+j}}{2} e^{-j^2 D_m \tau} cos(jx)\right) \end{pmatrix}.
\end{aligned}
$$

On the other hand, we have

$$
\lambda\begin{pmatrix} \varphi_1^* \\ \varphi_2^* \end{pmatrix} = \lambda\begin{pmatrix} \frac{a_0}{2} + \sum_{n=1}^{\infty} a_n cosnx \\ \frac{A_0}{2} + \sum_{n=1}^{\infty} A_n cosnx \end{pmatrix} = L\begin{pmatrix} \varphi_1^* \\ \varphi_2^* \end{pmatrix}.
$$

Comparing the coefficients, we obtain the following equalities:

$$
\frac{A_0}{2d_m}\frac{\beta_0}{2} + \sum_{n=1}^{\infty} \frac{A_n}{d_m + n^2 D_m}\frac{\beta_n}{2} = \lambda\frac{a_0}{2},
$$

$$
\begin{aligned}
& \frac{A_0}{2d_m}\beta_1 cosx + \frac{\beta_0}{2}\frac{A_1}{d_m + 1^2 D_m} cosx + \sum_{i=1}^{\infty} \frac{1}{2}\frac{A_{i+1}}{d_m + (i+1)^2 D_m}\beta_i cosx + \\
& \sum_{n=1}^{\infty} \frac{1}{2}\frac{A_n}{d_m + n^2 D_m}\beta_{n+1} cosx = \lambda a_1 cosx,
\end{aligned}
$$

$$\begin{aligned}&\frac{A_0}{2d_m}\beta_2 cos2x + \frac{\beta_0}{2}\frac{A_2}{d_m + 2^2 D_m}cos2x + \sum_{i=1}^{\infty}\frac{1}{2}\frac{A_{i+2}}{d_m + (i+2)^2 D_m}\beta_i cos2x\\ &+\frac{1}{2}\frac{A_1}{d_m + D_m}\beta_1 cos2x + \sum_{n=1}^{\infty}\frac{1}{2}\frac{A_n}{d_m + n^2 D_m}\beta_{n+2}cos2x = \lambda a_2 cos2x,\end{aligned}$$

$$\begin{aligned}&\frac{A_0}{2d_m}\beta_3 cos3x + \frac{\beta_0}{2}\frac{A_3}{d_m + 3^2 D_m}cos3x + \sum_{i=1}^{2}\frac{1}{2}\frac{A_{3-i}}{d_m + (3-i)^2 D_m}\beta_i cos3x +\\ &\sum_{i=1}^{\infty}\frac{1}{2}\frac{A_{i+3}}{d_m + (i+3)^2 D_m}\beta_i cos3x + \sum_{n=1}^{\infty}\frac{1}{2}\frac{A_n}{d_m + n^2 D_m}\beta_{n+3}cos(3x) = \lambda a_3 cos3x,\end{aligned}$$

$$\cdots,$$

$$\begin{aligned}&\frac{A_0}{2d_m}\beta_m cosmx + \frac{\beta_0}{2}\frac{A_m}{d_m + m^2 D_m}cosmx + \sum_{i=1}^{m-1}\frac{1}{2}\frac{A_{m-i}}{d_m + (m-i)^2 D_m}\beta_i cosmx\\ &+\sum_{i=1}^{\infty}\frac{1}{2}\frac{A_{i+m}}{d_m + (i+m)^2 D_m}\beta_i cosmx + \sum_{n=1}^{\infty}\frac{1}{2}\frac{A_n}{d_m + n^2 D_m}\beta_{n+m}cosmx = \lambda a_m cosmx,\end{aligned}$$

$$\cdots.$$

Moreover, we have

$$\frac{a_0}{2(d_h+\rho)}\frac{b_0}{2} + \sum_{n=1}^{\infty}\frac{b_n}{2}\frac{a_n}{(d_h+\rho) + n^2 D_h} = \lambda\frac{A_0}{2},$$

