

RESEARCH

Open Access



# Accelerating mosquito population replacement: a two-dimensional model with periodic release of *Wolbachia*-infected males

Hongpeng Guo<sup>1,2\*</sup>

\*Correspondence:

[ghp8013@gzhu.edu.cn](mailto:ghp8013@gzhu.edu.cn)

<sup>1</sup>School of Mathematics and Information Science, Guangzhou University, Guangzhou, 510006, China

<sup>2</sup>Center for Applied Mathematics, Guangzhou University, Guangzhou, 510006, China

## Abstract

This study investigates strategies for accelerating mosquito population replacement through the periodic release of *Wolbachia*-infected male mosquitoes using a two-dimensional time-switching model. We obtain the existence and stability of periodic solutions within this framework and establish several sufficient conditions for eradicating wild mosquitoes by varying the release amounts of infected males. Our results indicate that accelerated replacement is feasible as long as the *Wolbachia* infection is favorable. Despite *Wolbachia* infection brings a fitness costs, effective population replacement can still be achieved if the release waiting time does not exceed a certain threshold and the release amount is sufficient to match or surpass the capacity of wild mosquitoes. However, when the release waiting time exceeds this threshold, we identify a continuous, unbounded curve that separates two boundary equilibrium points, with solutions originating from either side converging to their respective boundary equilibrium points. Numerical simulations are presented to validate our theoretical findings, highlighting the potential of this approach for effective mosquito population control.

**Mathematics Subject Classification:** 34C25; 34D20; 34D23

**Keywords:** *Wolbachia*-infected male mosquitoes; Population replacement; Periodic solutions; Global asymptotic stability

## 1 Introduction

Dengue fever, one of the most prevalent mosquito-borne diseases, is a viral infection transmitted to humans through the bites of infected mosquitoes. Currently, about half of the global population is at risk of infecting dengue. The WHO Americas region has reported 4.5 million cases and 2300 deaths, the number of cases in Asia was also high: Bangladesh (321,000 cases), Malaysia (111,400 cases), Thailand (150,000 cases), and Vietnam (369,000 cases) [1]. So far, there is no effective vaccine that prevents dengue and other significant mosquito-borne diseases [2, 3]. Therefore, controlling mosquito populations to cut off transmission pathways remains crucial for preventing these diseases. The best way to control mosquito populations is through population suppression, commonly using chemical

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

insecticides. However, this method has high costs, environmental pollution, increased resistance, and unintended harm to non-target organisms [4].

A promising and environmentally friendly approach to controlling mosquito-borne diseases involves using the endosymbiotic bacterium *Wolbachia*. Infection with *Wolbachia* in *Aedes aegypti* can greatly reduce the mosquitoes' dengue transmission potential [5]. In mosquitoes, *Wolbachia* often causes cytoplasmic incompatibility (CI). This leads to early embryonic death when *Wolbachia*-infected males mate with uninfected females [6, 7]. On the contrary, *Wolbachia*-infected females can produce viable embryos after mating with either infected or uninfected males, bringing them a reproductive advantage over uninfected females. To reduce or even eradicate the wild mosquito population, *Wolbachia*-infected male mosquitoes are continuously released into control areas. This method induces sterility and effectively suppresses target *Aedes* mosquito populations. Thus, it can reduce the spread of mosquito-borne diseases.

Numerous publications have explored the dynamics of *Wolbachia* transmission using different dynamical equations. Notable works include studies on population suppression models [8–15] and population replacement models [16–24]. Among them, Huang and Su [8, 20] considered *Wolbachia*-driven dynamics with mating competition and incomplete CI; Liu and Zhang [10, 15] established delay differential equations with stage structure to study the release strategies of sterile mosquitoes and bifurcation structures, respectively; Farkas [16] developed an age-structured model and demonstrated significant differences in the existence and stability of equilibrium solutions compared to the unstructured model; Hu and Yang [17, 21] developed stochastic differential equation models to study *Wolbachia* invasion. Yu and Zheng [12, 23] established delay differential equation models to study the suppression and replacement of mosquito populations. Additionally, Huang [18] considered a reaction–diffusion model that describes the spatial dynamics of *Wolbachia* spread in a mixed population of infected and uninfected mosquitoes. They indicated that diffusion can lower the threshold value of the infection frequency above which *Wolbachia* can invade the entire population. Li [19] developed an impulsive mosquito population model with general birth and death rate functions to study the cytoplasmic incompatibility (CI) effect caused by the mating of *Wolbachia*-infected males and uninfected females. Yu and Zheng [22] formulated discrete dynamical models to study the persistence of *Wolbachia* infection through the release of *Wolbachia*-infected mosquitoes, which display rich dynamics, including bistable, semistable, and globally asymptotically stable equilibria. Finally, there has been significant interest in periodic succession models for mosquito suppression, as seen in works such as [11, 13, 14], along with other related literature.

Furthermore, *Wolbachia* can trigger resistance in mosquito vectors to various human pathogens [5, 25]. As a result, we can release *Wolbachia*-infected female mosquitoes into control areas, gradually replacing the wild population through the reproductive advantage conferred by CI. Subsequently, *Wolbachia* induces the host to express resistance to pathogens, ultimately leading to the interruption of mosquito-borne disease transmission in the release area. Population replacement is similar to vaccinating vector insects. Field applications of *Wolbachia*-based population replacement have been carried out in 15 countries, including Australia, Indonesia, Malaysia, Brazil, and Vietnam [26–28]. However, due to the limited resources in the production of *Wolbachia*-infected mosquitoes, the possible shortage of labors and mosquito factories and the continued release of female

mosquitoes raise the risk of mosquito bites for local residents, while male mosquitoes do not bite humans. Therefore, we propose an innovative approach: initially release a small number of infected females, which makes that there are both infected and uninfected mosquitoes in the wild, then followed by the release of *Wolbachia*-infected males impulsively and periodically at discrete time points  $T_n = nT$ ,  $n = 0, 1, 2, \dots$ . This will ultimately achieve vaccination of the wild mosquito population (complete population replacement).

The primary objective of this study is based on the *Wolbachia* dynamic model, further releasing infected male mosquitoes periodically to address the following inquiries: What is the optimal frequency for releasing infected males, and how many should be released each time to guarantee the successful completion of wild mosquito vaccination (population replacement)?

Based on the aforementioned discussion and as mentioned earlier, in Sect. 2, we present a periodic release policy derived from the population replacement model, aiming to accelerate the control of wild mosquitoes. In Sect. 3, we provide essential lemmas to establish the global existence and uniqueness of the semitrivial steady states. We present our main results in Sect. 4. To illustrate our findings, we provide numerical examples to validate our theoretical analysis in Sect. 5. The paper ends with a discussion in Sect. 6 and an outlook about future work.

## 2 Model formulation

Let  $R(t)$  be the numbers of *Wolbachia*-infected male mosquitoes at time  $t$ ,  $\mathfrak{R}$  is the release rate,  $\mu_i$ ,  $i = 1, 2$ , are the density-independent death rates of the infected mosquitoes and uninfected mosquitoes, respectively. Then the dynamic of newly released *Wolbachia*-infected male mosquitoes is governed by

$$\frac{dR}{dt} = \mathfrak{R} - \mu_1 R(t), \quad t > 0. \quad (2.1)$$

We let

$$T(t) = U_f(t) + U_m(t) + I_f(t) + I_m(t)$$

denote the total population size that already is in the wild, with  $U_f(t)$ ,  $U_m(t)$ ,  $I_f(t)$ , and  $I_m(t)$  standing for the numbers of uninfected female mosquitoes, uninfected male mosquitoes, infected female mosquitoes, and infected male mosquitoes at time  $t$ , respectively. Let  $\delta_i$ ,  $i = 1, 2$ , be the density-dependent death rates of the infected mosquitoes and uninfected mosquitoes, respectively. Let  $b_I$  (resp.  $b_U$ ) be the natural birth rate of infected (or uninfected) mosquitoes and  $0 \leq \delta \leq 1$  be the proportion of individuals born female, thus the proportion of male mosquitoes born is  $1 - \delta$ . As in [29, 30], here we assume that the released infected male mosquitoes only affect the mating behavior of the wild healthy mosquitoes, without impacting their other behaviors (i.e., ignoring interspecific and intraspecific com-

petition). With perfect maternal transmission and complete CI [31–33], we have

$$\begin{cases} \frac{dI_f}{dt} = \delta b_1 I_f - \delta_1 I_f T(t) - \mu_1 I_f, \\ \frac{dI_m}{dt} = (1 - \delta) b_1 I_f - \delta_1 I_m T(t) - \mu_1 I_m, \\ \frac{dU_f}{dt} = \delta b_U U_f \frac{U_m}{R + I_m + U_m} - \delta_2 U_f T(t) - \mu_2 U_f, \\ \frac{dU_m}{dt} = (1 - \delta) b_U U_f \frac{U_m}{R + I_m + U_m} - \delta_2 U_m T(t) - \mu_2 U_m. \end{cases} \tag{2.2}$$

To reduce the dimension of the model, we set

$$x(t) = I_f + I_m \text{ and } y(t) = U_f + U_m. \tag{2.3}$$

There is equal sex determination, which means  $\delta = 1/2$  with  $I_f = I_m$  and  $U_f = U_m$ . Also, for convenience, rename the system parameters as  $b_1 = b_I/2$  and  $b_2 = b_U/2$ . Then (2.2) is reduced to

$$\begin{cases} \frac{dx}{dt} = x [b_1 - \mu_1 - \delta_1(x + y)], \\ \frac{dy}{dt} = y \left[ b_2 \frac{y}{x+y+2R(t)} - \mu_2 - \delta_2(x + y) \right], \\ \frac{dR}{dt} = \mathfrak{R} - \mu_1 R(t). \end{cases} \tag{2.4}$$

Notice that female mosquitoes can survive for more than five months with sufficient food, while the male mosquito life expectancy is only six to seven days in general [34]. Then the period during which a male mosquito can effectively mate a female mosquito is very short compared with the life span of female mosquitoes. And the only role that the *Wolbachia*-infected male mosquitoes released into the wild play in the interactive dynamics is just to mate with wild uninfected females, so that the wild female mosquito that mates with a *Wolbachia*-infected male mosquito either does not reproduce or produces eggs that will not hatch. Thus the death of those released *Wolbachia*-infected male mosquitoes can be ignored, and the number of released *Wolbachia*-infected male mosquitoes  $R(t)$  can be treated as a known function. This idea is due to Yu and Li [13, 35], and later Zheng et al. [36–38] extended this idea in mathematical modeling.

Considering the release cost, *Wolbachia*-infected male mosquitoes are released at regular intervals. Our main concerns here are the release period and the release amount: to manage the release starts at time  $t = 0$  such that  $R(t) = 0$  for  $t \leq 0$ , and that a constant amount  $r/2$  of *Wolbachia*-infected male mosquitoes are released after a constant waiting period  $T$  so that infected males are released impulsively and periodically at discrete time points  $T_n = nT$ ,  $n = 0, 1, 2, \dots$ . Let  $\bar{T}$  be the sexual lifespan of *Wolbachia*-infected male mosquitoes. Then there are three possible release strategies  $T < \bar{T}$ ,  $T = \bar{T}$ , and  $T > \bar{T}$ . In this paper, we consider focus on the case of  $T > \bar{T}$ .

For the case of  $T > \bar{T}$ ,  $R(t)$  becomes a piecewise constant, and a  $T$ -periodic function is defined as

$$R(t) = \begin{cases} r/2, & t \in [nT, nT + \bar{T}), \\ 0, & t \in [nT + \bar{T}, (n + 1)T), \end{cases} \tag{2.5}$$

for  $n = 0, 1, 2, \dots$ , where  $r$  is a constant. Then system (2.4) becomes the following two subsystems:

$$\begin{cases} \frac{dx}{dt} = x [b_1 - \mu_1 - \delta_1(x + y)], \\ \frac{dy}{dt} = y \left[ b_2 \frac{y}{x + y + r} - \mu_2 - \delta_2(x + y) \right] \end{cases} \tag{2.6}$$

for  $t \in [nT, nT + \bar{T})$ ,  $n = 0, 1, 2, \dots$ ,

$$\begin{cases} \frac{dx}{dt} = x [b_1 - \mu_1 - \delta_1(x + y)], \\ \frac{dy}{dt} = y \left[ b_2 \frac{y}{x + y} - \mu_2 - \delta_2(x + y) \right] \end{cases} \tag{2.7}$$

for  $t \in [nT + \bar{T}, (n + 1)T)$ ,  $n = 0, 1, 2, \dots$ . Here, we extend continuously to  $(0, 0)$  by the special case

$$\frac{y}{x + y} \Big|_{(0,0)} = 0,$$

and maintain this remediation in our following discussion without further notice. As we examine the issue of mosquito population replacement, it is important to note that the equilibrium point  $(0, 0)$  is always unstable. Define

$$\kappa_1 = \frac{b_1 - \mu_1}{\delta_1}, \quad \kappa_2 = \frac{b_2 - \mu_2}{\delta_2}. \tag{2.8}$$

$\kappa_1$  and  $\kappa_2$  measure the carrying capacity for a single population of infected and uninfected mosquitoes, respectively. If  $\kappa_1 > \kappa_2$ , we say that *Wolbachia* infection is favorable for infected mosquitoes, or *Wolbachia* infection brings a fitness benefit. On the other hand, if  $\kappa_1 < \kappa_2$ , we say that *Wolbachia* infection brings a fitness cost. Our main interest in this paper is to study how often, and in what amount, should the *Wolbachia*-infected male mosquitoes be released, so that the entire wild mosquito population can be accelerated replaced by *Wolbachia*-infected mosquitoes. This is achieved if the solutions of systems (2.6)–(2.7) approach steady-state  $(\kappa_1, 0)$ .

