The Role of Preferential Mating and Wolbachia Infection on the *Aedes Aegypti* Population Dynamics

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Abstract

Wolbachia, an endosymbiont bacteria, is common in various invertebrates and known for host reproductive manipulation strategies as well as for slowing the replication of certain viruses. When infected by Wolbachia, Aedes aegypti mosquitoes become resistant to transmitting some mosquito-borne diseases (MBD) such as dengue or other diseases prevalent in tropical and subtropical regions. Releasing a large number of Wolbachia infected mosquitoes in the environment is assumed to be a more effective strategy than other various methods to control the spread of MBD. However, evaluation of such Wolbachia-based interventions over a long term temporal scale is limited in the literature. The Wolbachia's host manipulation strategy, Cytoplasmic Incompatibility (CI), benefits the Wolbachia in the form of decreasing the number of non-infected mosquitoes, by casuing the cytoplasm of Wolbachia male mosquitoes to be incompatible with non-Wolbachia females, the eggs produced which would become non-infected mosquitoes are instead non-viable. Additionally, changes in mating preference could impact the benefit from CI, as it requires that infected males mate with non-infected females. In this work we develop models that capture the life cycle and mating preference of mosquitoes with and without Wolbachia. Our research primarily focuses on the effects of preferential mating on the population dynamics of mosquitoes. The analysis of models suggest that Wolbachia persists and dominates in the mosquito population as long as a sufficiently large Wolbachia infected mosquito population is obtained i.e. there exists a critical population size[11]. This critical population size is a function of mating-related factors and stage progression rates. This study shows that increasing same infection status preferential mating increases the critical population size, with the non-infected same status preferences being more critical than the Wolbachia same status preference. Additionally, this study shows that the effect of preferential mating is diminished when a constant recruitment of Wolbachia infected adults is applied and increased and when the Wolbachia infected mosquito population proportion is increased.

1 Introduction

Aedes aegypti are prominent transmitters of mosquito-borne diseases (MBDs) in subtropical and tropical areas, like dengue, zika, yellow fever, and others. This article mostly refers to dengue, one of the most common MBD that reports cases across the Americas, South-East Asia and Western Pacific exceeding 1.2 million in 2008 and over 3.34 million in 2016 [3]. Control methods such as insecticides and target cleaning, while very effective in the short-term, have had little lasting effect in the fight against dengue in the long-term and must be reapplied continuously. A recently developed, long-term control method uses Wolbachia, an endosymbiont bacterium, which inhibits the ability for mosquitoes to transmit many MBDs, including dengue [5]. Some of the most commonly used strains of Wolbachia for releases strategies are the wMel and wMelPop strains[13]. Other strains that have been successfully implanted or found in *Aedes aegypti* are wAlbA, wAlbB, wMelCS, wPip, wRi, and wAu[6, 13].

Wolbachia in *Aedes aegypti*

Wolbachia is passed down from mother to offspring (vertical transmission). Vertical transmission may fail and the chance of failure increases as the Wolbachia bacterium density within the mother decreases (often due to heat stress) [13]. In *Aedes aegypti*, Wolbachia manipulates the microRNA (aae-miR-2940) of its host, which regulates transcripts of a DNA methyltransferase (AaDnmt2) that dengue uses to replicate [21]. Through this regulation, dengue replication is suppressed, and its ability to invade into the salivary glands of its host decreases. Since the dengue density is low within the host, the female mosquitoes are less able to spread the disease when blood feeding, as they transmit MBDs through spitting and biting on their prey. This method has had success in a few locations including: Medellin, Colombia [7]; Cairns, Australia; and Townsville, Australia [12]. Most notably, in Townsville, Australia, since the establishment of Wolbachia infected mosquitoes, no local dengue transmissions has been reported. However, the sustainability of this method in the long-term and the range of locations where the method is viable are still unclear.

A major concern is the fitness of Wolbachia infected mosquitoes in the competition against wild non-infected mosquito populations. One of the effects that Wolbachia has on a host mosquito is shortening its lifespan, which significantly impacts its ability to compete for mating with non-infected mosquitoes, this decrease in lifespan is different for each strain. For example, the wMelPop strain reduces the lifespan of Wolbachia infected mosquitoes to 50% of the lifespan of non-infected mosquitoes, which is much more drastic than the lifespan reduction of other strains. Since studies suggest that this itself would result in the Wolbachia infected mosquitoes being unable to persist in the population, the wMelPop strain will not be considered for the analysis of the proposed model [10]. However, Wolbachia gains a reproductive advantage through the host reproductive manipulation strategy known as "cytoplasmic incompatibility" (CI), which causes the incompatibility of crossings between non-infected females and Wolbachia infected males, reducing the offspring of the non-infected population since the eggs produced by this cross will not be able to hatch[20].