$$\begin{aligned}&e^{-D_m\tau}b_1\frac{a_0}{2(d_h+\rho)}cosx + \frac{b_0}{2}\frac{a_1}{(d_h+\rho) + D_h}e^{-D_m\tau}cosx\\ &+\sum_{n=1}^{\infty}\frac{b_i}{2}e^{-D_m\tau}cosx\frac{a_{i+1}}{(d_h+\rho) + (i+1)^2 D_h}\\ &+\sum_{n=1}^{\infty}\frac{b_{n+1}}{2}e^{-1^2 D_m\tau}cosx\frac{a_n}{(d_h+\rho) + n^2 D_h} = \lambda A_1 cosx,\end{aligned}$$

$$
\begin{aligned}
& e^{-2^2 D_m \tau} b_2 \frac{a_0}{2(d_h+\rho)} cos2x + \frac{b_0}{2} \frac{a_2}{(d_h+\rho)+2^2 D_h} e^{-2^2 D_m \tau} cos2x \\
& + \sum_{i=1}^{\infty} \frac{b_i}{2} e^{-2^2 D_m \tau} cos2x \frac{a_{i+2}}{(d_h+\rho)+(i+2)^2 D_h} \\
& \frac{b_1}{2} e^{-2^2 D_m \tau} cos2x \frac{a_1}{(d_h+\rho)+D_h} + \sum_{n=1}^{\infty} \frac{b_{n+2}}{2} e^{-2^2 D_m \tau} cos2x \frac{a_n}{(d_h+\rho)+n^2 D_h} = \lambda A_2 cos2x,
\end{aligned}
$$

$$\ldots,$$

$$
\begin{aligned}
& e^{-m^2 D_m \tau} b_m \frac{a_0}{2(d_h+\rho)} cosmx + \frac{b_0}{2} \frac{a_m}{(d_h+\rho)+m^2 D_h} e^{-m^2 D_m \tau} cosmx \\
& + \sum_{i=1}^{\infty} \frac{b_i}{2} e^{-m^2 D_m \tau} cosmx \frac{a_{m+i}}{(d_h+\rho)+(m+i)^2 D_h} \\
& + \sum_{i=1}^{m-1} \frac{b_i}{2} e^{-m^2 D_m \tau} cosmx \frac{a_{m-i}}{(d_h+\rho)+(m-i)^2 D_h} \\
& + \sum_{n=1}^{\infty} \frac{b_{n+m}}{2} e^{-m^2 D_m \tau} \frac{a_n}{(d_h+\rho)+n^2 D_h} cosmx = \lambda A_m cosmx,
\end{aligned}
$$

$$\ldots.$$

Our next step is to determine the matrix

$$
L_M = \begin{pmatrix} 0 & J = (J_{ij})_{(M+1)\times(M+1)} \\ K = (K_{ij})_{(M+1)\times(M+1)} & 0 \end{pmatrix}
$$

such that

$$
L_M \begin{pmatrix} \frac{a_0}{2} & a_1 & \cdots & a_M & \frac{A_0}{2} & A_1 & \cdots & A_M \end{pmatrix}^T = \lambda \begin{pmatrix} \frac{a_0}{2} & a_1 & \cdots & a_M & \frac{A_0}{2} & A_1 & \cdots & A_M \end{pmatrix}^T
$$

