Modelling Malaria Control by Introduction of Larvivorous Fish

Yijun Lou · Xiao-Qiang Zhao

Abstract Malaria creates serious health and economic problems which call for integrated management strategies to disrupt interactions among mosquitoes, the parasite and humans. In order to reduce the intensity of malaria transmission, malaria vector control may be implemented to protect individuals against infective mosquito bites. As a sustainable larval control method, the use of larvivorous fish is promoted in some circumstances. To evaluate the potential impacts of this biological control measure on malaria transmission, we propose and investigate a mathematical model describing the linked dynamics between the host–vector interaction and the predator–prey interaction. The model, which consists of five ordinary differential equations, is rigorously analysed via theories and methods of dynamical systems. We derive four biologically plausible and insightful quantities (reproduction numbers) that completely determine the community composition. Our results suggest that the introduction of larvivorous fish can, in principle, have important consequences for malaria dynamics, but also indicate that this would require strong predators on larval mosquitoes. Integrated strategies of malaria control are analysed to demonstrate the biological application of our developed theory.

Keywords Vector borne diseases · Disease control · Malaria transmission · Predator–prey model · Larvivorous fish · Global attractivity

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1 Introduction

Human malaria is a parasitic disease which is caused by the genus *Plasmodium*, and it is spread among humans by female *Anopheles* mosquitoes. Currently, approximately two billion people are at risk of *Plasmodium falciparum* malaria (Snow et al. 2005), which primarily affects poor populations in tropical and subtropical areas. Malaria is also a major hindrance to economic development. The economic impacts of malaria include costs of health care, decreased school attendance and work productivity due to the disease, loss of investment and tourism (Greenwood et al. 2005).

The Global Malaria Eradication Programme, using two key tools: chloroquine for treatments and prevention and dichloro-diphenyl-trichloroethane (DDT) for vector control, was launched by WHO in 1955 (World Health Organization 2000). With the emergence of chloroquine-resistant *Plasmodium* parasites and DDT-resistant *Anopheles* mosquitoes, the goal for global eradication of malaria was officially abandoned in 1972 (Brito 2001). After that, more effective interventions, including drug combinations with an artemisinin derivative and anti-vector measures, were delivered (Greenwood et al. 2008). However, global warming, drug resistance and insecticide resistance may deteriorate malaria burden. Although malaria vaccine research has progressed rapidly over the past few years, it is likely to be at least a decade before an efficacious vaccine is available for widespread use in malaria-endemic countries (Greenwood et al. 2005). Without this kind of prospect vaccines in the near future, vector control becomes an essential component. Contemporary vector control strategies include indoor residual spraying (IRS) and insecticide treated nets (ITNs). These programmes target the adult female mosquito population to shorten the length of its life stage rather than reduce the vector population. However, harmful effects of chemicals on mosquitoes and non-target populations, emerging resistance to insecticides, logistical difficulties and prohibitive costs call for other vector-targeted malaria control strategies (Ghosh and Dash 2007; Walker and Lynch 2007). On the contrary, unlike adult mosquitoes, immature mosquitoes cannot escape from their breeding sites until the adult stage and hence, they cannot easily avoid control measures (Killeen et al. 2002). Larval control of *Anopheles* mosquitoes is a well-proven effective tool that has been neglected, but deserves renewed consideration for malaria control in the twenty first century (Walker and Lynch 2007).

Manipulating an auto-reproducing predator into the ecosystem may provide sustained biological control of the vector population (Chandra et al. 2008). Larvivorous fish which feeds on immature stages of mosquitoes has been introduced as a successful intervention tool against *Anopheles* mosquitoes (Chandra et al. 2008). In order to control malaria, introduction of larvivorous fish has been shown to be an efficient and suitable intervention tool for larval control in many circumstances (see Chandra et al. 2008; Ghosh and Dash 2007; Greenwood et al. 2005; Howard et al. 2007; Singh et al. 2006; Walker and Lynch 2007 and references therein). For example, one year after the release of larvivorous fish, malaria in three villages in India (Puram, Bodapatt and Banganatham) was eradicated (Ghosh et al. 2005). According to World Health Report 2009 (World Health Organization 2010), introduction of larvivorous *Gambusia* fish is promoted by almost all affected countries in rice-growing areas.
in the European region. Integrated malaria management, such as a combination of IRS, early detection, prompt treatments and larvivorous fish, can successfully bring malaria under control (Singh et al. 2006). In order to achieve an optimal strategy, sound insights into the dynamics among larvivorous fish, the vector and human populations are desirable. Our main object is to model and investigate this interaction.

In the larvivorous fish–mosquitoes–humans interaction, there exist two sub-interactions: the predator–prey (larvivorous fish and larval mosquitoes) and vector–host (adult mosquitoes and humans) interactions. To model this process, we can use the eco-epidemiological modelling idea. Eco-epidemiological models have been investigated for a long period, and some mathematical modelling works about eco-epidemiological interactions have been published recently (see, e.g. Auger et al. 2009; Hilker and Schmitz 2008; Moore et al. 2010; Oliveira and Hilker 2010 and references therein). However, there is just one paper (Moore et al. 2010), to the authors’ knowledge, studying the impact of predator–prey interactions on the transmission of vector-borne diseases. Moreover, the models in Moore et al. (2010) assume the predation on the adult mosquitoes and the analysis mainly focuses on the basic reproduction number and the local stability of equilibria. Until now, there has been little systematic analysis on the consequences of the larvivorous fish to the malaria transmission.

To gain insights into the transmission dynamics of malaria with the introduction of larvivorous fish, we couple the Ross–Macdonald model with an age-structured prey–predator model. The population dynamics is governed by a system of five ordinary differential equations. In order to get qualitative dynamics, we first study the subsystem describing the predator–prey interaction between larvivorous fish and mosquitoes. Then we use the limiting system to obtain the information for the whole model. We derive biologically plausible and insightful quantities (the mosquito, predator and disease reproduction numbers) that allow us to completely determine community compositions. In comparison with the study of Moore, Borer and Hosseini (Moore et al. 2010), our model focuses on the impact of the predator–larval (immature) vector interaction on the transmission of vector-borne pathogens. Moreover, since larviciding is an important tool to contain malaria transmission, the model allows us to study the integrated use of larvicides and larvivorous fish. On the other hand, we rigorously analyse the global dynamics of this system.

The article is organised as follows. The next section presents the eco-epidemiological model. We first study the predator free system, and then investigate the dynamics of the model with predators. Section 3 provides numerical simulations and the last section offers a discussion.

2 The Model and Mathematical Results

In this section, we introduce and investigate an eco-epidemiological model, which combines two submodels, one describing the age-structured prey–predator dynamics of mosquitoes and larvivorous fish, and the other describing disease spread between mosquitoes and humans.
2.1 Model Formulation

The model is based on monitoring the temporal dynamics of the host (humans), vector (mosquitoes), and predator (larvivorous fish) population sizes.

Following (Li 2009; Wonham et al. 2004), we simplify the biological cycle of female mosquitoes into two stages: the larval state \(L_v\) and adult one \(N_v\), with birth into the larval stage and natural death in each stage. From the viewpoint of the epidemiology, adult mosquitoes contribute to the transmission of disease, and larval control is an important measure for vector control. We suppose that the infectiousness does not affect vector’s egg-laying rate \(g\) and death rate \(d_v\). For the immature mosquitoes, the natural death rate and the maturation rate are \(d_L\) and \(\lambda_v\), respectively.

As noted in Li (2009), Reiskind and Lounibos (2009), larval crowding or competition is common in container-breeding mosquitoes. We use \(\alpha\) to denote the density-dependent development mortality of larvae. To account for the predation of immature mosquitoes by predators, we take the linear response form with a constant rate \(\gamma\), similar to that in the Lotka–Volterra model. Following the modelling idea of the classical Ross–Macdonald model (Aron and May 1982), the adult female mosquito population and the human population are divided into two epidemiological categories: the susceptible class and infectious class. Letting \(S_v\) and \(I_v\) be the population sizes of susceptible and infectious mosquitoes, we have \(N_v = S_v + I_v\). Assume \(\beta\) is the mosquito biting rate, that is, \(\beta\) is the average number of bites per mosquito per unit time.