### 3 Useful lemmas and the main result of the subsystem of (2.6)–(2.7)

To process further and discuss the global asymptotic stability of  $(\kappa_1, 0)$ , we need to first study the stability of semitrivial  $T$ -periodic steady state  $(0, \hat{y}(t))$  of (2.6)–(2.7), where  $\hat{y}(t)$

is a  $T$ -periodic solution of the following equations:

$$\begin{cases} \frac{dy}{dt} = y \left[ b_2 \frac{y}{y+r} - \mu_2 - \delta_2 y \right], & \text{for } t \in [nT, nT + \bar{T}), \\ \frac{dy}{dt} = y [b_2 - \mu_2 - \delta_2 y], & \text{for } t \in [nT + \bar{T}, (n+1)T), \end{cases} \tag{3.1}$$

where  $n = 0, 1, 2, \dots$

If the release period equals the sexual lifespan of infected males, i.e.,  $T = \bar{T}$ , model (3.1) becomes

$$\frac{dy}{dt} = y \left[ b_2 \frac{y}{y+r} - \mu_2 - \delta_2 y \right], \forall t > 0. \tag{3.2}$$

For the equilibria of system (3.2), besides  $E_0 = 0$ , its component satisfies

$$y^2 + (r - \kappa_2)y + \frac{\mu_2 r}{\delta_2} = 0. \tag{3.3}$$

The corresponding discriminant for (3.3) is

$$\Delta_r = r^2 - \frac{2(b_2 + \mu_2)}{\delta_2} r + \kappa_2^2. \tag{3.4}$$

It is easy to see that

$$\begin{cases} \Delta_r = 0, & \text{if } r = r_1^* \text{ or } r = r_2^*, \\ \Delta_r > 0, & \text{if } 0 \leq r < r_1^* \text{ or } r > r_2^*, \\ \Delta_r < 0, & \text{if } r \in (r_1^*, r_2^*), \end{cases} \tag{3.5}$$

where

$$r_1^* = \frac{(b_2 + \mu_2) - 2\sqrt{b_2\mu_2}}{\delta_2}, \quad r_2^* = \frac{(b_2 + \mu_2) + 2\sqrt{b_2\mu_2}}{\delta_2}.$$

With the above preparation, we summarize the existence and stability results for the equilibria of system (3.2).

**Lemma 3.1**

- (1) If  $0 < r < r_1^*$ , then system (3.2) has the trivial equilibrium  $E_0 = 0$  and two positive equilibria

$$E_1(r) = \frac{(\kappa_2 - r) - \sqrt{\Delta_r}}{2}, \quad E_2(r) = \frac{(\kappa_2 - r) + \sqrt{\Delta_r}}{2}.$$

Furthermore,  $E_0$  and  $E_2$  are both asymptotically stable and  $E_1$  is unstable;

- (2) If  $r = r_1^*$ , then system (3.2) has the trivial equilibrium  $E_0 = 0$  and a unique positive equilibrium  $E^*(r) = \frac{\kappa_2 - r}{2}$ . The equilibrium  $E_0 = 0$  is asymptotically stable and  $E^*$  is semistable, i.e., stable from the right side and unstable from the left side;

(3) If  $r > r_1^*$ , then  $E_0 = 0$  is the only nonnegative steady-state of system (3.2) and is globally asymptotically stable.

From Lemma 3.1, we know that the wild mosquito population goes to extinction as long as the number of released infected mosquitoes remains greater than  $r_1^*$ , i.e.,  $r > r_1^*$ . Hence, in this paper, to achieve the goal of accelerated population replacement, we focus on the case of

$$T > \bar{T}, r > r_1^*. \tag{3.6}$$

Let  $y(T) = y(T; 0, \nu) = \nu$ , then  $y(t) = y(t; 0, \nu)$  is a  $T$ -periodic solution of model (3.1). To find such a periodic solution of model (3.1), we only need to find an initial value  $\nu > 0$  such that  $y(T; 0, \nu) = \nu$ . To further process, we denote

$$h(\nu) := y(T; 0, \nu), \bar{h}(\nu) := y(\bar{T}; 0, \nu). \tag{3.7}$$

Then  $h(\nu)$  and  $\bar{h}(\nu)$  are two continuously differentiable functions in  $\nu$  and  $h(0) = \bar{h}(0) = 0$ . For every  $\nu > 0$ , define two function series  $\{h_n\}$  and  $\{\bar{h}_n\}$  by

$$h_n(\nu) := y(nT; 0, \nu), \bar{h}_n(\nu) := y(nT + \bar{T}; 0, \nu), \quad n = 0, 1, 2, \dots \tag{3.8}$$

By induction, we have

$$h_{n+1}(\nu) = y(T; 0, h_n(\nu)) = h(h_n(\nu)), \bar{h}_{n+1}(\nu) = \bar{h}(\bar{h}_n(\nu)), n = 0, 1, 2, \dots \tag{3.9}$$

Before proceeding further, we first need to solve the initial value problem (3.1) with  $y(0) = \nu$ . That is,

$$\frac{dy}{dt} = \left[ \frac{b_2 y}{y + r} - \mu_2 - \delta_2 y \right] y = \frac{-\delta_2 y \left[ (y - E^*(r))^2 - \frac{\Delta_r}{4} \right]}{y + r}. \tag{3.10}$$

Then, (3.10) is equivalent to

$$\begin{cases} \left[ \frac{\alpha}{y} + \frac{\beta(y - E^*(r))}{(y - E^*(r))^2 - \frac{\Delta_r}{4}} + \frac{\gamma}{(y - E^*(r))^2 - \frac{\Delta_r}{4}} \right] dy = -\delta_2 dt \text{ for } \Delta_r < 0, \\ \left[ \frac{\alpha}{y} + \frac{\nu}{y - E_1(r)} + \frac{\sigma}{y - E_2(r)} \right] dy = -\delta_2 dt \text{ for } \Delta_r > 0, \\ \left[ \frac{\alpha}{y} + \frac{\beta}{y - E^*(r)} + \frac{\gamma}{(y - E^*(r))^2} \right] dy = -\delta_2 dt \text{ for } \Delta_r = 0, \end{cases} \tag{3.11}$$

where

$$\alpha = \frac{\delta_2}{\mu_2}, \quad \beta = -\alpha = -\frac{\delta_2}{\mu_2}, \quad \gamma = 1 + \alpha E^*(r) = 1 - \beta E^*(r) = \sqrt{\frac{b_2}{\mu_2}},$$

$$\nu = \frac{r + E_1(r)}{E_1(r)(E_1(r) - E_2(r))}, \quad \sigma = -\frac{r + E_2(r)}{E_2(r)(E_1(r) - E_2(r))}.$$

To this end, we study the following equivalent problem for the case  $\Delta_r < 0$ :

$$d \left( \ln \left( y^\alpha \left( (y - E^*(r))^2 - \frac{\Delta_r}{4} \right)^{\frac{\beta}{2}} e^{\frac{\gamma}{\sqrt{-\frac{\Delta_r}{4}}} \tan^{-1} \left( \frac{y - E^*(r)}{\sqrt{-\frac{\Delta_r}{4}}} \right)} \right) \right) = -\delta_2 dt. \tag{3.12}$$

Integrating (3.12) from 0 to  $\bar{T}$ , we see

$$\begin{aligned} & \bar{h}^\alpha(\nu) \left( (\bar{h}(\nu) - E^*(r))^2 - \frac{\Delta_r}{4} \right)^{\frac{\beta}{2}} e^{\frac{\gamma}{\sqrt{-\frac{\Delta_r}{4}}} \tan^{-1} \left( \frac{\bar{h}(\nu) - E^*(r)}{\sqrt{-\frac{\Delta_r}{4}}} \right)} \\ &= \nu^\alpha \left( (\nu - E^*(r))^2 - \frac{\Delta_r}{4} \right)^{\frac{\beta}{2}} e^{\frac{\gamma}{\sqrt{-\frac{\Delta_r}{4}}} \tan^{-1} \left( \frac{\nu - E^*(r)}{\sqrt{-\frac{\Delta_r}{4}}} \right)} e^{-\delta_2 \bar{T}}. \end{aligned} \tag{3.13}$$

By similar computation as above, one can conclude that if  $\Delta_r > 0$ , then (3.13) becomes

$$\left[ \frac{\bar{h}(\nu)}{\nu} \right]^\alpha \left[ \frac{\bar{h}(\nu) - E_1(r)}{\nu - E_1(r)} \right]^\nu \left[ \frac{\bar{h}(\nu) - E_2(r)}{\nu - E_2(r)} \right]^\sigma = e^{-\delta_2 \bar{T}}. \tag{3.14}$$

And for the case  $\Delta_r = 0$ , (3.13) becomes

$$\bar{h}^\alpha(\nu) (\bar{h}(\nu) - E^*(r))^\beta e^{-\frac{\gamma}{\bar{h}(\nu) - E^*(r)}} = \nu^\alpha (\nu - E^*(r))^\beta e^{-\frac{\gamma}{\nu - E^*(r)}} e^{-\delta_2 \bar{T}}. \tag{3.15}$$

Moreover, for  $t \in (\bar{T}, T]$ , we need to solve the initial value problem (3.1) with  $y(\bar{T}^+) = y(\bar{T})$ . By a series of calculations, we can verify that

$$\frac{h(\nu)}{\kappa_2 - h(\nu)} = \left( \frac{\bar{h}(\nu)}{\kappa_2 - \bar{h}(\nu)} \right) e^{\kappa_2 \delta_2 (T - \bar{T})}. \tag{3.16}$$

It follows from (3.13)–(3.15) and (3.16) that function  $h(\nu)$  is implicitly determined.

Since  $h(\nu) \rightarrow 0, \bar{h}(\nu) \rightarrow 0$  as  $\nu \rightarrow 0$ , we have, from (3.13), (3.14), or (3.15),

$$\lim_{\nu \rightarrow 0} \frac{\bar{h}(\nu)}{\nu} = e^{-\frac{\delta_2 \bar{T}}{\alpha}}, \tag{3.17}$$

and from (3.16) that

$$\lim_{\nu \rightarrow 0} \frac{h(\nu)}{\bar{h}(\nu)} = e^{\kappa_2 \delta_2 (T - \bar{T})}.$$

Therefore

$$\lim_{\nu \rightarrow 0} \frac{h(\nu)}{\nu} = \lim_{\nu \rightarrow 0} \left( \frac{h(\nu)}{\bar{h}(\nu)} \cdot \frac{\bar{h}(\nu)}{\nu} \right) = e^{\kappa_2 \delta_2 (T - T^*)}, \tag{3.18}$$

where  $T^* = \frac{b_2}{b_2 - \mu_2} \bar{T}$ .

**Lemma 3.2** *Assume that  $T > T^*$ . If  $r > r_1^*$ , then system (3.1) has a unique  $T$ -periodic solution.*



*Proof* From (3.18) we see that  $\lim_{\nu \rightarrow 0} \frac{h(\nu)}{\nu} > 1$  for  $T > T^*$ . Hence, there is a sufficiently small  $\epsilon > 0$  such that

$$h(\nu) > \nu \text{ for } \nu \in (0, \epsilon). \tag{3.19}$$

Since solution  $y(t) = y(t; 0, \kappa_2)$  is strictly decreasing for  $t \in (0, \bar{T}]$ , we have  $\bar{h}(\kappa_2) < \kappa_2$ , and so  $h(\kappa_2) < \kappa_2$ . Therefore, there must be  $\nu_0 \in (\epsilon, \kappa_2)$  such that

$$h(\nu_0) = \nu_0, \quad h'(\nu_0) \leq 1, \text{ and } h(\nu) > \nu \text{ for } \nu \in (0, \nu_0). \tag{3.20}$$

This means  $y(t; 0, \nu_0)$  is a  $T$ -periodic solution of equation (3.1).