From the above equalities, we have $J = (J_1, J_2)$ with

$$J_1 = \begin{pmatrix} \frac{1}{d_m}\frac{\beta_0}{2} & \frac{1}{d_m+1^2D_m}\frac{\beta_1}{2} & \frac{1}{d_m+2^2D_m}\frac{\beta_2}{2} & \cdots \\ \frac{\beta_1}{d_m} & \frac{1}{d_m+D_m}\frac{\beta_0}{2} + \frac{\beta_{1+1}}{2(d_m+D_m)} & \frac{\beta_1}{d_m+2^2D_m}\frac{1}{2} + \frac{\beta_{2+1}}{2}\frac{1}{d_m+2^2D_m} & \cdots \\ \frac{\beta_2}{d_m} & \frac{\beta_1}{2(d_m+D_m)} + \frac{\beta_{1+2}}{2(d_m+D_m)} & \frac{\beta_0}{d_m+2^2D_m}\frac{1}{2} + \frac{\beta_{2+2}}{2}\frac{1}{d_m+2^2D_m} & \cdots \\ \frac{\beta_3}{d_m} & \frac{\beta_2}{2(d_m+D_m)} + \frac{\beta_{1+3}}{2(d_m+D_m)} & \frac{\beta_1}{d_m+2^2D_m}\frac{1}{2} + \frac{\beta_{2+3}}{2}\frac{1}{d_m+2^2D_m} & \cdots \\ \cdots & \cdots & \cdots & \cdots \\ \frac{\beta_n}{d_m} & \frac{\beta_{n-1}}{2(d_m+D_m)} + \frac{\beta_{1+n}}{2(d_m+D_m)} & \frac{\beta_{n-2}}{d_m+2^2D_m}\frac{1}{2} + \frac{\beta_{2+n}}{2}\frac{1}{d_m+2^2D_m} & \cdots \\ \cdots & \cdots & \cdots & \cdots \end{pmatrix}$$

and

$$J_2 = \begin{pmatrix} \cdots & \frac{1}{d_m+m^2D_m}\frac{\beta_m}{2} & \cdots \\ \cdots & \frac{\beta_{m-1}}{2(d_m+m^2D_m)} + \frac{\beta_{1+m}}{2(d_m+m^2D_m)} & \cdots \\ \cdots & \frac{\beta_{m-2}}{2(d_m+m^2D_m)} + \frac{\beta_{2+m}}{2(d_m+m^2D_m)} & \cdots \\ \cdots & \frac{\beta_{m-3}}{2(d_m+m^2D_m)} + \frac{\beta_{3+m}}{2(d_m+m^2D_m)} & \cdots \\ \cdots & \cdots & \cdots \\ \cdots & \frac{\beta_{|n-m|}}{2(d_m+m^2D_m)} + \frac{\beta_{n+m}}{2(d_m+m^2D_m)} & \cdots \\ \cdots & \cdots & \cdots \end{pmatrix}.$$

Moreover, we obtain that $K = (K_1, K_2)$ with K_1=

$$\begin{pmatrix} \frac{1}{(d_h+\rho)}\frac{b_0}{2} & \frac{1}{(d_h+\rho)+D_h}\frac{b_1}{2} & \frac{1}{(d_h+\rho)+2^2D_h}\frac{b_2}{2} \\ \frac{b_1}{(d_h+\rho)}e^{-D_m\tau} & \frac{e^{-D_m\tau}}{(d_h+\rho)+D_h}\frac{b_0}{2} + \frac{e^{-1^2D_m\tau}b_{1+1}}{2((d_h+\rho)+D_h)} & \frac{b_{2-1}e^{-D_m\tau}}{(d_h+\rho)+2^2D_h}\frac{1}{2} + \frac{b_{2+1}e^{-1^2D_m\tau}}{2}\frac{1}{(d_h+\rho)+2^2D_h} \\ \frac{b_2}{(d_h+\rho)}e^{-2^2D_m\tau} & \frac{e^{-2^2D_m\tau}}{(d_h+\rho)+D_h}\frac{b_1}{2} + \frac{e^{-2^2D_m\tau}b_{1+2}}{2((d_h+\rho)+D_h)} & \frac{b_{2-2}e^{-2^2D_m\tau}}{(d_h+\rho)+2^2D_h}\frac{1}{2} + \frac{b_{2+2}e^{-2^2D_m\tau}}{2}\frac{1}{(d_h+\rho)+2^2D_h} \\ \cdots & \cdots & \cdots \\ \frac{b_n}{(d_h+\rho)}e^{-n^2D_m\tau} & \frac{e^{-n^2D_m\tau}}{(d_h+\rho)+D_h}\frac{b_{n-1}}{2} + \frac{e^{-n^2D_m\tau}b_{n+1}}{2((d_h+\rho)+D_h)} & \frac{b_{n-2}e^{-n^2D_m\tau}}{(d_h+\rho)+2^2D_h}\frac{1}{2} + \frac{b_{2+n}e^{-n^2D_m\tau}}{2}\frac{1}{(d_h+\rho)+2^2D_h} \\ \cdots & \cdots & \cdots \end{pmatrix}$$