The force of infection for susceptible mosquitoes can be represented as

\[
c\beta S_v \frac{I_h}{N_h},
\]

where \(c\) is the transmission probability from infectious humans to mosquitoes, \(I_h\) and \(N_h\) are population sizes of infectious and total humans, respectively.

For the predator (larvivorous fish) population \(P\), we assume that \(k\) is the tropical conversion efficiency and \(d_p\) is the mortality rate.

Due to the fact that the total human population for a specified region remains almost constant, we suppose that the total human population is unchanged, being \(N_h\), to keep our mathematical modelling as simple as possible. Letting \(S_h\) and \(I_h\) be the population sizes of susceptible and infectious humans, we get \(N_h = S_h + I_h\). Hence, we only need to keep track of the population size of infectious humans. Based on the conservation of bites, that is, the total number of bites made by mosquitoes equals to the number of bites received by humans (Bowman et al. 2005), the average number of bites per human receives per unit time is \(\beta \frac{N_v}{N_h}\). Suppose the transmission probability per bite from infectious mosquitoes to humans is \(b\), then the infection rate per susceptible human is given by

\[
b\beta \frac{N_v}{N_h} \frac{I_v}{N_v} = b\beta \frac{I_v}{N_h}.
\]

This cross-infection between the host and vector populations is modelled as mass-action mechanism normalized by the host density, see, e.g. (Wonham et al. 2006). Let \(d_h\) be the average mortality rate of humans and \(\rho\) the recovery rate, i.e. \(1/\rho\) is the human infection period.
Based on the above assumptions, the community dynamics can be described by the following system:

\[
\begin{align*}
\frac{dL_v(t)}{dt} &= gN_v - d_L L_v - \alpha L_v^2 - \lambda_v L_v - \gamma L_v P, \\
\frac{dS_v(t)}{dt} &= \lambda_v L_v - c\beta S_v \frac{I_h}{N_h} - d_v S_v, \\
\frac{dI_v(t)}{dt} &= c\beta S_v \frac{I_h}{N_h} - d_v I_v, \\
\frac{dP(t)}{dt} &= k\gamma L_v P - d_p P, \\
\frac{dI_h(t)}{dt} &= b\beta (N_h - I_h) \frac{I_v}{N_h} - (d_h + \rho) I_h.
\end{align*}
\] (1)

For the sake of simplicity, it is convenient to use a change of variable \( N_v = S_v + I_v \). It is easy to see that system (1) is equivalent to the following one:

\[
\begin{align*}
\frac{dL_v(t)}{dt} &= gN_v - d_L L_v - \alpha L_v^2 - \lambda_v L_v - \gamma L_v P, \\
\frac{dN_v(t)}{dt} &= \lambda_v L_v - d_v N_v, \\
\frac{dI_v(t)}{dt} &= c\beta (N_v - I_v) \frac{I_h}{N_h} - d_v I_v, \\
\frac{dP(t)}{dt} &= k\gamma L_v P - d_p P, \\
\frac{dI_h(t)}{dt} &= b\beta (N_h - I_h) \frac{I_v}{N_h} - (d_h + \rho) I_h.
\end{align*}
\] (2)

Our first task is to show that the mathematical model is biologically meaningful.

**Theorem 2.1** System (2) has a unique and bounded solution with the initial value

\[
(L_v^0, N_v^0, I_v^0, P^0, I_h^0) \in X := \{(L_v, N_v, I_v, P, I_h) \in \mathbb{R}_{+}^5 : I_v \leq N_v, I_h \leq N_h\}.
\]

Moreover, the compact set

\[
\Gamma := \left\{(L_v, N_v, I_v, P, I_h) \in X : L_v \leq \frac{g\lambda_v}{\alpha d_v}, N_v \leq \frac{g}{\alpha} \left( \frac{\lambda_v}{d_v} \right)^2, P \leq \frac{k(g\lambda_v)^2}{\alpha(d_v)^2 \min\{d_L + \lambda_v, d_p\}} \right\}
\]

attracts all positive solutions in \( X \).

**Proof** It follows from Smith (1995, Theorem 5.2.1) that system (2) admits a unique nonnegative solution \((L_v(t), N_v(t), I_v(t), P(t), I_h(t))\) through an initial value \(0 \).
\((L_v^0, N_v^0, I_v^0, P^0, I_h^0) \in X \) with the maximal interval of existence \([0, \sigma)\) for some \(\sigma > 0\). Note that for any \((L_v, N_v, I_v, P, I_h) \in X\), if \(I_h = N_h, \frac{dI_h}{dt} \leq 0\) it then follows from Smith (1995, Remark 5.2.1) that \(I_h(t) \leq N_h\) for all \(t \in [0, \sigma)\).

According to Zhao and Jing (1996, Corollary 3.2), it is easy to observe that the following system

\[
\begin{align*}
\frac{du_1(t)}{dt} &= g_2 - \alpha u_1^2, \\
\frac{du_2(t)}{dt} &= \lambda u_1 - d_v u_2,
\end{align*}
\]

admits a globally asymptotically stable equilibrium \((\frac{g_1}{\alpha d_v} \frac{g}{\alpha (d_v)^2})\) with respect to all initial values in \(\mathbb{R}_+^2 \setminus \{(0, 0)\}\). Since

\[
\begin{align*}
\frac{dL_v(t)}{dt} &\leq gN_v - \alpha L_v^2, \\
\frac{dN_v(t)}{dt} &\leq \lambda L_v - d_v N_v,
\end{align*}
\]

according to the comparison principle (see, e.g. Smith and Waltman 1995, Theorem B.1), there exist \(M_1\) and \(M_2\) such that

\(L_v(t) \leq M_1, \quad N_v(t) \leq M_2, \quad \forall t \in [0, \sigma)\).

Note that

\[
\frac{d(kL_v(t) + P(t))}{dt} \leq kgN_v - \min\{d_L + \lambda_v, d_p\}(kL_v + P)
\]

\[\leq kgM_2 - \min\{d_L + \lambda_v, d_p\}(kL_v + P), \quad \forall t \in [0, \sigma)\].

By the comparison principle, we obtain that \(P(t)\) is bounded on \([0, \sigma)\). Thus, we see that \(\sigma = \infty\) and the solution exists globally.

From the previous arguments, we can see that \(\limsup_{t \to \infty} (L_v(t), N_v(t)) \leq (\frac{g_1}{\alpha d_v} \frac{g}{\alpha (d_v)^2})\) and \(\limsup_{t \to \infty} P(t) \leq \frac{k(g\lambda_v)^2}{\alpha (d_v)^2 \min\{d_L + \lambda_v, d_p\}}\). Hence, \(\Gamma\) is globally attractive. \(\square\)

The above lemma shows that solutions starting in the region \(X\) remain there for all time \(t \geq 0\). Biologically, we may restrict our attention to this closed set \(X\). Before we investigate the dynamics of our model with larvivorous fish, we would like to study the case where the predator is not introduced. There are two reasons to start with this situation. Firstly, it facilitates us to compare with the case where the predator is introduced. Secondly, it is mathematically easier to deal with the predator-free system, while still enables us to clearly illustrate the main mathematical ideas used in this paper.
2.2 Malaria Transmission Without the Predator

In this subsection, we consider the situation where there is no predator, that is \( P = 0 \). The predator-free model is given by

\[
\begin{align*}
\frac{dL_v(t)}{dt} &= gN_v - d_L L_v - \alpha L_v^2 - \lambda_v L_v, \\
\frac{dN_v(t)}{dt} &= \lambda_v L_v - d_v N_v, \\
\frac{dI_v(t)}{dt} &= c\beta(N_v - I_v) \frac{I_h}{N_h} - d_v I_v, \\
\frac{dI_h(t)}{dt} &= b\beta(N_h - I_h) \frac{I_v}{N_h} - (d_h + \rho)I_h.
\end{align*}
\] (3)