Now we prove the uniqueness of the  $T$ -periodic solution of equation (3.1) by contradiction. Assume that equation (3.1) has another  $T$ -periodic solution  $\nu_1 \in (\nu_0, \kappa_2)$  such that

$$h(\nu_1) = \nu_1, \quad h'(\nu_1) \leq 1, \text{ and } h(\nu) < \nu \text{ for } \nu \in (\nu_1, \kappa_2). \tag{3.21}$$

It follows from (3.20) that there exists  $\nu_2 \in [\nu_0, \nu_1]$  such that one of the following cases holds:

$$\text{case 1: } \quad h'(\nu_0) \leq 1, h'(\nu_2) \geq 1, \text{ and } h'(\nu_1) \leq 1. \tag{3.22}$$

$$\text{case 2: } \quad \nu_0 = \nu_2 \text{ and } h'(\nu_0) = 1; \text{ furthermore, } h'(\nu_1) \leq 1. \tag{3.23}$$

$$\text{case 3: } \quad h'(\nu_0) \leq 1; \text{ furthermore, } \nu_1 = \nu_2 \text{ and } h'(\nu_1) = 1. \tag{3.24}$$

$$\text{case 4: } \quad h'(\nu_0) = h'(\nu_2) = 1 \text{ and } h'(\nu_1) \leq 1. \tag{3.25}$$

$$\text{case 5: } \quad h'(\nu_0) = 1, h'(\nu_2) \leq 1, \text{ and } h'(\nu_1) = 1. \tag{3.26}$$

$$\text{case 6: } \quad h'(\nu_0) \leq 1 \text{ and } h'(\nu_2) = h'(\nu_1) = 1. \tag{3.27}$$

Note that we have assumed  $r > r_1^*$ . We first show that cases (3.22)–(3.27) would not happen separately in three regions, namely  $r \in (r_1^*, r_2^*)$ ,  $r = r_2^*$ , and  $r > r_2^*$ . See Table 1 for specific parameter symbols in different cases.

I) For the case  $r \in (r_1^*, r_2^*)$ , we know  $\Delta_r < 0$ . Set

$$F(\nu) = \nu^\alpha \left( (\nu - E^*(r))^2 - \frac{\Delta_r}{4} \right)^{\frac{\beta}{2}} e^{\frac{\gamma}{\sqrt{-\Delta_r}} \tan^{-1} \left( \frac{\nu - E^*(r)}{\sqrt{-\Delta_r}} \right)}.$$

**Table 1** Symbols for the three cases I), II), III)

$r$	$l_1$	$l_2$	$l_3 = P_1(0)$	$P_1(\kappa_2)$
$(r_1^*, \kappa_2)$	$> 0$	$< 0$	$> 0$	$< 0$
$\kappa_2$	$> 0$	$< 0$	$= 0$	$< 0$
$(\kappa_2, r_2^*)$	$< 0$	$> 0$	$< 0$	$< 0$
$r$	$\tilde{l}_1$	$\tilde{l}_2$	$\tilde{l}_3 = P_2(0)$	–
$r_2^*$	$> 0$	$> 0$	$< 0$	–
$r$	$q_1$	$q_2$	$q_3 = P_3(0)$	–
$r > r_2^*$	$> 0$	$> 0$	$< 0$	–

Simple calculation yields

$$F'(v) = \left( \frac{\alpha}{v} + \frac{\beta(v - E^*(r)) + \gamma}{((v - E^*(r))^2 - \frac{\Delta r}{4})} \right) F(v).$$

Then equation (3.13) becomes

$$F(\bar{h}(v)) = F(v)e^{-\delta_2 \bar{T}}. \tag{3.28}$$

Taking the derivative with respect to  $v$  in (3.28) yields

$$F'(\bar{h}(v))\bar{h}'(v) = F'(v)e^{-\delta_2 \bar{T}},$$

which implies that

$$\left( \frac{\alpha}{\bar{h}(v)} + \frac{\beta(\bar{h}(v) - E^*(r)) + \gamma}{((\bar{h}(v) - E^*(r))^2 - \frac{\Delta r}{4})} \right) \bar{h}'(v) = \left( \frac{\alpha}{v} + \frac{\beta(v - E^*(r)) + \gamma}{((v - E^*(r))^2 - \frac{\Delta r}{4})} \right),$$

or, equivalently,

$$\bar{h}'(v) = \frac{\bar{h}(v)((\bar{h}(v) - E^*(r))^2 - \frac{\Delta r}{4})(v + r)}{v((v - E^*(r))^2 - \frac{\Delta r}{4})(\bar{h}(v) + r)}.$$

Taking the derivative with respect to  $v$  in (3.16), we obtain

$$\begin{aligned} \frac{h'(v)}{h(v)(\kappa_2 - h(v))} &= \frac{\bar{h}'(v)}{\bar{h}(v)(\kappa_2 - \bar{h}(v))}. \\ \bar{h}(v) &= \frac{m\kappa_2 h(v)}{(m - 1)h(v) + \kappa_2}. \\ \bar{h}(v) - E^*(r) &= \frac{(m\kappa_2 - E^*(r)(m - 1))h(v) - \kappa_2 E^*(r)}{(m - 1)h(v) + \kappa_2}. \\ \bar{h}(v) + r &= \frac{(m\kappa_2 + (m - 1)r)h(v) + r\kappa_2}{(m - 1)h(v) + \kappa_2}. \\ \kappa_2 - \bar{h}(v) &= \frac{\kappa_2(\kappa_2 - h(v))}{(m - 1)h(v) + \kappa_2}. \end{aligned}$$

By simple algebra, we see

$$h'(v) = \frac{h(v) \left[ ((m\kappa_2 - E^*(r)(m - 1))h(v) - \kappa_2 E^*(r))^2 - \frac{\Delta r}{4}(\kappa_2 + (m - 1)h(v))^2 \right] (v + r)}{v\kappa_2 \left[ (v - E^*(r))^2 - \frac{\Delta r}{4} \right] [\kappa_2 r + (m\kappa_2 + r(m - 1))h(v)]}, \tag{3.29}$$

where  $m = e^{-\kappa_2 \delta_2 (T - \bar{T})}$ . We further obtain

$$\begin{aligned}
 h'(v_0) &= \frac{\left[ ((m\kappa_2 - E^*(r)(m-1))v_0 - \kappa_2 E^*(r))^2 - \frac{\Delta r}{4}(\kappa_2 + (m-1)v_0)^2 \right] (v_0 + r)}{\kappa_2 \left[ (v_0 - E^*(r))^2 - \frac{\Delta r}{4} \right] [\kappa_2 r + (m\kappa_2 + r(m-1))v_0]}, \\
 h'(v_1) &= \frac{\left[ ((m\kappa_2 - E^*(r)(m-1))v_1 - \kappa_2 E^*(r))^2 - \frac{\Delta r}{4}(\kappa_2 + (m-1)v_1)^2 \right] (v_1 + r)}{\kappa_2 \left[ (v_1 - E^*(r))^2 - \frac{\Delta r}{4} \right] [\kappa_2 r + (m\kappa_2 + r(m-1))v_1]}, \\
 h'(v_2) &= \frac{\left[ ((m\kappa_2 - E^*(r)(m-1))v_2 - \kappa_2 E^*(r))^2 - \frac{\Delta r}{4}(\kappa_2 + (m-1)v_2)^2 \right] (v_2 + r)}{\kappa_2 \left[ (v_2 - E^*(r))^2 - \frac{\Delta r}{4} \right] [\kappa_2 r + (m\kappa_2 + r(m-1))v_2]}.
 \end{aligned}
 \tag{3.30}$$

Set

$$P_1(v) = l_1 v^2 + l_2 v + l_3, \tag{3.31}$$

where

$$l_1 = \left( E^*(r)^2 - \frac{\Delta r}{4} \right) (1 - m) + (2m\kappa_2 E^*(r) + r\kappa_2 - m\kappa_2^2), \tag{3.32}$$

$$\begin{aligned}
 l_2 &= \left[ r \left( E^*(r)^2 - \frac{\Delta r}{4} \right) - 2r\kappa_2 E^*(r) \right] (1 - m) \\
 &\quad - \left[ r\kappa_2^2(m+1) + 2\kappa_2 \left( E^*(r)^2 - \frac{\Delta r}{4} \right) \right],
 \end{aligned}
 \tag{3.33}$$

$$l_3 = (\kappa_2^2 - r\kappa_2) \left( E^*(r)^2 - \frac{\Delta r}{4} \right) + 2r\kappa_2^2 E^*(r). \tag{3.34}$$

Then cases 1–6 can be equivalently written as follows:

$$P_1(v_0) \leq 0, P_1(v_1) \leq 0, P_1(v_2) \geq 0.$$

$$P_1(v_0) = 0, P_1(v_1) \leq 0.$$

$$P_1(v_0) \leq 0, P_1(v_1) = 0.$$

$$P_1(v_0) = 0, P_1(v_1) \leq 0, P_1(v_2) = 0.$$

$$P_1(v_0) = 0, P_1(v_1) = 0, P_1(v_2) \leq 0.$$

$$P_1(v_0) \leq 0, P_1(v_1) = 0, P_1(v_2) = 0.$$

We see that

$$\begin{aligned}
 P_1(\kappa_2) &= - \left( E^*(r)^2 - \frac{\Delta r}{4} \right) m\kappa_2^2 - r m\kappa_2 \left( E^*(r)^2 - \frac{\Delta r}{4} \right) \\
 &\quad + (m\kappa_2^3 + r m\kappa_2^2)(-\kappa_2 + 2E^*(r)).
 \end{aligned}
 \tag{3.35}$$

Since  $r \in (r_1^*, r_2^*)$ , we see  $-\kappa_2 + 2E^*(r) = -r < 0$ ,  $E^*(r)^2 - \frac{\Delta r}{4} = \frac{b_2}{\delta_2} r > 0$ . Hence, we have  $P_1(\kappa_2) < 0$ .

Next, we subdivide the condition  $r \in (r_1^*, r_2^*)$  into three cases:

$$r \in (r_1^*, \kappa_2), \quad r = \kappa_2, \quad \text{and} \quad r \in (\kappa_2, r_2^*).$$

$I_1$ )  $r \in (r_1^*, \kappa_2)$ . In this case,  $P_1(0) > 0$  and  $P_1(\kappa_2) < 0$ . It is easy to see *case 1*, *cases 3–6* are impossible. We now focus on *case 2*.

Let  $\lambda > 1$  be small enough such that

$$\lambda m < 1, \quad r < \frac{\left[\frac{\kappa_2 \mu_2}{\delta_2} + \kappa_2^2\right](1 - \lambda m)}{\frac{\lambda \mu_2}{\delta_2}(1 - m) + \kappa_2(1 - \lambda m)},$$

and  $h(v) - \lambda v$  has three roots  $\tilde{v}_1, \tilde{v}_2$ , and  $\tilde{v}_3$  with

$$0 < \tilde{v}_1 < v_0 < \tilde{v}_2 < \tilde{v}_3 < v_1$$

and

$$h'(\tilde{v}_1) \leq \lambda, \quad h'(\tilde{v}_2) \geq \lambda, \quad h'(\tilde{v}_3) \leq \lambda.$$

From (3.29), we have

$$h'(\tilde{v}_i) = \frac{\lambda \left[ ((m\kappa_2 - E^*(r)(m - 1)) \lambda \tilde{v}_i - \kappa_2 E^*(r))^2 - \frac{\Delta r}{4} (\kappa_2 + (m - 1) \lambda \tilde{v}_i)^2 \right] (\tilde{v}_i + r)}{\kappa_2 \left[ (\tilde{v}_i - E^*(r))^2 - \frac{\Delta r}{4} \right] \left[ \kappa_2 r + (m\kappa_2 + r(m - 1)) \lambda \tilde{v}_i \right]}, \tag{3.36}$$

$$i = 1, 2, 3.$$

Set

$$P_\lambda(v) = l_1(\lambda)v^2 + l_2(\lambda)v + l_3(\lambda), \tag{3.37}$$

where

$$l_1(\lambda) = \left( E^*(r)^2 - \frac{\Delta r}{4} \right) (1 - m)^2 \lambda^2 + \lambda m \kappa_2^2 (\lambda m - 1) - 2E^*(r) \lambda^2 \kappa_2 m (m - 1) - \lambda \kappa_2 r (m - 1),$$

$$l_2(\lambda) = \left( E^*(r)^2 - \frac{\Delta r}{4} \right) (r \lambda^2 (m - 1)^2 + 2\lambda \kappa_2 (m - 1)) + \kappa_1^2 r (\lambda^2 m^2 - 1) + 2\lambda r E^*(r) \kappa_2 (m - 1) (1 - \lambda m),$$

$$l_3(\lambda) = \left( E^*(r)^2 - \frac{\Delta r}{4} \right) [\kappa_2^2 (1 - \lambda m) + r \lambda \kappa_2 (m - 1)] + 2E^*(r) r \kappa_2^2 (1 - \lambda m).$$

Thus, from  $h'(\tilde{v}_1) \leq \lambda, h'(\tilde{v}_2) \geq \lambda, h'(\tilde{v}_3) \leq \lambda$ , we obtain

$$l_1(\lambda) \tilde{v}_1^2 + l_2(\lambda) \tilde{v}_1 + l_3(\lambda) \leq 0,$$

$$l_1(\lambda) \tilde{v}_2^2 + l_2(\lambda) \tilde{v}_2 + l_3(\lambda) \geq 0, \tag{3.38}$$

$$l_1(\lambda) \tilde{v}_3^2 + l_2(\lambda) \tilde{v}_3 + l_3(\lambda) \leq 0.$$

As  $r < \frac{\left[ \frac{\kappa_2 \mu_2}{\delta_2} + \kappa_2^2 \right] (1 - \lambda m)}{\frac{\lambda \mu_2}{\delta_2} (1 - m) + \kappa_2 (1 - \lambda m)}$ , we have

$$P_\lambda(0) = l_3(\lambda) > 0. \tag{3.39}$$

And from (3.38) we see

$$P_\lambda(\tilde{v}_1) \leq 0, P_\lambda(\tilde{v}_2) \geq 0, P_\lambda(\tilde{v}_3) \leq 0. \tag{3.40}$$

It thus follows that the quadratic polynomial  $P_\lambda(v)$  has a root in each of the three intervals  $(0, \tilde{v}_1]$ ,  $(\tilde{v}_1, \tilde{v}_2]$ , and  $(\tilde{v}_2, \tilde{v}_3]$ ; this is impossible, thus gives a contradiction.