Cytoplasmic Incompatibility

Since Wolbachia is vertically transmitted through the mother, a cross between a non-infected female and Wolbachia infected male would produce non-infected offspring, which would not be beneficial to the persistence of Wolbachia in the mosquito population. By decreasing the number of viable non-infected eggs, the proportion of Wolbachia infected eggs over the total number of eggs increases, though CI can fail if Wolbachia densities are not sufficiently high within the male mosquito [13]. Alternatively, through vertical transmission, a Wolbachia infected female (F_W) will produce Wolbachia infected offspring with both non-infected male (M_N) and Wolbachia infected male (M_W). A non-infected Female (F_N) and non-infected male will naturally produced non-infected offspring. Fig. 1 summarizes the results of mating crosses.

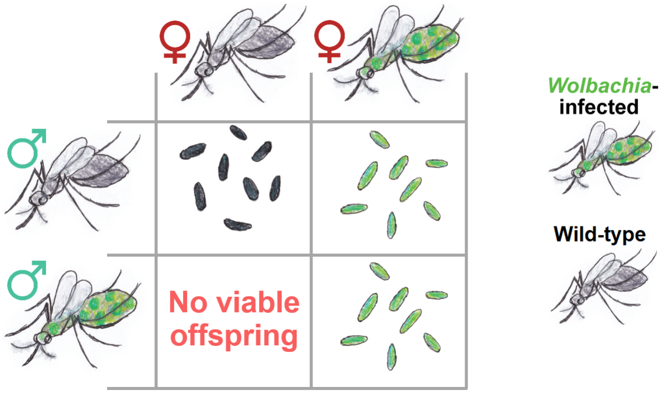


Figure 1: Outcome of Different Mating Crosses[14]

This complex interplay of life reduction and CI gives potentially complex population dynamics [20], resulting on the potential for the infected population to persist and reduce the transmission of dengue.

Preferential Mating

In the wild there is a 5 male to 3 female gender ratio within adults, this is known as the operational sex ratio, as the adults are the individuals that participate in mating [8]. *Aedes aegypti* are reported to mate in swarms where males gather then choose their partners relying on Wing Beat Frequency (WBF), ocular, and environmental cues [4]. These swarms are primarily composed of adult male *Aedes aegypti*, though other species of males, can mistakenly enter and cause mating interference as these cues can be similar between species [1]. One such expample are mating crosses between *Aedes aegypti* and *Aedes albopictus* which do not produce eggs, though female *Aedes aegypti* that mate with male *Aedes albopictus* may not wish to mate with male *Aedes aegypti* in the future, this process is called satyrization [1].

It has been observed that Wolbachia can alter some of these biological features including WBF, and physical mosquito size [2]. Small *Aedes aegypti* male mosquitoes are reported to prefer mating with smaller females. Under lab conditions, Wolbachia infected mosquitoes are larger in size, this could be a cause of preference against lab introduced Wolbachia infected mosquitoes. Another factor of mating preference could be tied to the reduction in Wolbachia infected mosquito lifespan, as older males have a preference for larger females[19].

Additionally, there have also been reports of existence of preferential mating in other species infected with Wolbachia: The two-spotted spider mites uninfected males are reported to prefer to mate with a non-infected partner, while an infected female would aggregate its offspring promoting sibling mating [18]. Thus, it's possible that Wolbachia infected males or non-infected males prefer partners from their own infection status. Here, a hypothesis-driven scenario with the potential for preferential mating in *Aedes aegypti* mosquitoes is analyzed. Preferential mating, egg laying rate, and hatch viability are considered inside the reproductive rate. Field studies suggest insignificant differences in the rate at which mosquitoes laid eggs when considering different infection statuses, thus for this work egg laying rates will be considered to be constant and equivalent [9].