Denote \( X_1 := \{(L_v, N_v, I_v, I_h) \in \mathbb{R}_+^4 : I_v \leq N_v, I_h \leq N_h\} \). Using the same argument as that in Theorem 2.1, we can show that \( X_1 \) is positively invariant for system (3). In the following, we first investigate the dynamics of the mosquito population when there is no predator on larvae. It is easy to see from system (3) that the mosquito population is described by the following age-structured growth equations:

\[
\begin{align*}
\frac{dL_v(t)}{dt} &= gN_v - d_L L_v - \alpha L_v^2 - \lambda_v L_v, \\
\frac{dN_v(t)}{dt} &= \lambda_v L_v - d_v N_v.
\end{align*}
\] (4)

Since one female mosquito can produce an average of \( g \) larvae per unit time which will survive to the adult stage with the probability of \( \frac{\lambda_v}{d_L + \lambda_v} \), and \( \frac{1}{d_v} \) gives the average lifespan of mosquitoes, an adult mosquito can produce \( g\lambda_v \frac{\lambda_v}{d_L + \lambda_v} \) adults in its lifetime. Denote \( R_v = \frac{g\lambda_v}{d_v(d_L + \lambda_v)} \). Borrowing the concept of the basic reproduction number (Anderson and May 1991; Diekmann et al. 2009), we call \( R_v \) the vector reproduction number. It is clear that when \( R_v \leq 1 \), system (4) has only one equilibrium \((0,0)\). However, system (4) admits a positive equilibrium \((L_v^*, N_v^*)\) when \( R_v > 1 \), where

\[
L_v^* = \frac{1}{\alpha} \left( g \frac{\lambda_v}{d_v} - (d_L + \lambda_v) \right) \quad \text{and} \quad N_v^* = \frac{\lambda_v}{d_v} \frac{d_L + \lambda_v}{\alpha} (R_v - 1).
\]

Let \( f(x) = \begin{pmatrix} g_{x_2} - d_{Lx_1} - \alpha x_1^2 - \lambda_v x_1 \\ \lambda_v x_1 - d_{ax_2} \end{pmatrix} \), then \( f : \mathbb{R}_+^2 \to \mathbb{R}^2 \) is a continuously differentiable map. Moreover, \( f \) admits the following properties:

1. \( f \) is cooperative on \( \mathbb{R}_+^2 \) and \( Df(x) = (\frac{\partial f_i}{\partial x_j})_{1 \leq i,j \leq 2} \) is irreducible for every \( x \in \mathbb{R}_+^2 \);
2. \( f(0) = 0 \) and \( f_i(x) \geq 0 \) for all \( x \in \mathbb{R}_+^2 \) with \( x_i = 0, i = 1, 2 \);
3. \( f \) is strictly sublinear on \( \mathbb{R}_+^2 \), i.e. \( f(px) > pf(x) \) for any \( p \in (0,1) \) and \((x_1, x_2) \in \text{Int}(\mathbb{R}_+^2)\).
Since $Df(0) = \left(\begin{array}{cc} -dL - \lambda_v g & 0 \\ \lambda_v & -d_v \end{array}\right)$, the spectral bound of $Df(0)$, $s(Df(0)) := \max\{\text{Re} \lambda : \det(\lambda - Df(0)) = 0\}$, has the same sign as $R_v - 1$. Hence, there exists a positive equilibrium $(L_v^*, N_v^*)$ for system (4) when $s(Df(0)) > 0$. It then follows from Zhao and Jing (1996, Corollary 3.2) that the subsequent result holds.

**Lemma 2.1** The following statements are valid:

(i) If $R_v \leq 1$, the trivial equilibrium $(0, 0)$ is globally asymptotically stable for system (4) in $\mathbb{R}^2_+$;

(ii) If $R_v > 1$, the positive equilibrium $(L_v^*, N_v^*)$ is globally asymptotically stable for system (4) in $\mathbb{R}^2_+ \setminus \{(0, 0)\}$.

The previous result indicates that the mosquito population will die out if the vector reproduction number is less than or equal to unity, while the mosquito population will eventually stabilize at a positive equilibrium $(L_v^*, N_v^*)$ if the vector reproduction number is greater than one. If $(L_v(t), N_v(t)) \to (L_v^*, N_v^*)$ as $t \to \infty$, the last two equations in system (3) give rise to the following limiting system:

\[
\begin{align*}
\frac{dI_v(t)}{dt} &= c\beta(N_v^* - I_v) \frac{I_h}{N_h} - d_v I_v, \\
\frac{dI_h(t)}{dt} &= b\beta(N_h - I_h) \frac{I_v}{N_h} - (d_h + \rho)I_h.
\end{align*}
\] (5)

It is clear that system (5) has the same form as the classical Ross–Macdonald model (Aron and May 1982). We can define the basic reproduction ratio of this system by the next generation operator approach (Diekmann et al. 2009; van den Driessche and Watmough 2002). This reproduction number turns out to be

\[
R_0 = \sqrt{b\beta \frac{1}{d_v} \frac{1}{(d_h + \rho)} c\beta \frac{1}{N_h} \frac{\lambda_v}{d_v} \frac{1}{\alpha} \left(\frac{\lambda_v}{d_v} - (d_L + \lambda_v)\right)}.
\]

Biologically, $(R_0)^2$ gives the average number of infected mosquitoes (humans) caused by one typical infected mosquito (human) in completely susceptible populations. It is easy to observe that when $R_0 \leq 1$, the limiting system (5) has only one trivial equilibrium $(0, 0)$. If $R_0 > 1$, system (5) has a positive equilibrium $(I_v^*, I_h^*)$ with

\[
I_v^* = \frac{(d_h + \rho)d_v N_h (R_0^2 - 1)}{bc\beta^2 + b\beta d_v},
\]

and

\[
I_h^* = \frac{bc\beta^2 N_v^* N_h - d_v (d_h + \rho) N_h^2}{bc\beta^2 N_v^* + c\beta (d_h + \rho) N_h} = \frac{d_v (d_h + \rho) N_h^2 (R_0^2 - 1)}{bc\beta^2 N_v^* + c\beta (d_h + \rho) N_h}.
\]

Let $B := [0, N_v^*] \times [0, N_h]$. It then follows that $\omega((I_v(0), I_h(0))) \subset B$, where $\omega((I_v(0), I_h(0)))$ is the omega limit set of $(I_v(0), I_h(0)) \in \mathbb{R}^2_+$ for the solution semiflow of system (5). Moreover, $B$ is positively invariant and system (5) is cooperative in $B$. By using Zhao and Jing (1996, Corollary 3.2) on the subset $B$, as argued in the proof...
of Lemma 2.1, we have the following threshold-type result for the classical Ross–Macdonald model.

**Lemma 2.2** The following statements are valid:

(i) If $R_0 \leq 1$, the trivial equilibrium $(0, 0)$ is globally asymptotically stable for system (5) in $\mathbb{R}_+^2$;

(ii) If $R_0 > 1$, the limiting system (5) admits a unique positive equilibrium $(I_v^*, I_h^*)$, and it is globally asymptotically stable for system (5) in $\mathbb{R}_+^2 \setminus \{(0, 0)\}$.

Lemmas 2.1 and 2.2 show that $R_v$ and $R_0$ are threshold parameters for vector sustainment and disease persistence, respectively. Our next task is to show that these two reproduction numbers also serve as important indexes for the global dynamics of the predator-free system (3). We refer the reader to Appendix A for a detailed proof.

**Theorem 2.2** Let $(L_v(t), N_v(t), I_v(t), I_h(t))$ be the solution of system (3) through $(L_v(0), N_v(0), I_v(0), I_h(0))$. The following statements are valid:

(i) If $R_v \leq 1$, $(0, 0, 0, 0)$ is globally attractive for system (3) in $X_1$;

(ii) If $R_v > 1$ and $R_0 \leq 1$, then $\lim_{t \to \infty} (L_v(t), N_v(t), I_v(t), I_h(t)) = (L_v^*, N_v^*, 0, 0)$ for all initial values in Int($X_1$);

(iii) If $R_v > 1$ and $R_0 > 1$, there exists a positive equilibrium $(L_v^*, N_v^*, I_v^*, I_h^*)$, and it is globally attractive for system (3) in Int($X_1$).

The previous theorem indicates that the long-time behaviour of solutions can be completely determined by two reproduction numbers, and that the parameter space can be divided into three regions to have different global attractors for system (3).