$I_2) r = \kappa_2$ . In this case we know  $l_3 = 0$ , which implies that  $P_1(0) = 0$ . Combined with the fact  $P_1(\kappa_2) < 0$ , we immediately know that cases 1–6 are impossible.

$I_3) r \in (\kappa_2, r_2^*)$ . In this case  $P_1(0) = l_3 < 0$  and  $P_1(\kappa_2) < 0$ , it is easy to see case 5 is impossible. For the cases 1–4 and case 6, we obtain that  $P_1(v)$  is a convex quadratic polynomial, hence  $l_1 < 0$ ,  $l_2 > 0$ , and  $l_3 < 0$ . It is easy to see that

$$0 > r l_1 - l_2 = 2r\kappa_2^2 + 2\kappa_2(E^*(r))^2 - \frac{\Delta_r}{4} > 0,$$

which leads to a contradiction.

II) For the case  $r = r_2^*$ , derivation (3.15) with respect to  $u$  gives

$$\begin{aligned} & \left( \frac{\alpha}{\bar{h}(v)} + \frac{\beta}{(\bar{h}(v) - E^*(r))} + \frac{\gamma}{(\bar{h}(v) - E^*(r))^2} \right) \bar{h}'(v) \\ & = \left( \frac{\alpha}{v} + \frac{\beta}{(v - E^*(r))} + \frac{\gamma}{(v - E^*(r))^2} \right), \end{aligned} \tag{3.41}$$

or, equivalently,

$$\bar{h}'(v) = \frac{\bar{h}(v)(\bar{h}(v) - E^*(r))^2(v + r)}{v(v - E^*(r))^2(\bar{h}(v) + r)}.$$

By simple algebra, we see that

$$h'(v) = \frac{h(v)[(m\kappa_2 - E^*(r)(m - 1))h(v) - \kappa_2 E^*(r)]^2(v + r)}{v\kappa_2[v - E^*(r)]^2[\kappa_2 r + (m\kappa_2 - r(1 - m))h(v)]}. \tag{3.42}$$

Similar to (3.31), we have

$$P_2(v) = \tilde{l}_1 v^2 + \tilde{l}_2 v + \tilde{l}_3, \tag{3.43}$$

where

$$\begin{aligned} \tilde{l}_1 &= E^*(r)^2(1 - m) + (2m\kappa_2 E^*(r) + r\kappa_2 - m\kappa_2^2), \\ \tilde{l}_2 &= [rE^*(r)^2 - 2r\kappa_2 E^*(r)](1 - m) - [r\kappa_2^2(m + 1) + 2\kappa_2 E^*(r)^2], \\ \tilde{l}_3 &= -r\kappa_2 E^*(r)^2 + 2\kappa_2^2 E^*(r)r + \kappa_2^2 E^*(r)^2 < 0 \text{ when } r = r_2^*. \end{aligned} \tag{3.44}$$

We obtain that  $P_2(v)$  is a convex quadratic polynomial, hence  $\tilde{l}_1 > 0$ ,  $\tilde{l}_2 > 0$ , and  $\tilde{l}_3 < 0$ . Thus, it is easy to see that *cases 1–2* and *cases 4–6* are impossible. *Case 3* can get the contradiction using the perturbation method similar to the proof  $I_1$ .

III) For the case  $r > r_2^*$ , set

$$\tilde{F}(v) = v^\alpha (v - E_1(r))^v (v - E_2(r))^\sigma. \tag{3.45}$$

Then

$$\tilde{F}'(v) = \left[ \frac{\alpha}{v} + \frac{v}{v - E_1(r)} + \frac{\sigma}{v - E_2(r)} \right] \tilde{F}(v). \tag{3.46}$$

From (3.14), we see

$$\tilde{F}(\bar{h}(v)) = \tilde{F}(v)e^{-\delta_2 \bar{T}}. \tag{3.47}$$

Taking the derivative with respect to  $v$  in (3.47) yields

$$\tilde{F}'(\bar{h}(v))\bar{h}'(v) = \tilde{F}'(v)e^{-\delta_2 \bar{T}},$$

which implies that

$$\left[ \frac{\bar{h}(v) + r}{\bar{h}(v)(\bar{h}(v) - E_1(r))(\bar{h}(v) - E_2(r))} \right] \bar{h}'(v) = \left[ \frac{v + r}{v(v - E_1(r))(v - E_2(r))} \right].$$

Similarly, a direct calculation gives

$$h'(v) = \frac{h(v)(v + r)[(m\kappa_2 + (1 - m)E_1(r))h(v) - \kappa_2 E_1(r)][(m\kappa_2 + (1 - m)E_2(r))h(v) - \kappa_2 E_2(r)]}{v\kappa_2(v - E_1(r))(v - E_2(r))[r\kappa_2 + (m\kappa_2 - r(1 - m))h(v)]}. \tag{3.48}$$

In addition, set

$$P_3(v) = q_1 v^2 + q_2 v + q_3, \tag{3.49}$$

where

$$q_1 = -\kappa_2^2 m + m\kappa_2(E_1(r) + E_2(r)) + (1 - m)E_1(r)E_2(r) + r\kappa_2, \tag{3.50}$$

$$q_2 = -r\kappa_2^2(m + 1) - r\kappa_2(1 - m)(E_1(r) + E_2(r)) + [r(1 - m) - 2\kappa_2]E_1(r)E_2(r), \tag{3.51}$$

$$q_3 = \kappa_2(\kappa_2 - r)E_1(r)E_2(r) + r\kappa_2^2(E_1(r) + E_2(r)). \tag{3.52}$$

Since  $r > r_2^*$ , we easily see

$$q_3 = 2r\kappa_2 \left( \kappa_2 + 2\frac{\mu_2}{\delta_2} \right) (\kappa_2 - r) < 0. \tag{3.53}$$

Hence, we obtain that  $P_3(v)$  is a convex quadratic polynomial with  $q_1 > 0$ ,  $q_2 > 0$ , and  $q_3 < 0$ . Same as case II). Hence, *cases 1–2* and *cases 4–6* cannot happen. *Case 3* can get the contradiction using the perturbation method similar to the proof  $I_1$ .  $\square$

**Lemma 3.3** *Assume that  $T = T^*$ . Then*

1. *If  $r_1^* < r < \kappa_2$ , then equation (3.1) has a unique  $T$ -periodic solution;*
2. *If  $r \geq \kappa_2$ , then  $h(v) < v$  for all  $v > 0$ .*

*Proof 1.* Since  $r_1^* < r < \kappa_2$ , then  $\Delta_r < 0$ . Hence, from (3.16) and (3.13), we see

$$\frac{h(v)}{v} = \frac{\kappa_2 - h(v)}{\kappa_2 - \bar{h}(v)} \cdot \frac{\left( (v - E^*(r))^2 - \frac{\Delta_r}{4} \right)^{\frac{\beta}{2\alpha}} e^{\frac{\gamma}{\alpha\sqrt{-\frac{\Delta_r}{4}}} \tan^{-1}\left(\frac{v - E^*(r)}{\sqrt{-\frac{\Delta_r}{4}}}\right)}}{\left( (\bar{h}(v) - E^*(r))^2 - \frac{\Delta_r}{4} \right)^{\frac{\beta}{2\alpha}} e^{\frac{\gamma}{\alpha\sqrt{-\frac{\Delta_r}{4}}} \tan^{-1}\left(\frac{\bar{h}(v) - E^*(r)}{\sqrt{-\frac{\Delta_r}{4}}}\right)}}. \tag{3.54}$$

Set

$$G(v) = (\kappa_2 - v)^\alpha \left( (v - E^*(r))^2 - \frac{\Delta_r}{4} \right)^{\frac{\beta}{2}} e^{\frac{\gamma}{\sqrt{-\frac{\Delta_r}{4}}} \tan^{-1}\left(\frac{v - E^*(r)}{\sqrt{-\frac{\Delta_r}{4}}}\right)} > 0 \text{ for } v \in (0, \kappa_2). \tag{3.55}$$

Clearly, we have  $h(v) = v$  if and only if  $G(v) = G(\bar{h}(v))$ , where  $v \in (0, \kappa_2)$ .

Taking the derivative of  $G(v)$ , we obtain

$$\begin{aligned} G'(v) &= \left[ -\frac{\alpha}{\kappa_2 - v} + \frac{\beta(v - E^*(r)) + \gamma}{(v - E^*(r))^2 - \frac{\Delta_r}{4}} \right] G(v) \\ &= \left[ -\frac{\alpha}{\kappa_2 - v} - \frac{\alpha}{v} + \frac{v + r}{v[(v - E^*(r))^2 - \frac{\Delta_r}{4}]} \right] G(v) \\ &= \frac{1}{v} \left[ -\frac{\alpha\kappa_2}{\kappa_2 - v} + \frac{v + r}{(v - E^*(r))^2 - \frac{\Delta_r}{4}} \right] G(v) \\ &= \frac{-(1 + \alpha\kappa_2)(v - \bar{v})}{(\kappa_2 - v)[(v - E^*(r))^2 - \frac{\Delta_r}{4}]} G(v), \end{aligned} \tag{3.56}$$

where  $\bar{v} = \kappa_2 - r$ , and  $\bar{v} > 0$  for  $r_1^* < r < \kappa_2$ ,  $\bar{v} = 0$  for  $r = \kappa_2$ ,  $\bar{v} < 0$  for  $\kappa_2 < r < r_2^*$ . This also implies

$$G'(v) > 0 \text{ for } 0 < v < \bar{v} \text{ and } G'(v) < 0 \text{ for } v \in (\bar{v}, \kappa_2). \tag{3.57}$$

This shows that  $G(v)$  is strictly increasing for  $v \in (0, \bar{v})$ , and  $G(v) > G(\bar{h}(v))$  for  $v \in (0, \bar{v})$ . Thus (3.19) holds and equation (3.1) has at least one  $T$ -periodic solution. Then, there must be  $v_0 \in (0, \kappa_2)$  such that

$$h(v_0) = v_0 \text{ and } h(v) > v \text{ for } v \in (0, v_0). \tag{3.58}$$

Now we prove the uniqueness of the  $T$ -periodic solution of equation (3.1) by contradiction. Assume that equation (3.1) has another  $T$ -periodic solution  $v_1 \in (v_0, \kappa_2)$  such that

$$h(v_1) = v_1 \text{ and } h(v) < v \text{ for } v \in (v_1, \kappa_2). \tag{3.59}$$

Based on the properties of the function  $G(v)$  and  $\bar{h}(v)$ , we can obtain the following fact:

$$\bar{v} < v_0 < v_1 \text{ and } \bar{v} > \bar{h}(v_0) > \bar{h}(v_1). \tag{3.60}$$

Following from (3.57), we then obtain

$$G(v_0) > G(v_1) = G(\bar{h}(v_1)) > G(\bar{h}(v_0)) = G(v_0), \tag{3.61}$$

which leads to a contradiction. Thus the uniqueness is confirmed.

2. Since  $\bar{v} = 0$  for  $r = \kappa_2$  and  $\bar{v} < 0$  for  $\kappa_2 < r < r_2^*$ ,  $G(v)$  is strictly decreasing for all  $v \in (0, \kappa_2)$ . Hence, from the above proof we have  $G(v) < G(\bar{h}(v))$  and

$$\frac{h(v)}{v} = \frac{\kappa_2 - h(v)}{\kappa_2 - v} \cdot \left( \frac{G(v)}{G(\bar{h}(v))} \right)^{\frac{1}{\alpha}} < \frac{\kappa_2 - h(v)}{\kappa_2 - v}, \tag{3.62}$$

which implies that  $h(v) < v$  for  $v \in (0, \kappa_2)$ .

