https://dx.doi.org/10.1016/j.actatropica.2024.107159

Effectiveness evaluation of mosquito suppression strategies on dengue transmission under changing temperature and precipitation

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Abstract

Widespread resurgence of dengue outbreaks has seriously threatened the global health. Due to lack of treatments and vaccines, one key strategy in dengue control is to reduce the vector population size. As an environment-friendly mosquito control approach, releasing male mosquitoes transinfected with specific *Wolbachia* strain into the field to suppress the wild mosquito population size has become wildly accepted. The current study evaluates the effectiveness of this suppression strategy on dengue control under changing temperature and precipitation profiles. We formulate a mathematical model which includes larval intraspecific competition, the maturation period for mosquitoes, the extrinsic incubation period (EIP) and intrinsic incubation period (IIP). The persistence of mosquitoes and disease is discussed in terms of two basic reproduction numbers ($\mathcal{R}_M$ and $\mathcal{R}_0$) and the release ratio p_w. Further numerical simulations are carried out to not only validate theoretical results, but also provide interesting quantitative observations. Sensitivity analysis on the reproduction numbers, peak size, peak time and the final epidemic size is performed with respect to model parameters, which highlights effective control measures against dengue transmission. Moreover, by assuming temperature and precipitation dependent mosquito-related parameters, the model can be used to project the effectiveness of releasing *Wolbachia*-carrying males under climatic variations. It is shown that the effectiveness of various control strategies is highly dependent on the changing temperature and precipitation profiles. In particular, the model projects that it is most challenging to control the disease at the favorable temperature (around $27 \sim 30$°C) and precipitation ($5 \sim 8$mm/day) range, during which the basic reproduction number $\mathcal{R}_0$ is very high and more *Wolbachia*-infected males should be released.

Keywords: Dengue control, mosquito suppression strategy, vector-host model, changing temperature, precipitation

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1. Background

As a type of mosquito-borne viral disease, dengue is mainly transmitted between humans through female *Aedes* mosquitoes, the geographic expansion of which facilitates the spread of dengue disease to almost 130 countries [42]. Caused by any of the four serotypes of dengue virus, clinical symptoms of dengue infection include mild dengue fever, severe dengue haemorrhagic and severe dengue shock syndrome [16]. Due to the absence of specific antiviral treatments and reliable vaccines, controlling the mosquito vector becomes one of the most effective approaches in dengue control [27]. Traditional mosquito control measures mainly rely on massive use of chemical insecticides, which are not environmental-friendly. In addition, widespread insecticide resistance in mosquitoes leads to unsatisfactory control effects [11]. Therefore, it is imperative to find other novel environmentally friendly and effective mosquito control methods.

One of the alternatives is *Wolbachia*-driven mosquito control [20]. *Wolbachia* is a genus of maternally transmitted endosymbiosis bacteria, which can naturally infect one to three quarters of insects including some mosquito species such as *Culex pipiens* and *Aedes albopictus* [28]. Due to lower density of *Wolbachia* in natural infection, *Wolbachia*-driven control programs artificially transinfect some chosen *Wolbachia*-strain into a target mosquito species and release these transinfected mosquitoes into the field [7]. Rather than male killing, feminization and parthenogenesis, the only reproductive manipulation of *Wolbachia* observed in mosquitoes is cytoplasmic incompatibility (CI), which render natural female mosquitoes laying nonviable eggs if they mated with released *Wolbachia*-infected males [21]. On the other hand, the *Wolbachia*-infected female mosquitoes can lay viable *Wolbachia*-infected eggs after mating with *Wolbachia*-infected or uninfected males.

Wolbachia-driven strategies can be classified into two classes based on the difference of objectives. One is *Wolbachia*-driven replacement strategy, where male and female *Wolbachia*-infected mosquitoes are released simultaneously to replace natural *Wolbachia*-free mosquitoes by establishing *Wolbachia*-infection in the wild [54]. The other is *Wolbachia*-driven suppression strategy, that is, only male *Wolbachia*-carrying mosquitoes are released to suppress the number of wild natural mosquitoes [47, 66]. Avoiding bite nuisance, releasing *Wolbachia*-infected male mosquitoes makes *Wolbachia*-driven suppression strategy more acceptable to local residents compared with *Wolbachia*-driven replacement strategy. Field release trials have been authorized in a number of regions in China [9], Singapore [51], United states [8] and Australia [3]. In China, successful suppression of wild mosquito population has been achieved on the Shazai island, where millions of *Wolbachia*-infected males from Guangzhou's 'mosquito factory' have been deployed regularly since 2015 [66].

Mathematical models can help design appropriate release strategies through investigating the population dynamics of wild mosquitoes. A large amount of mosquito population models have been developed for that purpose. The majority of existing population models focused on *Wolbachia* based replacement, i.e., the spread and establishment of *Wolbachia* in wild mosquito species. In general, the mosquito population is divided into natural *Wolbachia*-free and *Wolbachia*-infected subgroups. The most concerned problem is to predict the threshold infection frequency of *Wolbachia* under the influence of various factors, which include the intensity of CI and maternal transmission [2, 43, 63], the age/sex structure [19, 53], the developmental delay [4, 62] of immature mosquitoes, stochastic effects of environment [18, 22]

and discontinuous releasing modes [30, 57]. A number of other models in the form of discrete difference equations [60, 61, 64], ordinary differential equations [56, 65] and delay differential equations [24, 25, 55, 59], have been proposed and analysed to explore the *Wolbachia*-driven suppression effects.

Mosquito population models involving *Wolbachia* can be extended to epidemiological models by incorporating the interactive transmission process of dengue virus between humans and mosquitoes. Few vector-host models have been proposed to investigate the altered dynamics of dengue epidemic under the control of *Wolbachia*-driven strategy. Most of these limited numbers of *Wolbachia* relevant dengue epidemic modeling studies attempted to explore the invasion dynamics of *Wolbachia*-infected mosquitoes and verify whether successful establishment and spread of *Wolbachia* can effectively control the transmission of dengue virus [26, 29, 38, 52]. To evaluate the suppression effects of releasing male-only *Wolbachia*-infected mosquitoes, the interactive transmission dynamics between wild mosquitoes and humans should be considered in the model formulation while *Wolbachia*-infected males do not get involved in the spread of disease. By assuming an ideal (continuous proportional) release strategy with a fixed ratio, threshold dynamics of mosquito persistence and disease outbreak in terms of the release ratio can be thoroughly investigated through models incorporating aforementioned features [44, 58].

Even though existing modeling studies had made important contributions on exploring *Wolbachia*-driven control of mosquitoes and mosquito borne diseases, one important factor closely related to the growth of mosquitoes is often ignored, that is, the intra-specific competition during aquatic (especially larval) stages. Due to weak mobility and confined habitats, immature mosquitoes especially larvae may experience strong intra-specific competition for limited resources when larval density is high [33, 49]. It makes more sense in biology to incorporate the effects of larval density-dependent intra-specific competition in model formulation, which constitutes one of the motivations of the current study. Since only adult female mosquitoes are involved in the transmission of the dengue disease, we mainly model the population growth of adult female mosquitoes while considering the effects of density dependent larval survival in the recruitment term.

In ecology, uniform and cohort competition are two possible approximations of intraspecific competition in modeling studies [15, 41]. Uniform competition assumes that all larvae are functionally identical and compete equally with all others from the larval stage. This assumption is fairly simplistic and implies that the survival of each larva may depend on the total population size of the larval stage, which leads to a coupled stage-structured model and may make the theoretical analysis intractable (see references [13, 24, 25, 56]). By contrast, cohort competition assumes competition occurs within the same age cohort containing individuals that enter the age class simultaneously, which is more suitable for most insect species [41] and has been employed in several modeling studies on mosquito population [14, 31, 32]. In this study, we assume mosquito larvae experience cohort competition and lump all mosquitoes in immature stages into a joint larval stage. In this case, survival of immature individuals can be formulated as a function of the initial population size of the age cohort, i.e., the newly laid eggs. Detailed model formulation is provided in Section 2.

The mosquito population model incorporating density-dependent larval survival is further extended into a vector-host epidemiological model to investigate the transmission dynamics of dengue virus under the release of *Wolbachia*-infected male-only mosquitoes into the wild

population. In addition, the intrinsic period in infected humans and the extrinsic period in infected mosquitoes are included in the model, which yields a system of delay differential equations with three different delays. The persistence of the mosquito population and disease transmission is further characterized through two respective reproduction numbers.

As the vector of dengue virus, *Aedes* mosquito growth are strongly affected by climatic variations such as ambient temperature and precipitation [6]. Another focus of this paper is to investigate the sensitivity of the effectiveness of control strategies under consideration of larval intra-specific competition, varying temperatures and precipitations. Further observation can be gained by assuming temperature and precipitation-dependent parameters in the model.

The overall layout of this paper is provided as follows. In Section 2, the modeling framework of the mosquito population growth and the vector-host interaction is described in detail. Theoretical analysis including the well-posedness of the model, the existence of all equilibria and local stability of two boundary equilibria are provided. In Section 3, numerical simulations are performed to not only validate the theoretical results, but also explore the sensitivity of the basic reproduction numbers ($\mathcal{R}_M$ and $\mathcal{R}_0$) with respect to parameters, and quantify effectiveness of releasing *Wolbachia*-infected males under changing temperatures weather conditions. We summarize this paper in Section 4.

2. Model formulation and persistence analysis

In this section, we first describe the dynamics of adult mosquito population growth and further formulate a dengue model by incorporating the pathogen transmission between mosquitoes and humans. The main aspects considered in the model formulation include: larval competition during mosquito maturation, the released male *Wolbachia*-infected mosquitoes, the extrinsic incubation period (EIP) in infected mosquitoes, and the intrinsic incubation period (IIP) of dengue virus in infected human hosts. The model formulation will follow the diagram in Figure 1 for different time-dependent variables.

2.1. Mosquito growth model with larval competition

Although a mosquito undergoes three aquatic (including egg, larval and nymphal) immature stages and one adult stage during its life cycle, we mainly focused on the population growth of adult female mosquitoes, which can be described by a single equation through stock recruitment arguments. In fact, the dynamics of the population size of female adult mosquitoes $M(t)$ are governed by two processes: recruiting (developing) from the immature stage and death, that is

$$\frac{dM(t)}{dt} = R(t) - D(t), \tag{2.1}$$

where $R(t)$ is the recruitment rate at time t and $D(t)$ represents the death rate of adult mosquitoes.