### 2.3 Malaria Transmission with Predators

In this subsection, we study the malaria transmission when larvivorous fish is introduced as a control measure and investigate the dynamics of system (2). We first study the subsystem for the mosquito and predator populations. It is easy to see that population sizes of mosquitoes and their predators are governed by the following system:

$$
\begin{align*}
\frac{dL_v(t)}{dt} &= gN_v - d_LL_v - \alpha L_v^2 - \lambda_v L_v - \gamma L_v P, \\
\frac{dN_v(t)}{dt} &= \lambda_v L_v - d_v N_v, \\
\frac{dP(t)}{dt} &= k\gamma L_v P - d_P P. 
\end{align*}
$$

Since $P(t) \geq 0, \forall t \geq 0$, we have the following comparison relation:

$$
\begin{align*}
\frac{dL_v(t)}{dt} &\leq gN_v - d_LL_v - \alpha L_v^2 - \lambda_v L_v, \\
\frac{dN_v(t)}{dt} &= \lambda_v L_v - d_v N_v.
\end{align*}
$$
By the comparison principle and Lemma 2.1, we obtain that $L_v(t) \to 0$ and $N_v(t) \to 0$ as $t \to \infty$ when $R_v \leq 1$. Using the theory of internally chain transitive sets (see, e.g. Hirsch et al. 2001; Zhao 2003), as argued in the proof of Theorem 2.2, we have the following result.

**Theorem 2.3** Let $(L_v(t), N_v(t), P(t))$ be the solution of system (6) through $(L_v(0), N_v(0), P(0)) \in \mathbb{R}_+^3$. If $R_v \leq 1$, then $\lim_{t \to \infty} (L_v(t), N_v(t), P(t)) = (0, 0, 0)$.

Biologically, it is easy to see that $k\gamma \left( \frac{1}{\alpha} \left( g \frac{dL}{dv} - dL - \lambda v \right) \right)$ accounts for the mean number of the offspring which can be reproduced by index larvivorous fish when the larval mosquito population stabilizes at $L^*_v$ (recall that $L^*_v = \frac{1}{\alpha} \left( g \frac{dL}{dv} - dL - \lambda v \right)$), and that $\frac{1}{d_p}$ is the average lifespan of larvivorous fish. Hence, the product $k\gamma \frac{1}{d_p} \alpha \left( g \frac{dL}{dv} - dL - \lambda v \right)$ gives the expected number of larvivorous fish produced by typical larvivorous fish in its lifetime. Set $R_p = k\gamma \frac{1}{d_p} \alpha \left( g \frac{dL}{dv} - dL - \lambda v \right)$. Similar to the concept of the basic reproduction number, we call $R_p$ the predator reproduction number. The subsequent result shows that the predator cannot sustain itself if the predator reproduction number is not greater than unity.

**Theorem 2.4** Let $(L_v(t), N_v(t), P(t))$ be the solution of system (6) through $(L_v(0), N_v(0), P(0)) \in \mathbb{R}_+^3$ with $L_v(0) > 0$ and $N_v(0) > 0$. If $R_v > 1$ and $R_p \leq 1$, then

$$\lim_{t \to \infty} (L_v(t), N_v(t), P(t)) = (L^*_v, N^*_v, 0).$$

On the other hand, if the predator reproduction number exceeds one, that is $k\gamma \left( g \frac{dL}{dv} - dL - \lambda v \right) > d_p$, there exists a positive equilibrium $(\hat{L}_v, \hat{N}_v, \hat{P})$, where

$$\hat{L}_v = \frac{d_p}{k\gamma}, \quad \hat{N}_v = \frac{\lambda_v}{d_v} \hat{L}_v \quad \text{and} \quad \hat{P} = \frac{\alpha d_p}{k\gamma^2} (R_p - 1).$$

Our next goal is to show that when $R_p > 1$, the solutions of system (6) will converge to the unique positive equilibrium.

**Theorem 2.5** Let $(L_v(t), N_v(t), P(t))$ be the solution of system (6) through $(L_v(0), N_v(0), P(0)) \in \mathbb{R}_+^3$. If $R_p > 1$, then $\lim_{t \to \infty} (L_v(t), N_v(t), P(t)) = (\hat{L}_v, \hat{N}_v, \hat{P})$ for all $L_v(0) > 0$, $N_v(0) > 0$ and $P(0) > 0$.

The key ideas to prove Theorems 2.4 and 2.5 are similar. We first show that the system is uniformly persistent with respect to a specific set. By choosing suitable Lyapunov functions and using the LaSalle’s invariance principle (LaSalle 1976), we then obtain the global attractivity results. In our proof, we take a widely used type of Lyapunov functions (see, e.g. Guo and Li 2006; Korobeinikov and Maini 2004; Ma et al. 2003; Zhang et al. 2000 and references therein). For detailed proofs of Theorems 2.4 and 2.5, we refer the reader to Appendix B and Appendix C, respectively. We should point out that a similar result is given in Zhang et al. (2000) when there is a density-dependent death rate for the predator population.
Theorem 2.5 implies that the adult mosquito population will stabilize at $\hat{N}_v$ if the predator reproduction number ($R_p$) is greater than one. In this situation, if we denote
\[
R^c_0 = \sqrt{\frac{bc\beta^2}{(d_h + \rho)d_vN_h}} = \sqrt{\frac{1}{(d_h + \rho)}\frac{\lambda_v d_p}{d_v k\gamma}},
\]
the value of $(R^c_0)^2$ gives the average number of infectious mosquitoes (humans) reproduced by a typical infectious mosquito (human) in its infection period, with the introduction of larvivorous fish (a control measure). We call $R^c_0$ the control reproduction ratio. It then follows from Lemma 2.2 that when $R^c_0 > 1$, the classical Ross–Macdonald model (5) with $N^*_v$ replaced by $\hat{N}_v$ has a positive equilibrium $(\hat{I}_v, \hat{I}_h)$, where
\[
\hat{I}_v = \frac{(d_h + \rho)d_vN_h}{bc\beta^2 + b\beta d_v}((R^c_0)^2 - 1)
\]
and
\[
\hat{I}_h = \frac{d_v(d_h + \rho)N^2_h}{bc\beta^2 + c\beta(d_h + \rho)N_h}((R^c_0)^2 - 1).
\]
Using the theory of internally chain transitive sets (see, e.g. Hirsch et al. 2001; Zhao 2003), as argued in the proof of Theorem 2.2, we then have the following result.

**Theorem 2.6** Let $(L_v(t), N_v(t), I_v(t), P(t), I_h(t))$ be the solution of system (2) through $(L_v(0), N_v(0), I_v(0), P(0), I_h(0))$. The following statements are valid:

(i) If $R_v \leq 1$, $(0, 0, 0, 0, 0)$ is globally attractive for system (2) in $X$;

(ii) If $R_v > 1$, $R_p \leq 1$ and $R_0 \leq 1$,

\[
\lim_{t \to \infty} (L_v(t), N_v(t), I_v(t), P(t), I_h(t)) = (L^*_v, N^*_v, 0, 0, 0)
\]

for all initial values in $\text{Int}(X)$;

(iii) If $R_v > 1$, $R_p \leq 1$ and $R_0 > 1$,

\[
\lim_{t \to \infty} (L_v(t), N_v(t), I_v(t), P(t), I_h(t)) = (L^*_v, N^*_v, I^*_v, 0, I^*_h)
\]

for all initial values in $\text{Int}(X)$;

(iv) If $R_v > 1$, $R_p > 1$ and $R^c_0 \leq 1$,

\[
\lim_{t \to \infty} (L_v(t), N_v(t), I_v(t), P(t), I_h(t)) = (\hat{L}_v, \hat{N}_v, 0, \hat{P}, 0)
\]

for all initial values in $\text{Int}(X)$;

(v) If $R_v > 1$, $R_p > 1$ and $R^c_0 > 1$,

\[
\lim_{t \to \infty} (L_v(t), N_v(t), I_v(t), P(t), I_h(t)) = (\hat{L}_v, \hat{N}_v, \hat{I}_v, \hat{P}, \hat{I}_h)
\]

for all initial values in $\text{Int}(X)$.