If  $r > r_2^*$ , then from (3.14) we see

$$\frac{h(v)}{v} = \frac{\kappa_2 - h(v)}{\kappa_2 - \bar{h}(v)} \cdot \left( \frac{v - E_1(r)}{\bar{h}(v) - E_1(r)} \right)^{\frac{\nu}{\alpha}} \cdot \left( \frac{v - E_2(r)}{\bar{h}(v) - E_2(r)} \right)^{\frac{\sigma}{\alpha}}. \tag{3.63}$$

Set

$$G_1(v) = (\kappa_2 - v)^\alpha (v - E_1(r))^\nu (v - E_2(r))^\sigma > 0 \text{ for } v \in (0, \kappa_2). \tag{3.64}$$

Taking the derivative of  $G_1(v)$ , we obtain

$$\begin{aligned} G_1'(v) &= \left[ -\frac{\alpha}{\kappa_2 - v} + \frac{\nu}{v - E_1(r)} + \frac{\sigma}{v - E_2(r)} \right] G_1(v) \\ &= \frac{-(1 + \alpha\kappa_2)(v - \bar{v})}{(\kappa_2 - v)[(v - E^*(r))^2 - \frac{\Delta E}{4}]} G_1(v). \end{aligned} \tag{3.65}$$

Since  $r > r_2^*$ , we have  $\bar{v} < 0$ , which implies that  $G_1'(v) < 0$  for all  $v \in (0, \kappa_2)$ . By similar analysis as (3.62), we have  $h(v) < v$ .

The rest of the proof of the case  $r = r_2^*$  can be dealt with in the same spirit of the case  $r_1^* < r < \kappa_2$ , and so we omit the details here. The proof therefore is complete.  $\square$

**Lemma 3.4** *Assume  $T < T^*$ . If  $r \geq \kappa_2$ , then  $h(v) < v$  for all  $v > 0$ .*

*Proof* It follows from (3.18) that  $\lim_{v \rightarrow 0} \frac{h(v)}{v} < 1$  for  $T < T^*$ . Hence, there is sufficiently small  $\epsilon > 0$  such that

$$h(v) < v \text{ for } v \in (0, \epsilon). \tag{3.66}$$

Since solution  $y(t) = y(t; 0, \kappa_2)$  is strictly decreasing for  $t \in (0, \bar{T}]$ , hence  $\bar{h}(\kappa_2) < \kappa_2$ , which implies  $h(\kappa_2) < \kappa_2$ . Assume that there exists  $\tilde{v} \in (\epsilon, \kappa_2)$  such that  $h(\tilde{v}) \geq \tilde{v}$ . Then there must be  $v' \in (0, \tilde{v}]$  such that

$$h(v') = v', h'(v') \geq 1. \tag{3.67}$$



Thus, from (3.31), (3.43), and (3.49), we see

$$\begin{aligned}
 &l_1 v'^2 + l_2 v' + l_3 \geq 0 \text{ for } r \in [\kappa_2, r_2^*), \\
 &\tilde{l}_1 v'^2 + \tilde{l}_2 v' + \tilde{l}_3 \geq 0 \text{ for } r = r_2^*, \\
 &q_1 u'^2 + q_2 v' + q_3 \geq 0 \text{ for } r > r_2^*.
 \end{aligned}
 \tag{3.68}$$

For  $r \in [\kappa_2, r_2^*)$ , further calculation gives

$$\begin{aligned}
 &[(E^*(r)^2 - \frac{\Delta_r}{4}) + r\kappa_2]v'^2 + [r(E^*(r)^2 - \frac{\Delta_r}{4}) - 2r\kappa_2 E^*(r) - r\kappa_2^2 - 2\kappa_2(E^*(r)^2 - \frac{\Delta_r}{4})]v' + l_3 \\
 &\geq [m(E^*(r)^2 - \frac{\Delta_r}{4}) - 2m\kappa_2 E^*(r) + m\kappa_2^2]v'^2 \\
 &\quad + m[r(E^*(r)^2 - \frac{\Delta_r}{4}) - 2r\kappa_2 E^*(r) + r\kappa_2^2]v' > 0.
 \end{aligned}$$

Set

$$\begin{aligned}
 \tilde{G}_1(v) &= [(E^*(r)^2 - \frac{\Delta_r}{4}) + r\kappa_2]v^2 + [r(E^*(r)^2 - \frac{\Delta_r}{4}) - 2r\kappa_2 E^*(r) \\
 &\quad - r\kappa_2^2 - 2\kappa_2(E^*(r)^2 - \frac{\Delta_r}{4})]v + l_3.
 \end{aligned}$$

Hence,  $\tilde{G}_1(v) > 0$ .

The quadratic polynomial  $\tilde{G}_1(v)$  is concave up. Since  $\tilde{G}_1(0) = l_3 \leq 0$  for  $r \geq \kappa_2$ ,  $\tilde{G}_1(\kappa_2) = 0$  and  $\tilde{G}_1(v) < 0$  for  $u \in (0, \kappa_2)$ , it contradicts the assumption of  $\tilde{G}_1(v) > 0$ .

For the case  $r = r_2^*$ , we can use a proof similar to the above. Thus we omit it here.

For  $r > r_2^*$ , we obtain

$$\begin{aligned}
 &(E_1(r)E_2(r) + r\kappa_2)v'^2 + [(r - 2\kappa_2)E_1(r)E_2(r) - r\kappa_2(E_1(r) + E_2(r)) - r\kappa_2^2]v' + q_3 \\
 &\geq [\kappa_2^2 m - m\kappa_2(E_1(r) + E_2(r)) + mE_1(r)E_2(r)]v'^2 \\
 &\quad + [r m\kappa_2^2 - r m\kappa_2(E_1(r) + E_2(r)) + r mE_1(r)E_2(r)]v' \\
 &> 0.
 \end{aligned}
 \tag{3.69}$$

Set

$$\tilde{G}_2(v) = (E_1(r)E_2(r) + r\kappa_2)v^2 + [(r - 2\kappa_2)E_1(r)E_2(r) - r\kappa_2(E_1(r) + E_2(r)) - r\kappa_2^2]v + q_3.$$

Hence,  $\tilde{G}_2(v) > 0$ .

Clearly, quadratic polynomial  $\tilde{G}_2(v)$  is concave up. Since  $\tilde{G}_2(0) = q_3 = l_3 < 0$  for  $r > r_2^*$ ,  $\tilde{G}_2(\kappa_2) = 0$  and  $\tilde{G}_2(v) < 0$  for  $u \in (0, \kappa_2)$ . Thus, it contradicts the assumption of  $\tilde{G}_2(v) > 0$ . □

Based on the above discussion, we summarize the main results as follows.

**Theorem 3.1**

- (1) *The trivial equilibrium  $E_0$  of equation (3.1) is globally asymptotically stable if  $T \leq T^*$  and  $r \geq \kappa_2$ .*
- (2) *Equation (3.1) has a unique globally asymptotically stable  $T$ -periodic solution if one of the following statements is true:*

- (a)  $T > T^*$  and  $r > r_1^*$ .
- (b)  $T = T^*$  and  $r_1^* < r < \kappa_2$ .

#### 4 The global dynamics of systems (2.6)–(2.7)

Let  $H(t; 0, \omega)$  be a unique nonnegative global solution of systems (2.6)–(2.7) on  $[0, \infty)$ . Let  $\{Q_{1t}\}_{t \geq 0}$  and  $\{Q_{2t}\}_{t \geq 0}$  be solutions semiflow associated with system (2.6) and system (2.7), respectively. Since systems (2.6)–(2.7) are  $T$ -periodic, we consider their associated period map  $P$  defined as  $P(\omega) = H(T; 0, \omega)$  for  $\omega \in \mathbb{R}_+^2$ . Thus  $P(\omega) = Q_{2(T-\bar{T})}(Q_{1(T)}(\omega))$ ,  $\forall \omega \in \mathbb{R}_+^2$ , that is,  $P = Q_{2(T-\bar{T})} \circ Q_{1(T)}$ .

Let  $y^*(t) = y(t; 0, v_0)$  be the unique positive  $T$ -periodic solution of system (3.1). Then  $(0, y^*(t))$  is a semitrivial  $T$ -periodic solution of systems (2.6)–(2.7). Write  $\omega^* = (0, v_0)$ , let  $DP(\omega^*)$  be the Jacobian matrix of  $P$  at  $\omega^*$  and  $\rho(DP(\omega^*))$  be the spectral radius of the linear operator  $DP(\omega^*)$ .

**Lemma 4.1** *Assume that  $T > \bar{T}$ ,  $r > r_1^*$ , and one of the following two conditions is satisfied:*

- (1)  $T > T^*$ ,
- (2)  $T = T^*$  and  $r_1^* < r < \kappa_2$ .

*Then the following two statements are valid:*

(i) *If  $\kappa_1 < \kappa_2$  and  $T > \frac{\kappa_2 T^*}{\kappa_2 - \kappa_1}$ , then  $\rho(DP(\omega^*)) < 1$ , and hence,  $(0, y^*(t))$  is an asymptotically stable fixed point of  $P$ , i.e., the semitrivial  $T$ -periodic solution  $(0, y^*(t))$  of systems (2.6)–(2.7) is locally asymptotically stable.*

(ii) *If  $\kappa_1 > \kappa_2$ , then  $\rho(DP(\omega^*)) > 1$ , and hence  $(0, y^*(t))$  is an unstable fixed point of  $P$ , i.e., the semitrivial  $T$ -periodic solution  $(0, y^*(t))$  of systems (2.6)–(2.7) is unstable.*

*Proof* Let  $f_1(\omega)$  and  $f_2(\omega)$  be the right-hand side vector fields of systems (2.6) and (2.7), respectively. Then we have

$$Df_1(\omega) = \begin{bmatrix} \delta_1 \kappa_1 - 2\delta_1 u - \delta_1 v & -\delta_1 u \\ \frac{-b_2 v^2}{(u+v+r)^2} - \delta_2 v & \frac{2b_2 uv + b_2 v^2 + 2b_2 vr}{(u+v+r)^2} - \delta_2 u - 2\delta_2 v - \mu_2 \end{bmatrix}$$

and

$$Df_2(\omega) = \begin{bmatrix} \delta_1 \kappa_1 - 2\delta_1 u - \delta_1 v & -\delta_1 u \\ \frac{-b_2 v^2}{(u+v)^2} - \delta_2 v & \frac{2b_2 uv + b_2 v^2}{(u+v)^2} - \delta_2 u - 2\delta_2 v - \mu_2 \end{bmatrix}.$$

Let  $U_1(t, \omega) := Q_{1t}(\omega)$ ,  $U_2(t, \omega) := Q_{2t}(\omega)$  and  $V_1(t, \omega) = D_\omega U_1(t, \omega)$  and  $V_2(t, \omega) = D_\omega U_2(t, \omega)$ . Then, for any given  $\omega \in \mathbb{R}_+^2$ , the matrix functions  $V_1(t, \omega)$  and  $V_2(t, \omega)$  satisfy

$$\frac{dV_1(t)}{dt} = Df_1(U_1(t, \omega))V_1(t), \quad V_1(0) = I, \quad t \in [0, \bar{T}],$$

$$\frac{dV_2(t)}{dt} = Df_2(U_2(t, \omega))V_2(t), \quad V_2(\bar{T}) = I, \quad t \in [\bar{T}, T].$$

Since  $H = Q_{2T} \circ Q_{1\bar{T}}$ , the chain rule implies that  $DH(\omega^*) = DQ_{2T} \circ (Q_{1\bar{T}}(\omega^*))$ . Then  $D(Q_{1\bar{T}}(\omega^*)) = D_\omega U_1(t, \omega^*) = V_1(\bar{T}, \omega^*)$  and  $DQ_{2T}(Q_{1\bar{T}}(\omega^*)) = D_\omega U_2(t, \omega^*) = V_2(T,$

$Q_{1\bar{T}}(\omega^*)$ . Since  $\omega^* = (0, v_0)$ ,  $U_1(t, \omega^*) = (0, y_1^*(t))$  with

$$\begin{cases} (y_1^*(t))^\alpha ((y_1^*(t) - A)^2 + B)^{\frac{\beta}{2}} e^{\frac{\gamma}{\sqrt{B}} \tan^{-1}\left(\frac{y_1^*(t)-A}{\sqrt{B}}\right)} \\ = v_0^\alpha ((v_0 - A)^2 + B)^{\frac{\beta}{2}} e^{\frac{\gamma}{\sqrt{B}} \tan^{-1}\left(\frac{v_0-A}{\sqrt{B}}\right)} e^{-\delta_2 t} \text{ for } r_1^* < r < r_2^*, \\ \left[\frac{y_1^*(t)}{v_0}\right]^\alpha \left[\frac{y_1^*(t)-E_1}{v_0-E_1}\right]^\nu \left[\frac{y_1^*(t)-E_2}{v_0-E_2}\right]^\sigma = e^{-\delta_2 t} \text{ for } r > r_2^*, \\ (y_1^*(t))^\alpha ((y_1^*(t) - A)^\beta e^{-\frac{\gamma}{y_1^*(t)-A}} = v_0^\alpha (v_0 - A)^\beta e^{-\frac{\gamma}{v_0-A}} e^{-\delta_2 t} \text{ for } r = r_2^*. \end{cases} \tag{4.1}$$

$U_2(t, U_1(\bar{T}, \omega^*)) = (0, y_2^*(t))$  with

$$\frac{y_2^*(t)}{\kappa_2 - y_2^*(t)} = \left(\frac{y_1^*(\bar{T})}{\kappa_2 - y_1^*(\bar{T})}\right) e^{\kappa_2 \delta_2 (t - \bar{T})}.$$

