Mathematical Biosciences and Engineering

https://www.aimspress.com/journal/mbe

MBE, 23(8): 2393–2428.
DOI: 10.3934/mbe.2026087
Received: 25 April 2026
Revised: 25 June 2026
Accepted: 13 July 2026
Published: 03 August 2026

Research article

Optimal control approach to developing sex-structured release strategies for dengue prevention

Evan Gibbs[1,2,*], Jordy Cevallos–Chavez[3,4], Khaled Elhassan[5], Jimena Sanchez[6], Unnati Gohil[3] and Heliana Arias Castro[7]

[1] Department of Mathematics, York College of Pennsylvania, York, PA 17345, USA
[2] Department of Engineering Sciences and Applied Mathematics, Northwestern University, Evanston, IL 60208, USA
[3] Simon A. Levin Mathematical, Computational and Modeling Sciences Center, Arizona State University, 1031 Palm Walk, Tempe, AZ 85287, USA
[4] School of Human Evolution and Social Change, Arizona State University, 900 E Cady Mall, Tempe, AZ 85287, USA
[5] College of Arts and Sciences, Ohio State University, Columbus, OH 43210, USA
[6] Department of Mathematics, Scripps College, Claremont, CA 91711, USA
[7] Department of Mathematics, Universidad del Valle, Cali, Valle del Cauca 760032, Colombia

* **Correspondence:** Email: evangibbs2032@u.northwestern.edu.

Abstract: Dengue remains a public health challenge due to the persistence of *Aedes aegypti* populations and the limited effectiveness of medical and vector control interventions. The release of *Wolbachia*-infected mosquitoes has been used in multiple regions; yet, release protocols are often heuristically structured, with limited optimization. In particular, the impacts of mosquito sex structure and strain-specific effects remain unclear. This study develops a sex-structured dynamical model that links within-vector *Wolbachia* dynamics, such as cytoplasmic incompatibility and vertical transmission, with between-host dengue transmission. An optimal control framework is used to determine cost-effective releases of male and female mosquitoes over a finite intervention horizon, with mosquito dispersal on a finite time interval. The cost effectiveness of a release program relies on minimizing releases and dengue cases. The approach is applied to three *Wolbachia* strains, *w*AlbB, *w*Mel, and *w*MelPop, to assess how strain-specific fitness and viral blocking influence optimal release plans. The analysis identified sex-structured strategies that diverge from in-field protocols, supporting the notion that commonly used plans may benefit from optimization by sex. Additionally, differences were noted among strains, which suggests that optimal sex-structured releases may vary with *Wolbachia* strain used.

Keywords: *Wolbachia*; dengue; sex-structured model; optimal control; public health interventions

1. Introduction

Dengue is a vector-borne viral disease, primarily transmitted by the *Aedes aegypti* mosquito, with transmission disproportionately affecting regions of high population density and limited socioeconomic resources [1–5]. Over recent decades, the dengue incidence has substantially increased across endemic and emerging regions, driven, in part, by expanding climatic suitability for mosquito vectors, urbanization, and global mobility [1,4,5]. Originally native to sub-Saharan Africa, *Aedes aegypti* has spread throughout much of the Americas and other tropical regions, where it has become the dominant vector for dengue and other arboviruses, including yellow fever and chikungunya [3,6–8]. Its close association with human habitats and its efficiency in urban environments make humans the primary blood-meal source sustaining transmission [8, 9]. Classical dengue control strategies have focused on chemical insecticides and source reduction through the elimination of larval habitats [10]. Although dengue vaccines have become available, their population-level impact remains limited, as vaccine efficacy is partial and varies by serotype and host immune status [11, 12]. These limitations are compounded by the intrinsic heterogeneity of dengue, which consists of four antigenically distinct serotypes, complicating immunity and long-term control efforts [12, 13]. As a result, contemporary dengue management strategies have increasingly focused toward interventions that directly target mosquito populations. Despite these efforts, *Aedes aegypti* persist especially in warmer regions that permit year-round reproduction, with persistence pronounced in low-income countries where sustained vector control is difficult to maintain [4, 5].

Motivated by these challenges, biological vector control strategies based on *Wolbachia*-infection of mosquito populations have received a growing attention. *Wolbachia* is a maternally inherited endosymbiotic bacterium that infects a wide range of arthropods and can establish stably within mosquito populations [14]. In *Aedes aegypti*, *Wolbachia pipientis* has been shown to reduce the viral replication within mosquitoes, thereby lowering the transmission potential for dengue and other RNA viruses [15, 16]. In addition, *Wolbachia* infection induces cytoplasmic incompatibility, consequently altering mosquito reproductive dynamics such that offspring viability depends on the infection status of mating pairs [17]. Empirical evidence indicates that the strength of incompatibility varies across *Wolbachia* strains and environmental conditions [4, 18–21]. Large scale field implementations have been initiated by organizations such as the World Mosquito Program in regions of Latin America, Oceania, and Asia [4]. However, release strategies are frequently heuristically designed, and the systematic optimization of release protocols remains limited. Current field practices often rely on single sex releases or simplistic mixed sex-ratios [22]. In particular, differences in the effects of *Wolbachia* infection across male and female mosquitoes suggest that such release practices may be sub-optimal for wild mosquito populations of varying composition. While these releases can produce successful results, they may require prolonged release schedules or greater quantities of mosquitoes, thus increasing intervention costs. Sex-optimized releases can leverage the sex-driven distinctions between *Wolbachia*-infected mosquitoes, thereby minimizing costs and promoting an increased accessibility of interventions. Moreover, release outcomes strongly depend on the *Wolbachia* strain choice, as egg viability, fitness costs, and viral blocking efficacy vary substantially across strains [18–21, 23]. Among the most commonly used strains are *w*MelPop, *w*Mel, and *w*AlbB, which differ markedly in these biological characteristics.

This work addresses these gaps by introducing a sex-structured dynamical system that integrates the dynamics of the *Wolbachia* population with dengue transmission between-hosts. An associated

optimal control problem is formulated in which the control variables represent the proportion of maximal release rates of male and female *Aedes aegypti* mosquitoes. The objective functional balances the intervention costs with the cumulative human infection over a finite intervention horizon, thus ensuring that *Wolbachia*-infected mosquitoes are released on a fixed, finite time interval. The framework is applied to the *w*AlbB, *w*Mel, and *w*MelPop strains to assess how strain-specific biological differences influence optimal release strategies. The proposed framework allows for the analysis of sex-structured release strategies and their cost-effectiveness.

2. Sex-structured *Wolbachia*-dengue transmission model formulation

Mathematical models for *Wolbachia*-based mosquito release strategies have incorporated a variety of biological and ecological features of *Aedes aegypti*, including seasonally varying birth functions [24] and sex-structured population dynamics [25]. While these approaches have provided valuable insights into *Wolbachia* establishment and persistence, further development is needed to quantify how *Wolbachia* affects the pathogen transmission when vector sex is explicitly accounted for. This distinction is particularly relevant for dengue, as transmission is primarily driven by female mosquitoes, while reproductive interactions between male and female mosquitoes govern the inheritance and spread of *Wolbachia* within vector populations, as summarized in Table 1.

Table 1. Offspring viability outcomes of *Wolbachia* and wild mosquito reproduction.

Gender	Non-infected male	*Wolbachia*-infected male
Non-infected female	Non-infected offspring	Deceased offspring
Wolbachia-infected female	Infected offspring	Infected offspring

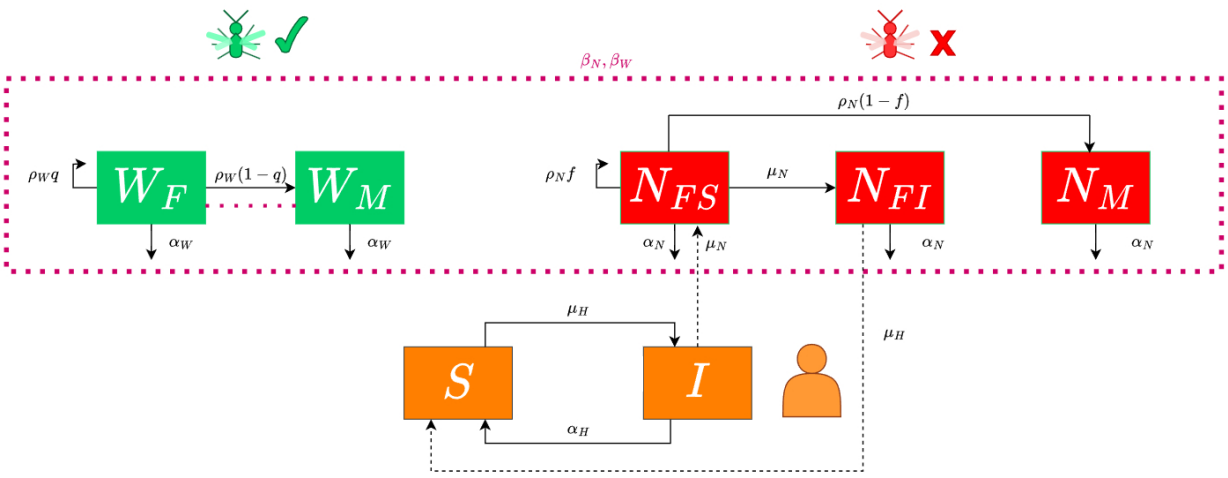

Figure 1. Flow diagram of the sex-structured *Wolbachia*-Dengue transmission model, which shows five distinct compartments for mosquitoes based upon sex, dengue presence (red compartments), and *Wolbachia*-infection (green compartments), as well as a human population (orange compartments) composed of dengue-infected and dengue-susceptible individuals.

To capture these mechanisms, a sex-structured model is formulated to describe the coupled dynamics of mosquito populations and dengue transmission in humans under *Wolbachia* intervention. The model builds upon the bi-dimensional *Wolbachia* framework proposed by Vicencio, Vasilieva, and Gajardo [26], extending it to incorporate dengue transmission through an explicit human component. The mosquito population is divided into wild, non-*Wolbachia*-infected males and females, denoted by (N_M) and (N_F), respectively, and *Wolbachia*-infected males and females, denoted by (W_M) and (W_F). As the proportion of *Wolbachia*-infected mosquitoes increases through vertical transmission and cytoplasmic incompatibility, the pool of vectors capable of transmitting dengue is reduced, which is consistent with intervention outcomes [27]. In order to quantify the epidemiological consequences of mosquito population changes, a human population is incorporated into the model. The human population is divided in two compartments: susceptible (S) or infected (I). The total population, denoted as H, is assumed to be constant and given by $H = S + I$. This coupling allows for the direct assessment of how *Wolbachia*-infected mosquito releases influence human dengue prevalence, which cannot be evaluated using mosquito-only models. The flow diagram of the mathematical model is shown in Figure 1, which illustrates the interactions between mosquito subpopulations and human disease states.

Within this framework, several biological assumptions are adopted to maintain tractability while preserving key transmission mechanisms. Human dengue infection is represented using two epidemiological classes, susceptible and infected, without a recovered (immune) class. Although infection with a given dengue serotype can confer long-term immunity to that serotype, it is possible to become infected from a different strain, thus leaving short-term immunity [28]. Accordingly, recovery is not assumed to confer permanent immunity at the population level, meaning that individuals who recover from the infected class (I) immediately move to the susceptible class (S). The model further assumes homogeneous mixing between humans and mosquitoes and treats all dengue serotypes equivalently. Only wild, non-*Wolbachia*-infected female mosquitoes are capable of transmitting dengue, while *Wolbachia*-infected mosquitoes are assumed to completely block transmission. Though literature suggests that this incompatibility can be imperfect, we assume perfect incompatibility because accurately identifying parameters characterizing such variability was infeasible for the problem formulation. Additionally, an assumption of complete incompatibility distinguishes the distinct biological roles of *Wolbachia*-infected male and female mosquitoes, thus leading to the identification of optimal release strategies primarily influenced by the sex of mosquitoes released. Under these assumptions, the governing system of equations is as follows:

$$\begin{aligned}
\frac{dN_{FI}}{dt} &= \mu_N N_{FS} I - \alpha_N N_{FI} - \beta_N N_{FI} P,\\
\frac{dN_{FS}}{dt} &= \rho_N f(N_{FI} + N_{FS})\left(\frac{N_M}{W_M + N_M}\right) - \alpha_N N_{FS} - \beta_N N_{FS} P - \mu_N N_{FS} I,\\
\frac{dN_M}{dt} &= \rho_N (1 - f)(N_{FI} + N_{FS})\left(\frac{N_M}{W_M + N_M}\right) - \alpha_N N_M - \beta_N N_M P,\\
\frac{dW_F}{dt} &= \rho_W q W_F - \alpha_W W_F - \beta_W W_F P,\\
\frac{dW_M}{dt} &= \rho_W (1 - q) W_F - \alpha_W W_M - \beta_W W_M P,\\
\frac{dI}{dt} &= \mu_H (H - I) N_{FI} - \alpha_H I,
\end{aligned} \tag{2.1}$$

with initial conditions $N_{FI}(0) \geq 0$, $N_{FS}(0) \geq 0$, $N_M(0) \geq 0$, $W_F(0) \geq 0$, $W_M(0) \geq 0$, and $I(0) \geq 0$. The entire mosquito population is $P = N_{FS} + N_{FI} + N_M + W_M + W_F$. While *Wolbachia*-infected mosquito subcategories remain split only by sex (W_M and W_F), wild *Wolbachia*-free females are split into two compartments, wild susceptible mosquitoes (N_{FS}) and infected with dengue (N_{FI}), thus reflecting the role of female mosquitoes as the primary vectors of transmission. Wild males are aggregated in a single compartment (N_M), as they do not take blood meals and therefore do not directly contribute to dengue transmission [29]. No vertical or horizontal transmission of dengue is assumed to occur within the mosquito population.

Distinct demographic parameters are assigned to wild and *Wolbachia*-infected mosquitoes to capture potential fitness differences. Natural birth rates (ρ_N, ρ_W) and natural death rates (α_N, α_W) are included for each. Female birth proportions (f, q) are separately specified for each population. Density-dependent competition terms (β_N, β_W) account for resource limitations during immature developmental stages, such as access to water and suitable habitats. In Table 2, the model parameters and their descriptions are presented.

The wild and *Wolbachia*-infected mosquito populations are given by the following:

$$N(t) = N_F(t) + N_M(t) \quad \text{and} \quad W(t) = W_F(t) + W_M(t), \tag{2.2}$$

with average lifespans of ${\alpha_N}^{-1}$ and ${\alpha_W}^{-1}$ for wild and *Wolbachia*-infected mosquitoes, respectively. The term $N_M/(N_M + W_M)$ denotes the probability that mating occurs between two wild (uninfected) mosquitoes. We assume $W_M + N_M > 0$, so that the mating probability term is well-defined. To ensure biological feasibility and non-trivial populations dynamics, it is assumed that $\rho_N > \alpha_N$ and $\rho_W > \alpha_W$. Additionally, to reflect strain-dependent fitness costs associated with *Wolbachia* infection, the model assumes $\rho_W \leq \rho_N$ and $\alpha_W \geq \alpha_N$, as shown in Table 3.

Dengue transmission between mosquitoes and humans is governed by three epidemiological parameters: the human-to-mosquito transmission rate (μ_N), the mosquito-to-human transmission rate (μ_H) and the recovery rate in humans (α_H). Parameter values are informed by data from Cali, Colombia, a location experiencing sustained circulation of all four serotypes and active *Wolbachia*-based release programs [30]. While parameter estimation based on a specific locality introduces certain limitations, *Aedes aegypti* populations exhibit similar ecological and epidemiological characteristics across subtropical regions, thus supporting broader qualitative interpretations of results. Prior to the analysis, the system (2.1) is proven to be biologically well-posed.