Let τ represent the developmental duration through all aquatic stages. Then, individuals newly recruited into the adult stage at time t are developed from eggs laid at a previous time instant $t-\tau$ (i.e., birth at $t-\tau$) and the survival through immature stages. Assume $B(t)$ is the egg laying rate at time t, which is dependent on the total number of egg-laying

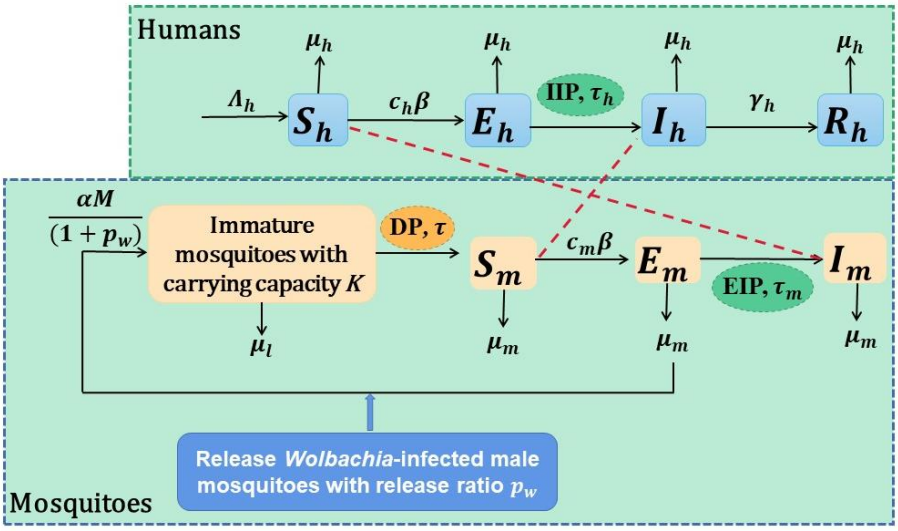

Figure 1: Schematic flow chart of the transmission of dengue virus under the impact of larval competition and released male *Wolbachia*-infected mosquitoes. Here, DP, IIP and EIP represent the developmental period, the intrinsic incubation period in infected humans and the extrinsic incubation period in infected mosquitoes, respectively.

adults $M(t)$ at time t. The recruitment rate $R(t)$ can be formulated as

$$R(t) = B(t-\tau) \times P(t-\tau, t)$$

where $P(t-\tau, t)$ measures the survival probability of individuals born at time $t-\tau$ to time instant t. Due to larval intra-specific competition, the survival probability $P(t-\tau, t)$ of immature mosquitoes may be influenced by density dependent effects. Under the assumption of cohort competition [41], this survival probability takes a function of the initial population size entering into this age cohort at previous time $t-\tau$, that implies $P(t-\tau, t)$ is a function of $B(t-\tau)$. In this manuscript, we are going to use the following Shepherd recruitment functional response [12], which is widely employed in ecological studies to quantify the varying trend of survival due to population density regulations [39, 41]:

$$P(t-\tau, t) = \frac{e^{-\mu_l \tau}}{1 + (B(t-\tau)/K)^{\theta}}.$$

In this Shepherd recruitment model, $e^{-\mu_l \tau}$ represents the survival probability through density-independent natural death with a rate μ_l, K is the threshold carrying capacity for immature mosquitoes, above which immature individual survival is determined dominantly by density-dependent intra-specific competition. The degree of compensation parameter θ (> 0) determines the shape of changing trend between larval survival and initial population size [12]: $\theta > 1$ implies a hump-shaped changing trend and the occurrence of overcompensation [12, 41], while $\theta \leq 1$ indicates a monotonically increasing trend (with $\theta = 1$) or without a far-end asymptotic maximum ($\theta < 1$). The case of $\theta = 1$ is equivalent to the Beverton-Holt model and compensation is expected to occur [5]. Recent experimental research showed that sur-

vivorship curves of larval mosquitoes were best fit when compensating density-dependence was considered in the model [10]. Therefore, we assume there is compensation for larval intra-specific competition, i.e., $\theta = 1$. Furthermore, assume adult mosquitoes are subject to natural mortality with background rate μ_m, that is, $D(t) = \mu_m M(t)$. Then (2.1) becomes the following delay differential equation for the growth of female adult mosquito population:

$$\frac{dM(t)}{dt} = B(t-\tau)P(t-\tau,t) - \mu_m M(t) = B(t-\tau)\frac{e^{-\mu_l \tau}}{1+B(t-\tau)/K} - \mu_m M(t). \qquad (2.2)$$

It remains to determine the term $B(t)$, which should be carefully argued due to the releasing of male-only *Wolbachia*-carrying mosquitoes. Assume male *Wolbachia*-carrying mosquitoes are deployed regularly. Due to cytoplasmic incompatibility (CI), *Wolbachia*-carrying eggs produced by wild female adults mated with *Wolbachia*-infected male mosquitoes will be nonviable. At time t, let $w(t)$ represent the amount of released male mosquitoes carrying *Wolbachia*. If we assume that this released amount is maintained to be proportionate to the population size of wild natural male mosquitoes, with the overflooding ratio p_w, then $w(t) = p_w M(t)$ under the $1:1$ female-male ratio assumption. Furthermore, we assume that male *Wolbachia*-carrying mosquitoes have the same mating ability as that of wild natural male mosquitoes. The mating probability between a *Wolbachia*-carrying male mosquito and a wild natural female mosquito becomes $\frac{w(t)}{M(t)+w(t)} = \frac{p_w}{1+p_w}$. Since the intensity of CI is assumed as 100%, a *Wolbachia*-infected male mated with a wild female mosquito will certainly produce nonviable eggs. Therefore, fertile eggs can only be produced by the mating between wild natural male and female mosquitoes, with the probability $1 - \frac{w(t)}{M(t)+w(t)} = \frac{1}{1+p_w}$. Assume the egg-laying rate of a wild natural female mosquito is denoted by α, then the birth rate of wild *Wolbachia*-free female mosquitoes under the impact of released *Wolbachia*-infected male mosquitoes at time t is $B(t) = \alpha\frac{1}{1+p_w}M(t)$. Substituting the form of the birth rate into (2.2) yields the following delay differential equation describing the growth of natural adult female mosquito population affected by released male *Wolbachia*-infected mosquitoes:

$$\frac{dM(t)}{dt} = \frac{\alpha M(t-\tau)e^{-\mu_l \tau}}{2(1+p_w)+2\alpha M(t-\tau)/K} - \mu_m M(t). \qquad (2.3)$$

Please note that $1/2$ is used to assume that the female-male ratio is $1:1$. Since released *Wolbachia*-infected male mosquitoes are only involved into the reproductive activity of wild mosquitoes and will die naturally in the end, the dynamics of *Wolbachia*-infected male mosquitoes are omitted in this paper.

2.2. Dengue disease transmission model

In this subsection, we extend model (2.3) by incorporating the cross-infections between mosquitoes and humans. Here, we assume that only a single dengue serotype is involved in the disease transmission. The wild female adult mosquito population is divided into subgroups of susceptible (S_m), exposed (E_m) and infected (I_m) mosquitoes. Then, $M(t) =$

$S_m(t) + E_m(t) + I_m(t)$. The human population is correspondingly separated into susceptible (S_h), exposed (E_h), infectious (I_h) and recovered (R_h) subgroups. Let $N_h(t)$ be the total size of humans at time t, then $N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t)$.

Susceptible humans can be infected with dengue virus if they are bitten by infected mosquitoes. The infection rate of susceptible humans can be described by

$$c_h \beta \frac{I_m(t)}{N_h(t)} S_h(t),$$

where β and c_h represent respectively the biting rate of mosquitoes and the transmission probability of dengue virus from mosquitoes to humans. Let τ_h represent the intrinsic incubation period (IIP) of dengue virus in infected human hosts, then the transfer rate from exposed to infectious state is

$$e^{-\mu_h \tau_h} c_h \beta \frac{I_m(t-\tau_h)}{N_h(t-\tau_h)} S_h(t-\tau_h),$$

where μ_h is the natural death rate of humans and $e^{-\mu_h \tau_h}$ represents the survival probability of infected humans during IIP.

Dengue virus can be transmitted to susceptible mosquitoes if they are feeding on the blood of infectious humans. The transmission rate of dengue virus from infected humans to susceptible mosquitoes is depicted by

$$c_m \beta \frac{I_h(t)}{N_h(t)} S_m(t),$$

where c_m is the transmission possibility from humans to mosquitoes. Considering a constant duration of the extrinsic incubation period (EIP) in infected mosquitoes τ_m, exposed mosquitoes transfer to infectious state at the rate

$$e^{-\mu_m \tau_m} c_m \beta \frac{I_h(t-\tau_m)}{N_h(t-\tau_m)} S_m(t-\tau_m),$$

where $e^{-\mu_m \tau_m}$ represents the survival probability of infected mosquitoes during EIP.

Based on the above arguments and model diagram in Figure 1, we obtain the following system of delay differential equations with three different discrete delays to describe the

cross-infections of dengue virus between humans and mosquitoes:

$$\begin{cases} \dfrac{dS_m(t)}{dt} = \dfrac{\alpha M(t-\tau)e^{-\mu_l \tau}}{2(1+p_w)+2\alpha M(t-\tau)/K} - \mu_m S_m(t) - c_m\beta \dfrac{I_h(t)}{N_h(t)} S_m(t), \\ \dfrac{dE_m(t)}{dt} = c_m\beta \dfrac{I_h(t)}{N_h(t)} S_m(t) - \mu_m E_m(t) - e^{-\mu_m\tau_m} c_m\beta \dfrac{I_h(t-\tau_m)}{N_h(t-\tau_m)} S_m(t-\tau_m), \\ \dfrac{dI_m(t)}{dt} = e^{-\mu_m\tau_m} c_m\beta \dfrac{I_h(t-\tau_m)}{N_h(t-\tau_m)} S_m(t-\tau_m) - \mu_m I_m(t), \\ \dfrac{dS_h(t)}{dt} = \Lambda_h - \mu_h S_h(t) - c_h\beta \dfrac{I_m(t)}{N_h(t)} S_h(t), \\ \dfrac{dE_h(t)}{dt} = c_h\beta \dfrac{I_m(t)}{N_h(t)} S_h(t) - \mu_h E_h(t) - e^{-\mu_h\tau_h} c_h\beta \dfrac{I_m(t-\tau_h)}{N_h(t-\tau_h)} S_h(t-\tau_h), \\ \dfrac{dI_h(t)}{dt} = e^{-\mu_h\tau_h} c_h\beta \dfrac{I_m(t-\tau_h)}{N_h(t-\tau_h)} S_h(t-\tau_h) - (\mu_h+\gamma_h) I_h(t), \\ \dfrac{dR_h(t)}{dt} = \gamma_h I_h(t) - \mu_h R_h(t). \end{cases} \tag{2.4}$$

The detailed descriptions of parameters in model (2.4) are listed in Table 1.

It is easy to verify the following integral formulae of $E_m(t)$ and $E_h(t)$ hold

$$\begin{aligned} E_m(t) &= \int_{t-\tau_m}^{t} e^{-\mu_m(t-\eta)} c_m\beta \frac{I_h(\eta)}{N_h(\eta)} S_m(\eta) d\eta \quad \text{and} \\ E_h(t) &= \int_{t-\tau_h}^{t} e^{-\mu_h(t-\eta)} c_h\beta \frac{I_m(\eta)}{N_h(\eta)} S_h(\eta) d\eta. \end{aligned} \tag{2.5}$$

with the biological compatibility conditions for initial values of E_m and E_h:

$$E_m(0) = \int_{-\tau_m}^{0} e^{\mu_m\eta} c_m\beta \frac{I_h(\eta)}{N_h(\eta)} S_m(\eta) d\eta \ \text{ and } \ E_h(0) = \int_{-\tau_h}^{0} e^{\mu_h\eta} c_h\beta \frac{I_m(\eta)}{N_h(\eta)} S_h(\eta) d\eta.$$

2.3. Persistence analysis

Theoretical analysis has been performed on model (2.4), which is presented in the Appendix. Two reproduction numbers, for the mosquito population $\mathcal{R}_M$ and for the disease transmission $\mathcal{R}_0$ can be introduced as follows:

$$\mathcal{R}_M = \frac{e^{-\mu_l\tau}\alpha}{2(1+p_w)\mu_m} \tag{2.6}$$

Table 1: Biological explanations and values for parameters of system (2.4).

Para.	Description
Λ_h	Recruitment rate of humans
μ_l	Per-capita natural death rate of larvae
μ_m	Per-capita natural death rate of adult mosquitoes
μ_h	Per-capita natural death rate of humans
τ	Maturation delay of larvae
τ_m	The extrinsic incubation period (EIP) in infected mosquitoes
τ_h	The intrinsic incubation period (IIP) of dengue virus in infected human hosts
α	The egg-laying rate of a wild natural female mosquitoes
p_w	The ratio of released *Wolbachia*-carrying males to wild males
β	Biting rate of mosquitoes
c_m	The transmission probability of dengue virus from humans to mosquitoes
c_h	The transmission probability of dengue virus from mosquitoes to humans
γ_h	Recovery rate of infectious humans
K	Threshold carrying capacity of larval mosquitoes (measuring larval density dependent effects)

and

$$\begin{aligned}\mathcal{R}_0 :=& \frac{e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h M^*}{(\mu_h+\gamma_h)\mu_m N_h^*}\\ =& \frac{e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h \mu_h}{(\mu_h+\gamma_h)\mu_m\Lambda_h}\frac{K(1+p_w)}{\alpha}\left(\frac{e^{-\mu_l\tau}\alpha}{2(1+p_w)\mu_m}-1\right)\\ =& \frac{e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h \mu_h}{(\mu_h+\gamma_h)\mu_m\Lambda_h}\frac{K(1+p_w)}{\alpha}(\mathcal{R}_M-1).\end{aligned} \tag{2.7}$$

These reproduction numbers can be used to characterize the existence and local stability of various equilibria for model (2.4).