Theorem 2.6 implies that the global dynamics of our model system can be completely determined by four threshold parameters: the vector reproduction number $R_v$, the basic reproduction number $R_0$, the predator reproduction number $R_p$ and the control reproduction number $R^c_0$, and there are five possible community compositions.
3 Numerical Simulations

In this section, we first present some simulations which illustrate our analytic results.

3.1 Different Community Components

Almost 200 fish species are known to feed on mosquito larvae (Jenkins 1964) and different species have different efficacy in controlling the disease in different ecological settings. Introduction of different fish species may give rise to different potential outcomes of our model (as shown in Theorem 2.6). To do this, we first choose a set of default parameters which are biologically accepted. By changing some coefficients to satisfy different conditions in Theorem 2.6, we simulate the long-time population sizes of the larval mosquitoes, infectious mosquitoes, infectious humans and the predator.

We adopt some parameter values from Hancock and Godfray (2007) and references therein except $d_h$, $N_h$, $\gamma$, $k$, and $d_p$. These values are roughly consistent with $P. falciparum$ transmitted by Anopheles Gambiae. We suppose that the life expectancy of humans is 70 years, then $d_h = \frac{1}{70 \times 365} \text{ d}^{-1}$. For illustration, we choose $\gamma = 0.01$, $k = 0.0005$, $d_p = \frac{1}{365}$, and $N_h = 1000$. The default parameters are summarized in Table 1.

To get potential community compositions of the model, we change the reproduction numbers by varying some parameters, while keeping others as default parameters. The observed population dynamics of four components (larval mosquitoes, infectious mosquitoes, infectious humans and the predator) are shown in Fig. 1.

In Fig. 2, we simulate the impact of larvivorous fish on the disease control. Here we assume that the maximum lifespan of an adult mosquito is 16 days (that is, $\frac{1}{d_v} \leq 16$) and the human biting rate of mosquitoes is between 0.1 and 0.3 (that is, $\beta \in [0.1, 0.3]$). It is easy to see from Fig. 2 that the high biting rate (corresponding to large values of $\beta$) and low efficacy of adulticiding (corresponding to small values of mosquito death rate $d_v$) make $R_0 > 1$ and $R_0^c > 1$. This indicates that the disease will eventually stabilize at a positive state (Theorem 2.6) and persist in the human population. When the human biting rate is 0.1, the disease will be eradicated if the adulticiding can ensure that the mean lifespan of mosquitoes is less than 12 days (this strategy results in $R_0 < 1$ in the top picture of Fig. 2). If the larvivorous fish is introduced and the adulticiding can ensure the mean lifespan of mosquitoes to be less than 15.7 days, the strategies combined with the larvivorous fish and the adulticiding can eradicate the disease (these combined strategies make $R_0^c < 1$ in the bottom picture of Fig. 2). On the other hand, when the mean lifespan of adult mosquitoes is 10 days,

<table>
<thead>
<tr>
<th>Parameter</th>
<th>$d_L$</th>
<th>$d_v$</th>
<th>$g$</th>
<th>$b$</th>
<th>$c$</th>
<th>$\beta$</th>
<th>$\rho$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>0.1</td>
<td>0.1</td>
<td>30</td>
<td>0.5</td>
<td>0.5</td>
<td>0.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Parameter</td>
<td>$d_h$</td>
<td>$N_h$</td>
<td>$\alpha$</td>
<td>$\lambda_v$</td>
<td>$\gamma$</td>
<td>$k$</td>
<td>$d_p$</td>
</tr>
<tr>
<td>Value</td>
<td>$\frac{1}{70 \times 365}$</td>
<td>1000</td>
<td>0.05</td>
<td>$\frac{1}{16}$</td>
<td>0.01</td>
<td>0.0005</td>
<td>$\frac{1}{365}$</td>
</tr>
</tbody>
</table>
the disease will be eradicated if people protect themselves to make the human biting rate of mosquitoes to be less than 0.14 ($R_0 < 1$ in the top picture of Fig. 2). If the larvivorous fish is introduced and the human biting rate of mosquitoes is less than...
Fig. 2 Two (basic/control) reproduction numbers as functions of $\beta$ (representing the use of bed nets) and $\frac{1}{d_v}$ (representing the use of adulticides). Parameters are chosen as those in Table 1 except $k$, $\beta$ and $d_v$. Here $k = 0.001$, $\beta$ and $d_v$ are variable.

0.16, the disease will die out ($R_0^c < 1$ in the bottom picture of Fig. 2). Hence, introduction of the larvae predator can be incorporated into an integrated strategy for disease control.

Next, we implement a case study for two fish species in specific ecological settings.

3.2 A Case Study

In this subsection, we investigate the efficacy of two different fish species, *Orechromis niloticus* L. and *Oreochromis spilurus*, on malaria transmission. We use same parameters as those in Table 1 except $k$, $\gamma$ and $d_p$, which represent the fish predation potential.

In Howard et al. (2007), Howard, Zhou and Omlin reported that *Orechromis niloticus* L. can dramatically cause a 94% reduction in the population size of larval mosquitoes *Anopheles gambiae s.l.* in Kisii Central District of western Kenya. From our
theoretical results, we can see that the equilibria for the population sizes of larval mosquitoes, $L^*_v$ and $\hat{L}_v$ (corresponding to two different settings without and with fish, respectively) can be expressed by:

$$L^*_v = \frac{1}{\alpha} \left( g \frac{\lambda_v}{d_v} - (d_L + \lambda_v) \right)$$  and  $$\hat{L}_v = \frac{d_p}{k \gamma}.$$

Hence, we have $\hat{L}_v = (1 - 94\%) L^*_v$, that is

$$\frac{d_p}{k \gamma} = 6\% \times \frac{1}{\alpha} \left( g \frac{\lambda_v}{d_v} - (d_L + \lambda_v) \right) = 22.26.$$

In this case, we can compute the reproduction numbers $R_0 = 2.28$ and $R^c_0 = 0.56$. Thus, the community components are similar to Fig. 1(d), implying that $O. niloticus$ can indirectly control malaria in this setting.

However, introducing $Oreochromis spilurus$ into the water storage container in Somalia produces a mean reduction of 52.8% in larval mosquitoes (Mohamed 2003). For the predation efficacy of $O. spilurus$, we have this relation: $\hat{L}_v = (1 - 52.8\%) L^*_v$, implying that the population size of larval mosquitoes is reduced to 47.2% of its saturated value by fish introduction. Hence, $\frac{d_p}{k \gamma} = 175.47$. In this case, $R_0 = 2.28$ and $R^c_0 = 1.57$. The final outcome of community components should be similar to Fig. 1(e). In this setting, the population sizes of infectious humans without and with fish are $I^*_h = 627.3$ and $\hat{I}_h = 367.6$, respectively. Although the disease remains endemic in the case of $O. spilurus$ introduction, the fish can drastically reduce the size of the infectious human population.

4 Discussion

In this paper, we discussed a mathematical model designed to describe vital dynamics of malaria transmission with vector predators, aiming to highlight practical procedures for the introduction of predators as a biological control method.

We coupled an age-structured prey–predator model with the Ross–Macdonald model. The age-structured prey–predator system describes the vector–larvivorous fish interaction with the structured mosquito population, while the Ross–Macdonald model describes the vital cross-transmission of malaria parasites between humans and mosquitoes.

In our model, the equations for mosquitoes and their predators can be decoupled and completely separated. We systematically used the behavioural process for sub-models to investigate the population changes on the long term. By utilizing the theories of monotone dynamical systems, Lyapunov functions, and internally chain transitive sets, we completely investigated the global dynamics of this model. We derived full characterization of the global behaviour of the model, and showed that the parameter space can be divided into five parts according to global attractors of the system.

Our main result (Theorem 2.6) indicates that three scenarios exist for disease eradication: (1) $R_v \leq 1$; (2) $R_0 \leq 1$; (3) $R^c_0 \leq 1$. In order to control the disease, we can use the larvicides or adulticides to reduce the vector reproduction number to be less
than unity (Scenario (1)). The integrated strategy combined with larviciding, adulticiding, bed nets, prompt treatments and vaccination can be used to reduce the basic reproduction number to be less than one (Scenario (2)). If the larvivorous fish is successfully introduced ($R_p > 1$), the integrated strategy combined with adulticiding, prompt treatments, bed nets, vaccination can be implemented to let Scenario (3) happen.