Super-infected *Aedes aegypti*

Super-infected *Aedes aegypti* mosquitoes are simultaneously infected with two or more avirulent Wolbachia strains, one viable combination is for instance, wMel and wAlbB, creating wMelwAlbB [9]. Studies have reported insignificant changes in fecundity, hatch rate, and lifespan in wMelwAlbB in comparison to wMel and wAlbB [9]. Furthermore, wMelwAlbB was found to block the DENV-2 strain (there are four dengue strains: DENV, DENV-2, DENV-3, DENV-4) more efficiently than wAlbB and wMel strains on their own [9]. DENV-2 infection rates in wMelwAlbB were consistently lower (69%) than both, wMel (89%) (Fisher's exact test, $p = 0.034$) and wAlbB (100%) alone [9]. These results suggest that the deployment of super-infected mosquitoes might be used to replace single infected vectors and may represent an effective strategy to help manage potential resistance by DENV-2 to field deployments of single infected strains [9].

Different strains produce diverse effects on the mosquitoes lifespan, mating preferences, egg count, and viability of eggs between the mating crosses. In this paper, each of the wMel, wAlbB, and wMelwAlbB strains are studied individually competing against a wild uninfected mosquito population.

Previous Work and Developments

Numerous mathematical models have been developed to determine the persistence of Wolbachia infected *Aedes aegypti* in the population.

In [11], Meksianic et al (2012) proposed a six compartmental model of stages for Wolbachia infected and non-infected adults and aquatic mosquitoes. While the adults are divided into male and female, the aquatic states already include the eggs, larvae, and pupae of both genders in each equation. Major assumptions are that CI is perfect and vertical transmission is imperfect. This model allows for the possibility that gender ratios change when mosquitoes mature into adults (the operational sex ratio), though they keep the gender ratio at 1:1.

In this paper, a system of ordinary differential equations to model the life cycle stages and status of infection that shows the effect that preferential mating has on *Aedes aegypti* population dynamics is developed. This model is used to find a range for the degree of preferential mating that the Wolbachia infected population can withstand, and if a larger release of Wolbachia infected mosquitoes from labs can counteract the negative effect of preferential mating.

2 Methodology

The proposed model is based on the six stage deterministic model by Ndii et al. [11], which models the competition for persistence between non-infected and Wolbachia infected mosquitoes. The new model includes changes to mating behavior based on mating preference, mating swarms, mating interference and affected by different adult death rates. The model consists of classifications of population that represent aquatic mosquitoes that are non-infected (A_N), adult males that are non-infected (M_N), and adult females that are non-infected (F_N). Similarly, mosquito populations that represent the Wolbachia infected classifications are considered (A_W, M_W, F_W). The model compartments and descriptions are shown in Table 1. The total adult male population is refered to as $P = M_W + M_N + \delta$, with δ being the density of interfering males from other species. For the simulations, the infection status of the mosquitoes are further specified by replacing the Wolbachia subscript (W) with the strain subscripts (wMel, wAlbB, wSuper) to get the densities of life stages with specific infection statuses (F_{wMel}, M_{wMel}, F_{wAlbB}, M_{wAlbB}, F_{wSuper}, M_{wSuper}).

Table 1: Model Compartments for wMel infected mosquitoes

Compartment	Description
A_N	Density of non-infected aquatic mosquitoes
A_W	Density of Wolbachia infected aquatic mosquitoes
F_N	Density of non-infected adult female mosquitoes
M_N	Density of non-infected adult male mosquitoes
F_W	Density of Wolbachia infected adult female mosquitoes
M_W	Density of Wolbachia infected adult male mosquitoes

Model Derivation

Significant model assumptions that distinguish the model from that of [11] are summarized in Table 2.

Table 2: Model Assumptions

Label	Description
(A1)	Mating preferences (MP) exists.
(A2)	Imperfect cytoplasmic incompatibility (CI) exists [13].
(A3)	Imperfect vertical transmission (VT) exists [13].
(A4)	Eggs from different mating pairs have different viability [9].
(A5)	There is no significant difference in the egg laying rate between different mating pair combinations [9].
(A6)	The Operational Sex Ratio (OSR), the 5:3 male to female sex ratio of mating adults, is the only relevant sex ratio to the model [8].
(A7)	The lifespans of all adult classes are different [9].
(A8)	Female mosquitoes make contact with males based on proportion of total males(including rare mating interference from other species), then select for mates.