Note that the amount of released *Wolbachia*-infected males is measured by the release ratio p_w. In view of (2.6) and (2.7), the release ratio p_w has negative effects on the basic reproduction numbers $\mathcal{R}_M$ and $\mathcal{R}_0$. Based on the formulae of $\mathcal{R}_M$ and $\mathcal{R}_0$, we obtain the corresponding threshold values of the release ratio p_w, which are shown as follows

$$\begin{cases}\mathcal{R}_M=1 \text{ if and only if } p_{w_1}^*=\dfrac{e^{-\mu_l\tau}\alpha}{2\mu_m}-1, \textit{and}\\ \mathcal{R}_0=1 \text{ if and only if } p_{w_2}^*=\dfrac{e^{-\mu_l\tau}\alpha}{2\mu_m}-1-\dfrac{\alpha\Lambda_h\mu_m(\mu_h+\gamma_h)}{\beta^2 c_m c_h e^{-\mu_m\tau_m-\mu_h\tau_h}\mu_h K}.\end{cases}$$

As the reproduction numbers, these critical release ratios of *Wolbachia*-infected males can serve as threshold values for mosquito control and disease prevention. We have the following

persistence results on the mosquito population and disease transmission in terms of the reproduction numbers ($\mathcal{R}_M$ and $\mathcal{R}_0$) and critical release ratios ($p^*_{w_1}$ and $p^*_{w_2}$).

(1) If $\mathcal{R}_M < 1$ (i.e., $p_w > p^*_{w_1}$), the dengue-free-mosquito-extinct (DFME) equilibrium is locally stable, which indicates that releasing a large amount of *Wolbachia*-infected males can drive the extinction of mosquito population and further wipe out the dengue disease;

(2) If $\mathcal{R}_M > 1$ and $\mathcal{R}_0 < 1$ (i.e., $p^*_{w_2} < p_w < p^*_{w_1}$), the dengue-free-mosquito-persistent (DFMP) equilibrium is locally stable, which implies that releasing a medium amount of *Wolbachia*-infected males can still eliminate the dengue disease even though the mosquito population persists;

(3) If $\mathcal{R}_0 > 1$ (i.e., $p_w < p^*_{w_2}$), the unique endemic equilibrium exists, which means that releasing a small amount of *Wolbachia*-infected males is inadequate to control both the mosquito population and dengue disease.

3. Results

This section presents numerical simulations to not only validate our theoretical results, but also investigate the integrated impact of larval competition K and releasing *Wolbachia*-infected males p_w on mosquito and dengue control under changing weather conditions. The *Wolbachia*-infected male mosquitoes are assumed to be continuously released to a hypothetical isolated natural *Wolbachia*-free mosquitoes inhabiting in Nansha district of Guangzhou, which is a metropolitan city in China and large-scale field release of *Wolbachia*-infected male mosquitoes are allowed to carry out. The per-capita death rate of humans μ_h can be estimated as $\mu_h = 3.5818 \times 10^{-5}$ by applying similar method as that in [48]. Based on the bulletin of 7th national population census [45], the total number of permanent residents in Nansha district is $N^*_h = 846,584$. Then, the daily recruitment of humans in Nansha district of Guangzhou is calculated approximately as $\Lambda_h = N^*_h \times \mu_h = 30.323$.

There are few references involving the intensity of larval intra-specific competition. We give a rough estimate of threshold carrying capacity of larval mosquitoes K within $[10^6, 10^7]$. The other parameters are estimated from related literature. The baseline value of all parameters in model (2.4) are listed in Table 2. Based on these parameter values, we simulate the behavior of solutions under different cases and implement relative sensitivity analysis of the basic reproduction numbers (for mosquito population $\mathcal{R}_M$ and dengue disease $\mathcal{R}_0$ respectively) with respect to all other parameters. Furthermore, various sensitivity analyses on the basic reproduction number of dengue disease ($\mathcal{R}_0$), the peak size (maximum number) of infected humans (I_h), the peak time (i.e. when the number of infected humans reaches the maximum) of infected humans (I_h) and the final size of humans are conducted to explore how threshold larval carrying capacity (K) and releasing ratio of *Wolbachia*-infected males (p_w) jointly influence dengue control.

In view of the effects of changing weather conditions, mosquito related parameters are further extended to be temperature (T) and precipitation (P) dependent. The functional relationships of these parameters with respect to temperatures and precipitations are shown in Table 3. The basic reproduction numbers ($\mathcal{R}_M$ and $\mathcal{R}_0$), the threshold value of releasing

Table 2: Baseline value of parameters in model (2.4).

Para.	Baseline/Range	Dimension	Reference
Λ_h	30.323	Humans $\times$Day^{-1}	Estimated
μ_h	3.5818 $\times 10^{-5}$	Day^{-1}	[48]
α	7.496	Day^{-1}	[48]
β	0.189	Day^{-1}	[48]
μ_l	0.0427	Day^{-1}	[48]
μ_m	0.09047	Day^{-1}	[48]
τ	14	Day	[35, 58]
τ_m	10	Day	[35]
τ_h	5	Day	[35]
p_w	$0 \sim 50$	Dimensionless	Assumed
c_m	0.65	Dimensionless	[35]
c_h	0.7	Dimensionless	[35]
γ_h	0.18	Day^{-1}	[35]
K	$10^6 \sim 10^7$	Dimensionless	Assumed

ratios ($p^*_{w_1}$ and $p^*_{w_2}$), the peak size (maximum number) of infected humans (I_h) and the final size of humans are employed as the indices to evaluate the control effects under varying temperature and precipitation profiles.

Table 3: Temperature and precipitation dependent parameters.

Name	Formulations	Resources
Adult mortality rate, $\mu_m(T)$	$\mu_m(T) = -\log(0.677\exp(-0.5((T-20.9)/13.2)^6)T^{0.1})$	[36, 48]
Biting rate, $\beta(T)$	$\beta(T) = 0.0943 + 0.0043T$	[37, 48]
Egg laying rate, $\alpha(T,P)$	$\alpha(T,P) = \alpha_1(T)\alpha_2(P)$ $= 33.2\exp(-0.5((T-70.3)/14.1)^2)(38.8-T)^{1.5}$ $\times\dfrac{1.05\exp(-0.05(P-10)^2)}{\exp(-0.05(P-10)^2)+0.05}$	[1, 37, 48]
Developmental period, $\tau(T)$	$\tau(T) = 133.95 - 8.464T + 0.149T^2$	[37, 48]
EIP, $\tau_m(T)$	$\tau_m(T) = 1.03(4+\exp(5.15-0.123T))$	[37, 48]
Immature death rate, $\mu_l(T,P)$	$\mu_l(T,P) = \mu_{l_1}(T)\mu_{l_2}(P)$ $= -\log(0.977\exp(-0.5((T-21.8)/16.6)^6))$ $\times[1+1.1P/(1+P)]$	[1, 37, 48]

3.1. Threshold dynamics of solutions

In view of the formulae in (2.6) and (2.7), the basic reproduction numbers for mosquito growth $\mathcal{R}_M$ and for disease transmission $\mathcal{R}_0$ are determined by the releasing ratio p_w and the threshold larval carrying capacity K. Assume K is set as 10^6. Figures 2-4 show different threshold behaviours of model (2.4) under different combinations of $\mathcal{R}_M$ and $\mathcal{R}_0$. As shown in Figure 2, the mosquitoes and the dengue disease will both eventually die out if the mosquito reproduction number is reduced to be less than 1, i.e., $\mathcal{R}_M = 0.9421 < 1$, by releasing a large amount of *Wolbachia*-infected male mosquitoes ($p_w = 30 > p^*_{w_1} = 28.2062$). While mosquito

population will persist and the dengue disease is effectively controlled if $\mathcal{R}_M = 2.6551 > 1$ and $\mathcal{R}_0 = 0.9928 < 1$ (see Figure 3). In this case, a medium amount of *Wolbachia*-infected males are released ($9.8678 = p^*_{w_2} < p_w = 10 < p^*_{w_1}$), which may raise the basic mosquito reproduction number $\mathcal{R}_M$ to be greater than one. In the case where $\mathcal{R}_M > 1$ and $\mathcal{R}_0 > 1$ ($p_w = 5 < p^*_{w_2}$), both mosquitoes and dengue virus coexist with humans, as shown in Figure 4.

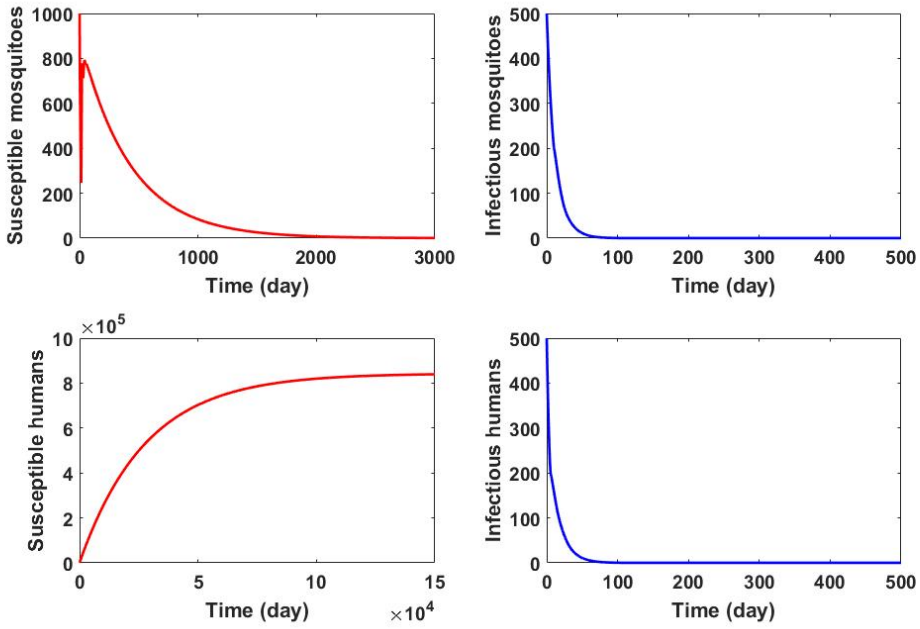

Figure 2: Solution profiles when $p_w = 30$ and other parameters are given in Table 2. In this case, $p_w > p^*_{w_1}$ and $\mathcal{R}_M = 0.9421 < 1$.