and

$$K_2 = \begin{pmatrix} \cdots & \frac{1}{(d_h+\rho)+m^2 D_h}\frac{b_m}{2} & \cdots \\ \cdots & \frac{b_{m-1}e^{-D_m\tau}}{2((d_h+\rho)+m^2D_h)} + \frac{b_{1+m}e^{-1^2D_m\tau}}{2((d_h+\rho)+m^2D_h)} & \cdots \\ \cdots & \frac{b_{m-2}e^{-2^2D_m\tau}}{2((d_h+\rho)+m^2D_h)} + \frac{b_{2+m}e^{-2^2D_m\tau}}{2((d_h+\rho)+m^2D_h)} & \cdots \\ \cdots & \cdots & \cdots \\ \cdots & \frac{b_{|n-m|}e^{-n^2D_m\tau}}{2((d_h+\rho)+m^2D_h)} + \frac{b_{n+m}e^{-n^2D_m\tau}}{2((d_h+\rho)+m^2D_h)} & \cdots \\ \cdots & \cdots & \cdots \end{pmatrix}.$$

Hence, we have

$$J_{1j} = \frac{\beta_{j-1}}{2(d_m+(j-1)^2D_m)} \text{ and } J_{ij} = \frac{\beta_{|i-j|}+\beta_{i+j-2}}{2(d_m+(j-1)^2D_m)}, \ \forall i \geq 2,$$

and

$$K_{1j} = \frac{b_{j-1}}{2((d_h+\rho)+(j-1)^2D_h)} \text{ and } K_{ij} = \frac{e^{-(i-1)^2D_m\tau}[b_{|i-j|}+b_{i+j-2}]}{2((d_h+\rho)+(j-1)^2D_h)}, \ \forall i \geq 2.$$

By matrices J and K, we can write out the matrix L_M. Since $\lim_{M\to\infty} r(L_M) = r(L)$, using Matlab, we can get spectral radius of L_M, which can be used to approximate $r(L)$.

Remark: In the case where all parameters are spatially-independent, i.e., $\beta(x) \equiv \frac{\beta_0}{2}$, and $\frac{e^{-d_m\tau}b\beta(x)}{H(x)}m^*(x) = \frac{b_0}{2}$, $\forall x \in \bar{\Omega}$, we have

$$L\begin{pmatrix} \varphi_1^* \\ \varphi_2^* \end{pmatrix} = L\begin{pmatrix} \frac{a_0}{2} + \sum\limits_{n=1}^{\infty} a_n cosnx \\ \frac{A_0}{2} + \sum\limits_{n=1}^{\infty} A_n cosnx \end{pmatrix} = \lambda\begin{pmatrix} \frac{a_0}{2} + \sum\limits_{n=1}^{\infty} a_n cosnx \\ \frac{A_0}{2} + \sum\limits_{n=1}^{\infty} A_n cosnx \end{pmatrix}.$$

Therefore, the following equalities hold

$$\begin{aligned} \frac{A_0}{2d_m}\frac{\beta_0}{2} &= \lambda\frac{a_0}{2}, \\ \frac{\beta_0}{2}\frac{A_n}{d_m+n^2D_m} &= \lambda a_n, \ n = 1,2,3\cdots \\ \frac{a_0}{2(d_h+\rho)}\frac{b_0}{2} &= \lambda\frac{A_0}{2}, \\ \frac{b_0}{2}\frac{a_n}{(d_h+\rho)+n^2D_h}e^{-n^2D_m\tau} &= \lambda A_n, n = 1,2,3\cdots. \end{aligned}$$