1. A_i represents the density of aquatic mosquitoes with infected status $i = \{N, W\}$ (N: non-infected; W: Wolbachia-infected):

   (a) It is assumed that A_i increases when females mate with a male of either infection status and is multiplied by the interference competition since there is a competition in which the aquatic mosquitoes could habituate. This is modeled with the product of

   $$\underbrace{F_i\left(\frac{\rho_{ii}M_i + \rho_{ij}M_j}{P}\right)}_{\text{mating preference due to infection status}} \overbrace{\left(1 - \frac{A_W + A_N}{K}\right)}^{\text{interference competition}},$$

   where the reproductive rate between female and male with different infection status $i, j = \{N, W\},\ i \neq j$ is represented by ρ_{ij}, where

   $$\rho_{ij} = (m_{ij} : \text{mating probability}) \cdot (e_{ij} : \text{egg laying rate}) \cdot (v_{ij} : \text{viability of pairing}).$$

      i. The mating probability is subject to mating preference and is incorporated by relating the mating probabilities (m_{ij}) to mating preference ratios p and q for (A1). Here, p represents the preference of non-infected females for non-infected males and $1 - p$ represents the preference of non-infected females for Wolbachia-infected males. Similarly, q represents the preference of Wolbachia-infected females for Wolbachia-infected males and $1 - q$ represents the preference of Wolbachia-infected females for non-Wolbachia males.

      ii. The egg laying rate of the crossings were found to have insignificant differences (A5).

iii. The viability of the eggs from each cross represents the average percentage of eggs that are viable (A4). For the non-Wolbachia infected female and Wolbachia-infected male crossing, this value tends to be very low due to cytoplasmic incompatibility (A2).

Table 3: Biological definition of ρ_{ij}

Parameter	**Description**	**Unit**
ρ_{ij}	Reproductive rate of $(F_i \cdot M_j)$	day^{-1}
m_{ij}	Probability of mating upon contact of $(F_i \cdot M_j)$	N/A
e_{ij}	Egg laying rate of $(F_i \cdot M_j)$	day^{-1}
v_{ij}	Viability of eggs from $(F_i \cdot M_j)$	N/A

Similarly, ρ_{ii} represents the reproductive rate of a cross between mosquitoes of the same infection status. That is, the contacts between females and males with different infection status is modeled by $F_i \frac{\rho_{ij} M_j}{P}$, and the contacts between females and males with the same infection status is modeled by $F_i \frac{\rho_{ii} M_i}{P}$. In these scenarios, we assume that mates are chosen out of a pool of males $P = M_W + M_N + \delta$, where δ represents mating interference from male mosquitoes from other species that mistakenly enter the mating swarm. Assumption (A8) considers that these crosses happen rarely, therefore δ will have a "very small" value(.0001). Lastly, female adult mosquitoes are laying their eggs in water sources with a total carrying capacity K.

(b) We assume that A_i decreases with a maturation rate γ_i and natural death rate μ_{Ai}.

2. F_i denotes the density of adult female mosquitoes with infection status i and it is assumed that

   (a) F_i increases when aquatic mosquitoes A_i mature at a growth rate γ_i with OSR $(1 - \epsilon_i)$ becoming female (A6).

      i. F_N increases with all aquatic mosquitoes from A_N.

      ii. F_N increases with a proportion of $(1 - \alpha_W)$ of aquatic mosquitoes from A_W that do not successfully inherit or loose their Wolbachia and mature to become non-infected females (A3).

      iii. F_W increases with a proportion of α_W aquatic mosquitoes from A_W (A3).

   (b) F_W increases with a constant recruitment rate Λ of adult Wolbachia-infected mosquitoes raised in ideal lab conditions.

   (c) F_i decreases with a natural death rate μ_{Fi} (A7).

3. Let M_i be the density of adult male mosquitoes with infection status $i = \{N, W\}$:

(a) M_i increases when aquatic mosquitoes A_i mature at a growth rate γ_i with OSR ϵ_i becoming male (A6).
    i. M_N increases with all aquatic mosquitoes from A_N.
    ii. M_N increases with a proportion of $(1 - \alpha_W)$ of aquatic mosquitoes from A_W that do not successfully inherit or loose their Wolbachia and mature to become non-infected males (A3).
    iii. M_W increases with a proportion of α_W aquatic mosquitoes from A_W (A3).

(b) M_W increases with a constant recruitment rate Λ of adult Wolbachia-infected mosquitoes raised in ideal lab conditions.

(c) M_i decreases with a natural death rate μ_{Mi} (A7).

Fig. 2 provides a visual representation of the assumptions of our proposed model which describes the Wolbaquia infected and non-infected mosquito population dynamics, from the aquatic to adult stage. Table 4 contains the complete description of the parameters of the model.