3.2. Sensitivity analysis of $\mathcal{R}_M$ and $\mathcal{R}_0$

The local sensitivity analysis of $\mathcal{R}_M$ and $\mathcal{R}_0$ is explored with respect to other parameters in Table 2. By virtue of the method provided in [35, 58], the relative sensitivity index is defined by

$$S_p^g = \frac{\tilde{p}}{\tilde{g}} \times \frac{\partial g}{\partial p}|_{p=\tilde{p}},$$

where g is a differentiable function of the parameter p, and $\tilde{g}$ is the value of g evaluated when p is set at the baseline value $\tilde{p}$ in Table 2. Figure 5 shows the relative indices of $\mathcal{R}_M$ and $\mathcal{R}_0$, which are sorted with the absolute values in descending order to highlight the significance of parameters. It can be seen from the figure that both $\mathcal{R}_M$ and $\mathcal{R}_0$ are most sensitive to adult mosquito death rate μ_m, which indicates that increased adult mosquitoes mortality rate may effectively control the mosquito population size and the spread of dengue virus disease. Compared with $\mathcal{R}_0$, the mosquito reproduction number $\mathcal{R}_M$ is more sensitive to the changes of the release ratio of *Wolbachia*-infected males p_w. As expected, disease related parameters such as the biting rate β, the transmission probabilities c_m, c_h play evident positive roles

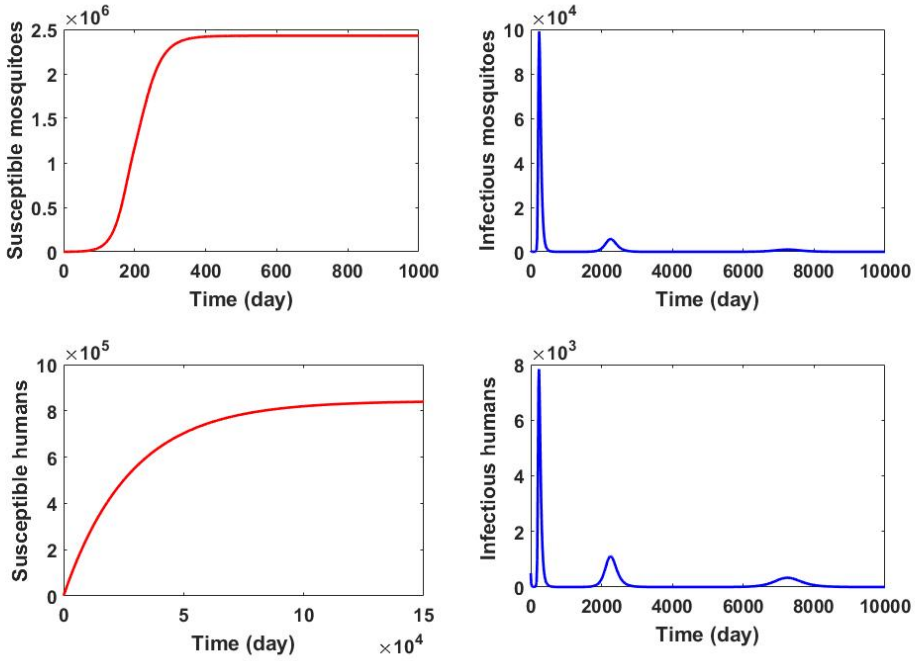

Figure 3: Solution profiles when $p_w = 10$ and other parameters are given in Table 2. In this case, $p^*_{w_2} < p_w < p^*_{w_1}$ and $\mathcal{R}_M = 2.6551 > 1$, $\mathcal{R}_0 = 0.9928 < 1$.

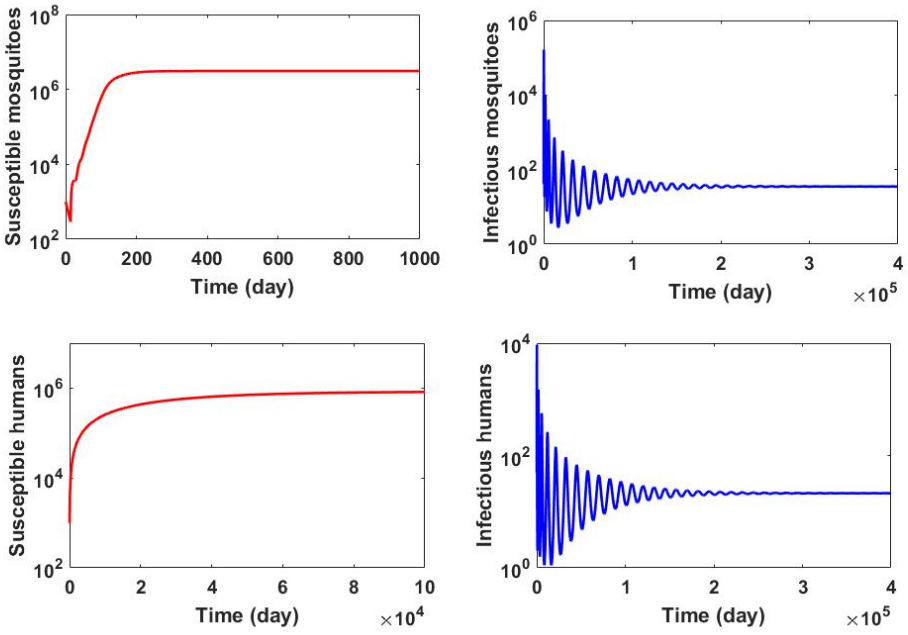

Figure 4: Solution profiles when $p_w = 5$ and other parameters are given in Table 2. In this case, $p_w < p^*_{w_2}$, which implies $\mathcal{R}_M = 4.8677 > 1$ and $\mathcal{R}_0 = 1.2654 > 1$.

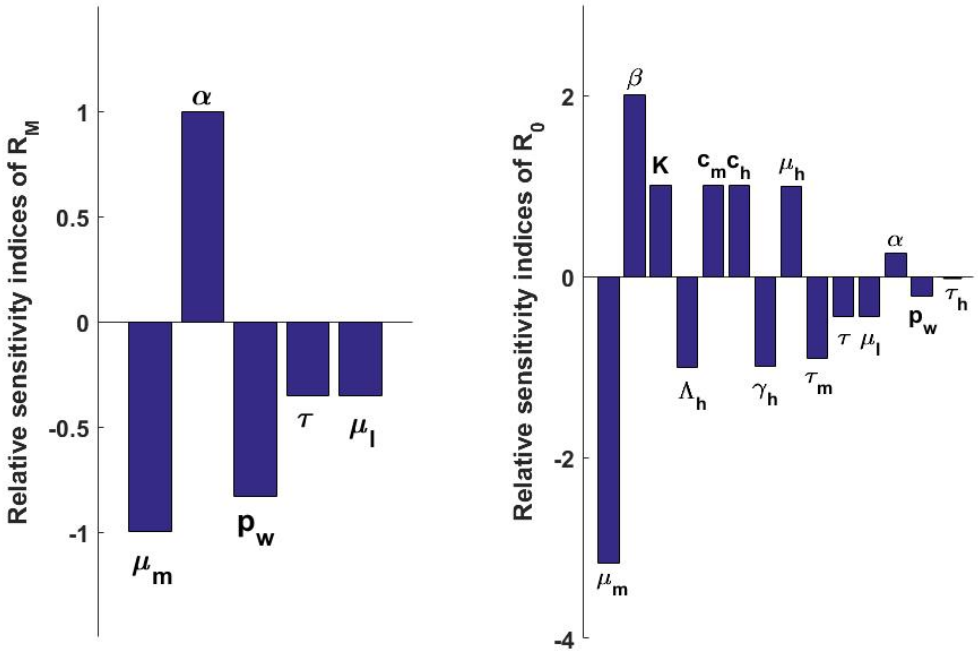

Figure 5: Relative sensitivity indices of $\mathcal{R}_M$ and $\mathcal{R}_0$ with respect to parameters in Table 1.

in the basic reproduction number $\mathcal{R}_0$, which is sensitive to the intensity of threshold larval carrying capacity K and human related parameters $(\Lambda_h, \mu_h, \gamma_h)$ as well. With the exception of the time delay induced by IIP (τ_h), the variations of mosquito developmental duration (τ) and EIP (τ_m) may have great impacts on values of $\mathcal{R}_M$ and $\mathcal{R}_0$ respectively. Hence, it is important to accurately measure the larval intra-specific competition, EIP and mosquito developmental delay, and incorporate these ingredients in the model formulation, which may in turn greatly improve the model projections. Unlike the sensitivity indices of μ_m and μ_l on $\mathcal{R}_0$, which are negative, that of μ_h is counter-intuitively positive. This positive index can be explained through the dilution effect of host in vector-borne disease transmission [34].

3.3. Combined control effects of p_w and K

The sensitivity analysis reported in Figure 5 implies that the basic reproduction number of dengue disease $\mathcal{R}_0$ is more sensitive to the carrying capacity of larval mosquitoes K than the release ratio p_w, which is a surprising result. In this subsection, we further investigate the combined effects of K and p_w on the control of dengue fever disease. The basic reproduction number $\mathcal{R}_0$, the peak size and time of infectious humans and the final size of humans are employed as the indices to evaluate the effectiveness. The contour plots in Figure 6 indicate all these indices are negatively correlated with p_w while positively correlated with K. The basic reproduction number, peak level of human infections and the final epidemic size are projected to have sharp decreases if the larval intra-specific competition is intensified (smaller K) and more *Wolbachia*-infected males (larger p_w) are released. The peak time of human infections

is sensitive to larval carrying capacity only when the release ratio is between 12 and 20. In order to eliminate the transmission of dengue fever, it is better to combine multiple control methods, which include releasing *Wolbachia*-infected male mosquitoes, cleaning the pooled water (i.e., intensify the larval competition with smaller K) and killing adult mosquitoes. Furthermore, it is interesting to observe that the relationship between the peak size and the carrying capacity K is not monotone. The peak size may take a smaller value when the release ratio is around 10 (when $K = 7 \times 10^6$). This implies that increasing the release ratio may not be always beneficial for disease control.

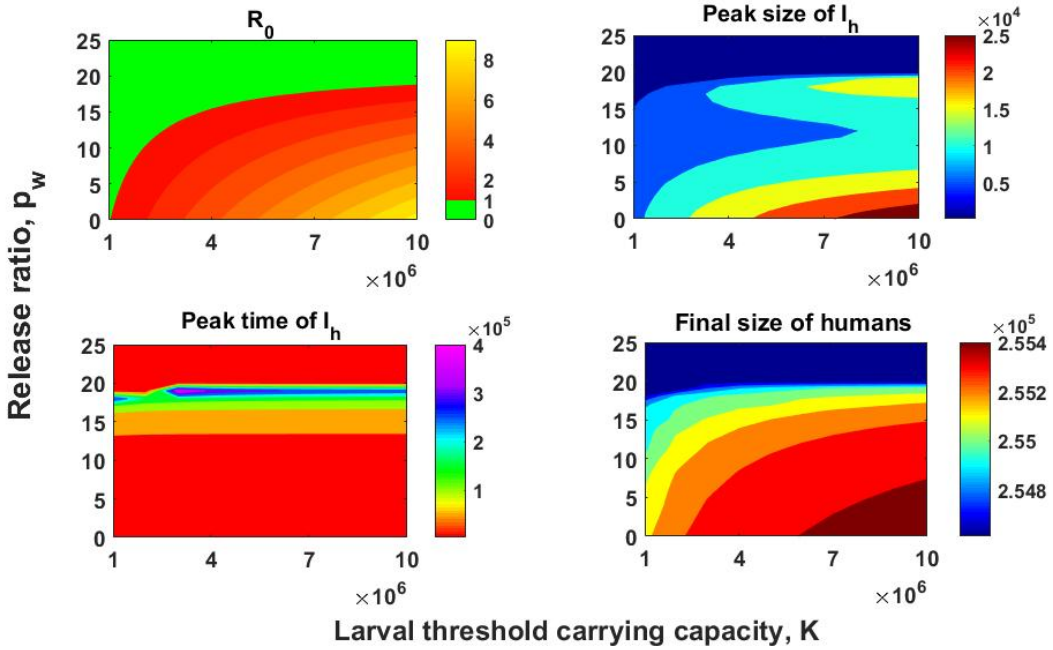

Figure 6: The contour plots depict the variation of $\mathcal{R}_0$, peak size and peak time of infectious humans and final size of humans with respect to K and p_w.

3.4. Effects of changing temperatures and precipitations

This subsection explores the impact of changing temperatures and daily precipitations on mosquito control and dengue prevention. According to the historical weather data in Guangzhou [50], the varying range of temperature and daily precipitation are chosen as $14 \sim 35$°C and $0 \sim 10$mm/day respectively. Figure 7 shows how the reproduction numbers $\mathcal{R}_M$ and $\mathcal{R}_0$ vary with changing temperatures and daily precipitations. The appropriate temperature range for mosquitoes to survive and transmit dengue virus are $20 \sim 32$°C and $23 \sim 30$ °C respectively.