If the predator is aggressive enough (for example, the fish *Orechromis niloticus* L.), $R_0^c$ can be reduced to be less than unity. In this case, the infection can be eradicated. Even though the fish is not so aggressive (for example, the fish *Oreochromis spilurus*) but can sustain itself, it is easy to observe that $R_0^c < R_0$ and $\hat{I}_h < I^*_h$ (see Sect. 3). Hence, the introduction of larvivorous fish has an important effect on malaria control. It may increase the extinction probability of malaria and reduce the prevalence of infection. On the other hand, larvivorous fish provides an opportunity to eradicate malaria locally in combination with other methods such as insecticide-treated nets (ITNs) and prompt treatments. Although the use of predators can not control the disease solely, it may dramatically decrease the population size of infectious humans and slow down the initial speed of disease spread, which in turn, will earn important time for vaccine and drug treatment development for other emerging mosquito borne diseases.

It is easy to see that the larval death rate $d_L$ is not incorporated in the expressions of the control reproduction number $R_0^c$ and the population size of infectious humans $\hat{I}_h$ at the positive equilibrium. Thus, increasing the larval death rate may not have effect on malaria transmission. As pointed out in Jacob et al. (1982), larviciding, a standard method to increase the larval death rate, may also increase the death rate of larvivorous fish $d_p$, which will subsequently increase $R_0^c$ and $\hat{I}_h$. In this sense, using the larvicides, a common method for malaria control, may have negative effects on malaria containing. Therefore, we should carefully design the integrated strategies, which calls for more field work.

In this work, the dynamics of a malaria model with larvivorous fish is fully investigated in the absence of the disease-induced death rate. Extension of our framework to include a disease-induced death rate is an interesting future work. Incorporating age-structured culling for malaria is also another interesting topic in the future. For more details about culling strategies for the vector population, we refer the reader to reference (Gourley et al. 2007). Note that we did not consider seasonal effects on mosquito dynamics in this paper. In the seasonally forced case, although we can get a similar result (see Lou and Zhao 2010; Zhao and Jing 1996) for the periodic Ross–Macdonald model via the theory of monotone dynamical systems, the Lyapunov function method may fail to work for the periodic prey–predator system. This is another challenging problem for future investigation.

We hope that this paper would lead to a better understanding of the vector-borne diseases with introduction of larval vector predators and provide new conceptual tools for the advancement of our knowledge to this important subject.

**Acknowledgement**  We are grateful to anonymous referees for their careful reading and helpful suggestions which led to an improvement of our original manuscript.
Appendix A: Proof of Theorem 2.2

Our key idea to prove Theorem 2.2 is to use the theory of internally chain transitive sets, see, e.g. (Hirsch et al. 2001; Zhao 2003).

Let $\Phi(t)$ be the solution semiflow of system (3) on $X_1$, that is,

$$
\Phi(t)(L_v(0), N_v(0), I_v(0), I_h(0)) = (L_v(t), N_v(t), I_v(t), I_h(t)).
$$

Then $\Phi(t)$ is compact for each $t > 0$. Let $\omega(L_v(0), N_v(0), I_v(0), I_h(0))$ be the omega limit set of $\Phi(t)(L_v(0), N_v(0), I_v(0), I_h(0))$. It then follows from Hirsch et al. (2001, Lemma 2.1′) (see also Zhao 2003, Lemma 1.2.1′) that $\omega$ is an internally chain transitive set for $\Phi(t)$.

(i) In the case where $R_v \leq 1$, we have $L_v(t) \to 0$, $N_v(t) \to 0$ and $I_v(t) \to 0$ as $t \to \infty$. Hence, we have $\omega = \{(0, 0, 0)\} \times \omega_1$ for some $\omega_1 \subset \mathbb{R}$. It is easy to see that

$$
\Phi(t)|_\omega(0, 0, 0, I_h(0)) = (0, 0, 0, \Phi_1(t)(I_h(0))),
$$

where $\Phi_1(t)$ is the solution semiflow associated with the following equation:

$$
\frac{dI_h}{dt} = -(d_h + \rho)I_h.
$$

(7)

Since $\omega$ is an internally chain transitive set for $\Phi(t)$, it easily follows that $\omega_1$ is an internally chain transitive set for $\Phi_1(t)$. Since $\{0\}$ is globally asymptotically stable for (7), Hirsch et al. (2001, Theorem 3.2 and Remark 4.6) implies that $\omega_1 = \{0\}$. Thus, we have $\omega = \{(0, 0, 0, 0)\}$, and hence

$$
\lim_{t \to \infty} (L_v(t), N_v(t), I_v(t), I_h(t)) = (0, 0, 0, 0).
$$

This proves the statement (i).

(ii) In the case where $R_v > 1$, we have $L_v(t) \to L^*_v$, $N_v(t) \to N^*_v$ as $t \to \infty$ for any $L_v(0) > 0$ and $N_v(0) > 0$. Thus, $\omega = \{(L^*_v, N^*_v)\} \times \omega_2$ for some $\omega_2 \subset \mathbb{R}^2$, and

$$
\Phi(t)|_\omega(L^*_v, N^*_v, I_v(0), I_h(0)) = (L^*_v, N^*_v, \Phi_2(t)(I_v(0), I_h(0))),
$$

where $\Phi_2(t)$ is the solution semiflow associated with the following system:

$$
\begin{align*}
\frac{dI_v(t)}{dt} &= c\beta(N^*_v - I_v) \frac{I_h}{N_h} - d_v I_v, \\
\frac{dI_h(t)}{dt} &= b\beta(N_h - I_h) \frac{I_v}{N_h} - (d_h + \rho)I_h.
\end{align*}
$$

(8)

Since $\omega$ is an internally chain transitive set for $\Phi(t)$, it is easy to see that $\omega_2$ is an internally chain transitive set for $\Phi_2(t)$. Since $R_0 \leq 1$, the trivial equilibrium $\{(0, 0)\}$ is globally asymptotically stable for system (8) according to Lemma 2.2. It then follows from Hirsch et al. (2001, Theorem 3.2 and Remark 4.6) that $\omega_2 = \{(0, 0)\}$. This proves $\omega = \{(L^*_v, N^*_v, 0, 0)\}$, and hence, the statement (ii) holds.
(iii) In the case where \( R_v > 1 \) and \( R_0 > 1 \), we have \( L_v(t) \to L_v^* \), \( N_v(t) \to N_v^* \) as \( t \to \infty \). We have \( \omega = \{(L_v^*, N_v^*)\} \times \omega_3 \) for some \( \omega_3 \subset \mathbb{R}^2 \), and

\[
\Phi(t)|_{\omega}(L_v^*, N_v^*, I_v(0), I_h(0)) = (L_v^*, N_v^*, \Phi_2(t)(I_v(0), I_h(0))),
\]

where \( \Phi_2(t) \) is the solution semiflow of system (8). Since \( \omega \) is an internally chain transitive set for \( \Phi(t) \), it follows that \( \omega_3 \) is an internally chain transitive set for \( \Phi_2(t) \).