Lemma 2.1. *The sex-structured Wolbachia-dengue transmission model,* (2.1)*, is well-posed. Consequently, the set*

$$\chi := \left\{(N_{FI}, N_{FS}, N_M, W_F, W_M, I) \in \mathbb{R}^6_+ \ : \ 0 \leq N_{FS}, N_{FI}, N_M, W_F, W_M, I \leq \tilde{K}\right\}$$

acts as an absorbing set of trajectories and is invariant, where

$$\tilde{K} := \max\left\{\tilde{N}_{FS}, \tilde{N}_{FI}, \tilde{N}_M, \tilde{W}_F, \tilde{W}_M, \tilde{I}\right\},$$

and $\tilde{N}_{FS}, \tilde{N}_{FI}, \tilde{N}_M, \tilde{W}_F, \tilde{W}_M$, and $\tilde{I}$ represent the finite carrying capacities of each subpopulation.

The proof is provided in Appendix A.

Table 2. Description of sex-structured *Wolbachia*-dengue transmission model parameters.

Parameter	Description	Units	Value	Reference
ρ_N	Per capita fecundity rate of uninfected insects	time^{-1}	4.55	[31, 32]
ρ_W (*w*MelPop)	Per capita fecundity rate of infected insects	time^{-1}	$0.5 \times \rho_N = 2.27$	[33–35]
ρ_W (*w*Mel)	Per capita fecundity rate of infected insects	time^{-1}	$0.9 \times \rho_N = 4.095$	[36]
ρ_W (*w*AlbB)	Per capita fecundity rate of infected insects	time^{-1}	$0.85 \times \rho_N = 3.8675$	[36]
α_N	Per capita mortality rate of uninfected insects	time^{-1}	0.03333	[31, 32]
α_W (*w*MelPop)	Per capita mortality rate of infected insects	time^{-1}	$2 \times \alpha_N = 0.06666$	[33–35]
α_W (*w*Mel)	Per capita mortality rate of infected insects	time^{-1}	$1.1 \times \alpha_N = 0.03666$	[36]
α_W (*w*AlbB)	Per capita mortality rate of infected insects	time^{-1}	α_N	[36]
β_N	Competition of uninfected insects	$(\text{mosquito} \times \text{time})^{-1}$	2.61×10^{-3}	[26]
β_W	Competition of infected insects	$(\text{mosquito} \times \text{time})^{-1}$	3.13×10^{-3}	[37, 38]
f	Female birth proportion (uninfected)	scalar	0.5	[39]
q	Female birth proportion (infected)	scalar	0.5556	[40, 41]
μ_N	Human→mosquito transmission rate	$(\text{time} \times \text{human})^{-1}$	0.0004762	[42]
μ_H	Mosquito→human transmission rate	$(\text{time} \times \text{mosquito})^{-1}$	0.001427	[42]
α_H	Per capita dengue recovery rate in humans	time^{-1}	0.1	[42]

Table 3. *w*MelPop, *w*Mel and *w*AlbB strain parameter relationships.

Strain	Fecundity rate (ρ_W)	Mortality rate (α_W)	References
*w*MelPop	$0.5 \times \rho_N$	$2 \times \alpha_N$	[33–35]
*w*Mel	$0.9 \times \rho_N$	$1.1 \times \alpha_N$	[36]
*w*AlbB	$0.85 \times \rho_N$	$\approx \alpha_N$	[36]

To incorporate strain-specific effects of *Wolbachia* infection, three commonly deployed strains are considered: *w*MelPop, *w*Mel, and *w*AlbB. These strains primarily differ in their impacts on mosquito fecundity and mortality, thereby reflecting strain-dependent fitness costs [43]. In Table 3, the corre-

sponding parameter values are shown.

Among the three strains, *w*AlbB is associated with minimal increases in mosquito mortality and primarily affects fitness through sensitivity to temperature [18]. In contrast, *w*MelPop induces substantial fitness costs, including increased mortality, while *w*Mel exhibits intermediate effects and is often associated with higher overall survival relative to *w*MelPop [20, 21]. These strain-dependent tradeoffs influence establishment success and intervention outcomes and are typically evaluated in relation to the local environmental conditions and viral suppression efficacy [19, 23]. Due to the infeasibility of identifying parameters that accurately capture the relationship between dengue suppression efficacy and strain for the present formulation, all three strains are assumed to equally suppress dengue transmission and to experience the same level of density-dependent competition, which is represented by a common competition parameter (β_W). The *w*MelPop strain is used as our baseline reference for this parameter.

3. Mathematical analysis

3.1. Basic reproduction number

The basic reproduction number, $\mathscr{R}_0$, characterizes the ability of dengue to invade and persist in a population through the human–mosquito transmission cycle. In the proposed model, dengue transmission is exclusively mediated by wild, *Wolbachia*-free female mosquitoes, while *Wolbachia*-infected mosquitoes are assumed to be incompetent vectors. Consequently, $\mathscr{R}_0$ depends on the equilibrium structure of the mosquito population and, in particular, on the availability of wild female mosquitoes.

Definition 3.1 (Basic reproduction number for dengue under *Wolbachia*-mediated vector structure)**.** The basic reproduction number, $\mathscr{R}_0$, is the expected number of secondary dengue infections generated by a single infected individual introduced into a fully susceptible host population, conditional on the mosquito population being at a given demographic equilibrium:

$$\mathscr{R}_0 = (Q_N - 1)\frac{H\alpha_N\mu_H\mu_N}{\alpha_H\beta_N\rho_N}.$$

Remark. $\mathscr{R}_0$ quantifies the transmission potential of dengue through the wild female mosquito population and decreases as *Wolbachia* reduces the availability of competent vectors. The basic reproduction number accounts for both stages of transmission (host to vector and vector to host). The calculation of $\mathscr{R}_0$ is completed at the equilibrium of dengue-free, wild mosquito domination ($\mathscr{E}_N$), which is described in Theorem 3.1. The explicit calculation of $\mathscr{R}_0$ is discussed in Appendix A.

The quantity

$$Q_N = \frac{f\rho_N}{\alpha_N} \tag{3.1}$$

represents the net reproductive threshold of wild female mosquitoes and plays a central role in determining whether dengue can persist. In particular, dengue transmission requires not only efficient human–vector contact but also sufficient demographic persistence of the wild mosquito population. This expression highlights the explicit coupling between the vector population structure and epidemiological dynamics.

To assess the influence of the model parameters on the dengue transmission potential, a local sensitivity analysis over $\mathscr{R}_0$ is performed. For a parameter p, the sensitivity index

$$\Upsilon_p := \frac{p}{\mathscr{R}_0} \cdot \frac{\partial \mathscr{R}_0}{\partial p} \tag{3.2}$$

quantifies the relative change in $\mathscr{R}_0$ induced by a relative change in p, evaluated at the wild-mosquito, dengue-free equilibrium.

Table 4. Normalized sensitivity indices of $\mathscr{R}_0$ related to Q_N.

Parameter (p)	Sensitivity index Υ_p
H	1
μ_H	1
μ_N	1
α_H	-1
β_N	-1
f	$\frac{Q_N}{Q_N - 1}$
ρ_N	$\frac{1}{Q_N - 1}$
α_N	$-\frac{1}{Q_N - 1}$

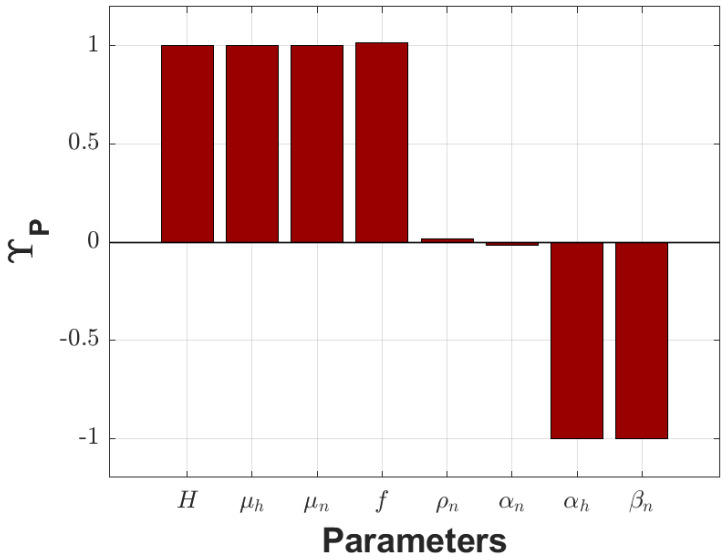

Figure 2. Bar plot of the normalized local sensitivity indices of $\mathscr{R}_0$, evaluated at the baseline parameter values shown in Table 2.

Importantly, although *Wolbachia*-related parameters do not explicitly appear in $\mathscr{R}_0$, their effects are indirect but structural: *Wolbachia* reduces the wild female mosquito population, thereby diminishing the pool of competent vectors. The resulting sensitivity indices, summarized in Table 4 and Figure 2, reveal that dengue invasion is most strongly promoted by increases in mosquito-to-human and human-to-mosquito transmission rates, as well as by increases in the net reproductive output of wild female

mosquitoes. Conversely, increased mosquito mortality and reduced human infectious periods substantially decrease $\mathscr{R}_0$.

3.2. Equilibria analysis

This section analyzes the equilibrium structure of the sex-structured *Wolbachia*-dengue transmission model (2.1). The system admits five biological equilibria: three are dengue-free and two are dengue-present equilibria. The equilibria are represented in form as $\mathscr{E} = (N_{FI}^*, N_{FS}^*, N_M^*, W_F^*, W_M^*, I^*)$.

Theorem 3.1. *Assuming $Q_N > 1$, $Q_W > 1$, and $q, f \in (0,1)$, System* (2.1) *admits five distinct equilibria:*

1) *A wild mosquito dominated, dengue free equilibrium $\mathscr{E}_N$;*
2) *A Wolbachia-dominated, dengue free equilibrium $\mathscr{E}_W$;*
3) *A coexistence, dengue free equilibrium, $\mathscr{E}_C$, provided $C > \dfrac{Q_N - 1}{Q_W - 1}$ & $C > \dfrac{(1-f)Q_N + (f+q)}{(Q_W-1)(q-f)}$ when $q > f$;*
4) *A wild dominated, dengue endemic equilibrium $\mathscr{E}_{DN}$ if $\mathscr{R}_0 > \dfrac{Q_N - 1}{\rho_N - 1}$ & $\mu_H f > 4Q_N\beta_N\alpha_H$;*
5) *A coexistence, dengue endemic equilibrium $\mathscr{E}_{DW}$ when $\alpha_W < 1$ & $\beta_N > \beta_W, C > \dfrac{Q_N - 1}{Q_W - 1}$ & $C > \dfrac{(1-f)Q_N + 1}{Q_W - 1}$ when $q > f$. Moreover, $\mathscr{R}_0 > \dfrac{\nu_1 + \nu_2}{\nu_0}$, where*

$$\nu_0 = Q_W(\alpha_W + q)\frac{\alpha_N}{f}\frac{Q_N}{Q_N - 1}, \quad \nu_1 = (1-f)\frac{\beta_W}{\alpha_W}\frac{Q_N}{\alpha_H} - q(1-q)\frac{\beta_N}{\alpha_N}\frac{Q_N}{f}, \quad \nu_2 = (q-f)\left(\frac{\beta_N}{\alpha_N} + \frac{\beta_W}{\alpha_W}\right).$$

They are defined by the following:

$$\mathscr{E}_N = \left(0,\ f(Q_N-1)\frac{\alpha_N}{\beta_N},\ (1-f)(Q_N-1)\frac{\alpha_N}{\beta_N},\ 0,\ 0,\ 0\right),$$

$$\mathscr{E}_W = \left(0,\ 0,\ 0,\ q(Q_W-1)\frac{\alpha_W}{\beta_W},\ (1-q)(Q_W-1)\frac{\alpha_W}{\beta_W},\ 0\right),$$

$$\mathscr{E}_C = \left(0, \frac{\alpha_W f\bar{\varphi_1}}{\bar{\varphi_2}}, \frac{\alpha_W(1-f)\bar{\varphi_1}}{\bar{\varphi_2}}, \frac{\alpha_W q\bar{\varphi_3}}{\bar{\varphi_2}}, \frac{\alpha_W(1-q)\bar{\varphi_3}}{\bar{\varphi_2}}, 0\right),$$

$$\mathscr{E}_{DN} = \left(\frac{f\left(1 - \dfrac{\rho_N - 1}{Q_N - 1}\mathscr{R}_0\right)}{\beta_n\mu_H(H\mu_N + f\rho_n)},\ \bar{\varphi_4}f\rho_N,\ (1-q)(Q_W-1)\frac{\alpha_W}{\beta_W},\ 0,\ 0,\ \frac{f\left(1 - \dfrac{\rho_N - 1}{Q_N - 1}\mathscr{R}_0\right)}{\mu_H\rho_N f^2 - \alpha_N\mu_H f + \alpha_H\beta_N}\right),$$

$$\mathscr{E}_{DW} = \left(\frac{\bar{\varphi_6}}{\mu_H\bar{\varphi_{13}}\bar{\varphi_{11}}},\ \frac{\bar{\varphi_{12}}\bar{\varphi_5}}{\beta_W\mu_H\bar{\varphi_{13}}\bar{\varphi_{11}}},\ \bar{\varphi_9},\ \bar{\varphi_8},\ \bar{\varphi_7},\ \frac{\bar{\varphi_6}}{\mu_N\bar{\varphi_5}}\right).$$

where

$$\begin{aligned}
\bar{\varphi_1} &= (C(Q_W-1)+1)(Q_W-1)(1-q),\\
\bar{\varphi_2} &= C(Q_W-1)(f-q) + (1-f)Q_N + (f+q),
\end{aligned}$$

$$
\begin{aligned}
\bar{\varphi_3} &= (C(Q_W-1)-(Q_N-1))(Q_W-1)(1-f),\\
\bar{\varphi_4} &= \frac{\mu_h\rho_N f^2-\alpha_N\mu_H f+\alpha_H\beta_N}{\beta_N\mu_H(H\mu_N+f\rho_N)},\\
\bar{\varphi_5} &= (1-q)\mu_H\rho_W q f\alpha_W\beta_N\left[\frac{1}{Q_W}\left(\frac{1}{\alpha_w}-1\right)+\frac{Q_N}{f}+\frac{\beta_W}{\alpha_W}\frac{\alpha_H}{\mu_H}+\frac{\beta_W}{\alpha_W}\frac{\alpha_N}{\beta_N}+\frac{\beta_W}{\beta_N}\right]\\
&\quad+\alpha_H\alpha_N\beta_W^2\left[(q-f)\left(1-\frac{\beta_N}{\beta_W}\right)+(1-f)Q_N\right],\\
\bar{\varphi_6} &= \bar{\varphi_{12}}\alpha_W\alpha_N\alpha_H\left(\mathscr{R}_0\frac{Q_NQ_W}{Q_N-1}\frac{\alpha_N(\alpha_W+q)}{f}-Q_N\left(\frac{\beta_W}{\alpha_W}\frac{1}{\alpha_H}(1-f)-\frac{\beta_N}{\alpha_N}\frac{1}{f}q(1-q)\right)-(q-f)\left(\frac{\beta_N}{\alpha_N}+\frac{\beta_W}{\alpha_W}\right)\right),\\
\bar{\varphi_7} &= \frac{(Q_W-1)(1-f)(1-q)\bar{\varphi_{10}}}{\beta_W\bar{\varphi_{11}}},\\
\bar{\varphi_8} &= \frac{q(Q_W-1)(1-f)\bar{\varphi_{10}}}{\beta_W\bar{\varphi_{11}}},\\
\bar{\varphi_9} &= \frac{(\alpha_W-q\rho_W)(1-f)(1-q)\bar{\varphi_{12}}}{\beta_W\bar{\varphi_{11}}},\\
\bar{\varphi_{10}} &= \alpha_W\beta_N\left[C(Q_W-1)-(Q_N-1)\right],\\
\bar{\varphi_{11}} &= \alpha_W\beta_N(q-f)\left[Q_W+\frac{1}{C}(1-Q_N(1-f))-1\right],\\
\bar{\varphi_{12}} &= 1-\left(\frac{1}{C}+Q_W\right),\\
\bar{\varphi_{13}} &= \frac{1}{C}\left(1+\frac{\mu_N}{\alpha_N}H\right)+Q_W-1.
\end{aligned}
$$

First, we discuss the analysis of the dengue-free equilibria $\mathscr{E}_N$, $\mathscr{E}_W$, and $\mathscr{E}_C$. Feasibility of $\mathscr{E}_N$ requires $Q_N > 1$. Let us recall that Q_N represents the demographic reproduction threshold for wild female mosquitoes. Similarly,

$$Q_W := q\rho_W/\alpha_W$$

governs feasibility of the *Wolbachia* equilibrium $\mathscr{E}_W$. These thresholds reflect purely vector-demographic conditions: $Q_N > 1$ ensures persistence of wild mosquitoes, while $Q_W > 1$ ensures self-sustainability of *Wolbachia*-infected mosquitoes. Notably, dengue elimination does not require *Wolbachia* establishment; the system may converge to $\mathscr{E}_N$ if wild mosquitoes dominate. However, such a state remains epidemiologically fragile, as persistence of competent wild vectors permits reinvasion of dengue.