Within the suitable temperature range (especially $25 \sim 30$°C), more daily precipitation facilitates mosquito growth while medium amount of precipitation is more favorable to the transmission of dengue virus. During the favorable temperature range ($23 \sim 30$°C) for dengue transmission, Figure 8 explores the effects of changing temperatures and precipitations on the peak size of infected humans and the final size of humans, which increase first with the temperature and reach the maximum values at around 27.5°C, and then decrease

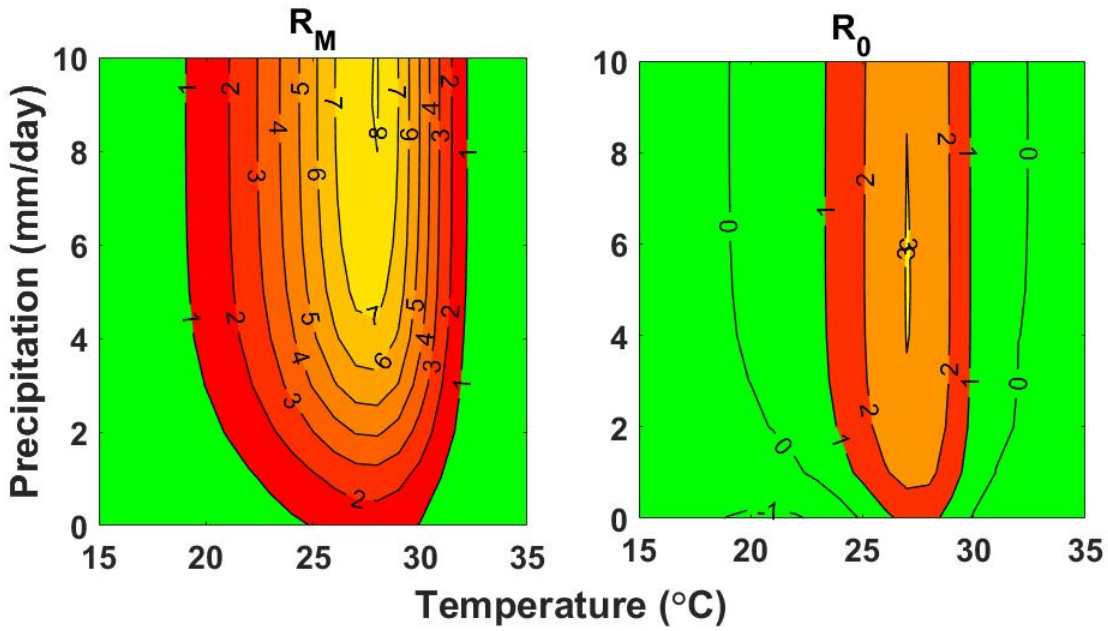

Figure 7: The variations of $\mathcal{R}_M$ and $\mathcal{R}_0$ with respect to varying temperature and daily precipitation. Different color schemes are employed to distinguish cases whether the basic reproduction number is less (green) or greater (red and yellow) than one.

once the temperature is greater than 27.5°C. Moreover, the variations of threshold release ratios $p^*_{w_1}$ and $p^*_{w_2}$ depicted in the contour plots of Figure 9 indicate that more *Wolbachia*-infected male mosquitoes are needed to be released for dengue control when temperature and precipitation are in some regions.

Compared with precipitation, temperature plays more significant roles in determining the magnitudes of reproduction numbers. The sensitivity of the basic reproduction number $\mathcal{R}_0$ with respect to temperature dependent parameters is further explored under four different temperatures when the daily rainfall is fixed at a moderate amount (i.e., $P = 5$ mm/day). Other than the biting rate β, the sensitivity index of $\mathcal{R}_0$ to all temperature dependent parameters first decreases between $21 \sim 27$°C and then increases when the temperature rises to 30°C, which are shown in Figure 10. In addition, the impact of temperature-independent parameter p_w on $\mathcal{R}_0$ is affected by varying temperatures, the changing trend of which is similar as those of temperature dependent parameters (see Figure 10). Therefore, it may become challenging to control dengue outbreaks when releasing *Wolbachia*-infected male mosquitoes at favorable temperatures and precipitations for mosquitoes.

4. Discussion

Frequent emergence and resurgence of dengue outbreaks brings a huge global health burden. The prevention and control of dengue transmission relies strongly on the mosquito control due to the absence of effective treatments and vaccines. Releasing mosquitoes transinfected by specific *Wolbachia* strain in the field to suppress or replace the wild mosquito population has become a wildly accepted environment-friendly control strategy. In this pa-

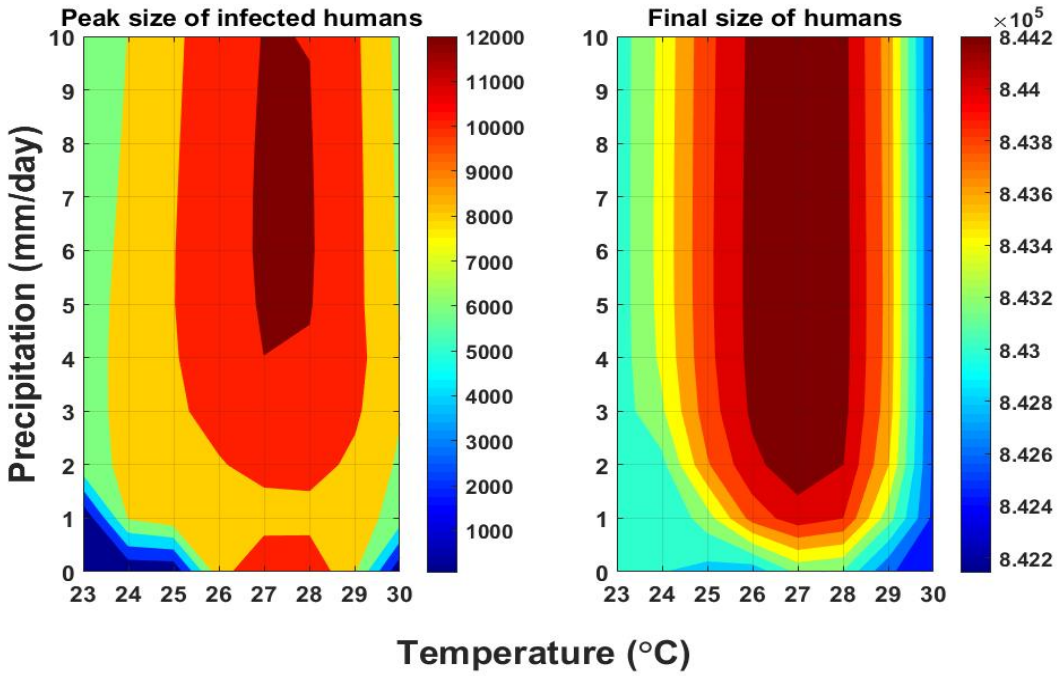

Figure 8: The plots depict the variations of peak size of infectious humans and final size of humans with respect to varying temperature and daily precipitation.

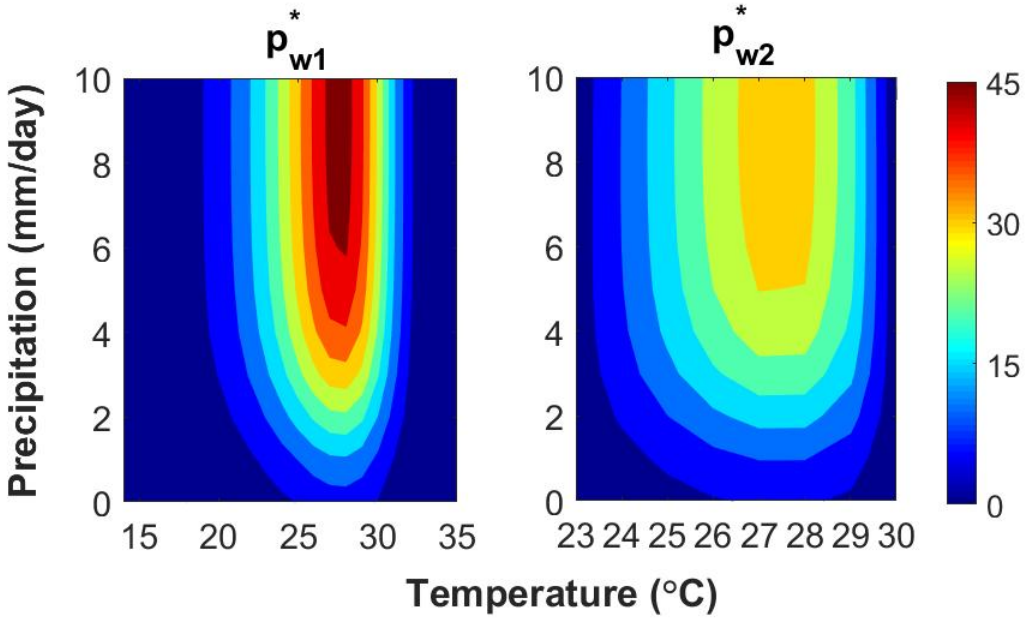

Figure 9: The threshold release ratios for mosquito control ($p^*_{w_1}$) and dengue extinction ($p^*_{w_2}$) vary with changing temperatures and daily precipitations.

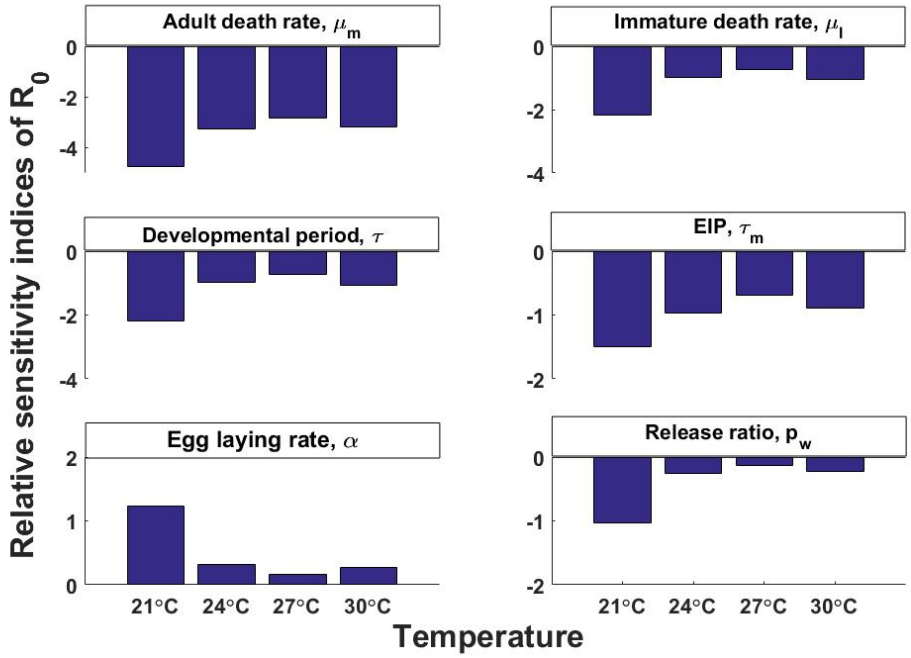

Figure 10: Relative sensitivity indices of the basic reproduction number $\mathcal{R}_0$ with respect to temperature dependent parameters under different temperatures and moderate daily precipitation (P is fixed at 5mm/day).

per, a vector-host epidemiological model is proposed to investigate the effects of releasing *Wolbachia*-infected male-only mosquitoes on dengue control. Different from existing models, the mosquito population model takes into consideration of the effects of larval intra-specific competition and the development duration of immature mosquitoes. By introducing the interactive transmission processes between humans and mosquitoes, this mosquito population model is further extended into a vector-host epidemic model incorporating extrinsic incubation period and intrinsic incubation period. Under the assumption of continuous proportional release strategy, we have conducted theoretical analysis, which includes the well-posedness of the model, the existence of all equilibria and local stability of two boundary equilibria in terms of the reproduction numbers, for mosquito persistence $\mathcal{R}_M$ and the disease transmission $\mathcal{R}_0$. Threshold release ratio of *Wolbachia*-infected males can be determined for mosquito control and disease prevention.