Solving these equations, we then obatin

$$\lambda = \pm\sqrt{\frac{1}{(d_h+\rho)}\frac{b_0}{2}\frac{1}{d_m}\frac{\beta_0}{2}}, \ A_i = a_i = 0, \ \forall i \geq 1.$$

It follows that

$$r(L) = \sqrt{\frac{1}{(d_h+\rho)}\frac{b_0}{2}\frac{1}{d_m}\frac{\beta_0}{2}} = \sqrt{\frac{1}{d_m}\frac{1}{(d_h+\rho)}e^{-d_m\tau}\frac{b\beta}{H}\frac{\mu}{d_m}c\beta},$$

which is consistent with Lemma 5.4.1.

Chapter 6

Conclusions and Future Work

This chapter presents the main conclusions of this thesis and the future work. First, we summarize the main results. Then we suggest some future research directions.

6.1 Research summary

Each year, approximately 2.2 billion people are affected by *Plasmodium falciparum* malaria worldwide, claiming about 515 million endemic cases [85]. Hence, there is an essential need for more information on the spatial and temporal patterns of disease burden, distribution and control strategies. Human malaria is caused by parasites belonging to the genus Plasmodium, which can be transmitted by several species of female anopheles mosquitoes. Since the pioneering work of Ronald Ross [73], who proved that mosquitoes transmit malaria and presented the first mathematical model for the disease, modeling of malaria has flourished (see, e.g., [5, 28, 49, 66, 70, 74] and references therein).

Mathematical models can provide an important approach to understanding risk and planning for disease control in heterogeneous environments, especially when the models are based on the ecology of the local vector populations and a sound understanding of the entomological parameters relevant for transmission ([47,48]). In this work, we have presented four epidemic models in the presence of spatial or temporal heterogeneity, with malaria transmission as our main topic.

To address the impact of seasonal fluctuations on disease transmission, we investigated the dynamics of a time-delayed periodic SIS epidemic model in chapter 2. We first considered a periodic single-species population model with time-delayed, and obtained four sets of conditions to ensure that the population will stabilize eventually at an oscillating state. When the disease invades the population and susceptibles contact infectives under the standard incidence law, we found an explicit formula for $\mathcal{R}_0$ in the form of the division of the average contact rate and the mass of the average disease induced death rate, disease recovery rate and death rate. Furthermore, we showed that there exists an endemic periodic solution and the disease remains endemic when $\mathcal{R}_0 > 1$, and the disease dies out when $\mathcal{R}_0 < 1$. In order to eradicate such a disease, we should decrease the average contact rate, or increase the average disease recovery rate to make $\mathcal{R}_0 < 1$.

Motivated by the compartmental models in [15,68,69], we formulated a mathematical malaria model in chapter 3 to address the age-structure of mosquitoes and the seasonal climate effects on malaria transmission. Our work shows that the prospects for the success of malaria control depend, in part, on the basic reproductive number for malaria. For our time-delayed and periodic model, we successfully defined the basic reproduction ratio, which can be numerically computed. This project allows us to study the trends of malaria risk associated with global warming.

To study the possible impact of the mobility of humans and mosquitoes on malaria transmission, we proposed a periodic Ross-Macdonald type model with diffusion and advection in chapter 4. For the periodic model without diffusion and advection, we showed that the basic reproduction ratio serves as a threshold parameter for disease transmission. In the appearance of diffusion and advection, we established the existence of the leftward and rightward spreading speeds and their coincidence with the minimum wave speeds in the left and right directions, respectively. For the model in a bounded domain, we obtained a threshold result on the global attractivity of either zero or the positive periodic solution.