In contrast, convergence to $\mathscr{E}_W$ eliminates all competent vectors and structurally prevents dengue transmission under the assumption of perfect cytoplasmic incompatibility. The coexistence equilibrium ($\mathscr{E}_C$) represents a balance between wild and *Wolbachia*-infected subpopulations and acts as a

separatrix between attraction regions. Feasibility of $\mathscr{E}_C$ relies on satisfying inequalities for the quantity $C := \dfrac{\alpha_W \beta_N}{\alpha_N \beta_W}$, which encodes the competition balance among populations. $\mathscr{E}_C$ may exist when the competition balance among wild and *Wolbachia* populations appropriately exceeds the replacement balance between populations under specific female birth ratios. The attainability of each equilibrium depends on the local stability, which is determined by the interaction between demographic thresholds and inter-specific competition parameters. Consequently, the long-term system behavior reduces to competitive exclusion: asymptotic dominance by either wild or *Wolbachia*-Infected mosquitoes.

Proposition 3.1. The wild-mosquito equilibrium $\mathscr{E}_N$ is locally asymptotically stable if $Q_N - 1 > C(Q_W - 1)$, while the *Wolbachia*-dominated equilibrium $\mathscr{E}_W$ is locally asymptotically stable if $Q_W > 1$.

This result is proven in detail in Appendix A.

The threshold $Q_W > 1$ ensures that *Wolbachia*-infected mosquitoes are demographically self-sustaining. When $Q_W < 1$, *Wolbachia* cannot persist, and the system converges to the wild-mosquito equilibrium $\mathscr{E}_N$. When $Q_W > 1$, the persistence of *Wolbachia* becomes possible, but dominance over the wild population depends on the competition balance encoded in C. The inequality

$$Q_N - 1 < C(Q_W - 1)$$

characterizes when wild mosquitoes outcompete *Wolbachia*-infected mosquitoes. Conversely, violation of this condition leads to *Wolbachia*-infected dominance. Thus, the system exhibits a competitive exclusion structure: asymptotic dynamics are governed by demographic reproduction thresholds and interspecific competition, thus leading to eventual dominance by one subpopulation. Note that the inequality that ensures stability of $\mathscr{E}_N$ is exactly the same as seen in the feasibility conditions for $\mathscr{E}_C$. When $\mathscr{E}_C$ exists, $\mathscr{E}_N$ must be locally asymptotically stable.

However, persistent coexistence with and without dengue is restricted to a narrow parameter regime and is structurally unstable under biologically reasonable conditions. Due to the complexity of the analytical solution of thresholds for $\mathscr{E}_C$ and $\mathscr{E}_{DW}$, the local stability was gauged via numerical methods. Intuitively, from a biological perspective, when considering the inheritive dominance of *Wolbachia* [16], it is unlikely that either would be stable.

As demonstrated in Figure 3, each basin of attraction plot shows convergence to two of the non-coexistence equilibria ($\mathscr{E}_{DN}$ and $\mathscr{E}_W$) and confirms the instability of either of the coexistence fixed points, $\mathscr{E}_C$ and $\mathscr{E}_{DW}$. When no dengue is present or is insufficiently spread, the region occupied by $\mathscr{E}_{DN}$ is effectively $\mathscr{E}_N$. There exists no region for a coexistence equilibrium for any strain choice, provided it would be stable for some choice of parameters, that is, there is no stable coexistence equilibrium that is attainable under reasonable, biological choices of parameters, only asymptotic domination by one sub-population.

We finish the section with a discussion of $\mathscr{E}_{DN}$ and $\mathscr{E}_{DW}$. Feasibility of $\mathscr{E}_{DN}$ requires that

$$\mathscr{R}_0 > \frac{Q_N - 1}{\rho_N - 1} \quad \text{and} \quad \mu_H f > 4 Q_N \beta_N \alpha_H.$$

In the inequality, $\mu_H f$ measures the effective contribution of wild female mosquitoes to dengue transmission from mosquitoes to humans. Additionally, $4Q_N\beta_N\alpha_H$ could be understood as the combined

effects of human recovery and density-dependent competition among uninfected mosquitoes. This expression says that mosquito-to-human transmission must be strong enough to overcome both human recovery and density-dependent limitation in the wild mosquito population. This means that dengue can only persist when transmission from mosquitoes to humans is sufficiently strong relative to the loss of infection through human recovery and regulation of the wild mosquito population by competition. Effectively, the human population must maintain their status as a reservoir of the disease. This is intimately related to the inequality involving $\mathscr{R}_0$, suggesting that not only must dengue spread efficiently among human hosts, but also must transfer between the host and vector populations enough to support this spread. The associated stability analysis for $\mathscr{E}_{DN}$ is not tractable.

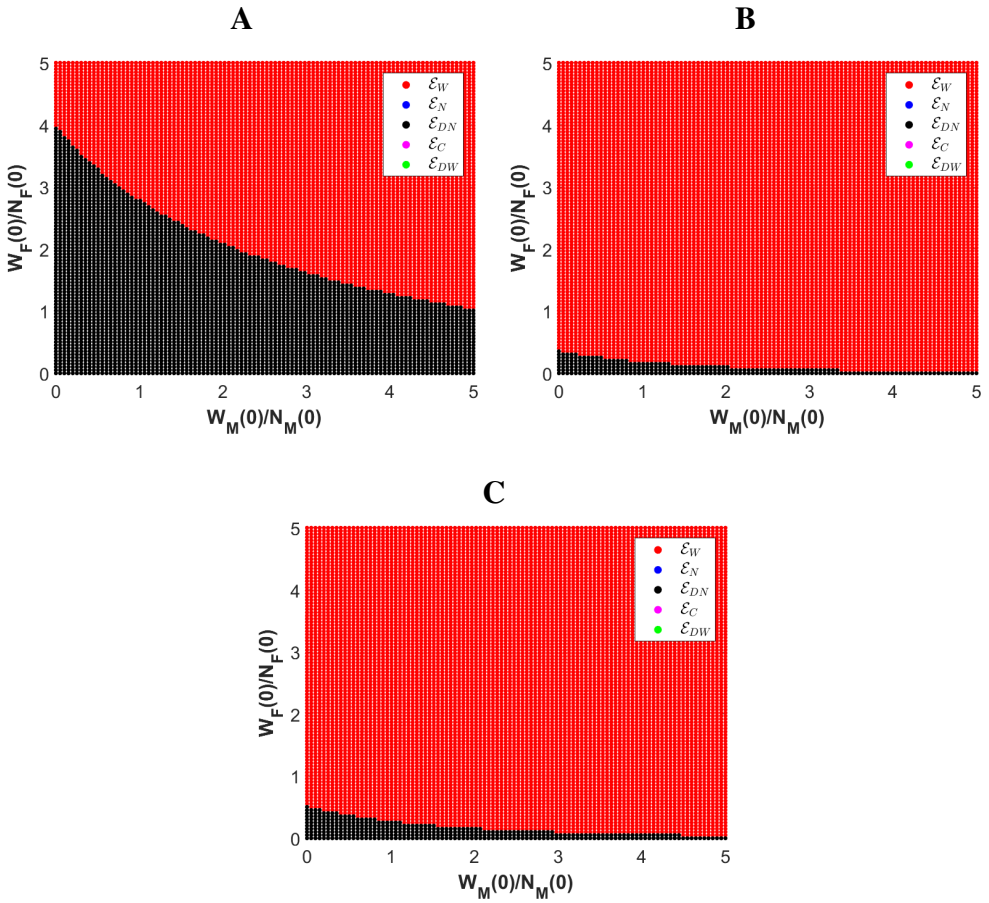

Figure 3. Basin of attraction plots for mosquito population equilibria convergence dynamics for *w*MelPop (***A***), *w*Mel (***B***), and *w*AlbB (***C***) strains with starting male and female wild mosquito populations of 1000, as well as 100 dengue-infected humans and mosquitoes. On the horizontal axis is the ratio of male *Wolbachia*-infected mosquitoes to male wild mosquitoes, whereas the vertical axis represents an identical ratio for female mosquitoes. In each plot, the red area displays convergence to a wild and dengue-free equilibrium, $\mathscr{E}_W$, the blue area represents convergence to a *Wolbachia* and dengue-free equilibrium, $\mathscr{E}_N$, the black area to a wild dominated, dengue endemic equilibrium, $\mathscr{E}_{DN}$, the magenta area to a coexistence, dengue free equilibrium, $\mathscr{E}_C$, and the green area to a coexistence, dengue endemic equilibrium, $\mathscr{E}_{DW}$.

Alternatively, $\mathscr{E}_{DW}$ is feasible under similar conditions as $\mathscr{E}_C$. While both need $q > f$ and $C > \dfrac{Q_N - 1}{Q_W - 1}$, $\mathscr{E}_C$ requires that

$$C > \frac{(1-f)Q_N + (f+q)}{(Q_W - 1)(q-f)}$$

while $\mathscr{E}_{DW}$ needs

$$C > \frac{(1-f)Q_N + 1}{Q_W - 1}.$$

Ultimately, *Wolbachia* and wild mosquito coexistence requires an appropriate competition balance guaranteed by $C > (Q_N - 1)/(Q_W - 1)$. However, what determines the persistence of dengue is dictated by the remaining two thresholds stated above, as well as the condition that $\mathscr{R}_0 > (\nu_1 + \nu_2)/\nu_0$. This section concludes with a summarization of the equilibria in Table 5.

Table 5. Summary table of subpopulations present in the five equilibria of the sex-structured *Wolbachia*-dengue transmission model, (2.1).

Equilibria	Wild mosquito	*Wolbachia* mosquito	Dengue infection
$\mathscr{E}_N$	Yes	No	No
$\mathscr{E}_W$	No	Yes	No
$\mathscr{E}_C$	Yes	Yes	No
$\mathscr{E}_{DN}$	Yes	No	Yes
$\mathscr{E}_{DW}$	Yes	Yes	Yes

3.3. Numerical simulations of the sex-structured Wolbachia-dengue transmission model

In this subsection, we provide numerical simulations of the sex-structured *Wolbachia*-dengue transmission model (2.1) under varying initial conditions of the subpopulations. Figure 4 demonstrates the two main cases when no *Wolbachia*-infected mosquitoes are present and when such mosquitoes are introduced to the system. For the case of a nonexistent *Wolbachia*-infected population, we consider that there exist both dengue-infected humans and mosquitoes. However, the same qualitative behavior holds true regardless of whether only one of the dengue-infected subpopulations is present to begin with. All subpopulations approach an equilibrium where dengue remains endemic, with dengue-infected mosquito and human subpopulations remaining significantly lower than uninfected populations, thus corroborating the estimates of [42]. Alternatively, when *Wolbachia*-infected mosquitoes are introduced to the system, the qualitative behavior of the dynamics dramatically changes. In this instance, *Wolbachia*-infected populations can overtake wild mosquito populations, thus leading to the eradication of dengue. However, the level and specifications of introduction of *Wolbachia*-infected mosquitoes play a large role in dictating the long term dynamics of the system. Sex-release ratios, *Wolbachia* strain, and quantity of release ultimately determine whether *Wolbachia* overtake will occur.

Figure 5 describes the dynamics for approaching the two equilibrium points, $\mathscr{E}_{DN}$ and $\mathscr{E}_W$, when accounting for *Wolbachia* presence in mosquito populations (under the 3 different *Wolbachia* strains). Regardless of the inheritive advantage *Wolbachia* has when *Wolbachia*-infected females reproduce, the plots of $\mathscr{E}_{DN}$ illustrate that too low of *Wolbachia* introduction can lead to the persistence of only wild

mosquitoes (and therefore also disease). This is of great importance for constructing release programs. Although economic feasibility of releases is crucial, over-minimizing the number of mosquitoes released can make the intervention virtually ineffective. Alternatively, for the plots demonstrating $\mathscr{E}_W$, *Wolbachia* mosquito overtake and persistence can be achieved when a sufficiently large amount of *Wolbachia*-infected mosquitoes are released. Even though a significant portion of the mosquitoes released initially die, with a sizable enough amount released, they can outlast the remaining wild mosquitoes, eventually driving down disease transmission.

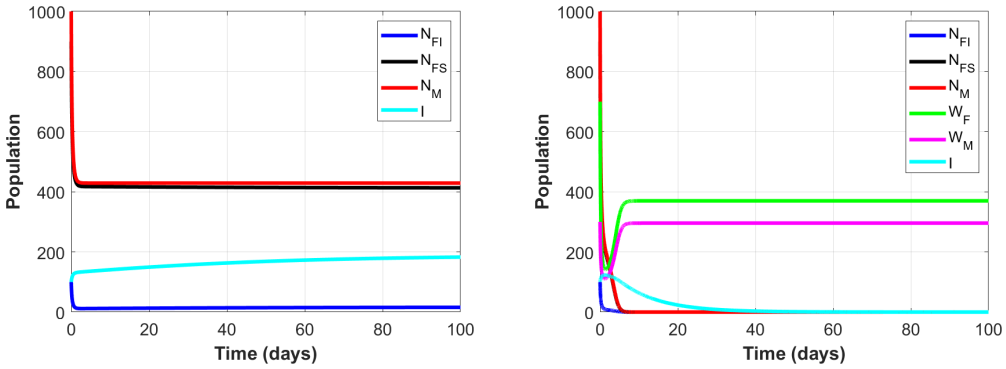

Figure 4. Dynamics of the sex-structured *Wolbachia*-dengue transmission model, (2.1), without and with (left to right) *Wolbachia*-infected mosquitoes. Dengue-infected wild female mosquitoes, N_{FI} (dark blue), non-dengue infected wild female mosquitoes, N_{FS} (black), wild male mosquitoes, N_M (red), *Wolbachia*-infected female mosquitoes, W_F (green), *Wolbachia*-infected male mosquitoes, W_M (magenta), and dengue-infected humans, I (turquoise).