Based on the estimated parameters, various quantitative simulations are further performed. A series of solution curves of susceptible and infected mosquitoes/humans are plotted to validate the threshold dynamics in terms of the reproduction numbers $\mathcal{R}_M$ and $\mathcal{R}_0$. Then, the sensitivity of $\mathcal{R}_M$ and $\mathcal{R}_0$ in terms of other parameters has been conducted. As expected, both $\mathcal{R}_M$ and $\mathcal{R}_0$ are most sensitive to parameters related to adult mosquitoes, which indicates that killing adult mosquitoes is the most efficient way to control both the mosquito population and the transmission of dengue disease. In addition, the release ratio p_w and the carrying capacity of larval mosquitoes K play relative important roles in determining $\mathcal{R}_M$, $\mathcal{R}_0$, the peak time and peak size of infectious humans and the final size of humans. Evident delays of peak time and reductions of $\mathcal{R}_0$, the peak size of infected humans and final epidemic size appear with larger release ratio and smaller larval carrying capacity

(intensified larval intra-specific competition). However, the changing trends of the peak size with respect to the release ratio p_w and threshold carrying capacity K are not monotone. In particular, the smallest peak size of infected humans may arise when medium amount of *Wolbachia*-infected males are released (i.e. $p_w = 10$) and relative weak intra-specific competition (i.e. $K = 7 \times 10^6$). Therefore, indiscriminately augmenting the population of *Wolbachia*-infected males in the field may not necessarily aid in disease control. It is crucial to accurately measure the intensity of intra-specific competition and assess the carrying capacity of the environment in field studies.

The model can be used to project the effect of changing temperatures and precipitations by assuming temperature and precipitation-dependent parameters. The variations of above-mentioned indices with changing weather conditions are simulated. It is surprisingly observed that the relationship between the disease transmission and effectiveness of control measure are very complicated as non-monotone relationships appear. In particular, the model projects that it is most challenging to control the disease at the favorable range of temperature (around $27 \sim 30$°C) and daily precipitation ($5 \sim 8$mm/day), during which the basic reproduction number is maximized and more *Wolbachia*-infected males should be released. To design dengue control strategies, it is essential to consider ambient temperature and precipitation when releasing *Wolbachia*-infected male mosquitoes into the field.

Although the model considers various pivotal aspects in *Wolbachia* against dengue transmission, including the intra-specific larval competition, the development durations in three different scales (the maturation period of immature mosquitoes τ, and two development durations needed for the pathogen within humans (IIP τ_h) and mosquitoes (EIP τ_m), the study has a few limitations. In order to guarantee the success of *Wolbachia*-driven mosquito control programs, it is essential to design more practical release strategies, such as discontinuous and impulsive releases. Furthermore, considering the existence of four different dengue serotypes that can cause infection, the single-serotype vector-host epidemiological model used in this study should be expanded to incorporate two or multi-strain dengue models. Additionally, it is crucial to assess the accuracy of the model used in this study. This can be achieved by calculating statistical indices such as the absolute error (AE), relative error (RE), mean absolute percentage error (MAPE), and the determinant coefficient R^{*2}, which measures the square of the correlation coefficient R^*, as well as the distance between indices of simulation and observation (DISO) [23]. These aspects can be addressed in future research.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

Kaihui Liu was supported by the National Natural Science Foundation of China (Grant No. 11901247), Foundation for High-Level Entrepreneurial and Innovative Talents of Jiangsu Province, and Research Grants for High-Level Talents of Jiangsu University. Qiong Li's research was partially supported by National Science Foundation of China (Grant No. 12250410241). Y. Lou's research was partially supported by the NSF of China (12071393) and The Hong Kong Research Grants Council (15304821).

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Appendix: Theoretical analysis

This appendix section conducts theoretical analysis on model (2.4). The well-posedness property of the model will be shown first, followed by the threshold dynamics of dengue transmission in terms of different basic reproduction numbers.

4.1. Well-posedness of the model

Set $\hat{\tau} = \max\{\tau, \tau_m, \tau_h\}$. Define $\mathbf{X} := C([-\hat{\tau}, 0], \mathbf{R}^7)$ and its positive cone $\mathbf{X}_+ := C([-\hat{\tau}, 0], \mathbf{R}^7_+)$. Then, $(\mathbf{X}, \mathbf{X}_+)$ is an ordered Banach space. Given a continuous function $v(t) : [-\hat{\tau}, \sigma) \to \mathbf{X}$ with $\sigma > 0$, denote $v_t \in \mathbf{X}$ as $v_t(\theta) = v(t + \theta)$ for all $\theta \in [-\hat{\tau}, 0]$ and $t \in [0, \sigma)$. Since model (2.4) describes the evolution dynamics of the dengue transmission, it is essential to verify the nonnegativity and boundedness of the solutions, which is established in the following theorem.

Proposition 4.1. *For any $\phi \in \boldsymbol{X}_+$, system (2.4) admits a unique nonnegative and bounded solution $y(t,\phi)$ with $y_0 = \phi$ on $[0,+\infty)$.*

Proof. It is easy to deduce that system (2.4) admits a unique solution $y(t,\phi)$ with $y_0 = \phi$ on $[0,\sigma_\phi)$, where $\sigma_\phi < \infty$. For any $\phi \in \mathbf{X}$, define

$$f(t,\phi) = \begin{pmatrix} \frac{e^{-\mu_l\tau}\alpha\sum_{i=1}^{3}\phi_i(-\tau)}{2(1+p_w)+2\alpha(\sum_{i=1}^{3}\phi_i(-\tau))/K} - \mu_m\phi_1(0) - c_m\beta\frac{\phi_6(0)}{\sum_{i=4}^{7}\phi_i(0)}\phi_1(0) \\ c_m\beta\frac{\phi_6(0)}{\sum_{i=4}^{7}\phi_i(0)}\phi_1(0) - \mu_m\phi_2(0) - e^{-\mu_m\tau_m}c_m\beta\frac{\phi_6(-\tau_m)}{\sum_{i=4}^{7}\phi_i(-\tau_m)}\phi_1(-\tau_m) \\ e^{-\mu_m\tau_m}c_m\beta\frac{\phi_6(-\tau_m)}{\sum_{i=4}^{7}\phi_i(-\tau_m)}\phi_1(-\tau_m) - \mu_m\phi_3(0) \\ \Lambda_h - \mu_h\phi_4(0) - c_h\beta\frac{\phi_3(0)}{\sum_{i=4}^{7}\phi_i(0)}\phi_4(0) \\ c_h\beta\frac{\phi_4(0)}{\sum_{i=4}^{7}\phi_i(0)}\phi_3(0) - \mu_h\phi_5(0) - e^{-\mu_h\tau_h}c_h\beta\frac{\phi_4(-\tau_h)}{\sum_{i=4}^{7}\phi_i(-\tau_h)}\phi_3(-\tau_h) \\ e^{-\mu_h\tau_h}c_h\beta\frac{\phi_4(-\tau_h)}{\sum_{i=4}^{7}\phi_i(-\tau_h)}\phi_3(-\tau_h) - (\mu_h+\gamma_h)\phi_6(0) \\ \gamma_h\phi_6(0) - \mu_h\phi_7(0) \end{pmatrix}$$

For $i = 1,3,4,6,7$, $f_i(t,\phi) \geq 0$ holds whenever $\phi_i(0) = 0$. It follows from [40, Theorem 3.4] that $y_i(t,\phi) \geq 0$, $i = 1,3,4,6,7$ holds for all $t \in [0,\sigma_\phi)$. In view of the integral formulae of $E_m(t)$ and $E_h(t)$ in (2.5), we obtain the nonnegativity of $y_i(t,\phi), i = 2,5$ for all $t \in [0,\sigma_\phi)$. On the other hand, the total sizes of mosquitoes and humans satisfy the following inequalities:

$$\begin{cases} \dfrac{dM(t)}{dt} = \dfrac{e^{-\mu_l\tau}\alpha M(t-\tau)}{2(1+p_w)+2\alpha M(t-\tau)/K} - \mu_m M(t) \leq \dfrac{Ke^{-\mu_l\tau}}{2} - \mu_m M(t), \\ \dfrac{dN_h(t)}{dt} = \Lambda_h - \mu_h N_h(t), \end{cases} \tag{4.1}$$

for all $t \in [0,\sigma_\phi)$. It easily follows from system (4.1) and the comparison principle that $M(t)$ and $N_h(t)$ are bounded on $[0,\sigma_\phi)$. Besides, $\dfrac{dM(t)}{dt}$ and $\dfrac{dN_h(t)}{dt}$ become negative whenever both $M(t)$ and $N_h(t)$ are greater than $\max\{\dfrac{Ke^{-\mu_l\tau}}{2}, \dfrac{\Lambda_h}{\mu_h}\}$. Therefore, we obtain that solutions of system (2.4) are ultimately bounded and globally exist on $[0,+\infty)$. Furthermore, we have

$$\limsup_{t\to\infty} M(t) \leq \frac{Ke^{-\mu_l\tau}}{2\mu_m} \text{ and } \limsup_{t\to\infty} N_h(t) \leq \frac{\Lambda_h}{\mu_h}.$$

□

4.2. Existence and stability of equilibria

In this subsection, we explore the existence and local stability of equilibria in terms of the reproduction numbers for mosquito population growth and the transmission of dengue diseases.

4.2.1. Existence of equilibria

The equilibria of system (2.4) can be obtained by solving the following algebraic equations:

$$\begin{cases} \dfrac{e^{-\mu_l\tau}\alpha M}{2(1+p_w)+2\alpha M/K} - \mu_m S_m - c_m\beta\dfrac{I_h}{N_h}S_m = 0, \\ c_m\beta\dfrac{I_h}{N_h}S_m - \mu_m E_m - e^{-\mu_m\tau_m}c_m\beta\dfrac{I_h}{N_h}S_m = 0, \\ e^{-\mu_m\tau_m}c_m\beta\dfrac{I_h}{N_h}S_m - \mu_m I_m = 0, \\ \Lambda_h - \mu_h S_h - c_h\beta\dfrac{I_m}{N_h}S_h = 0, \\ c_h\beta\dfrac{I_m}{N_h}S_h - \mu_h E_h - e^{-\mu_h\tau_h}c_h\beta\dfrac{I_m}{N_h}S_h = 0, \\ e^{-\mu_h\tau_h}c_h\beta\dfrac{I_m}{N_h}S_h - (\mu_h+\gamma_h)I_h = 0, \\ \gamma_h I_h - \mu_h R_h = 0. \end{cases} \tag{4.2}$$

In the absence of infections, i.e., $E_m = 0$, $I_m = 0$, $E_h = 0$ and $I_h = 0$ in (4.2), we obtain two dengue-free equilibria, which are dengue-free-mosquito-extinction (DFME) equilibrium $E_{01} = (0, 0, 0, N_h^*, 0, 0, 0)$ and dengue-free-mosquito-persistent (DFMP) equilibrium $E_{02} = (M^*, 0, 0, N_h^*, 0, 0, 0)$, where

$$N_h^* = S_h^* = \frac{\Lambda_h}{\mu_h} \quad \text{and} \quad M^* = \frac{K(1+p_w)}{\alpha}\left(\frac{e^{-\mu_l\tau}\alpha}{2(1+p_w)\mu_m} - 1\right).$$

Define

$$\mathcal{R}_M = \frac{e^{-\mu_l\tau}\alpha}{2(1+p_w)\mu_m}, \tag{4.3}$$

which is the reproduction number of mosquito growth. It is easy to deduce from above derivation that the DFMP equilibrium exists when $\mathcal{R}_M > 1$.