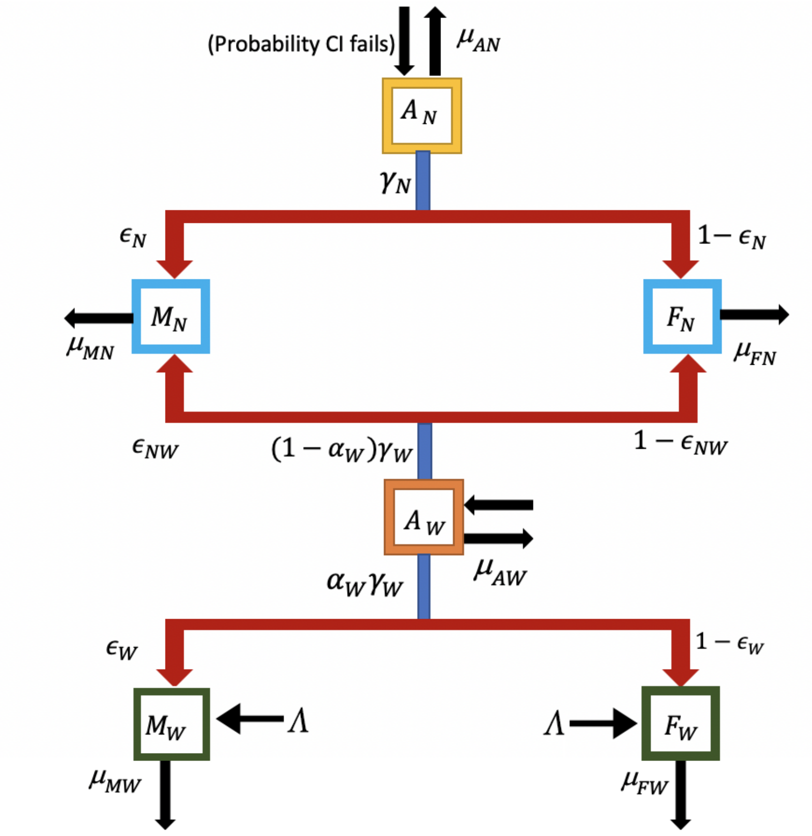


Figure 2: Schematic Representation of Model (1)

Table 4: Model Parameters

Parameter	**Description**	**Unit**
μ_{AN}, μ_{AW}	Aquatic mosquito death rate	day^{-1}
γ_N, γ_W	Aquatic mosquito maturation rate	day^{-1}
$\epsilon_N, \epsilon_M, \epsilon_{NW}$	Proportion of adults that are male	N/A
δ	Density of interfering species	*pop./pool*
$\mu_{FN}, \mu_{MN}, \mu_{FW}, \mu_{MW}$	Adult per capita death rate	day^{-1}
α_W	Probability of vertical transmission	N/A
K	Aquatic mosquito carrying capacity	*pop./pool*
Λ	Recruitment of Wolbachia mosquitoes	$(pop./pool)day^{-1}$
ρ_{ij}	Reproductive rate of $(F_i \cdot M_j)$	day^{-1}
m_{ij}	Mating probability of $(F_i \cdot M_j)$	N/A
e_{ij}	Egg laying rate of $(F_i \cdot M_j)$	day^{-1}
v_{ij}	Viability of eggs from $(F_i \cdot M_j)$	N/A

The mosquito population dynamics are represented by the following system of nonlinear ordinary differential equations

$$
\begin{aligned}
\frac{dA_N}{dt} &= F_N\left(\frac{\rho_{NW}M_W + \rho_{NN}M_N}{M_W + M_N + \delta}\right)\left(1 - \frac{A_N + A_W}{K}\right) - \mu_{AN}A_N - \gamma_N A_N, \\
\frac{dM_N}{dt} &= \epsilon_N\gamma_N A_N + \epsilon_{NW}(1-\alpha_W)\gamma_W A_W - \mu_{MN}M_N, \\
\frac{dF_N}{dt} &= (1-\epsilon_N)\gamma_N A_N + (1-\epsilon_{NW})(1-\alpha_W)\gamma_W A_W - \mu_{FN}F_N, \\
\frac{dA_W}{dt} &= F_W\left(\frac{\rho_{WW}M_W + \rho_{WN}M_N}{M_W + M_N + \delta}\right)\left(1 - \frac{A_N + A_W}{K}\right) - \mu_{AW}A_W - \gamma_W A_W, \\
\frac{dM_W}{dt} &= \Lambda + \epsilon_W\alpha_W\gamma_W A_W - \mu_{MW}M_W \\
\frac{dF_W}{dt} &= \Lambda + (1-\epsilon_W)\alpha_W\gamma_W A_W - \mu_{FW}F_W
\end{aligned}
\tag{1}
$$

3 Mathematical Analysis

In this section, we present the basic dynamics of our model. The following theorem shows that our model is biologically well-defined.