As can be seen from the plots of Figure 5, what defines a "sufficiently large" introduction of *Wolbachia*-infected mosquitoes varies depending on the strain. This is understood by the basin of attraction plots of Figure 3, that is, when the introduction of *Wolbachia* mosquitoes satisfies a large enough ratio of male *Wolbachia*-infected mosquitoes to male wild mosquitoes (and likewise with females), then convergence to a *Wolbachia* dominant equilibrium ($\mathscr{E}_W$) is guaranteed. These required ratios are dependent on the initial population sizes of wild mosquitoes. From Figure 3 , which represents the basins of attraction matched to the plots of Figure 5, to achieve convergence to this equilibrium, *w*MelPop requires the largest amount of mosquitoes, followed by *w*AlbB, and then *w*Mel. For a symmetric sex release, *w*MelPop dominance is reliant on an introduction where both of the sexes of *Wolbachia*-infected mosquitoes exceed double the number of same sex wild mosquitoes. Alternatively, *w*Mel and *w*AlbB can overtake the wild population with a female-only introduction of approximately 35% and 50% of the wild female population, respectively. Biologically, due to the high mortality and low fecundity induced by *w*MelPop, substantially more mosquitoes must be released to ensure *Wolbachia* establishment when compared to either *w*Mel or *w*AlbB. A similar analysis of required introduction amounts can be completed for initial populations of varying size, but the ultimate determinant of the success of *Wolbachia*-introduction rests on attaining these necessary sex-structured ratios for a given wild population.

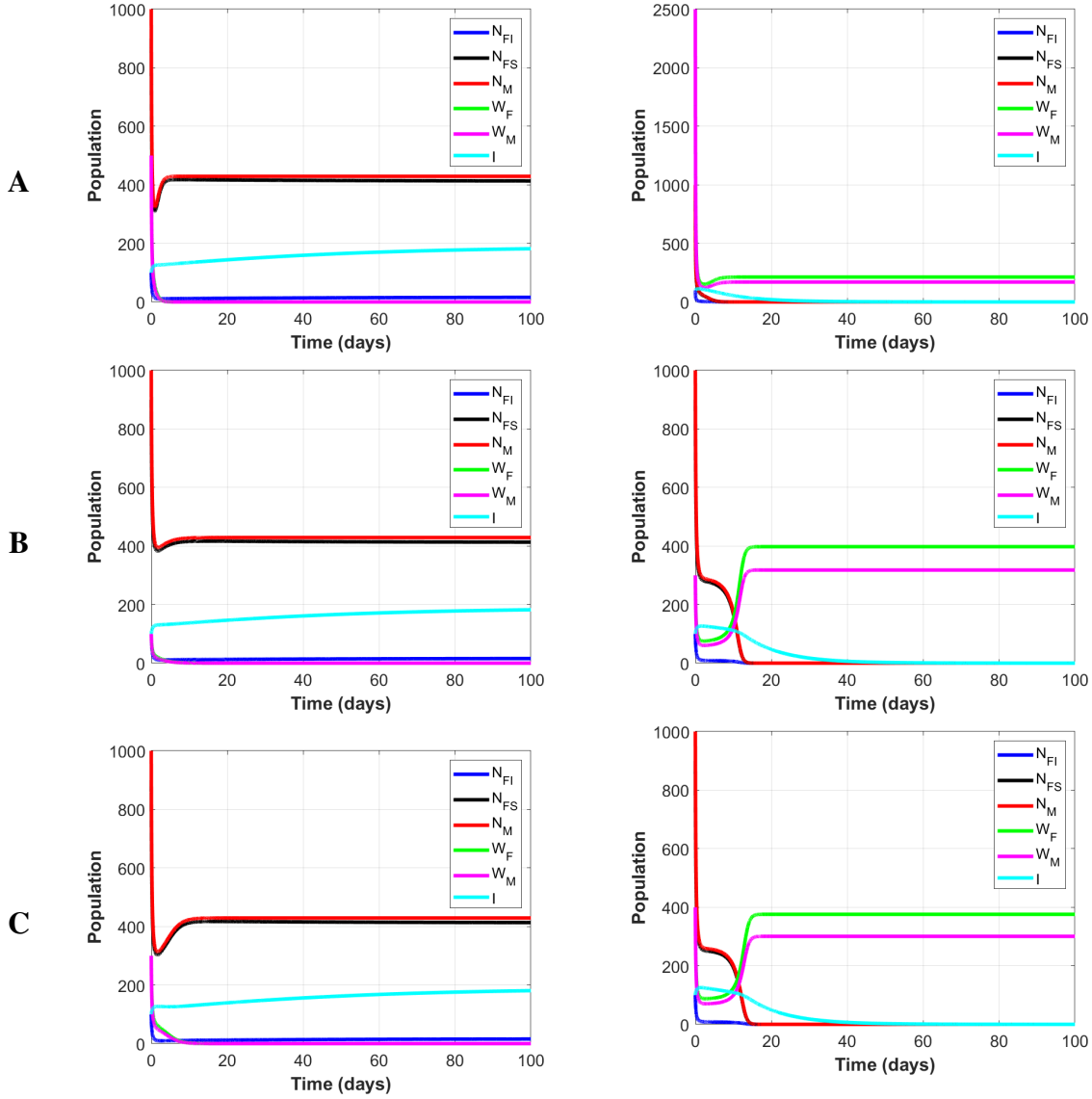

Figure 5. Dynamics of *w*MelPop (***A***), *w*Mel (***B***), and *w*AlbB (***C***) strains reaching $\mathscr{E}_{DN}$ (left) and $\mathscr{E}_W$ (right). Dengue-infected wild female mosquitoes, N_{FI} (dark blue), non-dengue infected wild female mosquitoes, N_{FS} (black), wild male mosquitoes, N_M (red), *Wolbachia*-infected female mosquitoes, W_F (green), *Wolbachia*-infected male mosquitoes, W_M (magenta), and dengue-infected humans, I (turquoise).

4. Formulation of the optimal control problem

4.1. Optimal control formulation

Effective *Aedes aegypti* release programs must balance reductions in human dengue infection with the logistical and economic costs associated with mosquito deployment. Although the long term cost of dengue infection substantially exceeds the per-unit cost of mosquito releases [44], the scale of release programs often represents a primary barrier to implementation, especially in resource-limited settings.

These considerations motivate the formulation of an optimal control problem to identify cost-effective release strategies for *Wolbachia*-infected mosquitoes [4].

In this section, an optimal control framework is introduced to investigate sex-structured mosquito release strategies. Existing release programs typically employ fixed male-female ratios, implicitly assuming that static release compositions are sufficient. The present formulation relaxes this assumption by allowing release proportions to dynamically vary over the course of the intervention, thereby enabling the identification of time-dependent, sex-specific strategies that minimize both the epidemiological burden and the intervention effort. Such continuous control strategies are intended to approximate in-field release protocols that are often discretely completed.

Our optimal control problem is stated on a fixed, finite time interval, $[0, T]$, representing the duration of the release program. Maximum feasible release rates for *Wolbachia*-infected male and female mosquitoes are denoted by L_M and L_F, respectively. The control variables $\boldsymbol{u}(t) = [u_1(t), u_2(t)]$ represent the proportions of these maximum release rates deployed at time t. Incorporating these controls into System (2.1) yields the controlled *Wolbachia*-dengue transmission model by (4.1), subject to nonnegative initial conditions for all state variables. Then System (2.1) becomes the following:

$$\begin{aligned}
\frac{dN_{FS}}{dt} &= \rho_N f(N_{FI} + N_{FS})\left(\frac{N_M}{W_M + N_M}\right) - \alpha_N N_{FS} - \beta_N N_{FS} P - \mu_N N_{FS} I,\\
\frac{dN_{FI}}{dt} &= \mu_N N_{FS} I - \alpha_N N_{FI} - \beta_N N_{FI} P,\\
\frac{dN_M}{dt} &= \rho_N (1-f)(N_{FI} + N_{FS})\left(\frac{N_M}{W_M + N_M}\right) - \alpha_N N_M - \beta_N N_M P,\\
\frac{dW_F}{dt} &= \rho_W q W_F - \alpha_W W_F - \beta_W W_F P + u_1 L_F,\\
\frac{dW_M}{dt} &= \rho_W (1-q) W_F - \alpha_W W_M - \beta_W W_M P + u_2 L_M,\\
\frac{dI}{dt} &= \mu_H (H - I) N_{FI} - \alpha_H I,
\end{aligned} \tag{4.1}$$

such that $N_{FS}(0) \geq 0$, $N_{FI}(0) \geq 0$, $N_M(0) \geq 0$, $W_F(0) \geq 0$, $W_M(0) \geq 0$, and $I(0) \geq 0$. For future use, we define the following:

$$\boldsymbol{f}(\boldsymbol{x}(t), \boldsymbol{u}(t)) = \left[\frac{dN_{FS}}{dt}, \frac{dN_{FI}}{dt}, \frac{dN_M}{dt}, \frac{dW_F}{dt}, \frac{dW_M}{dt}, \frac{dI}{dt}\right].$$

The objective is to minimize the functional $J(\boldsymbol{u})$ that is subject to $\boldsymbol{f}(\boldsymbol{x}(t), \boldsymbol{u}(t))$,

$$J(\boldsymbol{u}) = \int_0^T \left[a_0 I + \frac{1}{2} a_1 u_1^2(t) + \frac{1}{2} a_2 u_2^2(t)\right] dt, \tag{4.2}$$

where the weights a_0, a_1, and a_2 are nonnegative constants. The term involving $I(t)$ penalizes human infections, while the quadratic terms penalize mosquito release effort. Quadratic costs are used to reflect increasing marginal costs associated with high-intensity releases. Controls are restricted to the admissible set:

$$\mathscr{A} := \left\{u_i \in L^1(0, T) : u_i(t) \in [0, 1], \quad i = 1, 2\right\},$$

ensuring bounded and measurable release strategies. An optimal control $\boldsymbol{u}^*$ minimizes $J(\boldsymbol{u})$ over $\mathscr{A}$, with the associated state trajectory denoted by $\boldsymbol{x}^*$:

$$J(\boldsymbol{u}^*) = \min_{\boldsymbol{u}\in\mathscr{A}} J(\boldsymbol{u}). \tag{4.3}$$

The existence of an optimal control–state pair $(\boldsymbol{u}^*, \boldsymbol{x}^*)$ follows from the Filippov–Cesari Existence Theorem presented in [45]. Convexity of the integrand with respect to the control variables, compactness of the admissible control co-domain, and boundedness of state trajectories are satisfied under the present formulation. Consequently, there exists at least one admissible control that minimizes the objective functional subject to the controlled system (4.1).

Theorem 4.1. *There exists an optimal control $\boldsymbol{u}^*$ with $u_1, u_2 \in \mathscr{A}$ such that for $J(\boldsymbol{u})$ of (4.2)*

$$J(\boldsymbol{u}^*) = \min_{\boldsymbol{u}\in\mathscr{A}} J(\boldsymbol{u}),$$

subject to $\boldsymbol{f}(\boldsymbol{x}(t), \boldsymbol{u}(t))$ of the controlled Wolbachia-dengue transmission model (4.1).

Proof. The existence of an optimal control–state pair $(\boldsymbol{u}^*(t), \boldsymbol{x}^*(t))$ follows from the Filippov–Cesari Existence Theorem [45]. To apply this result, three conditions must be verified.

First, for each $(t, \boldsymbol{x})$, consider the set

$$N(t, \boldsymbol{x}) = \{(g(\boldsymbol{x}, \boldsymbol{u}) + \xi, \boldsymbol{f}(\boldsymbol{x}, \boldsymbol{u})) : \xi \le 0, \boldsymbol{u}(t) \in [0, 1]\}.$$

By construction, the integrand $g(\boldsymbol{x}, \boldsymbol{u})$ is convex in $\boldsymbol{u}$; therefore, $g(\boldsymbol{x}, \boldsymbol{u}) + \xi$ remains convex for any $\xi \le 0$. Moreover, the state dynamics $\boldsymbol{f}(\boldsymbol{x}, \boldsymbol{u})$ are affine in $\boldsymbol{u}$. Hence, the set $N(t, \boldsymbol{x})$ is convex for all $(t, \boldsymbol{x})$.

Second, the admissible control co-domain is compact. Indeed, the control functions satisfy $u_i(t) \in [0, 1]$, and the interval $[0, 1]$ is compact by the Heine–Borel Theorem [46].

Finally, solutions of the controlled system (4.1) are uniformly bounded on $(0, T)$. Since the model is well posed, each state variable admits a finite upper bound. Let

$$\boldsymbol{x}^{\max} = [N_{FS}^{\max},\ N_{FI}^{\max},\ N_M^{\max},\ W_F^{\max},\ W_M^{\max},\ I^{\max}],$$

and define $M := \max\left\{N_{FS}^{\max},\ N_{FI}^{\max},\ N_M^{\max},\ W_F^{\max},\ W_M^{\max},\ I^{\max}\right\}$. Then,

$$\begin{aligned} \|\boldsymbol{x}(t)\| &\le \|\boldsymbol{x}^{\max}\| \\ &= \sqrt{(N_{FS}^{\max})^2 + (N_{FI}^{\max})^2 + (N_M^{\max})^2 + (W_F^{\max})^2 + (W_M^{\max})^2 + (I^{\max})^2} \\ &\le \sqrt{6M}, \end{aligned}$$

and one may take $K = \sqrt{6M}$.

Since all conditions of the Filippov–Cesari Existence Theorem are satisfied, there exists an optimal pair $(\boldsymbol{x}^*(t), \boldsymbol{u}^*(t))$.

Theorem 4.2. *The optimal controls of (4.3) admit the following characterizations:*

$$u_1^*(t) = \min\left\{1, \max\left\{\frac{-\lambda_4 L_F}{a_1}, 0\right\}\right\}, \qquad u_2^*(t) = \min\left\{1, \max\left\{\frac{-\lambda_5 L_M}{a_2}, 0\right\}\right\}.$$

Proof. Let $(\boldsymbol{u}^*, \boldsymbol{x}^*)$ denote an optimal control–state pair minimizing the objective functional (4.2) over the admissible control set $\mathscr{A}$. Then,

$$J(\boldsymbol{u}^*, \boldsymbol{x}^*) \leq J(\boldsymbol{u}, \boldsymbol{x}^*)$$

for any choice of $\boldsymbol{u}$ with $u_1, u_2 \in \mathscr{A}$.