The disease-endemic (DE) equilibrium

$$E^* := (S_m^*, E_m^*, I_m^*, S_h^*, E_h^*, I_h^*, R_h^*)$$

can be discussed as follows. Adding up the first three equations of (4.2), we obtain the unique value of $M^* > 0$, which is determined by

$$\frac{e^{-\mu_l\tau}\alpha M^*}{2(1+p_w)+2\alpha M^*/K} = \mu_m M^*.$$

By substituting the above equation into the first equation in (4.2) and combining the second and third equations of (4.2), we get

$$\begin{cases} \mu_m(M^* - S_m^*) = c_m\beta S_m^* \dfrac{I_h^*}{N_h^*}, \\ \mu_m E_m^* = c_m\beta \dfrac{I_h^*}{N_h^*} S_m^*(1 - e^{-\mu_m\tau_m}), \\ \mu_m I_m^* = c_m\beta \dfrac{I_h^*}{N_h^*} S_m^* e^{-\mu_m\tau_m}. \end{cases}$$

It then follows that

$$S_m^* = M^* - e^{\mu_m\tau_m} I_m^* \quad \text{and} \quad E_m^* = (e^{\mu_m\tau_m} - 1)I_m^*. \tag{4.4}$$

Substituting the first identity in (4.4) into the third equation of (4.2) yields

$$I_m^* = \frac{e^{-\mu_m\tau_m} c_m\beta I_h^*}{\mu_m N_h^*}(M^* - e^{\mu_m\tau_m} I_m^*) = \frac{e^{-\mu_m\tau_m} c_m\beta M^* - 2c_m\beta I_m^*}{\mu_m N_h^*} I_h^*. \tag{4.5}$$

Since $N_h^* = \Lambda_h/\mu_h$, in view of the fifth and sixth equations in (4.2), we get the following equations

$$\begin{cases} \mu_h(N_h^* - S_h^*) = c_h\beta \dfrac{S_h^*}{N_h^*} I_m^*, \\ \mu_h E_h^* = c_h\beta \dfrac{S_h^*}{N_h^*} I_m^*(1 - e^{-\mu_h\tau_h}), \\ (\mu_h + \gamma_h) I_h^* = c_h\beta \dfrac{S_h^*}{N_h^*} I_m^* e^{-\mu_h\tau_h}. \end{cases}$$

Through similar calculations as above, we have

$$\begin{cases} S_h^* = N_h^* - \dfrac{e^{\mu_h\tau_h}(\mu_h + \gamma_h)}{\mu_h} I_h^*, \\ E_h^* = \dfrac{(e^{\mu_h\tau_h} - 1)(\mu_h + \gamma_h)}{\mu_h} I_h^*. \end{cases} \tag{4.6}$$

It follows from the seventh equation in (4.2) that

$$R_h^* = \frac{\gamma_h}{\mu_h} I_h^*. \tag{4.7}$$

To get the explicit form of the endemic equilibrium, it is imperative to determine I_m^* and I_h^*. Substituting the equation related to S_h^* in (4.6) into the sixth equation of (4.2), we get,

$$I_h^* = \frac{e^{-\mu_h\tau_h} c_h\beta}{(\mu_h + \gamma_h)N_h^*} \left[N_h^* - \frac{e^{\mu_h\tau_h}(\mu_h + \gamma_h)}{\mu_h} I_h^* \right] I_m^* = \left(\frac{e^{-\mu_h\tau_h} c_h\beta}{\mu_h + \gamma_h} - \frac{c_h\beta}{\mu_h N_h^*} I_h^* \right) I_m^*. \tag{4.8}$$

Define

$$\begin{aligned}\mathcal{R}_0 :=& \frac{e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h M^*}{(\mu_h+\gamma_h)\mu_m N_h^*}\\ =& \frac{e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h \mu_h}{(\mu_h+\gamma_h)\mu_m\Lambda_h}\frac{K(1+p_w)}{\alpha}\left(\frac{e^{-\mu_l\tau}\alpha}{2(1+p_w)\mu_m}-1\right),\\ =& \frac{e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h \mu_h}{(\mu_h+\gamma_h)\mu_m\Lambda_h}\frac{K(1+p_w)}{\alpha}(\mathcal{R}_M-1),\end{aligned} \tag{4.9}$$

which is the basic reproduction number of the dengue transmission. Combining the relations of I_m^* and I_h^* in (4.5) and (4.8), we obtain

$$\begin{cases} I_m^* = \dfrac{[e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h M^* - (\mu_h+\gamma_h)\mu_m N_h^*]\mu_h}{\beta c_h[e^{-\mu_h\tau_h}\beta c_m\mu_h+(\mu_h+\gamma_h)\mu_m]} = \dfrac{\mu_h\mu_m(\mu_h+\gamma_h)N_h^*(\mathcal{R}_0-1)}{\beta c_h[e^{-\mu_h\tau_h}\beta c_m\mu_h+(\mu_h+\gamma_h)\mu_m]},\\ I_h^* = \dfrac{[e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h M^* - (\mu_h+\gamma_h)\mu_m N_h^*]\mu_h N_h^*}{\beta c_m(\mu_h+\gamma_h)[e^{-\mu_m\tau_m}\beta c_h M^*+\mu_h N_h^*]} = \dfrac{\mu_m\mu_h(N_h^*)^2(\mathcal{R}_0-1)}{\beta c_m[e^{-\mu_m\tau_m}\beta c_h M^*+\mu_h N_h^*]}.\end{cases}$$

It easily follows that I_m^* and I_h^* are both positive if $\mathcal{R}_0>1$. In view of the relations shown in (4.4), (4.6) and (4.7), E_m^*, E_h^* and R_h^* are positive provided that I_m^* and I_h^* are positive. Moreover, the positivity of M^* and N_h^* implies that S_m^* and S_h^* always hold positive, which can be deduced from the following equations.

$$\begin{cases} S_m^* = M^* - \dfrac{e^{\mu_m\tau_m}[e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h M^* - (\mu_h+\gamma_h)\mu_m N_h^*]\mu_h}{\beta c_h[e^{-\mu_h\tau_h}\beta c_m\mu_h+(\mu_h+\gamma_h)\mu_m]}\\ \qquad = \dfrac{\mu_m(\mu_h+\gamma_h)}{\beta c_h[e^{-\mu_h\tau_h}\beta c_m\mu_h+(\mu_h+\gamma_h)\mu_m]}(\beta c_h M^* + e^{\mu_m\tau_m}\mu_h N_h^*),\\ S_h^* = N_h^* - \dfrac{e^{\mu_h\tau_h}(\mu_h+\gamma_h)}{\mu_h}\dfrac{[e^{-\mu_m\tau_m-\mu_h\tau_h}\beta^2 c_m c_h M^* - (\mu_h+\gamma_h)\mu_m N_h^*]\mu_h N_h^*}{\beta c_m(\mu_h+\gamma_h)[e^{-\mu_m\tau_m}\beta c_h M^*+2\mu_h N_h^*]}\\ \qquad = \dfrac{[\beta c_m\mu_h+(\mu_h+\gamma_h)\mu_m e^{\mu_h\tau_h}](N_h^*)^2}{\beta c_m(e^{-\mu_m\tau_m}\beta c_h M^*+2\mu_h N_h^*)}.\end{cases}$$

To sum up, we conclude that E^* is the unique disease-endemic equilibrium of system (2.4), which exists if and only if $\mathcal{R}_M>1$ and $\mathcal{R}_0>1$.

4.2.2. Local stability of dengue-free equilibria

The local stability of equilibria depends on the roots of the characteristic equation. Since model (2.4) involves delay differential equations with three different discrete delays, the characteristic equations are determined by

$$det(J+e^{-\lambda\tau_m}J_{\tau_m}+e^{-\lambda\tau}J_\tau+e^{-\lambda\tau_h}J_{\tau_h}-\lambda I)=0, \tag{4.10}$$

where J, J_{τ_m}, J_τ and J_{τ_h} are the Jacobian matrices related to non-delayed, τ_m-delayed, τ-delayed and τ_h-delayed variables respectively and I is the identity matrix. The local stability of the dengue-free-mosquito-extinction (DFME) equilibrium E_{01} is concluded in the subsequent proposition.

Proposition 4.2. *The dengue-free-mosquito-extinction (DFME) equilibrium E_{01} is locally asymptotically stable if $\mathcal{R}_M < 1$;*

Proof. All matrices evaluated at the DFME equilibrium E_{01} in (4.10) are

$$J = \begin{pmatrix} -\mu_m & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\mu_m & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\mu_m & 0 & 0 & 0 & 0 \\ 0 & 0 & -c_h\beta & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & c_h\beta & 0 & -\mu_h & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\mu_h+\gamma_h) & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma_h & -\mu_h \end{pmatrix},$$

$$J_{\tau_m} = \mathbf{0},$$

$$J_\tau = \begin{pmatrix} \frac{e^{-\mu_l\tau}\alpha}{2(1+p_w)} & \frac{e^{-\mu_l\tau}\alpha}{2(1+p_w)} & \frac{e^{-\mu_l\tau}\alpha}{2(1+p_w)} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$J_{\tau_h} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -e^{-\mu_h\tau_h}c_h\beta & 0 & 0 & 0 & 0 \\ 0 & 0 & e^{-\mu_h\tau_h}c_h\beta & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

These Jacobian matrices constitute the following characteristic matrix

$$\begin{pmatrix} P_{11}(\lambda) & P_{12}(\lambda) \\ 0 & P_{22}(\lambda) \end{pmatrix},$$

where

$$P_{11}(\lambda) = \begin{pmatrix} -\mu_m + \frac{e^{-\lambda\tau}e^{-\mu_l\tau}\alpha}{2(1+p_w)} - \lambda & \frac{e^{-\lambda\tau}e^{-\mu_l\tau}\alpha}{2(1+p_w)} \\ 0 & -\mu_m - \lambda \end{pmatrix},$$

$$P_{12}(\lambda) = \begin{pmatrix} \frac{e^{-\lambda\tau}e^{-\mu_l\tau}\alpha}{2(1+p_w)} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$P_{22}(\lambda) = \begin{pmatrix} -\mu_m - \lambda & 0 & 0 & 0 & 0 \\ -c_h\beta & -\mu_h - \lambda & 0 & 0 & 0 \\ c_h\beta - e^{-\lambda\tau_h}e^{-\mu_h\tau_h}c_h\beta & 0 & -\mu_h - \lambda & 0 & 0 \\ e^{-\lambda\tau_h}e^{-\mu_h\tau_h}c_h\beta & 0 & 0 & -(\mu_h + \gamma_h) - \lambda & 0 \\ 0 & 0 & 0 & \gamma_h & -\mu_h - \lambda \end{pmatrix}.$$

Thus, the characteristic equation is

$$[\lambda + \mu_m - \frac{e^{-\lambda\tau}e^{-\mu_l\tau}\alpha}{2(1+p_w)}](\lambda + \mu_h + \gamma_h)(\lambda + \mu_m)^2(\lambda + \mu_h)^3 = 0.$$

It is easy to deduce from the characteristic equation that the stability of E_{01} depends on the sign of one characteristic root determined by the following transcendental equation

$$\lambda + \mu_m - \frac{e^{-\lambda\tau}e^{-\mu_l\tau}\alpha}{2(1+p_w)} = 0. \tag{4.11}$$

According to [17, Theorem A.5], all roots of the equation

$$\lambda + a + be^{-\lambda\tau} = 0,$$

have negative real parts if and only if the following statements hold true:

(1) $a\tau > -1$

(2) $a + b > 0$

(3) $b < \zeta \sin\zeta - a\tau\cos\zeta$, where ζ is the root of

$$\zeta = \begin{cases} -a\tau\tan\zeta, & 0 < \zeta < \pi,\ a \neq 0, \\ \dfrac{\pi}{2}, & a = 0. \end{cases}$$