We claim that \( \omega_3 \neq \{(0,0)\} \) for all \( I_v(0) > 0 \) and \( I_h(0) > 0 \). Assume that, by contradiction, \( \omega = \{(L_v^*, N_v^*, 0, 0)\} \) for some \( I_v(0) > 0 \) and \( I_h(0) > 0 \). Then, we have

\[
\lim_{t \to \infty} (L_v(t), N_v(t), I_v(t), I_h(t)) = (L_v^*, N_v^*, 0, 0).
\]

Since \( R_0 > 1 \), there exists some \( \delta > 0 \) such that

\[
bc\beta^2 \frac{N_v^* - \delta}{(d_h + \rho)d_v N_h} > 1.
\]

Moreover, there exists some \( T_0 > 1 \) such that

\[
\left|(L_v(t), N_v(t), I_v(t), I_h(t)) - (L_v^*, N_v^*, 0, 0)\right| < \delta, \quad \forall t > T_0.
\]

Hence, we have

\[
\frac{dI_v(t)}{dt} \geq c\beta(N_v^* - \delta - I_v) \frac{I_h}{N_h} - d_v I_v,
\]

\[
\frac{dI_h(t)}{dt} = b\beta(N_h - I_h) \frac{I_v}{N_h} - (d_h + \rho) I_h,
\]

for all \( t > T_0 \). It then follows from Lemma 2.2 that the following system

\[
\frac{du_1(t)}{dt} = c\beta(N_v^* - \delta - u_1) \frac{u_2}{N_h} - d_v u_1,
\]

\[
\frac{du_2(t)}{dt} = b\beta(N_h - u_2) \frac{u_1}{N_h} - (d_h + \rho) u_2
\]

admits a positive equilibrium \( (u_1^*, u_2^*) \) such that

\[
\lim_{t \to \infty} (u_1(t), u_2(t)) = (u_1^*, u_2^*), \quad \forall (u_1(0), u_2(0)) \in \mathbb{R}^2_+ \setminus \{(0,0)\}.
\]

By the comparison principle, we have

\[
\liminf_{t \to \infty} (I_v(t), I_h(t)) \geq (u_1^*, u_2^*),
\]

a contradiction. Since \( \omega_3 \neq \{(0,0)\} \) and \( (I_v^*, I_h^*) \) is globally asymptotically stable for system (8) in \( \mathbb{R}^2_+ \setminus \{(0,0)\} \), it follows that \( \omega_3 \cap W^s((I_v^*, I_h^*)) \neq \emptyset \), where \( W^s((I_v^*, I_h^*)) \) is the stable set for \( (I_v^*, I_h^*) \). By Hirsch et al. (2001, Theorem 3.1 and Remark 4.6), we then get \( \omega_3 = \{(I_v^*, I_h^*)\} \). Thus, \( \omega = \{(L_v^*, N_v^*, I_v^*, I_h^*)\} \), and hence, the statement (iii) is valid.
Appendix B: Proof of Theorem 2.4

Denote $X_0 := \{(L_v, N_v, P) \in \mathbb{R}_+^3 : L_v > 0, N_v > 0\}$, $\partial X_0 := \mathbb{R}_+^3 \setminus X_0 = \{(L_v, N_v, P) \in \mathbb{R}_+^3 : L_v = 0 \text{ or } N_v = 0\}$ and $X_{\partial} := \{(L_v(0), N_v(0), P(0)) \in \partial X_0 : (L_v(t), N_v(t), P(t)) \in \partial X_0, \forall t \geq 0\}$. It is clear that $X_{\partial} = \{(L_v, N_v, P) \in \mathbb{R}_+^3 : L_v = 0, N_v = 0\}$.

By the form of system (6), it is easy to see that both $\mathbb{R}_+^3$ and $X_0$ are positively invariant. We first show that when $R_v > 1$, system (6) is uniformly persistent with respect to $(X_0, \partial X_0)$ in the sense that there exists some $\epsilon > 0$ such that

$$\liminf_{t \to \infty} L_v(t) > \epsilon \quad \text{and} \quad \liminf_{t \to \infty} N_v(t) > \epsilon$$

for all $(L_v(0), N_v(0), P(0)) \in X_0$.

Since $R_v > 1$, there exists some $\delta > 0$ such that $g \lambda_v \frac{d}{dv} \left( dL_v + \lambda_v + \gamma \delta \right) > 1$ and $\frac{1}{\alpha} (\frac{g \lambda_v}{d} - dL - \lambda_v - \gamma \delta) > \delta$. Then we have the following claim, which says that $(0, 0, 0)$ is a weaker repellor for $X_0$.

**Claim** $\limsup_{t \to \infty} \|(L_v(t), N_v(t), P(t))\| \geq \delta$ for any $(L_v(0), N_v(0), P(0)) \in X_0$.

Suppose, by contradiction, that

$$\limsup_{t \to \infty} \|(L_v(t), N_v(t), P(t))\| < \delta \quad \text{for some } (L_v(0), N_v(0), P(0)) \in X_0.$$

Then there exists a $T_0 > 0$ such that $L_v(t) < \delta$, $N_v(t) < \delta$ and $P(t) < \delta$ for $t \geq T_0$. Thus, we have

$$\frac{dL_v(t)}{dt} \geq g N_v - dL_v - \alpha L_v^2 - \lambda_v L_v - \gamma \delta L_v,$$

$$\frac{dN_v(t)}{dt} = \lambda_v L_v - d_v N_v,$$

for all $t \geq T_0$. By Lemma 2.1, there exists a positive globally asymptotically stable equilibrium $(u_1^*, u_2^*)$ for the following system:

$$\frac{du_1(t)}{dt} = gu_2 - dL u_1 - \alpha u_1^2 - \lambda_v u_1 - \gamma \delta u_1,$$

$$\frac{du_2(t)}{dt} = \lambda_v u_1 - d_v u_2.$$

Moreover, $u_1^* = \frac{1}{\alpha} (g \frac{\lambda_v}{d} - dL - \lambda_v - \gamma \delta)$ and $u_2^* = \frac{\lambda_v}{d} u_1^*$. Hence, $\limsup_{t \to \infty} L_v(t) \geq \lim_{t \to \infty} u_1(t) = u_1^* > \delta$, a contradiction.

Let $\Psi(t)$ be the solution semiflow associated with system (6). Then $(0, 0, 0)$ is a compact and isolated invariant set for $\Psi(t)$ in $\partial X_0$, and $\Omega(X_{\partial}) := \bigcup_{x \in X_{\partial}} \omega(x) = (0, 0, 0)$. Furthermore, no subset of $(0, 0, 0)$ forms a cycle in $\partial X_0$. In view of the claim above, $(0, 0, 0)$ is an isolated invariant set for $\Psi(t)$ in $X$ and $W^s((0, 0, 0)) \cap X_0 = \emptyset$. By (Thieme 1993, Theorem 4.6), $\Psi(t)$ is uniformly persistent with respect to $(X_0, \partial X_0)$. Thus, we have $\omega((L_v, N_v, P)) \subset X_0$ for any $(L_v, N_v, P) \in X_0$.

Define a function $V_1 : X_0 \to \mathbb{R}$ by
\[ V_1 = \left( L_v - L_v^* - L_v^* \ln \frac{L_v}{L_v^*} \right) \]
\[ \quad + \frac{g}{d_v} \left( N_v - N_v^* - N_v^* \ln \frac{N_v}{N_v^*} \right) + \frac{1}{k} P, \quad \forall (L_v, N_v, P) \in X_0. \]

It then follows that
\[
V'_1(L_v, N_v, P) = \left( 1 - \frac{L_v^*}{L_v} \right) \left( gN_v - (d_L + \lambda_v)L_v - \alpha L_v^2 - \gamma L_v P \right) \]
\[ \quad + \frac{g}{d_v} \left( 1 - \frac{N_v^*}{N_v} \right) (\lambda_v L_v - d_v N_v) \]
\[ \quad + \frac{1}{k} (k \gamma L_v P - d_p P) \]
\[ = gN_v - gL_v^* \frac{N_v}{L_v} - (d_L + \lambda_v)L_v - (d_L + \lambda_v)\alpha L_v^2 - \gamma L_v P + (d_L + \lambda_v)\alpha L_v^* L_v + \gamma L_v^* P \]
\[ \quad + \gamma L_v^* P + \frac{g}{d_v} \lambda_v L_v - gN_v - \frac{gN_v^*}{d_v} \lambda_v \frac{L_v}{N_v} + gN_v^* + \gamma L_v P - \frac{d_p}{k} P. \]