By the Pontryagin Maximum Principle [47], there exists an adjoint vector $\boldsymbol{\lambda}(t)$, consisting of absolutely continuous functions, such that the Hamiltonian

$$\begin{aligned} H(t, \boldsymbol{x}, \boldsymbol{u}, \boldsymbol{\lambda}) = \; & g(t, \boldsymbol{x}, \boldsymbol{u}) + \boldsymbol{\lambda} f(t, \boldsymbol{x}, \boldsymbol{u}) \\ = \; & a_0 I(t) + \frac{a_1}{2} u_1^2(t) + \frac{a_2}{2} u_2^2(t) + a_3 + \lambda_1(t) \frac{dN_{FS}}{dt} + \lambda_4(t) \frac{dW_F}{dt} + \lambda_2(t) \frac{dN_{FI}}{dt} + \lambda_3(t) \frac{dN_M}{dt} \\ & + \lambda_5(t) \frac{dW_M}{dt} + \lambda_6(t) \frac{dI}{dt}, \end{aligned}$$

satisfies the adjoint system

$$\boldsymbol{\lambda}'(t) = -\frac{\partial H}{\partial \boldsymbol{x}}, \quad \boldsymbol{\lambda}(T) = 0,$$

and the optimality condition

$$H(t, \boldsymbol{x}^*(t), \boldsymbol{u}^*(t), \boldsymbol{\lambda}) = \min_{u \in \mathscr{A}} H(t, \boldsymbol{x}^*(t), \boldsymbol{u}(t), \boldsymbol{\lambda}(t)) \quad \textbf{a.e.} \quad t \in [0, T].$$

Since the Hamiltonian is quadratic in the control variables, its second derivatives satisfy the following:

$$\frac{\partial^2 H(t, \boldsymbol{x}, \boldsymbol{u}, \boldsymbol{\lambda})}{\partial u_1^2} = a_1 > 0, \quad \text{and} \quad \frac{\partial^2 H(t, \boldsymbol{x}, \boldsymbol{u}, \boldsymbol{\lambda})}{\partial u_2^2} = a_2 > 0,$$

which imply convexity with respect to $\boldsymbol{u}$. Therefore, the stationary conditions yield the following:

$$\left.\frac{\partial H}{\partial u_1}\right|_{u_1 = u_1^*} = a_1 u_1^*(t) + \lambda_4(t) L_F = 0 \qquad \left.\frac{\partial H}{\partial u_2}\right|_{u_2 = u_2^*} = a_2 u_2^*(t) + \lambda_5(t) L_M = 0,$$

where H is convex at $\boldsymbol{u}^*$, so H attains a minimum at $\boldsymbol{u}^*$ ($H(t, \boldsymbol{x}^*, \boldsymbol{u}, \boldsymbol{\lambda}) \geq H(t, \boldsymbol{x}^*, \boldsymbol{u}^*, \boldsymbol{\lambda})$ for any $\boldsymbol{u}$). If we solve for ${u_1}^*$ and ${u_2}^*$, then we attain the following characterization:

$$u_1^*(t) = \begin{cases} 0 & \text{if } \dfrac{\partial H}{\partial u_1} > 0 \\ \dfrac{-\lambda_4 L_F}{a_1} & \text{if } \dfrac{\partial H}{\partial u_1} = 0 \\ 1 & \text{if } \dfrac{\partial H}{\partial u_1} < 0 \end{cases} \quad u_2^*(t) = \begin{cases} 0 & \text{if } \dfrac{\partial H}{\partial u_2} > 0 \\ \dfrac{-\lambda_5 L_M}{a_2} & \text{if } \dfrac{\partial H}{\partial u_2} = 0 \\ 1 & \text{if } \dfrac{\partial H}{\partial u_2} < 0 \end{cases}$$

Projecting these expressions onto the admissible control set [0, 1] gives the following characterizations:

$$u_1^*(t) = \min\left\{1, \max\left\{\frac{-\lambda_4 L_F}{a_1}, 0\right\}\right\} \quad \text{and} \quad u_2^*(t) = \min\left\{1, \max\left\{\frac{-\lambda_5 L_M}{a_2}, 0\right\}\right\}.$$

4.2. Optimal control results

Closed-form solutions to the optimal control problem are not available due to the nonlinear structure of the system. Therefore, numerical solutions are computed using GPOPS-II, a next-generation optimal control software package [48]. Simulations are conducted using parameter values representative of Cali, Colombia, a region with sustained dengue transmission and active *Wolbachia* intervention programs [30, 42]. The three *Wolbachia* strains, *w*MelPop, *w*Mel, and *w*AlbB, are considered. Model parameters, control bounds, and initial conditions are summarized in Tables 6 and 7. The objective functional weights a_1 and a_2 are chosen to be equivalent so that the solution of optimal controls does not prioritize a given sex of *Wolbachia* based upon the associated weight alone. These weights ensure that optimal control solutions are structured by the biological effects of each sex on dengue existence and *Wolbachia* persistence. To ensure all entries of the objective functional (4.2) are comparable, a_0 was appropriately scaled according the units of I, u_1, and u_2.

Table 6. Optimal control parameters for release program and objective functional, $J(\boldsymbol{u})$.

Parameter	Description	Value	Units	Reference
L_F	Maximum release rate for female *Wolbachia*-infected mosquitoes.	100	mosquito $\times$ (time)$^{-1}$	Assumed
L_M	Maximum release rate for male *Wolbachia*-infected mosquitoes.	100	mosquito $\times$ (time)$^{-1}$	Assumed
H	Total human population.	$\frac{\tilde{P}}{1.4727}$	human	[42], Appendix A
a_0	Weight placed on infected humans, I.	$\frac{1000}{H}$	–	Assumed
a_1	Weight placed on u_1.	1	–	Assumed
a_2	Weight placed on u_2.	1	–	Assumed
T	Length of release program.	70	–	Gauged via [4]

Table 7. Initial conditions used for the optimal control calculations based on [42] .

Initial condition	Value	Units
$N_{FS}(0)$	$0.485 \times 1.4727 \times H$	mosquito
$N_{FI}(0)$	$0.03 \times 1.4727 \times H$	mosquito
$N_M(0)$	$0.485 \times 1.4727 \times H$	mosquito
$W_F(0)$	0	mosquito
$W_M(0)$	0	mosquito
$I(0)$	$0.01 \times H$	human

Figure 6 presents the optimal control solutions and corresponding system dynamics for each strain. In all cases, the optimal strategy exhibits a sex-asymmetric release pattern, with maximal female re-

leases maintained slightly longer than male releases before both are rapidly reduced. The duration of this delay varies by strain, with *w*MelPop requiring the longest sustained releases, consistent with its higher fitness costs. Across all strains, optimized controls substantially reduce human dengue prevalence relative to the scenarios without intervention. Replacement of wild mosquitoes by *Wolbachia*-infected populations is achieved under all optimized strategies, with strain-dependent differences in the time required for establishment. These results demonstrate that dynamically optimized, sex-structured release strategies may outperform commonly used heuristic approaches and that strain-specific biological characteristics play a critical role in shaping effective intervention programs.

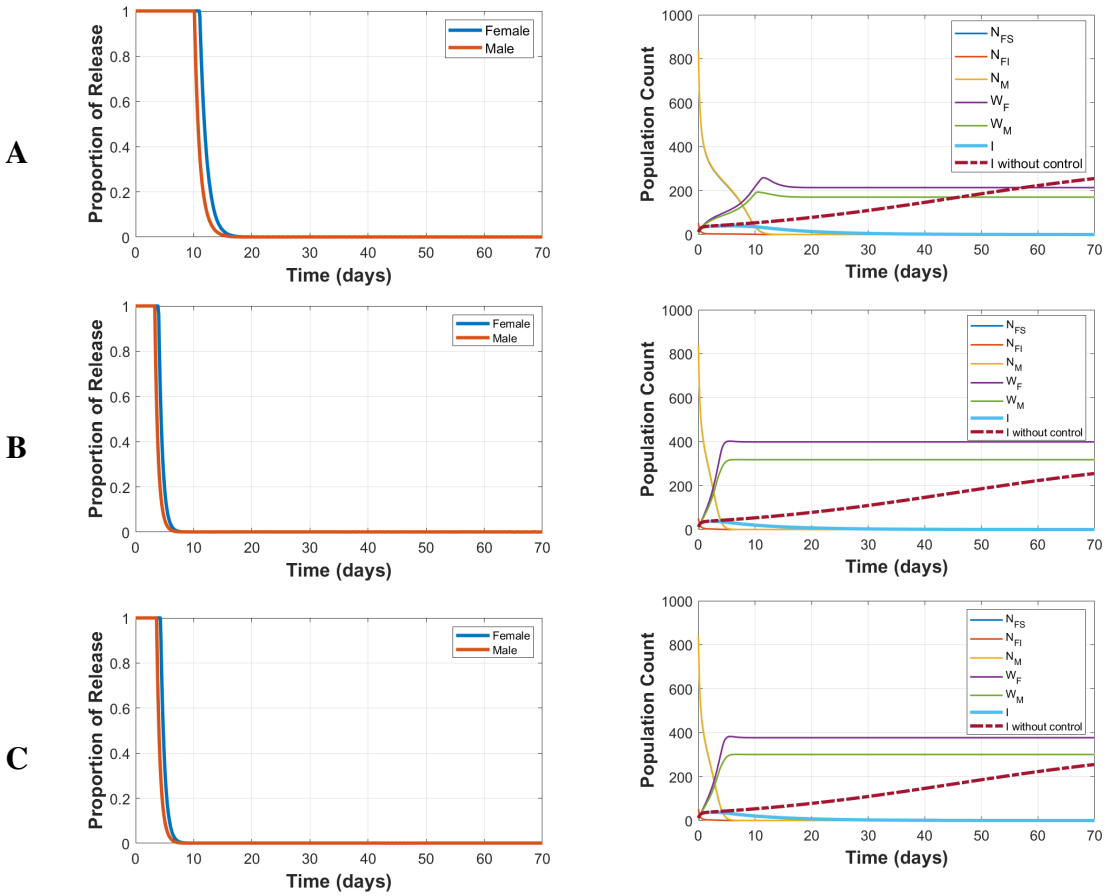

Figure 6. Optimal control solutions for *w*MelPop (***A***), *w*Mel (***B***), and *w*AlbB (***C***) scenarios. On the left, the optimal control solutions for female (blue) and male (orange) *Wolbachia*-infected mosquito release are illustrated. On the right, the population dynamics under the optimal control strategy are given. Non-dengue-infected wild female mosquitoes, N_{FS} (dark blue), dengue-infected wild female mosquitoes, N_{FI} (orange), wild male mosquitoes, N_M (yellow), *Wolbachia*-infected female mosquitoes, W_F (purple), *Wolbachia*-infected male mosquitoes, W_M (green), dengue-infected humans, I (turquoise), and for comparison, dengue-infected humans, I, under no control strategy (dashed maroon) are displayed.

A comparison can also be directly made between heuristic strategies and the optimized sex-structured strategies. In Figure 7, the optimized strategies and system dynamics for all-male *Wolbachia* releases for each strain are shown. Regardless of strain, the most optimized all-male *Wolbachia* release results in significantly more dengue cases when compared to the sex-structured protocol. No establishment of a *Wolbachia* population is achieved due to the incompatibility of *Wolbachia*-infected male mosquitoes with the wild population. A comparison of the final objective functional values across control strategies is found in Table 8. Sex-structured optimized release strategies outperform all-male releases at least ten-fold for each strain.

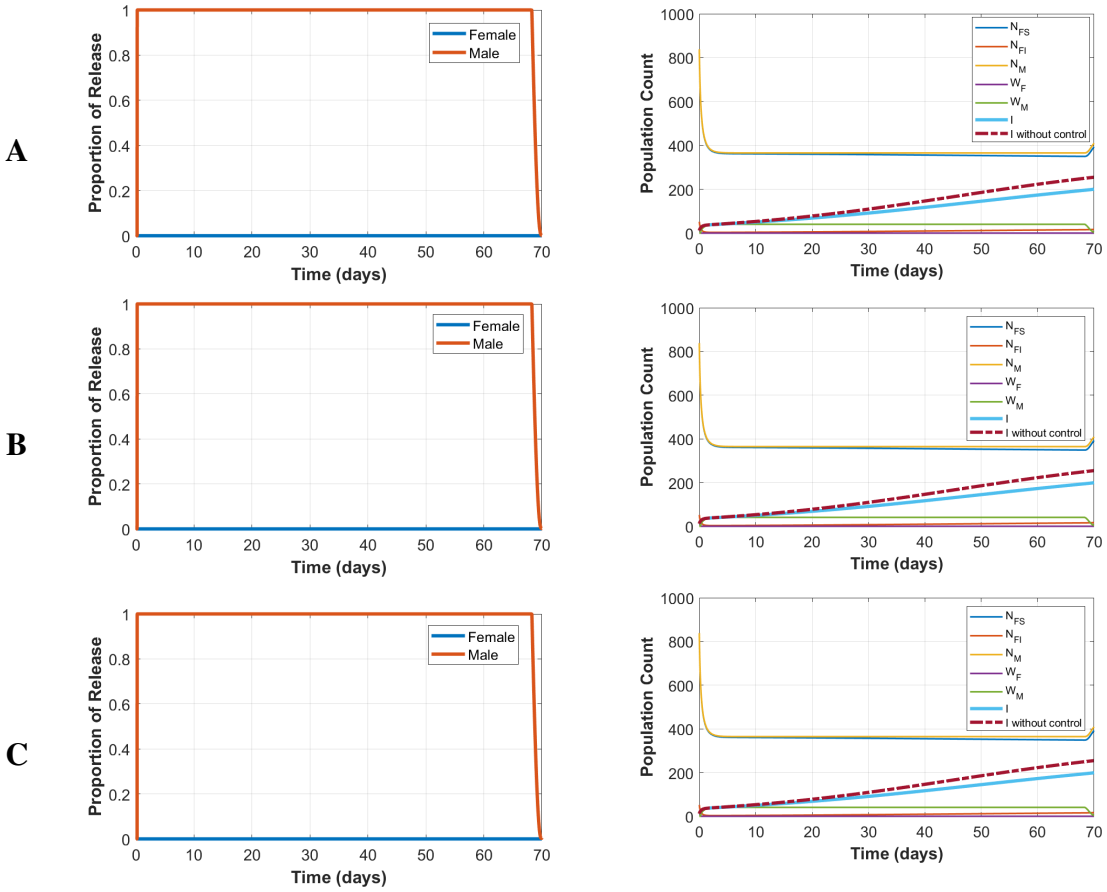

Figure 7. Optimized all-male release solutions for *w*MelPop (***A***), *w*Mel (***B***), and *w*AlbB (***C***) scenarios. On the left, the release solutions for female (blue) and male (orange) *Wolbachia*-infected mosquito release are illustrated. On the right, the population dynamics under the control strategy are given. Non-dengue-infected wild female mosquitoes, N_{FS} (dark blue), dengue-infected wild female mosquitoes, N_{FI} (orange), wild male mosquitoes, N_M (yellow), *Wolbachia*-infected female mosquitoes, W_F (purple), *Wolbachia*-infected male mosquitoes, W_M (green), dengue-infected humans, I (turquoise), and for comparison, dengue-infected humans under no control strategy, I (dashed maroon), are displayed.

In Figure 8, the optimized strategies and system dynamics for sex-symmetric *Wolbachia* releases for each strain are presented. Optimized symmetric *Wolbachia* release results in comparable system dynamics to the optimized sex-structured releases. However, the sex-structured release programs still

incrementally outperform the heuristic, symmetric release, as noted in Table 8. Altogether, these results further suggest that specified, scenario dependent sex-structured optimization may help improve the efficacy of *Wolbachia*-release programs that utilize preexisting heuristic release structuring.

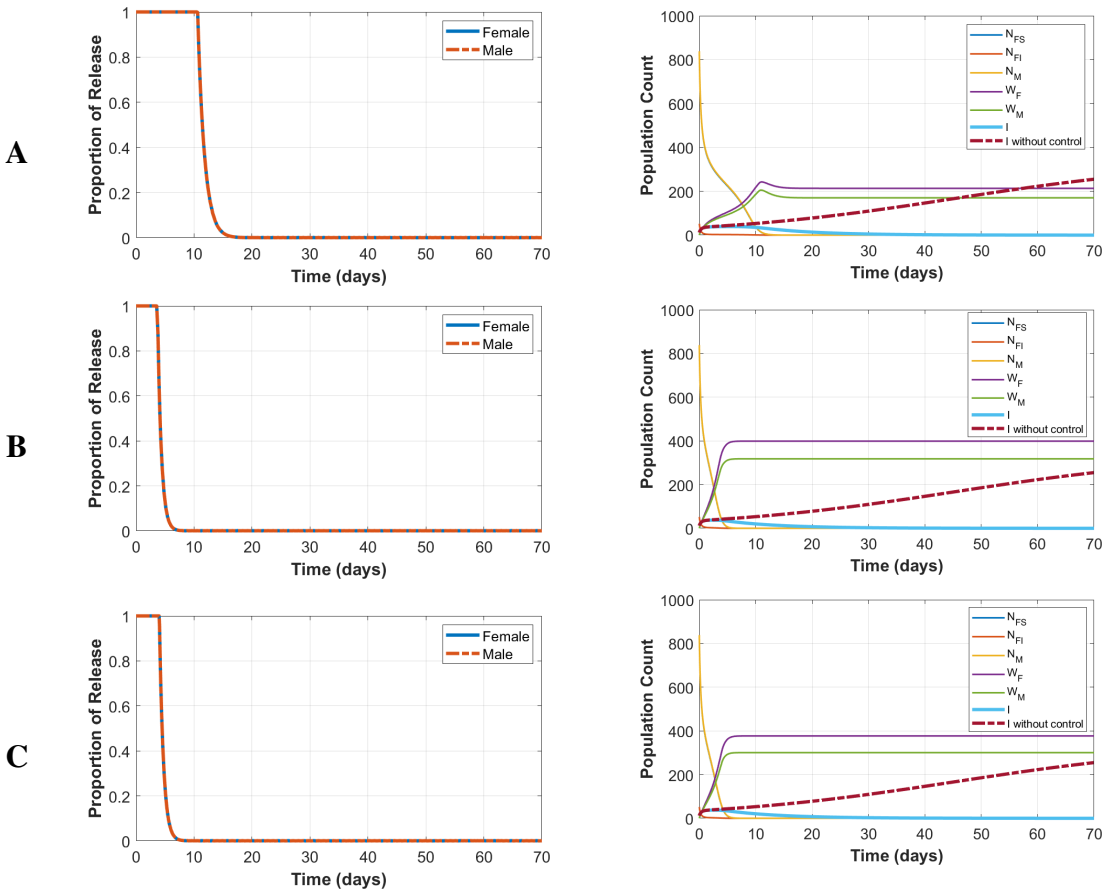

Figure 8. Optimized sex-symmetric release solutions for *w*MelPop (***A***), *w*Mel (***B***), and *w*AlbB (***C***) scenarios. On the left, the release solutions for female (blue) and male (orange) *Wolbachia*-infected mosquito release are illustrated. On the right, the population dynamics under the control strategy are given. Non-dengue-infected wild female mosquitoes, N_{FS} (dark blue), dengue-infected wild female mosquitoes, N_{FI} (orange), wild male mosquitoes, N_M (yellow), *Wolbachia*-infected female mosquitoes, W_F (purple), *Wolbachia*-infected male mosquitoes, W_M (green), dengue-infected humans, I (turquoise), and for comparison, dengue-infected humans under no control strategy, I (dashed maroon), are displayed.