Furthermore,  $y_2^*(T) = v_0$ ,  $y_1^*(\bar{T}) = y_2^*(\bar{T})$ , and

$$y^*(t) = \begin{cases} y_1^*(t), & t \in (nT, nT + \bar{T}], \\ y_2^*(t), & t \in (nT + \bar{T}, (n + 1)T], \end{cases} \tag{4.2}$$

for  $n = 0, 1, 2, \dots$ . Hence,

$$Df_1(U_1(t, \omega^*)) = \begin{bmatrix} \delta_1 \kappa_1 - \delta_1 y_1^*(t) & 0 \\ \frac{-b_2 (y_1^*(t))^2}{(y_1^*(t)+r)^2} - \delta_2 y_1^*(t) & \frac{b_2 (y_1^*(t))^2 + 2b_2 y_1^*(t)r}{(y_1^*(t)+r)^2} - 2\delta_2 y_1^*(t) - \mu_2 \end{bmatrix}$$

and

$$Df_2(U_2(t, U_1(\bar{T}, \omega^*))) = \begin{bmatrix} \delta_1 \kappa_1 - \delta_1 y_2^*(t) & 0 \\ -b_2 - \delta_2 y_2^*(t) & b_2 - \mu_2 - 2\delta_2 y_2^*(t) \end{bmatrix}.$$

It then follows that

$$V_1(\bar{T}, \omega^*) = \begin{bmatrix} e^{\int_0^{\bar{T}} [\delta_1 \kappa_1 - \delta_1 y_1^*(t)] dt} & 0 \\ * & e^{\int_0^{\bar{T}} \left[ \frac{b_2 (y_1^*(t))^2 + 2b_2 y_1^*(t)r}{(y_1^*(t)+r)^2} - 2\delta_2 y_1^*(t) - \mu_2 \right] dt} \end{bmatrix}$$

and

$$V_2(T, U_1(\bar{T}, \omega^*)) = \begin{bmatrix} e^{\int_{\bar{T}}^T [\delta_1 \kappa_1 - \delta_1 y_2^*(t)] dt} & 0 \\ ** & e^{\int_{\bar{T}}^T [b_2 - \mu_2 - 2\delta_2 y_2^*(t)] dt} \end{bmatrix}.$$

Thus, the matrix  $DH(\omega^*)$  has two positive eigenvalues  $\tau_1$  and  $\tau_2$  given by

$$\begin{aligned} \tau_1 &= e^{\int_0^{\bar{T}} [\delta_1 \kappa_1 - \delta_1 y_1^*(t)] dt} \cdot e^{\int_{\bar{T}}^T [\delta_1 \kappa_1 - \delta_1 y_2^*(t)] dt}, \\ \tau_2 &= e^{\int_0^{\bar{T}} \left[ \frac{b_2 (y_1^*(t))^2 + 2b_2 y_1^*(t)r}{(y_1^*(t)+r)^2} - 2\delta_2 y_1^*(t) - \mu_2 \right] dt} \cdot e^{\int_{\bar{T}}^T [b_2 - \mu_2 - 2\delta_2 y_2^*(t)] dt}. \end{aligned}$$

Since  $(0, y_1^*(t))$  satisfies equation (2.6), it follows that

$$\frac{(y_1^*(t))'}{y_1^*(t)} = \left[ b_2 \frac{y_1^*(t)}{y_1^*(t) + r} - \mu_2 - \delta_2 y_1^*(t) \right].$$

Integrating the above equation for  $t$  from 0 to  $\bar{T}$ , we then obtain

$$\ln y_1^*(\bar{T}) - \ln v_0 = \int_0^{\bar{T}} b_2 \frac{y_1^*(t)}{y_1^*(t) + r} dt - \mu_2 \bar{T} - \delta_2 \int_0^{\bar{T}} y_1^*(t) dt. \tag{4.3}$$

Since  $(0, y_2^*(t))$  satisfies equation (2.7), it follows that

$$\frac{(y_2^*(t))'}{y_2^*(t)} = [b_2 - \mu_2 - \delta_2 y_2^*(t)].$$

Integrating the above equation for  $t$  from  $\bar{T}$  to  $T$ , we then obtain

$$\ln v_0 - \ln y_2^*(\bar{T}) = (b_2 - \mu_2)(T - \bar{T}) - \delta_2 \int_{\bar{T}}^T y_2^*(t) dt. \tag{4.4}$$

From (4.3), (4.4) and using the fact that  $y_2^*(T) = v_0, y_1^*(\bar{T}) = y_2^*(\bar{T})$ , we have

$$\delta_2 \left( \int_0^{\bar{T}} y_1^*(t) dt + \int_{\bar{T}}^T y_2^*(t) dt \right) = \int_0^{\bar{T}} b_2 \frac{y_1^*(t)}{y_1^*(t) + r} dt - \mu_2 \bar{T} + (b_2 - \mu_2)(T - \bar{T}), \tag{4.5}$$

this implies the following inequality:

$$\kappa_2(T - T^*) < \int_0^T y^*(t) dt < \kappa_2 T, \tag{4.6}$$

from which we calculate

$$e^{\delta_1(\kappa_1 - \kappa_2)T} < \tau_1 = e^{\delta_1 \kappa_1 T - \delta_1 \int_0^T y^*(t) dt} < e^{\delta_1[(\kappa_1 - \kappa_2)T + \kappa_2 T^*]}$$

and

$$\tau_2 = e^{-(b_2 - \mu_2)(T - T^*) - b_2 \int_0^{\bar{T}} \frac{(y^*(t))^2}{(y^*(t) + r)^2} dt} < 1.$$

- (i) If  $\kappa_1 < \kappa_2, T > \frac{\kappa_2 T^*}{\kappa_2 - \kappa_1}$ , then  $\tau_1 < 1$ , proving the local asymptotic stability of the semitrivial  $T$ -periodic solution  $(0, y^*(t))$  of systems (2.6)–(2.7).
- (ii) If  $\kappa_1 > \kappa_2$ , then we have  $\tau_1 > 1$ , which makes the semitrivial  $T$ -periodic solution  $(0, y^*(t))$  of systems (2.6)–(2.7) unstable.

This completes the proof. □

**Corollary 4.1** *The boundary equilibrium  $(\kappa_1, 0)$  of systems (2.6)–(2.7) is always locally asymptotically stable.*

*Proof* The proof of Corollary 4.1 is very similar to the proof of Lemma 4.1. Note that the corresponding matrices  $V_1(t, (\kappa_1, 0))$  and  $V_2(t, (\kappa_1, 0))$  are

$$V_1(\bar{T}, (\kappa_1, 0)) = V_2(T, U_1(\bar{T}, (\kappa_1, 0))) = \begin{bmatrix} e^{\int_0^{\bar{T}} -\delta_1 \kappa_1 dt} & * \\ 0 & e^{\int_0^{\bar{T}} [-\delta_2 \kappa_1 - \mu_2] dt} \end{bmatrix},$$

$$V_2(T, U_1(\bar{T}, (\kappa_1, 0))) = \begin{bmatrix} e^{\int_{\bar{T}}^T -\delta_1 \kappa_1 dt} & * \\ 0 & e^{\int_{\bar{T}}^T [-\delta_2 \kappa_1 - \mu_2] dt} \end{bmatrix}.$$

Therefore, the corresponding two positive eigenvalues  $\tau_3$  and  $\tau_4$  are given by

$$\tau_3 = e^{-\delta_1 \kappa_1 T} < 1, \quad \tau_4 = e^{-(\delta_2 \kappa_1 + \mu_2) T} < 1. \quad \square$$

Now, we focus on the global dynamics for systems (2.6)–(2.7).

**Theorem 4.1** *Assume that  $\kappa_1 > \kappa_2$ . Then  $(\kappa_1, 0)$  is globally asymptotically stable.*

*Proof* From Corollary 4.1, we know that the boundary equilibrium  $(\kappa_1, 0)$  of systems (2.6)–(2.7) is locally asymptotically stable. Next, we are ready to prove that every solution of systems (2.6)–(2.7) goes to  $(\kappa_1, 0)$ . If  $(0, y^*(t))$  exists, as in the proof of Lemma 4.1, we know that  $(0, y^*(t))$  is an unstable semitrivial  $T$ -periodic solution of systems (2.6)–(2.7) under the condition  $\kappa_1 > \kappa_2$ .

The next proof investigates whether systems (2.6)–(2.7) have a positive  $T$ -periodic solution under  $\kappa_1 > \kappa_2$ . Now we show the nonexistence of the  $T$ -periodic solution of (2.6)–(2.7) by contradiction. Let  $(x^*(t), y^*(t))$  be a positive  $T$ -periodic solution of systems (2.6)–(2.7).

$$\begin{cases} \frac{(x^*)'}{x^*} = \delta_1 [\kappa_1 - (x^* + y^*)], \\ \frac{(y^*)'}{y^*} = \left[ b_2 \frac{y^*}{x^* + y^* + r} - \mu_2 - \delta_2 (x^* + y^*) \right] \end{cases} \tag{4.7}$$

for  $t \in [nT, nT + \bar{T})$ ,  $n = 0, 1, 2, \dots$

$$\begin{cases} \frac{(x^*)'}{x^*} = \delta_1 [\kappa_1 - (x^* + y^*)], \\ \frac{(y^*)'}{y^*} = \left[ b_2 \frac{y^*}{x^* + y^*} - \mu_2 - \delta_2 (x^* + y^*) \right] \end{cases} \tag{4.8}$$

for  $t \in [nT + \bar{T}, (n + 1)T)$ ,  $n = 0, 1, 2, \dots$ . Integrating the first equation of (4.7) for  $t$  from 0 to  $\bar{T}$  and the first equation of (4.8) for  $t$  from  $\bar{T}$  to  $T$ , we then obtain

$$\begin{cases} \ln x^*(\bar{T}) - \ln x^*(0) = \int_0^{\bar{T}} \delta_1 [\kappa_1 - (x^* + y^*)] dt, \\ \ln x^*(T) - \ln x^*(\bar{T}) = \int_{\bar{T}}^T \delta_1 [\kappa_1 - (x^* + y^*)] dt, \end{cases} \tag{4.9}$$

which implies that  $\int_0^T (x^* + y^*) dt = \kappa_1 T$ .

Similarly, integrating the second equation of (4.7) for  $t$  from 0 to  $\bar{T}$  and the second equation of (4.8) for  $t$  from  $\bar{T}$  to  $T$ , we then obtain

$$\begin{cases} \ln y^*(\bar{T}) - \ln y^*(0) = \int_0^{\bar{T}} \left[ b_2 \frac{y^*}{x^* + y^* + r} - \mu_2 - \delta_2(x^* + y^*) \right] dt, \\ \ln y^*(T) - \ln y^*(\bar{T}) = \int_{\bar{T}}^T \left[ b_2 \frac{y^*}{x^* + y^*} - \mu_2 - \delta_2(x^* + y^*) \right] dt, \end{cases} \tag{4.10}$$

which particularly implies

$$\int_0^{\bar{T}} \left[ b_2 \frac{y^*}{x^* + y^* + r} - \mu_2 \right] dt + \int_{\bar{T}}^T \left[ b_2 \frac{y^*}{x^* + y^*} - \mu_2 \right] dt = \delta_2 \kappa_1 T. \tag{4.11}$$

Then we see  $\kappa_1 \leq \kappa_2$ , which leads to a contradiction. Thus, Lemma 2.2 of [39] implies that for any initial value  $(u, v) \in \text{Int}(\mathbb{R}_+^2)$ , every solution of systems (2.6)–(2.7) goes to  $(\kappa_1, 0)$  because here the map  $H$  satisfied the  $\leq_K$  monotonicity and convergence. Hence,  $(\kappa_1, 0)$  is globally asymptotically stable.  $\square$

**Theorem 4.2** *Assume that  $\kappa_1 < \kappa_2$ . If  $T \leq T^*$  and  $r \geq \kappa_2$ , then  $(\kappa_1, 0)$  is globally asymptotically stable.*

*Proof* The local asymptotic stability of  $(\kappa_1, 0)$  can follow from Corollary 4.1. We now focus on the global attractivity of  $(\kappa_1, 0)$ . First, consider the following system:

$$\begin{cases} \frac{d\bar{y}}{dt} = \bar{y} \left[ b_2 \frac{\bar{y}}{\bar{y} + 2r} - \delta_2(\bar{y} + r) \right], & t \in (nT, nT + \bar{T}], n = 0, 1, 2, \dots, \\ \frac{d\bar{y}}{dt} = \bar{y} [b_2 - \delta_2\bar{y}], & t \in (nT + \bar{T}, (n + 1)T], n = 0, 1, 2, \dots \end{cases} \tag{4.12}$$

Since  $T \leq T^*$  and  $r \geq \kappa_2$ , it follows from Theorem 3.1 that

$$\lim_{t \rightarrow +\infty} \bar{y} = 0.$$

Suppose that  $(x, y)$  is the solution of systems (2.6)–(2.7). We see  $y \leq \bar{y}$  under the condition  $y(0) \leq \bar{y}(0)$ , which implies that  $\lim_{t \rightarrow +\infty} y = 0$ . For any given sufficiently small  $\epsilon > 0$ , there exists  $T_0 > 0$  such that  $y < \epsilon$  for  $t > T_0$ .