It is widely known in malariology that spatial heterogeneity and extrinsic incubation period (EIP) of the parasite in infected mosquitoes may affect the malaria transmission while the movement of human and mosquito populations leads to malaria spread. To understand the effects of these factors on malaria epidemic, we formulated and analyzed a nonlocal and time-delayed reaction-diffusion model in chapter 5. For this mathematical model, we derived a biologically meaningful threshold index, the basic reproduction ratio $\mathcal{R}_0$. The basic reproduction ratio for this model is characterized as the spectral radius of the next generation operator and can be numerically calculated. Mathematically, we showed that $\mathcal{R}_0 = 1$ defines a threshold. The disease will not invade if $\mathcal{R}_0 < 1$ and the disease becomes established in a previously uninfected populations if $\mathcal{R}_0 > 1$. For the model with spatially independent parameters, $\mathcal{R}_0$ can be explicitly calculated. Using a fluctuation method developed in [90], we got a set of sufficient conditions to guarantee that the disease will become established and stabilize at a unique spatially-homogeneous steady state. In particular, if $\mathcal{R}_0 > 1$ is large enough, the positive steady state is globally attractive. This work allows us to design an optimal spatial control strategy.

In summary, we have created a framework to study the malaria transmission which allows temporal or spatial variations. The framework permits the early warning system (e.g., forecasting the malaria risk with global warming in chapter 3) and assessment of spatial control strategies (e.g. spatial vaccination program in chapter 5).

6.2 Future work

Inevitably and perhaps encouragingly, there are several issues remaining worthy to study, both in terms of model analysis and construction. In this section, we enumerate some of these possible directions.

6.2.1 Global stability of the disease-endemic state

Although we have shown in chapter 3 that there exists at least one positive periodic state (disease-endemic state) when the basic reproduction ratio is greater than unity. What we were not able to accomplish in this work was the uniqueness, multiplicity, and stability of positive periodic solution for the model.

In chapter 5, it was shown in Theorem 5.3.2 that there exists a positive steady state for system (5.6) when $\mathcal{R}_0$ exceeds unity, its uniqueness and global attractivity still remain open. We expect to get some appropriate conditions as in Theorem 5.4.1 to guarantee the global attractivity of the positive steady state for system (5.6) when $\mathcal{R}_0 > 1$.

6.2.2 Bifurcation analysis of periodic models

As noted in chapter 3, the disease will die out if $\mathcal{R}_0 < 1$, provided that the invasion intensity is not strong. However, this case may not happen when the invasion intensity is strong. It was shown, even for some autonomous malaria models, that the stable disease free equilibrium coexists with a stable endemic equilibrium when $\mathcal{R}_0 < 1$ [66]. If the backward bifurcation exists, the solution through some suitable initial data may converge to the stable endemic equilibrium even $\mathcal{R}_0 < 1$. This phenomenon is called backward bifurcation (see, for instance [36,77,93] and the references therein for further discussion on backward bifurcation). In this scenario, the classical requirement of reducing basic reproduction ratio to be less than unity becomes only a necessary, but not sufficient condition, to control the disease. Bifurcation analysis of the periodic malaria models–presumably using the framework in [50] and other analytical results–is a desirable next step to enhance the mathematical understanding of epidemical models.

6.2.3 Sophistication of HIV-malaria co-infection dynamics

As pointed out in [1], it has been shown that HIV increases the risk of malaria infection and the development of clinical malaria, while malaria induces HIV–I replication *in vitro* and *in vivo*. Dual infection with HIV and malaria fuels the spread of both diseases in sub-Saharan Africa [1, 11]. It may be important to incorporate HIV-malaria coinfection into models, which always turn out to be high dimensional systems (see, e.g., [1,66]). The model analysis would be mathematically challenging and the complex dynamics may be biologically interesting.

6.2.4 Incorporation of additional drug-resistant phenomena

Antimalarial drugs are used for malaria treatment. However, the efficiency of antimalarial drugs has been decreasing dramatically over the past few decades, due to the emergence of drug-resistance. Malaria parasites have demonstrated some level of resistance to almost every anti-malarial drug currently available, significantly increasing the cost and complexity of achieving parasitological cure [8]. Currently, antimalarial drug resistance becomes a major public health problem hindering the control of malaria. Moreover, population movement (spatial heterogeneity) has introduced resistant parasites to areas previously free of drug resistance [7]. The models in this thesis would be augmented with the inclusion of drug-resistance phenomena, such as those in [4, 7, 28].

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