Table 8. Objective functional value results for all strains across varying control strategies.

Release strategy	*w*MelPop	*w*Mel	*w*AlbB
Optimized male-only release	6532.633	6511.244	6508.825
Optimized symmetric release	643.257	432.876	442.399
Optimal control sex-structured release	643.119	432.776	442.296

5. Conclusions

The continued global expansion of dengue fever highlights the need for effective strategies that limit transmission at the vector level, particularly given the absence of broadly preventative medical treatments. This study developed and analyzed a sex-structured mathematical model describing the interaction between *Wolbachia* dynamics in *Aedes aegypti* mosquitoes and dengue transmission in humans. By incorporating mosquito sex structure, the model captures mechanisms governing both *Wolbachia* inheritance and dengue transmission that are absent from non-sex-structured formulations.

Our mathematical analysis and calculations of $\mathscr{R}_0$ as well as its associated sensitivity analysis reinforce the need for *Wolbachia* release programs to sufficiently establish *Wolbachia* in mosquito populations, as persistent coexistence is unlikely to occur. It was shown that sufficient introductions of *Wolbachia*-infected mosquitoes rely on attaining specific *Wolbachia* to wild mosquitoes sex-ratios that are dependent on the initial wild population sizes. If such ratios of release are not met, then in real life, a mosquito population remains susceptible to dengue reestablishment via movement of infected humans. Ultimately, self-directed establishment of small *Wolbachia* batches is improbable and keeps the population at risk.

An optimal control problem was subsequently used to investigate release strategies under three most commonly deployed *Wolbachia* strains (*w*MelPop, *w*Mel, and *w*AlbB). The results indicate that commonly used heuristic strategies, such as single-sex or fixed-ratio releases, are generally suboptimal when both intervention costs and human infection burden are considered. In contrast, optimized sex-structured release strategies exhibit non-trivial temporal patterns, including sex-asymmetric release schedules that vary by strain. These findings suggest that sex structure plays a critical role in shaping effective *Wolbachia* deployment strategies and that its omission may lead to inefficient or costly interventions.

This work does not prescribe a specific release strategy or strain choice, but it has demonstrated that accounting for mosquito sex structure is essential to optimize *Wolbachia*-based dengue control. Future work should refine strain-specific parametrization, incorporate additional epidemiological complexity, and continue to compare optimized strategies against existing heuristic practices. Overall, this study highlights the nontrivial role of sex structure in vector populations and provides a quantitative framework to improve the design and evaluation of *Wolbachia* release programs particularly in resource-limited settings.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Acknowledgments

This research was conducted as part of the 2025 Simon A. Levin Mathematical, Computational, and Modeling Sciences Center Quantitative Research in the Life and Social Sciences Program (QRLSSP) at Arizona State University (ASU) and has been partially supported by The College of Liberal Arts and Sciences of Arizona State University. We would also like to thank Dr. Fabio Milner, Co-Director of the Simon A. Levin Mathematical, Computational and Modeling Sciences Center and Dr. John Nagy

for their support during the QRLSSP. Researcher Dr. Heliana Arias-Castro was partially supported by the Vice-Rectorate for Research (Vicerrectoría de Investigaciones) of Universidad del Valle through project code CI 71397.

Conflict of interest

The authors declare there is no conflict of interest.

References

1. ECDC, *Mosquito Factsheet*, 2023. Available from: https://www.ecdc.europa.eu/en/disease-vectors/facts/mosquito-factsheets/aedes-aegypti.
2. Mayo Clinic, *Dengue Fever–Symptoms and Causes*, 2024. Available from: https://www.mayoclinic.org/diseases-conditions/dengue-fever/symptoms-causes/syc-20353078.
3. J. R. Powell, Mosquito-borne human viral diseases: Why *Aedes aegypti*, *Am. J. Trop. Med. Hyg.*, **98** (2018), 1563. https://doi.org/10.4269/ajtmh.17-0866
4. World Mosquito Program, *Global Progress*, 2025. Available from: https://www.worldmosquitoprogram.org/en/global-progress.
5. WHO, *Dengue and Severe Dengue*, 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.
6. O. B. Dick, J. L. S. Martín, R. H. Montoya, J. Del Diego, B. Zambrano, G. H. Dayan, The history of dengue outbreaks in the Americas, *Am. J. Trop. Med. Hyg.*, **87** (2012), 584–593. https://doi.org/10.4269/ajtmh.2012.11-0770
7. R. W. Patch, Sacraments and disease in Mérida, Yucatán, Mexico, 1648–1727, *Historian*, **58** (1996), 731–743. https://doi.org/10.1111/j.1540-6563.1996.tb00971.x
8. M. Stensmyr, Mosquito biology: How a quest for water spawned a thirst for blood, *Curr. Biol.*, **30** (2020), R1046–R1049. https://doi.org/10.1016/j.cub.2020.07.030
9. L. Maschue, *How Urbanization Impacts the Mosquito Population*, 2025. Available from: https://www.vdci.net/blog/how-urbanization-impacts-the-mosquito-population/.
10. USEPA, *Pesticides Used to Control Adult Mosquitoes*, 2024. Available from: https://www.epa.gov/mosquitocontrol/pesticides-used-control-adult-mosquitoes.
11. CDC, *Vaccine Eligibility & Recommendations*, 2025. Available from: https://www.cdc.gov/dengue/hcp/vaccine/eligibility.html#:~:text=If%20you%20vaccinate%20a%20person,highest%20risk%20for%20severe%20disease.
12. WHO, *Vaccines and Immunization: Dengue*, 2025. Available from: https://www.who.int/news-room/questions-and-answers/item/dengue-vaccines.
13. Nature Education, *Dengue Viruses*, 2026. Available from: https://www.nature.com/scitable/topicpage/dengue-viruses-22400925/.
14. J. H. Werren, L. Bald, M. E. Clark, *Wolbachia*: Master manipulators of invertebrate biology, *Nat. Rev. Microbiol.*, **6** (2008), 741–751. https://doi.org/10.1038/nrmicro1969

15. L. A. Moreira, I. Iturbe-Ormaetxe, J. A. Jeffery, G. Lu, A. T. Pyke, L. M. Hedges, et al., A *Wolbachia* symbiont in *Aedes aegypti* limits infection with dengue, chikungunya, and plasmodium, *Cell*, **139** (2009), 1268–1278. https://doi.org/10.1016/j.cell.2009.11.042

16. S. Safaei, M. Derakhshan-Sefidi, A. Karimi, *Wolbachia*: A bacterial weapon against dengue fever-A narrative review of risk factors for dengue fever outbreaks, *New Microbes New Infect.*, **65** (2025), 101578. https://doi.org/10.1016/j.nmni.2025.101578

17. J. Engelstadter, S. Charlat, A. Pomiankowski, G. D. Hurst, The evolution of cytoplasmic incompatibility types: integrating segregation, inbreeding and outbreeding, *Genetics*, **172** (2006), 2601–2611. https://doi.org/10.1534/genetics.105.050302

18. R. Barelds, *How Do Different Wolbachia Strains Influence Aedes Aegypti Virus Transmission*, 2022. Available from: https://fse.studenttheses.ub.rug.nl/28076/.

19. H. A. Flores, J. T. de Bruyne, T. B. O'Donnell, V. T. Nhu, N. T. Giang, T. X. Trang, et al., Multiple *Wolbachia* strains provide comparative levels of protection against dengue virus infection in *Aedes aegypti*, *PLoS Pathogens*, **16** (2020), e1008433. https://doi.org/10.1371/journal.ppat.1008433

20. M. V. Mancini, T. H. Ant, C. S. Herd, J. Martinez, S. M. Murdochy, D. D. Gingell, et al., High temperature cycles result in maternal transmission and dengue infection differences between *Wolbachia* strains in *Aedes aegypti*, *MBio*, **12** (2021), e00250-21. https://doi.org/10.1128/mbio.00250-21

21. S. A. Ritchie, M. Townsend, C. J. Paton, A. G. Callahan, A. A. Hoffmann, Application of *w*MelPop *Wolbachia* strain to crash local populations of *Aedes aegypti*, *PLoS Negl. Trop. Dis.*, **9** (2015), e0003930. https://doi.org/10.1371/journal.pntd.0003930

22. S. Ong, *Wolbachia Goes to Work in the War on Mosquitoes*, 2021. Available from: https://www.nature.com/nature-index/news/wolbachia-goes-to-work-war-on-mosquitoes.

23. T. Walker, P. H. Johnson, L. A. Moreira, I. Iturbe-Ormaetxe, F. D. Frentiu, C. J. McMeniman, et al., The *w*Mel *Wolbachia* strain blocks dengue and invades caged *Aedes aegypti* populations, *Nature*, **476** (2011), 450–453. https://doi.org/10.1038/nature10355

24. D. Cardona Salgado, D. E. Campo Duarte, L. S. Sepúlveda Salcedo, O. Vasilieva, M. Svinin, Optimal release programs for dengue prevention using *Aedes aegypti* mosquitoes transinfected with *w*mel or *w*melpop *Wolbachia* strains, *Math. Biosci. Eng.*, **18** (2021), 2952–2990. https://doi.org/10.3934/mbe.2021149

25. S. T. Ogunlade, A. I. Adekunle, E. S. McBryde, M. T. Meehan, Modelling the ecological dynamics of mosquito populations with multiple co-circulating *Wolbachia* strains, *Sci. Rep.*, **12** (2022), 20826. https://doi.org/10.1038/s41598-022-25242-x

26. D. Vicencio, O. Vasilieva, P. Gajardo, Monotonicity properties arising in a simple model of *Wolbachia* invasion for wild mosquito populations, *Math. Biosci. Eng.*, **20** (2022), 1148–1175. https://doi.org/10.3934/mbe.2023053

27. P. A. Ryan, A. P. Turley, G. Wilson, T. P. Hurst, K. Retzki, J. Brown-Kenyon, et al., Establishment of *w*Mel *Wolbachia* in *Aedes aegypti* mosquitoes and reduction of local dengue transmission in Cairns and surrounding locations in northern Queensland, Australia, *Gates Open Res.*, **3** (2020), 1547. https://doi.org/10.12688/gatesopenres.13061.2

28. D. C. C. Management, *Immunity*, 2018. Available from: https://www.cdc.gov/dengue/training/cme/ccm/page45893.html.

29. N. Kurnia, Y. Kaitana, C. L. Salaki, L. C. Mandey, J. S. B. Tuda, T. E. Tallei, Study of dengue virus transovarial transmission in Aedes spp in ternate city Using streptavidin-biotin-peroxidase complex immunohistochemistry, *Infect. Dis. Rep.*, **14** (2022), 765–771. https://doi.org/10.3390/idr14050078

30. World Mosquito Program, *View the Latest Updates from the World Mosquito Program in Cali*, 2023. Available from: https://www.worldmosquitoprogram.org/en/global-progress/colombia/cali.

31. D. E. Campo-Duarte, O. Vasilieva, D. Cardona-Salgado, M. Svinin, Optimal control approach for establishing *w*melpop *Wolbachia* infection among wild *Aedes aegypti* populations, *J. Math. Biol.*, **76** (2018), 1907–1950. https://doi.org/10.1007/s00285-018-1213-2

32. M. C. Domínguez, F. F. L. Almeida, W. R. Almirón, Population dynamics of Aedes aegypti (Diptera: Culicidae) in the city of Córdoba, *Rev. Soc. Entomol. Argent.*, **59** (2000), 41–50.

33. A. A. Hoffmann, Facilitating *Wolbachia* invasions, *Austral Entomol.*, **53** (2013), 125–132. https://doi.org/10.1111/aen.12068

34. M. J. Lau, P. A. Ross, A. A. Hoffmann, Infertility and fecundity loss of *Wolbachia*-infected *Aedes aegypti* hatched from quiescent eggs is expected to alter invasion dynamics, *PLoS Negl. Trop. Dis.*, **15** (2021), e0009179. https://doi.org/10.1371/journal.pntd.0009179

35. C. J. McMeniman, S. L. O'Neill, A virulent *Wolbachia* infection decreases the viability of the dengue vector *Aedes aegypti* during periods of embryonic quiescence, *PLoS Negl. Trop. Dis.*, **4** (2010), e748. https://doi.org/10.1371/journal.pntd.0000748

36. X. Zhang, S. Tang, R. A. Cheke, H. Zhu, Modeling the effects of augmentation strategies on the control of dengue fever with an impulsive differential equation, *Bull. Math. Biol.*, **78** (2016), 1968–2010. https://doi.org/10.1007/s11538-016-0208-7

37. P. R. Crain, J. W. Mains, E. Suh, Y. Huang, P. H. Crowley, S. L. Dobson, *Wolbachia* infections that reduce immature insect survival: Predicted impacts on population replacement, *BMC Evol. Biol.*, **11** (2011), 290. https://doi.org/10.1186/1471-2148-11-290

38. S. De Oliveira, D. A. M. Villela, F. B. S. Dias, L. A. Moreira, R. M. De Freitas, How does competition among wild type mosquitoes influence the performance of *Aedes aegypti* and dissemination of *Wolbachia pipientis*, *PLoS Negl. Trop. Dis.*, **11** (2017), e0005947. https://doi.org/10.1371/journal.pntd.0005947

39. L. P. Lounibos, R. L. Escher, Sex ratios of mosquitoes from long-term censuses of florida tree holes, *J. Am. Mosq. Control Assoc.*, **24** (2008), 11–15. https://doi.org/10.2987/5656.1

40. H. Asgharian, P. L. Chang, P. J. Mazzoglio, I. Negri, *Wolbachia* is not all about sex: male-feminizing *Wolbachia* alters the leafhopper *Zyginidia pullula* transcriptome in a mainly sex-independent manner, *Front. Microbiol.*, **5** (2014), 430. https://doi.org/10.3389/fmicb.2014.00430

41. L. O'Connor, C. Plichart, A. C. Sang, C. L. Brelsfoard, H. C. Bossin, S. L. Dobson, Open release of male mosquitoes infected with a *Wolbachia* biopesticide: Field performance and infection containment, *PLoS Negl. Trop. Dis.*, **6** (2012), e1797. https://doi.org/10.1371/journal.pntd.0001797

42. J. H. Arias, H. J. Martínez, L. S. Sepúlveda, O. Vasilieva, Estimación de los parámetros de dos modelos para la dinámica del dengue y su vector en cali, colombia, *Ing. Cienc.*, **14** (2018), 69–92. https://doi.org/10.17230/ingciencia.14.28.3

43. R. M. de Freitas, F. G. Sauer, K. Kliemke, G. A. Garcia, M. G. Pavan, M. R. David, et al., *Wolbachia* strains *wMel* and *wAlbB* differentially affect *Aedes aegypti* traits related to fecundity, *Microbiol. Spectrum*, **12** (2024), e00128–24. https://doi.org/10.1128/spectrum.00128-24

44. J. A. Suaya, D. S. Shepard, J. B. Siqueira, C. T. Martelli, L. C. Lum, L. H. Tan, et al., Cost of dengue cases in eight countries in the Americas and Asia: A prospective study, *Am. J. Trop. Med. Hyg.*, **80** (2009), 846–855. https://doi.org/10.4269/ajtmh.2009.80.846

45. M. Martcheva, *An Introduction to Mathematical Epidemiology*, Springer, 2015. https://doi.org/10.1007/978-1-4899-7612-3

46. W. Rudin, *Principles of Mathematical Analysis*, *3rd edition*, McGraw-Hill, New York, 1976.

47. S. Lenhart, J. T. Workman, *Optimal Control Applied to Biological Models*, Chapman and Hall/CRC, 2007. https://doi.org/10.1201/9781420011418

48. R. O. R. LLC., *GPOPS-II: Next-Generation Optimal Control Software*, 2013. Available from: https://www.gpops2.com/.

Appendix

A. Model formulation and mathematical analysis

We provide detailed proofs of selected theoretical results presented in the sections Sex-Structured Wolbachia-Dengue Transmission Model Formulation and Mathematical Analysis.