For  $t > T_0$ , consider the following system:

$$\begin{cases} \frac{d\underline{x}}{dt} = \delta_1 \underline{x} [\kappa_1 - \epsilon - \underline{x}] \\ \frac{d\bar{x}}{dt} = \delta_1 \bar{x} [\kappa_1 - \bar{x}]. \end{cases} \tag{4.13}$$

We have  $\underline{x} \leq x \leq \bar{x}$  under conditions  $\underline{x}(T_0) \leq x(T_0) \leq \bar{x}(T_0)$  and  $t \geq T_0$ . The arbitrariness of  $\epsilon$  allows us to conclude that  $\lim_{t \rightarrow +\infty} x = \kappa_1$ . This completes the proof.  $\square$

**Theorem 4.3** *Assume that  $\kappa_1 < \kappa_2$ . If  $T > \frac{\kappa_2}{\kappa_2 - \kappa_1} T^*$ , then systems (2.6)–(2.7) admit a unique positive  $T$ -periodic solution initiating from  $w(\bar{u}, \bar{v})$ . Furthermore, there exists a continuous,*

unbounded, and one-dimensional curve  $\mathcal{H} \subset R^2$  such that both  $0$  and  $\bar{w}$  are in  $\mathcal{H}$ , and the following statements are valid:

- 1) Assume that  $\bar{w}(\bar{u}, \bar{v}) \in \mathcal{H}$ , and for any  $w(u, v)$  such that  $u > \bar{u}$  and  $v < \bar{v}$  we have  $\lim_{t \rightarrow +\infty} H(t; 0, \bar{w}) - (\kappa_1, 0) = 0$ ;
- 2) Assume that  $\bar{w}(\bar{u}, \bar{v}) \in \mathcal{H}$ , and for any  $w(u, v)$  such that  $u < \bar{u}$  and  $v > \bar{v}$  we have  $\lim_{t \rightarrow +\infty} H(t; 0, \bar{w}) - (0, \hat{y}(t)) = 0$ .

*Proof* The proof 1) and 2) and the existence of positive periodic solutions follow from Theorem 2.4 (saddle-point structure) of [39]. Here we only prove the uniqueness of positive periodic solutions. Suppose for contradiction that periodic systems (2.6)–(2.7) have two different  $T$ -periodic positive solutions  $(x_1(t), y_1(t))$  and  $(x_2(t), y_2(t))$ , then  $x_1(0) = x_1(T)$ ,  $y_1(0) = y_1(T)$ ,  $x_2(0) = x_2(T)$ ,  $y_2(0) = y_2(T)$ . There are four possible cases that determine the relationship between the initial values of  $x_1(0)$  and  $x_2(0)$ , and  $y_1(0)$  and  $y_2(0)$ :

$$(1) \begin{cases} x_1(0) < x_2(0) \\ y_1(0) > y_2(0) \end{cases} \quad (2) \begin{cases} x_1(0) > x_2(0) \\ y_1(0) < y_2(0) \end{cases} \quad (3) \begin{cases} x_1(0) < x_2(0) \\ y_1(0) < y_2(0) \end{cases} \quad (4) \begin{cases} x_1(0) > x_2(0) \\ y_1(0) > y_2(0) \end{cases}.$$

By Theorem 5.1 of [40], if (1) or (2) holds, then for all  $t \in [0, T]$

$$(1)' \begin{cases} x_1(t) < x_2(t) \\ y_1(t) > y_2(t) \end{cases} \quad \text{or} \quad (2)' \begin{cases} x_1(t) > x_2(t) \\ y_1(t) < y_2(t) \end{cases}.$$

Therefore, from (4.11) we can easily get

$$\int_0^{\bar{T}} \left[ b_2 \frac{y_1(t)}{x_1(t) + y_1(t) + r} - \mu_2 \right] dt + \int_{\bar{T}}^T \left[ b_2 \frac{y_1(t)}{x_1(t) + y_1(t)} - \mu_2 \right] dt = \delta_2 \kappa_1 T \tag{4.14}$$

and

$$\int_0^{\bar{T}} \left[ b_2 \frac{y_2(t)}{x_2(t) + y_2(t) + r} - \mu_2 \right] dt + \int_{\bar{T}}^T \left[ b_2 \frac{y_2(t)}{x_2(t) + y_2(t)} - \mu_2 \right] dt = \delta_2 \kappa_1 T. \tag{4.15}$$

We set

$$\begin{cases} F_1(\xi, \eta) = \frac{b_2 \eta}{\xi + \eta + r}, \\ F_2(\xi, \eta) = \frac{b_2 \eta}{\xi + \eta}. \end{cases}$$

Taking the partial derivative of  $F_1(\xi, \eta)$  and  $F_2(\xi, \eta)$  with  $\xi$  and  $\eta$ , respectively, we have

$$\begin{cases} \frac{\partial F_1(\xi, \eta)}{\partial \xi} = \frac{-b_2 \eta}{(\xi + \eta + r)^2} < 0, \\ \frac{\partial F_1(\xi, \eta)}{\partial \eta} = \frac{b_2(\xi + r)}{(\xi + \eta + r)^2} > 0, \\ \frac{\partial F_2(\xi, \eta)}{\partial \xi} = \frac{-b_2 \eta}{(\xi + \eta)^2} < 0, \\ \frac{\partial F_2(\xi, \eta)}{\partial \eta} = \frac{b_2 \xi}{(\xi + \eta)^2} > 0. \end{cases}$$

This is a contradiction to (4.14) and (4.15).

We will now prove that it is impossible for cases (3) and (4) to hold. It follows from systems (2.6)–(2.7) that

$$\delta_1 \int_0^T [x_1(t) + y_1(t)]dt = (b_1 - \mu_1)T \tag{4.16}$$

and

$$\delta_1 \int_0^T [x_2(t) + y_2(t)]dt = (b_1 - \mu_1)T. \tag{4.17}$$

From (4.16) and (4.17), there must exist  $t^* \in (0, T)$  such that one of the following two cases holds:

- (a)  $x_1(t^*) < x_2(t^*), y_1(t^*) \geq y_2(t^*),$
- (b)  $x_1(t^*) \geq x_2(t^*), y_1(t^*) < y_2(t^*).$

Again by Theorem 5.1 [40], for case (a), we have  $x_1(t) < x_2(t), y_1(t) \geq y_2(t)$  for  $t \in (t^*, T]$ . Therefore  $y_1(T) \geq y_2(T)$ , by the periodicity of  $y(t)$  and case (3), this is a contradiction. For case (b), we have  $x_1(t) \geq x_2(t), y_1(t) < y_2(t)$  for  $t \in (t^*, T]$ . Therefore  $x_1(T) \geq x_2(T)$ , by the periodicity of  $x(t)$  and case (4), this also is a contradiction.  $\square$

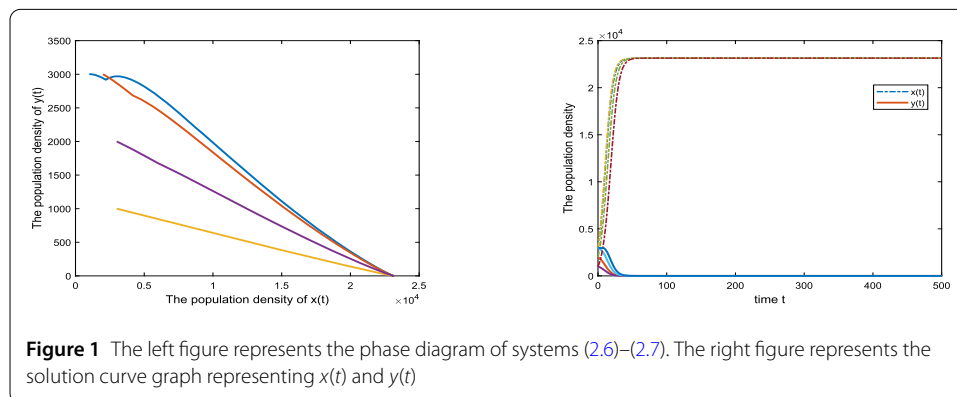
### 5 Numerical examples

In this section, we first provide numerical examples to demonstrate our analytic results for systems (2.6)–(2.7).

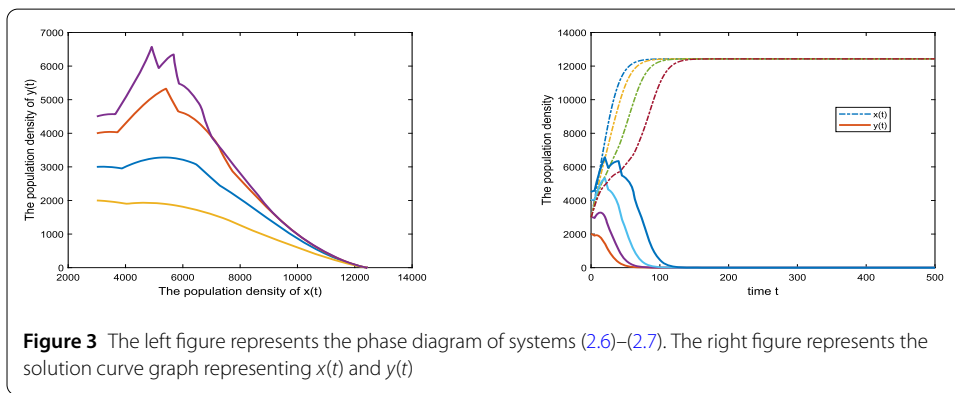
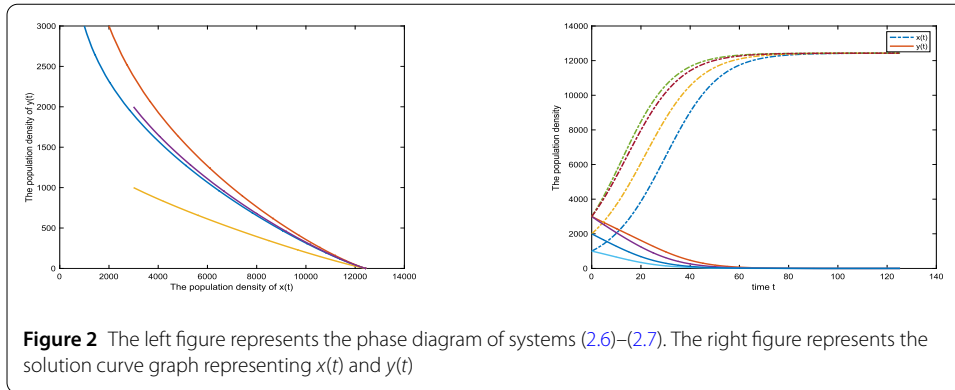
*Example 5.1* Given the parameters

$$\begin{aligned} b_1 = 0.1988, \quad b_2 = 0.1077, \quad \mu_1 = \mu_2 = 0.002, \quad T = 20 \\ \delta_1 = \delta_2 = 8.5034 \times 10^{-6}, \quad \bar{T} = 5, \quad r = 4720, \end{aligned} \tag{5.1}$$

we calculate that  $\kappa_1 = 23,144 > \kappa_2 = 12,430$ . Given four initial values (1000, 3000), (2000, 3000), (3000, 1000), and (3000, 2000), it follows from Theorem 4.1 that  $(\kappa_1, 0)$  is always globally asymptotically stable as shown in Fig. 1.







*Example 5.2* Given the parameters

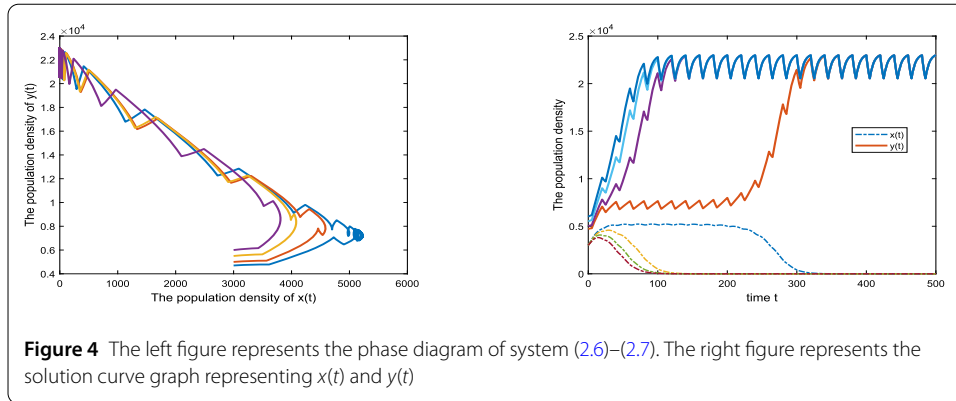
$$\begin{aligned}
 b_1 &= 0.1077, & b_2 &= 0.1988, & \mu_1 &= \mu_2 = 0.002, & T &= 5.01 \\
 \delta_1 &= \delta_2 = 8.5034 \times 10^{-6}, & \bar{T} &= 5, & r &= 47,200,
 \end{aligned}
 \tag{5.2}$$

we calculate that  $\kappa_1 = 12,430 < \kappa_2 = 23,144$ ,  $T^* = 5.0508$ . Given the initial values (1000, 3000), (2000, 3000), (3000, 1000), (3000, 2000), it follows from Theorem 4.2 that  $T \leq T^*$  and  $r \geq \kappa_2$ ,  $(\kappa_1, 0)$  is always globally asymptotically stable as shown in Fig. 2.