Obviously, equation (4.11) satisfies the first criterion. On the other hand, it is easy to check that the second statement holds true if $\mathcal{R}_M < 1$. It follows from $a = \mu_m \neq 0$ that $0 < \zeta < \pi$. Besides, the equation $\zeta = -\mu_m\tau\tan\zeta$ implies that $\tan\zeta < 0$ for $\tau > 0$, which further indicates that $\dfrac{\pi}{2} < \zeta < \pi$. Therefore, the third statement holds true since $\zeta\sin\zeta - a\tau\cos\zeta \geq 0 > -e^{-\mu_l\tau}\alpha\beta_w$. We conclude that the DFME equilibrium E_{01} is locally stable when $\mathcal{R}_M < 1$. □

Next, we explore the stability of the dengue-free-mosquito-persistent (DFMP) equilibrium E_{02} by applying similar statements as that in Proposition 4.2. The matrices evaluated at

E_{02} in (4.10) are

$$J = \begin{pmatrix} -\mu_m & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\mu_m & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\mu_m & 0 & 0 & 0 & 0 \\ 0 & 0 & -c_h\beta & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & c_h\beta & 0 & -\mu_h & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\mu_h+\gamma_h) & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma_h & -\mu_h \end{pmatrix},$$

$$J_{\tau_m} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -e^{-\mu_m\tau_m}c_m\beta\dfrac{M^*}{N_h^*} & 0 \\ 0 & 0 & 0 & 0 & 0 & e^{-\mu_m\tau_m}c_m\beta\dfrac{M^*}{N_h^*} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$J_\tau = \begin{pmatrix} \dfrac{2(1+p_w)\mu_m^2}{e^{-\mu_l\tau}\alpha} & \dfrac{2(1+p_w)\mu_m^2}{e^{-\mu_l\tau}\alpha} & \dfrac{2(1+p_w)\mu_m^2}{e^{-\mu_l\tau}\alpha} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$J_{\tau_h} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -e^{-\mu_h\tau_h}c_h\beta & 0 & 0 & 0 & 0 \\ 0 & 0 & e^{-\mu_h\tau_h}c_h\beta & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

The characteristic matrix at E_{02} becomes $\begin{pmatrix} Q_{11}(\lambda) & Q_{12}(\lambda) \\ 0 & Q_{22}(\lambda) \end{pmatrix}$ with

$$Q_{11}(\lambda) = \begin{pmatrix} -\mu_m - \lambda + e^{-\lambda\tau}\dfrac{2(1+p_w)\mu_m^2}{e^{-\mu_l\tau}\alpha} & e^{-\lambda\tau}\dfrac{2(1+p_w)\mu_m^2}{e^{-\mu_l\tau}\alpha} \\ 0 & -\mu_m - \lambda \end{pmatrix},$$

$$Q_{12}(\lambda)=\begin{pmatrix} e^{-\lambda\tau}\dfrac{2(1+p_w)\mu_m^2}{e^{-\mu_l\tau}\alpha} & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & -e^{-\lambda\tau_m}e^{-\mu_m\tau_m}c_m\beta\dfrac{M^*}{N_h^*} & 0 \end{pmatrix},$$

$$Q_{22}(\lambda)=\begin{pmatrix} -\mu_m-\lambda & 0 & 0 & e^{-\lambda\tau_m}e^{-\mu_m\tau_m}c_m\beta\dfrac{M^*}{N_h^*} & 0\\ -c_h\beta & -\mu_h-\lambda & 0 & 0 & 0\\ c_h\beta-e^{-\lambda\tau_h}e^{-\mu_h\tau_h}c_h\beta & 0 & -\mu_h-\lambda & 0 & 0\\ e^{-\lambda\tau_h}e^{-\mu_h\tau_h}c_h\beta & 0 & 0 & -(\mu_h+\gamma_h)-\lambda & 0\\ 0 & 0 & 0 & \gamma_h & -\mu_h-\lambda \end{pmatrix}.$$

By direct computation, the characteristic equation at E_{02} is

$$(\lambda+\mu_m)(\lambda+\mu_h)^3(\lambda+\mu_m-\frac{2(1+p_w)\mu_m^2}{e^{-\mu_l\tau}\alpha}e^{-\lambda\tau})f(\lambda)=0,$$

where

$$f(\lambda)=(\lambda+\mu_h+\gamma_h)(\lambda+\mu_m)-c_mc_h\beta^2e^{-\mu_m\tau_m-\mu_h\tau_h}\frac{M^*}{N_h^*}e^{-(\tau_m+\tau_h)\lambda}.$$

It is clear that the stability of E_{02} depends on the sign of the roots determined by

$$\lambda+\mu_m-\frac{2(1+p_w)\mu_m^2}{e^{-\mu_l\tau}\alpha}e^{-\lambda\tau}=0 \qquad \text{and} \qquad f(\lambda)=0.$$

By applying arguments analogous to those in the proof of Proposition 4.2, we obtain that all roots of $\lambda+\mu_m-\dfrac{2(1+p_w)\mu_m^2}{e^{-\mu_l\tau}\alpha}e^{-\lambda\tau}=0$ have negative real parts if and only if $\mathcal{R}_M>1$. To get the stability of E_{02}, it is imperative to investigate the roots of $f(\lambda)=0$, which is summarized in the following lemmas.

Lemma 4.3. *All roots of $f(\lambda)=0$ have negative real parts if and only if $\mathcal{R}_M>1$ and $\mathcal{R}_0<1$.*

Proof. It is clear that $f(\lambda)$ is increasing with respect to λ, and $f(\lambda)\to+\infty$ as $\lambda\to+\infty$. To guarantee all roots of $f(\lambda)=0$ have negative real parts, $f(0)>0$ must hold, which yields that

$$\mathcal{R}_0=\frac{\beta^2c_mc_he^{-\mu_m\tau_m-\mu_h\tau_h}M^*}{(\mu_h+\gamma_h)\mu_mN_h^*}<1.$$

Then we claim that condition $\mathcal{R}_0<1$ is sufficient to guarantee that all roots of $f(\lambda)=0$ have negative real parts. Assume that $\lambda=x+iy$ with $y>0$ ($y<0$ is similar) is the root of $f(\lambda)=0$, then the real part and the imaginary part satisfy

$$\begin{aligned} c_mc_h\beta^2e^{-\mu_m\tau_m-\mu_h\tau_h}\frac{M^*}{N_h^*}e^{-(\tau_m+\tau_h)x}\cos((\tau_m+\tau_h)y) =& x^2-y^2+(\mu_m+\mu_h+\gamma_h)x+\mu_m(\mu_h+\gamma_h),\\ c_mc_h\beta^2e^{-\mu_m\tau_m-\mu_h\tau_h}\frac{M^*}{N_h^*}e^{-(\tau_m+\tau_h)x}\sin((\tau_m+\tau_h)y) =& -2xy-(\mu_m+\mu_h+\gamma_h)y. \end{aligned}$$

We then prove that $x<0$ holds. If not, assume $x=0$, the above equations involving real

and the imaginary parts are reduced to

$$\begin{aligned} c_m c_h \beta^2 e^{-\mu_m \tau_m - \mu_h \tau_h} \frac{M^*}{N_h^*} \cos((\tau_m + \tau_h)y) &= -y^2 + \mu_m(\mu_h + \gamma_h), \\ c_m c_h \beta^2 e^{-\mu_m \tau_m - \mu_h \tau_h} \frac{M^*}{N_h^*} \sin((\tau_m + \tau_h)y) &= -(\mu_m + \mu_h + \gamma_h)y. \end{aligned}$$

It follows from the sum of squares of the above two equations that

$$(c_m c_h \beta^2 e^{-\mu_m \tau_m - \mu_h \tau_h} \frac{M^*}{N_h^*})^2 = [y^2 + (\mu_h + \gamma_h)^2](y^2 + \mu_m^2).$$

Hence,

$$\frac{(c_m c_h \beta^2 e^{-\mu_m \tau_m - \mu_h \tau_h} \frac{M^*}{N_h^*})^2}{\mu_m^2(\mu_h + \gamma_h)^2} = [1 + \frac{1}{(\mu_h + \gamma_h)^2}](1 + \frac{y^2}{\mu_m^2}) > 1,$$

that is

$$\mathcal{R}_0 = \frac{c_m c_h \beta^2 e^{-\mu_m \tau_m - \mu_h \tau_h} M^*}{\mu_m(\mu_h + \gamma_h) N_h^*} > 1,$$

a contradiction. On the other hand, if we assume $x > 0$, then

$$\begin{aligned} &(c_m c_h \beta^2 e^{-\mu_m \tau_m - \mu_h \tau_h} \frac{M^*}{N_h^*})^2 e^{-2(\tau_m + \tau_h)x} \\ =&[x^2 - y^2 + (\mu_m + \mu_h + \gamma_h)x + \mu_m(\mu_h + \gamma_h)]^2 + [2xy + (\mu_m + \mu_h + \gamma_h)y]^2 \\ =&(x^2 + y^2)^2 + x(\mu_m + \mu_h + \gamma_h)[2x^2 + 2y^2 + (\mu_m + \mu_h + \gamma_h)x + 2\mu_m(\mu_h + \gamma_h)x] \\ &+ 2\mu_m(\mu_h + \gamma_h)x^2 + [(\mu_m^2 + \mu_h + \gamma_h)^2]y^2 + \mu_m^2(\mu_h + \gamma_h)^2 \\ >&\mu_m^2(\mu_h + \gamma_h)^2. \end{aligned}$$

Therefore,

$$\mathcal{R}_0^2 = \frac{(c_m c_h \beta^2 e^{-\mu_m \tau_m - \mu_h \tau_h} \frac{M^*}{N_h^*})^2}{\mu_m^2(\mu_h + \gamma_h)^2} > e^{2\tau_m + \tau_h x} > 1,$$

which contradicts with $\mathcal{R}_0 < 1$ as well. □

Based on the above statements and Lemma 4.3, the local stability of the dengue-free-mosquito-persistent (DFMP) equilibrium E_{02} is concluded in the following theorem.

Proposition 4.4. *The dengue-free-mosquito-persistent (DFMP) equilibrium E_{02} is locally asymptotically stable if $\mathcal{R}_M > 1$ and $\mathcal{R}_0 < 1$.*

Remark 4.5. *Note that the amount of released Wolbachia-infected males is measured by the release ratio p_w. In view of (4.3) and (4.9), the release ratio p_w has negative effects on the reproduction numbers $\mathcal{R}_M$ and $\mathcal{R}_0$. Based on the formulae of $\mathcal{R}_M$ and $\mathcal{R}_0$, we obtain the*

corresponding threshold values of the release ratio p_w, which are shown as follows

$$\begin{cases} \mathcal{R}_M = 1, \text{ if and only if } p^*_{w_1} = \dfrac{e^{-\mu_l \tau}\alpha}{2\mu_m} - 1, \\ \mathcal{R}_0 = 1, \text{ if and only if } p^*_{w_2} = \dfrac{e^{-\mu_l \tau}\alpha}{2\mu_m} - 1 - \dfrac{\alpha \Lambda_h \mu_m (\mu_h + \gamma_h)}{\beta^2 c_m c_h e^{-\mu_m \tau_m - \mu_h \tau_h} \mu_h K}. \end{cases}$$

Therefore, the above threshold results in terms of the reproduction numbers can be rephrased into the following statements related to the threshold release ratios $p^*_{w_1}$ and $p^*_{w_2}$.

(1) If $p_w > p^*_{w_1}$, the dengue-free-mosquito-extinct (DFME) equilibrium is locally stable, which indicates that releasing a large amount of Wolbachia-infected males can drive the extinction of mosquito population and further wipe out the dengue disease;

(2) If $p^*_{w_2} < p_w < p^*_{w_1}$, the dengue-free-mosquito-persistent (DFMP) equilibrium is locally stable, which implies that releasing a medium amount of Wolbachia-infected males can still eliminate the dengue disease even though the mosquito population persists;

(3) If $p_w < p^*_{w_2}$, the unique endemic equilibrium exists, which means that releasing a small amount of Wolbachia-infected males is inadequate to control both the mosquito population and dengue disease.