A.1. Well-possedness of the sex-structured Wolbachia-dengue transmission model

Lemma A.1. *The sex-structured Wolbachia-dengue transmission model (2.1) is well-posed.*

Proof. With assumptions of the sex-structured *Wolbachia*-dengue transmission model (2.1),

$$\begin{aligned}
\left.\frac{dN_{FS}}{dt}\right|_{N_{FS}=0} &= \rho_N f N_{FI}\left(\frac{N_M}{W_M+N_M}\right) \geq 0\\
\left.\frac{dN_{FI}}{dt}\right|_{N_{FI}=0} &= \mu N_{FS} I \geq 0\\
\left.\frac{dN_M}{dt}\right|_{N_M=0} &= 0\\
\left.\frac{dW_F}{dt}\right|_{W_F=0} &= 0\\
\left.\frac{dW_M}{dt}\right|_{W_M=0} &= p_W(1-q)W_F \geq 0\\
\left.\frac{dI}{dt}\right|_{I=0} &= \mu_H H N_{FI} \geq 0,
\end{aligned}$$

that is, no subpopulation ever becomes negative, for when each subpopulation is 0, their rate of change is nonnegative, provided all other subpopulations are also required to be nonnegative. Hence, the model system (2.1) is invariant in the positive cone $\mathbb{R}^6_+$.

Next, we show that each subpopulation is bounded. To expedite a portion of this process, note that $N_F = N_{FI} + N_{FS}$, meaning $N_{FI}, N_{FS} \leq N_F$. If we can establish an upper bound on N_F, then this is also an upper bound for N_{FI} and N_{FS}.

For the wild female mosquito population,

$$\begin{aligned}\frac{dN_F}{dt} &= \rho_N f N_F\left(\frac{N_M}{N_M + W_M}\right) - \alpha_N N_F - \beta_N N_F P \\ &\leq \rho_N N_F - \alpha_N N_F - \beta_N N_F^2 \\ &= \beta_N N_F\left(\frac{\rho_N - \alpha_N}{\beta_N} - N_F\right).\end{aligned}$$

Hence,

$$\left.\frac{dN_F}{dt}\right|_{N_F=\tilde{N}_F} \leq 0$$

and $\dfrac{dN_F}{dt} < 0$ when $N_F > \tilde{N}_F$, where $\tilde{N}_F := \dfrac{\rho_N - \alpha_N}{\beta_N}$.

This inequality portrays a representation of logistic growth that identifies what can be considered as a "carrying capacity" of N_F. $\tilde{N}_F$ is not necessarily the actual "carrying capacity" of N_F however. Yet, given

$$\left.\frac{dN_F}{dt}\right|_{N_F>\tilde{N}_F} < 0,$$

then for any t, $N_F(t) \leq \max\left\{\tilde{N}_F, N_F(0)\right\}$. As $N_F \geq 0$, for any t,

$$\begin{aligned}0 \leq N_F(t) &\leq \max\left\{\tilde{N}_F, N_F(0)\right\} \\ |N_F(t)| &\leq \max\left\{\tilde{N}_F, N_F(0)\right\}.\end{aligned}$$

Therefore, N_F is bounded as desired. We denote the upper bound of N_F by $N_F^{\max}$ where $N_F^{\max} \geq N_{FI}^{\max}, N_{FS}^{\max}$.
Through a similar argument, for the wild male mosquito population, N_M,

$$\begin{aligned}\frac{dN_M}{dt} &= \rho_N f N_F\left(\frac{N_M}{N_M + W_M}\right) - \alpha_N N_M - \beta_N N_M P \\ &\leq \rho_N N_F N_M - \alpha_N N_M - \beta_N N_M^2 \\ &\leq \beta_N N_M\left(\frac{N_F^{\max}\rho_N - \alpha_N}{\beta_N} - N_M\right)\end{aligned}$$

which leads us to

$$\left.\frac{dN_M}{dt}\right|_{N_M=\tilde{N}_M} \leq 0$$

and $\frac{dN_M}{dt} < 0$ when $N_M > \tilde{N}_M$, where $\tilde{N}_M := \frac{N_F^{\max}\rho_N - \alpha_N}{\beta_N}$.

Continuing the same method, for any $t, N_M(t) \leq \max\left\{\tilde{N}_M, N_M(0)\right\}$, and for any t

$$\begin{aligned} 0 \leq N_M(t) &\leq \max\left\{\tilde{N}_M, N_M(0)\right\} \\ |N_M(t)| &\leq \max\left\{\tilde{N}_M, N_M(0)\right\}, \end{aligned}$$

thus showing N_M is bounded.

Next, for the *Wolbachia*-infected female population, W_F, realize,

$$\begin{aligned} \frac{dW_F}{dt} &= \rho_W q W_F - \alpha_W W_F - \beta_W W_F P \\ &\leq \rho_W W_F - \alpha_W W_F - \beta_W W_F^2 \\ &= \beta_W W_F \left(\frac{\rho_W - \alpha_W}{\beta_W} - W_F\right), \end{aligned}$$

suggesting

$$\left.\frac{dW_F}{dt}\right|_{W_F=\tilde{W}_F} \leq 0$$

and $\frac{dW_F}{dt} < 0$ when $W_F > \tilde{W}_F$, where $\tilde{W}_F := \frac{\rho_W - \alpha_W}{\beta_w}$.
Hence, for any $t, W_F(t) \leq \max\left\{\tilde{W}_F, W_F(0)\right\}$, and

$$\begin{aligned} 0 \leq W_F(t) &\leq \max\left\{\tilde{W}_F, W_F(0)\right\} \\ |W_F(t)| &\leq \max\left\{\tilde{W}_F, W_F(0)\right\}, \end{aligned}$$

showing W_F is bounded. We denote the upper bound of W_F by $W_F^{\max}$.

Likewise, for the *Wolbachia*-infected male population, W_M,

$$\begin{aligned} \frac{dW_M}{dt} &= \rho_W q W_F - \alpha_W W_M - \beta_W W_M P \\ &\leq \rho_W W_F^{\max} - \alpha_W W_M \\ &= \alpha_W \left(\frac{W_F^{\max}\rho_W}{\alpha_W} - W_M\right), \end{aligned}$$

indicating

$$\left.\frac{dW_M}{dt}\right|_{W_M=\tilde{W}_M} \leq 0$$

and $\frac{dW_M}{dt} < 0$ when $W_M > \tilde{W}_M$, where $\tilde{W}_M := \frac{W_F^{\max}\rho_W}{\alpha_W}$.

Therefore, for any t, $W_M(t) \leq \max\left\{\tilde{W}_M, W_M(0)\right\}$, and t,

$$\begin{aligned} 0 \leq W_M(t) &\leq \max\left\{\tilde{W}_M, W_M(0)\right\} \\ |W_M(t)| &\leq \max\left\{\tilde{W}_M, W_M(0)\right\}, \end{aligned}$$

proving W_M is bounded.
Finally, for the boundedness of the infected human population,

$$\begin{aligned} \frac{dI}{dt} &= \mu_H(H-I)N_{FI} - \alpha_H I \\ &\leq \mu_H(H-I)N_{FI}^{\max} - \alpha_H I \\ &= \mu_H H N_{FI}^{\max} - \mu_H I N_{FI}^{\max} - \alpha_H I \\ &= (\mu_H N_{FI}^{\max} + \alpha_H)\left(\frac{\mu_H H N_{FI}^{\max}}{\mu_H N_{FI}^{\max} + \alpha_H} - I\right) \end{aligned}$$

for which it is seen

$$\left.\frac{dI}{dt}\right|_{I=\frac{\mu_H H N_{FI}^{\max}}{\mu_H N_{FI}^{\max}+\alpha_H}} \leq 0$$

and $\frac{dI}{dt} < 0$ when $I > \frac{\mu_H H N_{FI}^{\max}}{\mu_H N_{FI}^{\max} + \alpha_H}$.

Thus, for any t, $I(t) \leq \max\{\tilde{I}, I(0)\}$ where $\tilde{I} = \frac{\mu_H H N_{FI}^{\max}}{\mu_H N_{FI}^{\max}+\alpha_H}$. Then, it follows that for any t:

$$\begin{aligned} 0 \leq I(t) &\leq \max\{\tilde{I}, I(0)\} \\ |I(t)| &\leq \max\{\tilde{I}, I(0)\}, \end{aligned}$$

thus showing I is bounded.

Specifically, the compact set

$$\chi := \left\{(N_{FI}, N_{FS}, N_M, W_F, W_M, I) \in \mathbb{R}_+^6 \ : \ 0 \leq N_{FI}, N_{FS}, N_M, W_F, W_M, I \leq \tilde{K}\right\}$$

where

$$\tilde{K} := \max\left\{\tilde{N}_{FS}, \tilde{N}_{FI}, \tilde{N}_M, \tilde{W}_F, \tilde{W}_M, \tilde{I}\right\},$$

acts as an absorbing set of trajectories and is invariant. Thus, the sex-structured *Wolbachia*-dengue transmission model (2.1) is well-posed.

A.2. Proof of the dengue-free equilibria and their stability

Proof. Under the pretense of no dengue, we have that $N_{FI} = I = 0$, that is, an equilibrium point will be of the form $\mathscr{E} = (0, N_{FS}^*, N_M^*, W_F^*, W_M^*, 0)$. For simplicity, we define $N_{FS} = N_F$ and will write a dengue-free equilibrium in the form $\mathscr{E} = (N_F^*, N_M^*, W_F^*, W_M^*)$, as we already know $N_{FI} = I = 0$. An equilibrium point, $\mathscr{E} = (N_F^*, N_M^*, W_F^*, W_M^*)$, for our system will satisfy the following:

$$\begin{aligned}
\left.\frac{dN_F}{dt}\right|_{(N_F,N_M,W_F,W_M)=\mathscr{E}} &= 0\\
\left.\frac{dN_M}{dt}\right|_{(N_F,N_M,W_F,W_M)=\mathscr{E}} &= 0\\
\left.\frac{dW_F}{dt}\right|_{(N_F,N_M,W_F,W_M)=\mathscr{E}} &= 0\\
\left.\frac{dW_M}{dt}\right|_{(N_F,N_M,W_F,W_M)=\mathscr{E}} &= 0.
\end{aligned}$$

Suppose $\mathscr{E}_N := \left(N_F^{\mathscr{E}_N}, N_M^{\mathscr{E}_N}, W_F^{\mathscr{E}_N}, W_M^{\mathscr{E}_N}\right)$ with

$$N_F^{\mathscr{E}_N} = \frac{f(f\rho_N - \alpha_N)}{\beta_N}, \quad N_M^{\mathscr{E}_N} = \frac{(1-f)(f\rho_N - \alpha_N)}{\beta_N}, \quad W_F^{\mathscr{E}_N} = W_M^{\mathscr{E}_N} = 0.$$

If $W_M = W_F = 0$, then $\dfrac{dW_M}{dt} = \dfrac{dW_F}{dt} = 0$.

Alternatively, if $N_F = \dfrac{f(f\rho_N - \alpha_N)}{\beta_N}$ and $N_M = \dfrac{(1-f)(f\rho_N - \alpha_N)}{\beta_N}$,

$$\begin{aligned}
\frac{dN_F}{dt} &= \rho_N f\left(\frac{f(f\rho_N - \alpha_N)}{\beta_N}\right) - \alpha_N\left(\frac{f(f\rho_N - \alpha_N)}{\beta_N}\right) - \beta_N\left(\frac{f(f\rho_N - \alpha_N)}{\beta_N}\right)\left(\frac{-(\alpha_N - f\rho_N)}{\beta_N}\right)\\
&= \frac{f(f\rho_N - \alpha_N)}{\beta_N}(\rho_N f - \alpha_N) - \frac{f(f\rho_N - \alpha_N)}{\beta_N}(\rho_N f - \alpha_N)\\
&= 0, \quad \text{as desired.}
\end{aligned}$$

$\dfrac{dN_M}{dt} = \rho_N(1-f)N_F - \alpha_N N_M - \beta_N N_M(N_F + N_M)$ provided $W_F = W_M = 0$, then by substituting N_F and N_M from before,

$$\begin{aligned}
\frac{dN_M}{dt} &= \rho_N(1-f)N_F - \alpha_N N_M - \beta_N N_M(N_F + N_M)\\
&= \frac{(1-f)(f\rho_N - \alpha_N)}{\beta_N}(\rho_N f - \alpha_N) - \frac{(1-f)(f\rho_N - \alpha_N)}{\beta_N}(\rho_N f - \alpha_N)\\
&= 0.
\end{aligned}$$

Hence,

$$\mathscr{E}_N = \left(\frac{f(f\rho_N - \alpha_N)}{\beta_N}, \frac{(1-f)(f\rho_N - \alpha_N)}{\beta_N}, 0, 0\right)$$

is an equilibrium. Moreover, as $N_F, N_M, W_F, W_M \geq 0$, it follows that

$$f\rho_N - \alpha_N > 0 \implies \frac{f\rho_N}{\alpha_N} > 1.$$

We define $Q_N := \frac{f\rho_N}{\alpha_N}$. From a biological perspective, the inequality $\frac{f\rho_N}{\alpha_N} > 1$ implies that $\mathscr{E}_N$ can only be attained when the average number female wild mosquitoes introduced (birthed) over a set period of time exceeds the average deaths of wild mosquitoes over an equivalent length of time. Ultimately, a population of wild mosquitoes must be self-sustaining. This a biologically reasonable requirement. To analyze the stability of $\mathscr{E}_N$, we first calculate the eigenvalues of the Jacobian, J, of the condensed system of (2.1) evaluated at $\mathscr{E}_N$.