*Example 5.3* Given the parameters

$$\begin{aligned}
 b_1 &= 0.1077, & b_2 &= 0.1988, & \mu_1 &= \mu_2 = 0.002, & T &= 20 \\
 \delta_1 &= \delta_2 = 8.5034 \times 10^{-6}, & \bar{T} &= 5, & r &= 4720,
 \end{aligned}
 \tag{5.3}$$

we calculate that  $\kappa_1 = 12,430 < \kappa_2 = 23,144$ , and  $T > \frac{\kappa_2}{\kappa_2 - \kappa_1} T^* = 10.9111$ . Given four initial values (3000, 4500), (3000, 4000), (3000, 3000), and (3000, 2000), it follows from Theorem 4.3 that there exists a continuous, unbounded, and one-dimensional curve, separating the attraction domains of  $(\kappa_1, 0)$  and  $(0, \hat{y}(t))$ , shown in Fig. 3.



*Example 5.4* Given the parameters

$$\begin{aligned}
 b_1 &= 0.1077, & b_2 &= 0.1988, & \mu_1 &= \mu_2 = 0.002, & T &= 20 \\
 \delta_1 &= \delta_2 = 8.5034 \times 10^{-6}, & \bar{T} &= 5, & r &= 4720,
 \end{aligned}
 \tag{5.4}$$

we calculate that  $\kappa_1 = 12,430 < \kappa_2 = 23,144$ , and  $T > \frac{\kappa_2}{\kappa_2 - \kappa_1} T^* = 10.9111$ . Given four initial values (3000, 4700), (3000, 5000), (3000, 5500), and (3000, 6000), it follows from Theorem 4.3 that there exists a continuous, unbounded, and one-dimensional curve, separating the attraction domains of  $(\kappa_1, 0)$  and  $(0, \hat{y}(t))$ , shown in Fig. 4.

### 6 Conclusion

Population replacement involves infecting wild mosquitoes with *Wolbachia*, while population suppression aims to fundamentally eliminate mosquitoes and reduce the problems caused by mosquito bites. Therefore, a continuous release of *Wolbachia*-infected or sterile male mosquitoes is a direct and efficient strategy to prevent mosquito-borne diseases. In this work, we assume that there are both *Wolbachia*-infected and uninfected mosquitoes in the target area initially. To speed up the process of replacing the mosquito population, we further release infected male mosquitoes at regular intervals. We do this to determine the optimal number and frequency of releases needed to accelerate population replacement.

Our research differs from previous studies as we have developed a model for accelerated mosquito replacement that considers the periodic release of infected male mosquitoes. In this model, we introduced two measures, namely  $\kappa_1 = (b_1 - \mu_1)/\delta_1$  and  $\kappa_2 = (b_2 - \mu_2)/\delta_2$ , which determine the carrying capacity of infected and uninfected mosquito populations, respectively. If  $\kappa_1 > \kappa_2$ , it indicates that *Wolbachia* infection is favorable for infected mosquitoes. On the other hand, if  $\kappa_1 < \kappa_2$ , it means that the infection brings a fitness cost. Through the analysis of system (3.1), by defining a threshold value  $T^*$  of releasing waiting time, we found that population replacement can be achieved as long as one of the following conditions holds: (i)  $\kappa_1 > \kappa_2$ ; (ii)  $\kappa_1 < \kappa_2$ ,  $T \leq T^*$ , and  $r \geq \kappa_2$ . While in the case of  $\kappa_1 < \kappa_2$  and  $T > \frac{\kappa_2}{\kappa_2 - \kappa_1} T^*$ , system (3.1) has a continuous, unbounded, and one-dimensional curve  $\mathcal{H} \subset \mathbb{R}^2$  such that both 0 and  $\bar{w}(\bar{u}, \bar{v})$  (a unique positive T-periodic solution) are located in  $\mathcal{H}$ . This curve divides the  $(\kappa_1, 0)$  and  $(0, \hat{y}(t))$  on each side, and the solution from both sides converges to their two equilibrium points. Unfortunately, we are currently unable to

provide a precise expression or providing sharp estimates for curve  $\mathcal{H}$ , this will be a part of our future work. Additionally, future research will explore the integration of environmental and spatial factors into our mosquito population replacement models. Understanding how variables such as habitat, temperature fluctuations, and resource availability influence the dynamics of mosquito populations will be crucial.

#### Acknowledgements

The author would like to thank all of the anonymous reviewers for their helpful comments.

#### Author contributions

HG: Writing—original draft, numerical simulation, review & editing, and approving the final manuscript.

#### Funding

This work was supported by the National Natural Science Foundation of China (No: 12301621).

#### Data availability

Not applicable.

#### Declarations

##### Competing interests

The author declares no competing interests.

Received: 27 September 2024 Accepted: 26 January 2025 Published online: 05 February 2025

#### References

1. World Health Organization: dengue and severe dengue. <https://www.who.int/en/news-room/fact-sheets/detail/dengue-and-severe-dengue>
2. Norrby, R.: Outlook for a dengue vaccine. *Clin. Microbiol. Infect.* **20**, 92–94 (2014)
3. Daily, J.P.: Malaria vaccine trials—beyond efficacy end points. *N. Engl. J. Med.* **367**, 2349–2351 (2012)
4. Nkya, T.E.: Impact of environment on mosquito response to pyrethroid insecticides: facts, evidences and prospects. *Insect Biochem. Mol. Biol.* **43**, 407–416 (2013)
5. Bian, G.W., Xu, Y., Lu, P., et al.: The endosymbiotic bacterium *Wolbachia* induces resistance to dengue virus in *Aedes aegypti*. *PLoS Pathog.* **6**, e1000833 (2010)
6. Hoffmann, A.A., Turelli, M.: Cytoplasmic incompatibility in insects. In: O'Neill, S.L., et al. (eds.) *Influential Passengers: Inherited Microorganisms and Arthropod Reproduction*, pp. 42–80. Oxford University Press, London (1997)
7. Laven, H.: Cytoplasmic inheritance in *Culex*. *Nature* **177**, 141–142 (1956)
8. Huang, M., Tang, M., Yu, J., Zheng, B.: The impact of mating competitiveness and incomplete cytoplasmic incompatibility on *Wolbachia*-driven mosquito population suppression. *Math. Biosci. Eng.* **16**, 4741–4757 (2019)
9. Liu, Y., Jiao, F., Hu, L.: Modeling mosquito population control by a coupled system. *J. Math. Anal. Appl.* **506**, 125671 (2022)
10. Liu, K., Lou, Y.: A periodic delay differential system for mosquito control with *Wolbachia* incompatible insect technique. *Nonlinear Anal., Real World Appl.* **73**, 103867 (2023)
11. Liu, Y., Yu, J., Li, J.: A mosquito population suppression model by releasing *Wolbachia*-infected males. *Bull. Math. Biol.* **84**, 121 (2022)
12. Yu, J.: Modelling mosquito population suppression based on delay differential equations. *SIAM J. Appl. Math.* **78**, 3168–3187 (2018)
13. Yu, J., Li, J.: Global asymptotic stability in an interactive wild and sterile mosquito model. *J. Differ. Equ.* **269**, 6193–6215 (2020)
14. Zheng, B., Yu, J., Li, J.: Modeling and analysis of the implementation of the *Wolbachia* incompatible and sterile insect technique for mosquito population suppression. *SIAM J. Appl. Math.* **81**, 718–740 (2021)
15. Zhang, X., Liu, Q., Zhu, H.: Modeling and dynamics of *Wolbachia*-infected male releases and mating competition on mosquito control. *J. Math. Biol.* **81**, 243–276 (2020)
16. Farkas, J., Hinow, P.: Structured and unstructured continuous models for *Wolbachia* infections. *Bull. Math. Biol.* **72**, 2067–2088 (2010)
17. Hu, L., Tang, M., Wu, Z., et al.: The threshold infection level for *Wolbachia* invasion in random environments. *J. Differ. Equ.* **266**, 4377–4393 (2019)
18. Huang, M., Yu, J., Hu, L., Zheng, B.: Qualitative analysis for a *Wolbachia* infection model with diffusion. *Sci. China Math.* **59**, 1249–1266 (2016)
19. Li, Y., Liu, X.: An impulsive model for *Wolbachia* infection control of mosquito-borne diseases with general birth and death rate functions. *Nonlinear Anal., Real World Appl.* **37**, 412–432 (2017)
20. Su, Y., Zheng, B., Zou, X.: *Wolbachia* dynamics in mosquitoes with incomplete CI and imperfect maternal transmission by a DDE system. *Bull. Math. Biol.* **84**, 95 (2022)
21. Yang, J., Chen, Z., Tan, Y., et al.: Threshold dynamics of a stochastic mathematical model for *Wolbachia* infections. *J. Biol. Dyn.* **17**, 2231967 (2023)
22. Yu, J., Zheng, B.: Modeling *Wolbachia* infection in mosquito population via discrete dynamical models. *J. Differ. Equ. Appl.* **25**, 1549–1567 (2019)

23. Zheng, B., Tang, M., Yu, J.: Modeling Wolbachia spread in mosquitoes through delay differential equations. *SIAM J. Appl. Math.* **74**, 743–770 (2014)
24. Zheng, B., Tang, M., Yu, J., Qiu, J.: Wolbachia spreading dynamics in mosquitoes with imperfect maternal transmission. *J. Math. Biol.* **76**, 235–263 (2018)
25. Dutra, H.L., Rocha, M.N., Dias, F.B., et al.: Wolbachia blocks currently circulating Zika virus isolates *Aedes aegypti* mosquitoes. *Cell Host Microbe* **19**, 771–774 (2016)
26. Hoffmann, A.A., Montgomery, B.L., Popvici, J., et al.: Successful establishment of Wolbachia in *Aedes* populations to suppress dengue transmission. *Nature* **476**, 454–457 (2011)
27. Nazim, W.A., Hoffmann, A.A., NoorAfizah, A., et al.: Establishment of Wolbachia strain wAlbB in Malaysian populations of *Aedes aegypti* for dengue control. *Curr. Biol.* **29**, 4241–4248 (2019)
28. Utarini, A., Indriani, C., Ahmad, R.A., et al.: Efficacy of Wolbachia-infected mosquito deployments for the control of dengue. *N. Engl. J. Med.* **384**, 2177–2186 (2021)
29. Farkas, J., Hinow, P.: Structured and unstructured continuous models for Wolbachia infections. *Bull. Math. Biol.* **72**, 2067–2088 (2010)
30. Keeling, M., Jiggins, F., Read, J.: The invasion and coexistence of competing Wolbachia strains. *Heredity* **91**, 382–388 (2003)
31. Mcmeniman, C., Lane, R., Cass, B., et al.: Stable introduction of a life-shortening Wolbachia infection into the mosquito *Aedes aegypti*. *Science* **323**, 141–144 (2009)
32. Walker, T., Johnson, P., Moreira, L., et al.: The *ωMelWolbachia* strain blocks dengue and invades caged *Aedes aegypti* populations. *Nature* **476**, 450–453 (2011)
33. Yeap, H., Mee, P., Walker, T., et al.: Dynamics of the “popcorn” Wolbachia infection in outbred *Aedes aegypti* informs prospects for mosquito vector control. *Genetics* **187**, 583–595 (2011)
34. VDCI: Understanding the Life Cycle of the Mosquito. <https://www.vdci.net/mosquito-biology-101-life-cycle>
35. Yu, J., Li, J.: Dynamics of interactive wild and sterile mosquitoes with time delay. *J. Biol. Dyn.* **13**, 1–15 (2019)
36. Zheng, B., Li, J., Yu, J.: Existence and stability of periodic solutions in a mosquito population suppression model with time delay. *J. Differ. Equ.* **315**, 159–178 (2022)
37. Zheng, B.: Impact of releasing period and magnitude on mosquito population in a sterile release model with delay. *J. Math. Biol.* **85**, 18 (2022)
38. Zheng, B., Yu, J.: Existence and uniqueness of periodic orbits in a discrete model on Wolbachia infection frequency. *Adv. Nonlinear Anal.* **11**, 212–224 (2022)
39. Hsu, S., Zhao, X.: A Lotka-Volterra competition model with seasonal succession. *J. Math. Biol.* **64**, 109–130 (2012)
40. Cantrell, R., Cosner, C.: *Spatial Ecology via Reaction-Diffusion Equations*. Wiley, Chichester (2003)

## Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Submit your manuscript to a SpringerOpen<sup>®</sup> journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

---

Submit your next manuscript at ► [springeropen.com](https://www.springeropen.com)

---