Since \( \gamma L_v^* = \frac{d_p}{k}, \quad N_v^* = \frac{\lambda_v}{d_v} L_v^* \) and \( gN_v^* = (d_L + \lambda_v)\alpha (L_v^*)^2 \), we further have
\[
V'_1(L_v, N_v, P) \]
\[ = -gL_v^* \frac{N_v}{L_v} - (d_L + \lambda_v)L_v - \alpha L_v^2 + (d_L + \lambda_v)L_v^* + \alpha L_v^* L_v \]
\[ \quad + \frac{g}{d_v} \lambda_v L_v - \frac{gN_v^*}{d_v} \lambda_v \frac{L_v}{N_v} + gN_v^* \]
\[ \leq -2gN_v^* - (d_L + \lambda_v)L_v - \alpha L_v^2 + (d_L + \lambda_v)L_v^* + \alpha L_v^* L_v + \frac{g\lambda_v}{d_v} L_v + gN_v^* \]
\[ = -g\frac{N_v^*}{d_v} - (d_L + \lambda_v)L_v - \alpha L_v^2 + (d_L + \lambda_v)\alpha L_v^* L_v + \frac{\lambda_v}{d_v} L_v \]
\[ = -(d_L + \lambda_v)L_v^* - \alpha (L_v^*)^2 - (d_L + \lambda_v)L_v - \alpha L_v^2 + (d_L + \lambda_v)L_v^* \]
\[ \quad + \alpha L_v^* L_v + \frac{g\lambda_v}{d_v} L_v \]
\[ = -\alpha (L_v^*)^2 - (d_L + \lambda_v)L_v - \alpha L_v^2 + \alpha L_v^* L_v + \frac{g\lambda_v}{d_v} L_v \]
\[ \leq \left( -\alpha L_v^* - (d_L + \lambda_v) + \frac{\lambda_v}{d_v} \right) L_v = 0. \]

Now we find the invariant set of \( \Psi (t) \) that is contained in the set
\[ \{ (L_v, N_v, P) \in X_0 : V'_1(L_v, N_v, P) = 0 \}. \]
If \( V'_1 = 0 \), we have \( L_v = L^*_v \) and \( N_v = N^*_v \). Consequently, \( \frac{dL_v(t)}{dt} = -\gamma L^*_v P \). This implies that \( P = 0 \). Thus, the only compact invariant subset of the set where \( V'_1 = 0 \) is the singleton \( \{(L^*_v, N^*_v, 0)\} \). By LaSalle’s invariance principle (LaSalle 1976), we obtain that \( (L^*_v, N^*_v, 0) \) is globally attractive in \( X_0 \).

Appendix C: Proof of Theorem 2.5

Denote \( Y_0 := \{(L_v, N_v, P) \in \mathbb{R}^3_+ : L_v > 0, N_v > 0, P > 0\}, \partial Y_0 := \mathbb{R}^3_+ \setminus Y_0 = \{(L_v, N_v, P) \in \mathbb{R}^3_+ : L_v = 0 \text{ or } N_v = 0 \text{ or } P = 0\} \) and \( Y_0 := \{(L_v(0), N_v(0), P(0)) \in \partial Y_0 : (L_v(t), N_v(t), P(t)) \in \partial Y_0, t \geq 0\} \). It is easy to see that \( Y_\partial = \{(L_v, N_v, P) \in \mathbb{R}^3_+ : L_v = 0 \text{ or } N_v = 0 \text{ or } P = 0\} \) and \( \partial Y_0 = \{(L_v(t), N_v(t), P(t)) \in \partial Y_0 \} \). By a similar argument as that in the proof of Theorem 2.4, we can show that if \( R_p > 1 \), system (6) is uniformly persistent with respect to \( (Y_0, \partial Y_0) \) in the sense that there exists some \( \epsilon > 0 \) such that \( \liminf_{t \to \infty} L_v(t) > \epsilon \), \( \liminf_{t \to \infty} N_v(t) > \epsilon \) and \( \liminf_{t \to \infty} P(t) > \epsilon \) for any \( (L_v(0), N_v(0), P(0)) \in Y_0 \).

Thus, we have \( \omega((L_v, N_v, P)) \subset Y_0 \) for any \( (L_v, N_v, P) \in Y_0 \).

Define a function \( V_2 : Y_0 \to \mathbb{R} \) by

\[
V_2(L_v, N_v, P) = \left( L_v - \hat{L}_v - \hat{L}_v \ln \frac{L_v}{\hat{L}_v} \right) + \frac{g}{d_v} \left( N_v - \hat{N}_v - \hat{N}_v \ln \frac{N_v}{\hat{N}_v} \right) + \frac{1}{k} \left( P - \hat{P} - \hat{P} \ln \frac{P}{\hat{P}} \right).
\]

We then have

\[
V'_2(L_v, N_v, P) = \left( 1 - \frac{\hat{L}_v}{L_v} \right) (gN_v - (d_L + \lambda_v)L_v - \alpha L^2_v - \gamma L_v P)
+ \frac{g}{d_v} \left( 1 - \frac{\hat{N}_v}{N_v} \right) (\lambda_v L_v - d_v N_v)
+ \frac{1}{k} \left( 1 - \frac{\hat{P}}{P} \right) (k\gamma L_v P - d_p P)
= gN_v - (d_L + \lambda_v)L_v - \alpha L^2_v - \gamma L_v P - g\hat{L}_v \frac{N_v}{L_v} + (d_L + \lambda_v)\hat{L}_v + \alpha \hat{L}_v L_v
+ \gamma \hat{L}_v P + \frac{g}{d_v} \lambda_v L_v - gN_v - \frac{g\hat{N}_v \lambda_v}{d_v} \frac{L_v}{\hat{N}_v} + g\hat{N}_v
+ \gamma L_v P - \frac{d_p}{k} P - \gamma \hat{P} L_v + \frac{d_p \hat{P}}{k}.
\]

Since \( \gamma \hat{L}_v = \frac{d_p}{k} \), \( (d_L + \lambda_v)\hat{L}_v + \alpha (\hat{L}_v)^2 + \frac{d_p}{k} \hat{P} = g\hat{N}_v \) and \( d_L + \lambda_v + \alpha \hat{L}_v + \gamma \hat{P} = \frac{g\hat{N}_v}{\hat{L}_v} \), it follows that

\[\square\]
\[ V'_2(L_v, N_v, P) = -(d_L + \lambda_v)L_v - \alpha(L_v)^2 - g\hat{L}_v \frac{N_v}{L_v} + g\hat{N}_v - \alpha(\hat{L}_v)^2 + \alpha\hat{L}_v L_v + \frac{g}{d_v}\lambda_v L_v - \frac{g\hat{N}_v\lambda_v L_v}{N_v} + g\hat{N}_v - \gamma \hat{P} L_v \]
\[ = -\frac{g\hat{N}_v}{L_v} L_v + \alpha\hat{L}_v L_v - \alpha(L_v)^2 - \alpha(\hat{L}_v)^2 + \alpha\hat{L}_v L_v + \frac{g\lambda_v}{d_v} L_v \]
\[ - \left( g\hat{L}_v \frac{N_v}{L_v} - 2g\hat{N}_v + g\frac{\hat{N}_v\lambda_v L_v}{N_v} \right). \]

Note that \( \frac{\hat{N}_v}{L_v} = \frac{\lambda_v}{d_v} \), we further obtain
\[ V'_2(L_v, N_v, P) = -\alpha\left( (L_v)^2 - 2\hat{L}_v L_v + (\hat{L}_v)^2 \right) - g\hat{N}_v \left( \frac{d_v}{\lambda_v} \frac{N_v}{L_v} - 2 + \frac{\lambda_v}{d_v} \frac{L_v}{N_v} \right) \leq 0. \]

Now we find the invariant set of \( \Psi(t) \) that is contained in the set
\[ \{(L_v, N_v, P) \in Y_0 : V'_2(L_v, N_v, P) = 0\}. \]

If \( V'_2 = 0 \), we have \( L_v = \hat{L}_v \) and \( N_v = \hat{N}_v \). Consequently, \( \frac{dL_v(t)}{dt} = \gamma \hat{L}_v (\hat{P} - P) \).
This implies \( P = \hat{P} \), and the largest compact invariant subset of the set where \( V'_2 = 0 \)
is \( \{(\hat{L}_v, \hat{N}_v, \hat{P})\} \). It then follows from LaSalle’s invariance principle that \( (\hat{L}_v, \hat{N}_v, \hat{P}) \) is globally attractive in \( Y_0 \).

References