$$\begin{pmatrix} \sigma_5 - N_F\beta_N - \sigma_3 - \alpha_N & \sigma_0 & -N_F\beta_N & -N_F\beta_N - \frac{N_F\sigma_5}{(N_M+W_M)} \\ -N_M\beta_N - N_M\sigma_4 & \sigma_6 & -N_M\beta_N & \sigma_1 - N_M\beta_N \\ -W_F\beta_W & -W_F\beta_W & q\rho_W - W_F\beta_W - \alpha_W - \sigma_2 & -W_F\beta_W \\ -W_M\beta_W & -W_M\beta_W & -W_M\beta_W - \rho_W(q-1) & -\alpha_W - W_M\beta_W - \sigma_2 \end{pmatrix} \tag{A.1}$$

is the Jacobian matrix, J, and

$$\sigma_0 = -\frac{N_F(\beta_N N_M^2 + 2\beta_N N_M W_M + \beta_N W_M^2 - f\rho_N W_M)}{(N_M + W_M)^2}, \qquad \sigma_1 = \frac{N_F\, N_M\, \rho_N\, (f-1)}{(N_M + W_M)^2},$$

$$\sigma_2 = \beta_W\, P, \qquad \sigma_3 = \beta_N\, P, \qquad \sigma_4 = \frac{\rho_N(f-1)}{N_M + W_M}, \qquad \sigma_5 = \frac{N_M f\rho_N}{N_M + W_M},$$
$$\sigma_6 = \sigma_1 - N_M\beta_N - \sigma_3 - N_F\sigma_4 - \alpha_N.$$

The eigenvalues, $\boldsymbol{\lambda}$, of $J(\mathscr{E}_N)$ are as follows:

$$\boldsymbol{\lambda}\,(J(\mathscr{E}_N)) = \begin{pmatrix} \frac{\alpha_N\beta_W - \alpha_W\beta_N - \beta_W\, f\,\rho_N + \beta_N\, q\,\rho_W}{\beta_N} \\ \alpha_N - f\,\rho_N \\ -f\,\rho_N \\ -\frac{\alpha_W\beta_N - \alpha_N\beta_W + \beta_W\, f\,\rho_N}{\beta_N} \end{pmatrix}.$$

All eigenvalues $\boldsymbol{\lambda}\,(J(\mathscr{E}_N))$ must be negative for $\mathscr{E}_N$ to be stable, requiring new thresholds relating the parameters of the sex-structured *Wolbachia*-dengue transmission model (2.1). By formalizing these thresholds, we can better understand the necessary biological conditions for *Wolbachia*-infected mosquitoes to overtake the wild mosquito populations (and vice versa). Conveniently, the third eigenvalue satisfies $-f\rho_N < 0$ and the second eigenvalue $\alpha_N - f\rho_N < 0$ as $Q_N > 1$. Additionally, $\alpha_N\beta_W - \alpha_W\beta_N - \beta_W f\rho_N < \alpha_N\beta_W - \alpha_W\beta_N - \beta_W f\rho_N + \beta_N q\rho_W$. It suffices to find the threshold for negativity for the first eigenvalue, which will immediately imply the negativity of the last eigenvalue.

We want $\alpha_N\beta_W - \alpha_W\beta_N - \beta_W f\rho_N + \beta_N q\rho_W < 0$. Then, we can see the following:

$$\alpha_N\beta_W - \alpha_W\beta_N - \beta_W f\rho_N + \beta_N q\rho_W < 0$$
$$\alpha_N\beta_W + \beta_N q\rho_W < \alpha_W\beta_N + \beta_W f\rho_N$$

$$\frac{\alpha_N\beta_W + \beta_N q\rho_W}{\alpha_W\beta_N + \beta_W f\rho_N} < 1$$
$$\frac{\alpha_W\beta_N + \beta_W f\rho_N}{\alpha_N\beta_W + \beta_N q\rho_W} > 1$$
$$\frac{\frac{\alpha_W\beta_N}{\alpha_N\beta_W} + Q_N}{1 + \frac{\beta_N q P_W}{\alpha_N\beta_W}} > 1$$
$$\frac{\alpha_W\beta_N}{\alpha_N\beta_W} + Q_N > 1 + \frac{\alpha_W\beta_N}{\alpha_N\beta_W} Q_W$$
$$Q_N > 1 + C(Q_W - 1)$$

where $C := \dfrac{\alpha_W\beta_N}{\alpha_N\beta_W}$ and $Q_W := \dfrac{q\rho_W}{\alpha_W}$. Therefore, our threshold for stability is $Q_N > 1 + C(Q_W - 1)$ for $\mathscr{E}_N$.

Next, suppose $\mathscr{E}_{\boldsymbol{W}} := \left(N_F^{\mathscr{E}_W}, N_M^{\mathscr{E}_W}, W_F^{\mathscr{E}_W}, W_M^{\mathscr{E}_W}\right)$, where

$$N_F^{\mathscr{E}_W} = N_M^{\mathscr{E}_W} = 0, \quad W_F^{\mathscr{E}_W} = \frac{q(q\rho_W - \alpha_W)}{\beta_W}, \quad W_M^{\mathscr{E}_W} = \frac{(q\rho_W - \alpha_W)(1-q)}{\beta_W}.$$

When $N_F = N_M = 0$,

$$\frac{dN_F}{dt} = \frac{dN_M}{dt} = 0.$$

Then, for

$$W_F = \frac{q(q\rho_W - \alpha_W)}{\beta_W}, \quad W_M = \frac{(q\rho_W - \alpha_W)(1-q)}{\beta_W},$$

$$\begin{aligned}
\frac{dW_F}{dt} &= \rho_W q\left(\frac{q(q\rho_W - \alpha_W)}{\beta_W}\right) - \alpha_W\left(\frac{q(q\rho_W - \alpha_W)}{\beta_W}\right) - \beta_W\left(\frac{q(q\rho_W - \alpha_W)}{\beta_W}\right)\left(\frac{(q\rho_W - \alpha_W)}{\beta_W}\right) \\
&= \frac{q(q\rho_W - \alpha_W)}{\beta_W}(\rho_W q - \alpha_W) - \frac{q(q\rho_W - \alpha_W)}{\beta_W}(\rho_W q - \alpha_W) \\
&= 0, \\
\frac{dW_M}{dt} &= \rho_W(1-q)\left(\frac{q(q\rho_W - \alpha_W)}{\beta_W}\right) - \alpha_W\left(\frac{(1-q)(q\rho_W - \alpha_W)}{\beta_W}\right) - \beta_W\left(\frac{(1-q)(q\rho_W - \alpha_W)}{\beta_W}\right)\left(\frac{(q\rho_W - \alpha_W)}{\beta_W}\right) \\
&= \frac{(1-q)(q\rho_W - \alpha_W)}{\beta_W}(\rho_W q - \alpha_W) - \frac{(1-q)(q\rho_W - \alpha_W)}{\beta_W}(\rho_W q - \alpha_W) \\
&= 0, \quad \text{as needed.}
\end{aligned}$$

Therefore,

$$\mathscr{E}_{\boldsymbol{W}} = \left(0, 0, \frac{q(q\rho_W - \alpha_W)}{\beta_W}, \frac{(q\rho_W - \alpha_W)(1-q)}{\beta_W}\right)$$

is a valid equilibrium. Provided $N_F, N_M, W_F, W_M \geq 0$,

$$q\rho_W - \alpha_W > 0 \implies Q_W > 1.$$

This suggests that the feasibility of $\mathscr{E}_{\boldsymbol{W}}$ relies on the average female birth rate of *Wolbachia*-infected mosquitoes exceeding the average death rate of *Wolbachia*-infected mosquitoes.

Using the same Jacobian as before, J, the eigenvalues, $\boldsymbol{\lambda}$, of $J(\mathscr{E}_{\boldsymbol{W}})$ are as follows:

$$\boldsymbol{\lambda}\left(J(\mathscr{E}_{\boldsymbol{W}})\right) = \begin{pmatrix} \alpha_W - q\rho_W \\ -q\rho_W \\ -\frac{\alpha_N\beta_W - \alpha_W\beta_N + \beta_N q\rho_W}{\beta_W} \\ -\frac{\alpha_N\beta_W - \alpha_W\beta_N + \beta_N q\rho_W}{\beta_W} \end{pmatrix}$$

We can see $-q\rho_W < 0$ and $\alpha_W - q\rho_W < 0$ as $Q_W > 1$. We need $\alpha_W\beta_N - \alpha_N\beta_W - \beta_N qP_W < 0$, provided the last two eigenvalues are equivalent. Note, $\alpha_W\beta_N - \alpha_N\beta_W - \beta_N qP_W = \beta_N(\alpha_W - q\rho_W) - \alpha_N\beta_W$, and as $\alpha_W - q\rho_W < 0$ and $-\alpha_N\beta_W < 0$, $\alpha_W\beta_N - \alpha_N\beta_W - \beta_N qP_W < 0$. Thus, we only require $Q_W > 1$ for the stability of $\mathscr{E}_{\boldsymbol{W}}$.
Finally, for $\mathscr{E}_{\boldsymbol{C}} = (N_F^{\mathscr{E}_C}, N_M^{\mathscr{E}_C}, W_F^{\mathscr{E}_C}, W_M^{\mathscr{E}_C})$, where

$$\begin{aligned} N_F^{\mathscr{E}_C} &= \frac{f(q\rho_W - \alpha_W)(q-1)\sigma_3}{\sigma_1} \\ N_M^{\mathscr{E}_C} &= \frac{(1-f)(q\rho_W - \alpha_W)(1-q)\sigma_3}{\sigma_1} \\ W_F^{\mathscr{E}_C} &= \frac{q(q\rho_W - \alpha_W)(1-f)\sigma_2}{\sigma_1} \\ W_M^{\mathscr{E}_C} &= \frac{(q-1)(\alpha_W - q\rho_W)(f-1)\sigma_2}{\sigma_1} \end{aligned}$$

and

$$\begin{aligned} \sigma_1 &:= \beta_W\left(\beta_N q^2\rho_W - \alpha_N\beta_W f + \alpha_W\beta_N f + \alpha_N\beta_W q - \alpha_W\beta_N q - \beta_W f\rho_N + \beta_W f^2\rho_N - \beta_N f q\rho_W\right) \\ \sigma_2 &:= \alpha_N\beta_W - \alpha_W\beta_N - \beta_W f\rho_N + \beta_N q\rho_W \\ \sigma_3 &:= \alpha_N\beta_W - \alpha_W\beta_N + \beta_N q\rho_W, \end{aligned}$$

it can be shown that $\mathscr{E}_{\boldsymbol{C}}$ is an equilibrium, which is omitted due to its algebraic terseness. The stability of $\mathscr{E}_{\boldsymbol{C}}$ is left to the numerical solution. Furthermore, all equilibria can be rewritten in terms of Q_N and Q_W as done in Theorem 3.1.

A.3. Boundedness of the mosquito population

Proof. Take $P = N_{FS} + N_{FI} + N_M + W_F + W_M$. Note,

$$\begin{aligned} \frac{dP}{dt} &= \rho_N f(N_{FI} + N_{FS})\left(\frac{N_M}{W_M + N_M}\right) - \alpha_N N_{FS} - \beta_N N_{FS} P - \mu_N N_{FS} \\ &\quad + \mu_N N_{FS} I - \alpha_N N_{FI} - \beta_N N_{FI} P \\ &\quad + \rho_N(1-f)(N_{FI} + N_{FS})\left(\frac{N_M}{W_M + N_M}\right) - \alpha_N N_M - \beta_N N_M P \\ &\quad + \rho_W q W_F - \alpha_W W_F - \beta_W W_F P + u_1 L_F \end{aligned}$$

$$
\begin{aligned}
&+ \rho_W(1-q)W_F - \alpha_W W_M - \beta_W W_M P + u_2 L_M \\
&\leq \rho_N P - \alpha_N P - \beta_N P^2 \\
&= \beta_N P\left(\frac{\rho_N - \alpha_N}{\beta_N} - P\right).
\end{aligned}
$$

Thus, $|P| \leq \dfrac{\rho_N - \alpha_N}{\beta_N}$. We denote $\tilde{P} = \dfrac{\rho_N - \alpha_N}{\beta_N}$.

A.4. Computation of the basic reproduction number

We determine the reproduction number using the Van den Driessche and Watmough approach [47], a technique often used for compartmental disease transition models. Following the procedure, we create a next generation matrix to computationally solve for $\mathscr{R}_0$ [45].

For this model, the infected compartments consist of the dengue-infected, wild female mosquitoes alongside the dengue-infected humans. The remaining subpopulations are considered non-infected, and thus, are not accounted for in the next generation matrix calculation. We continue with

$$
\begin{aligned}
\frac{dN_{FI}}{dt} &= \mu_N N_{FS} I - \alpha_N N_{FI} - \beta_N N_{FI} P, \\
\frac{dI}{dt} &= \mu_H (H - I) N_{FI} - \alpha_H I.
\end{aligned}
$$

The rate of new infections ($\mathscr{F}_i$) and transitional terms ($\mathscr{V}_i$) from $\dfrac{dN_{FI}}{dt}$ and $\dfrac{dI}{dt}$ can be put into matrices as follows:

$$
\mathscr{F}_i = \begin{bmatrix} \mu_H N_{FS} I \\ \mu_H (H - I) N_{FI} \end{bmatrix},
$$

$$
\mathscr{V}_i = \begin{bmatrix} \alpha_N N_{FI} + \beta_N N_{FI}(N_{FS} + N_{FI} + N_M + W_F + W_M) \\ \alpha_H I \end{bmatrix}.
$$

Recall that there are three disease-free equilbria by Theorem 3.1. Take

$$
\mathscr{E}_{\boldsymbol{N}} = (0, \frac{f(f\rho_N - \alpha_N)}{\beta_N}, \frac{(f-1)(\alpha_N - f\rho_N)}{\beta_N}, 0, 0, 0).
$$

Linearizing around the disease-free equilibrium for new dengue infections, we attain the following:

$$
F_N = \begin{bmatrix} 0 & -\frac{f\mu_N(\alpha_N - f\rho_N)}{\beta_N} \\ H\mu_H & 0 \end{bmatrix}.
$$

The same is done for the transitional terms, providing

$$
V_N = \begin{bmatrix} \alpha_N - \beta_N(\frac{f(\alpha_N - f\rho_N)}{\beta_N} - \frac{(\alpha_N - f\rho_N)(f-1)}{\beta_N}) & 0 \\ 0 & \alpha_H \end{bmatrix}.
$$

Then, we use F_N and V_N to solve for the next generation matrix:

$$K_N = F_N V_N^{-1} = \begin{bmatrix} 0 & -\frac{f\mu_N(\alpha_N - f\rho_N)}{\beta_N \alpha_H} \\ \frac{H\mu_H}{f\rho_N} & 0 \end{bmatrix}.$$

Adhering to the same methodology of [45], it follows that the next-generation reproduction number, $\mathscr{R}_0^{NG}$, is given by the following:

$$\mathscr{R}_0^{NG} = \sqrt{\frac{H\mu_H\mu_N(f\rho_N - \alpha_N)}{\alpha_H\rho_N\beta_N}}.$$

Finally, to solve for the basic reproduction number, $\mathscr{R}_0$,

$$\begin{aligned} \mathscr{R}_0 &= \left(\mathscr{R}_0^{NG}\right)^2 = \frac{H\mu_H\mu_N(f\rho_N - \alpha_N)}{\alpha_H\rho_N\beta_N} \\ &= \frac{H\mu_H\mu_N\alpha_N(Q_N - 1)}{\alpha_H\rho_N\beta_N}. \end{aligned}$$

$\mathscr{R}_0$ accounts for both host to vector and vector to host (human to human) transmission while $\mathscr{R}_0^{NG}$ accounts for only one transmission cycle (host to vector). For the sex-structured *Wolbachia*-dengue transmission model (2.1), $\mathscr{R}_0$ helps with observing the spread of dengue in both mosquito and human populations.