Theorem 1 (Positively Invariant). *All model parameters are bounded and non-negative, the domain* (2) *as follows.*

$$
\begin{aligned}
&0 \leq A_N + A_W \leq K \\
&0 \leq M_N \leq \frac{K[\epsilon_N \gamma_N + \epsilon_{NW}(1-\alpha_W)\gamma_W]}{\mu_{MN}} \\
&0 \leq F_N \leq \frac{(1-\epsilon_N)\gamma_N K + (1-\epsilon_{NW})(1-\alpha_W)\gamma_W K}{\mu_{FN}} \\
&0 \leq M_W \leq \frac{\Lambda + \epsilon_W \alpha_W \gamma_W K}{\mu_{MW}} \\
&0 \leq F_W \leq \frac{\Lambda + (1-\epsilon_W)\alpha_W \gamma_W K}{\mu_{FW}}
\end{aligned}
\tag{2}
$$

We begin by analyzing our model (1) by, first, finding the possible equilibrium solutions of the form $(A_N^*, M_N^*, F_N^*, A_W^*, M_W^*, F_W^{,})$. First, by setting $A_N' = 0$ we obtain

$$A_N^* = \frac{F_N^*(K - A_W^*)(\rho_{NN} M_N^* + \rho_{NW} M_W^*)}{KP(\gamma + \mu_{AN}) + F_N^*(\rho_{NN} M_N^* + \rho_{NW} M_W^*)}$$

Hence, $A_N^* > 0$ if and only if $K > A_W^*$. Then, by setting $M_N' = 0$, $M_W' = 0$, $F_N' = 0$ and $F_W' = 0$, we obtain the following equilibrium solutions with respect to A_N and A_W:

$$M_N{}^* = \frac{\gamma_N \epsilon_N A_N + \epsilon_{NW}\gamma_W(1-\alpha_W)A_W}{\mu_{MN}}, \qquad M_W{}^* = \frac{\Lambda + \epsilon_W \alpha_W \gamma_W A_W}{\mu_{MW}},$$

$$F_N{}^* = \frac{\gamma_N(1-\epsilon_N)A_N + (1-\epsilon_{NW})\gamma_W(1-\alpha_W)A_W}{\mu_{FN}}, \qquad F_W{}^* = \frac{\Lambda + (1-\epsilon_W)\alpha_W \gamma_W A_W}{\mu_{FW}}$$

Then, we proceed to substitute these expressions into $A_N' + A_W' = 0$, which simplifies into a cubic polynomial:

$$c_3 A_W^3 + c_2 A_W^2 + c_1 A_W + c_0 = 0,$$

where c_3, c_2, c_1 and c_1 are coefficients in terms of the parameters of the system and A_N. Therefore, the system may have up to three positive equilibrium solutions depending on the number of positive roots this cubic polynomial has.

Due to the complexity of the coefficients of this polynomial, we decided to focus on two biologically meaningful cases and obtain the existence conditions of equilibrium and stability conditions. Those cases are described as follow

1. The case of $\Lambda = 0$, which represents no continuous release of laboratory adult infected mosquitoes (Theorem 2).

2. The case of $\rho_{NW} = 0$, $\alpha_W = 1$. In this case, cytoplasmic incompatibility perfectly prevents all eggs from a non-infected female and Wolbachia infected male cross from being viable and vertical transmission perfectly transmits infection status to all offspring (Theorem 3).

Theorem 2 below provides conditions of existence and stability of equilibrium points when $\Lambda = 0$ in model (1).

Theorem 2 (No release of laboratory infected mosquitoes)**.** *Let $\Lambda = 0$, $\delta \neq 0$, then the following represents some of the possible equilibrium scenarios:*

1. *$E_1 = (0, 0, 0, 0, 0, 0)$ represents the extinction equilibrium. This equilibrium always exists and is locally asymptotically stable.*
2. *$E_2 = (A_N^*, M_N^*, F_N^*, 0, 0, 0)$ represents the equilibrium where only non-infected mosquitoes persist. This equilibrium only exists when*

$$R_W = \frac{4abcd}{K(a - bd)^2} < 1 \tag{3}$$

where

$$a = (1 - \epsilon_N)\gamma_N^2 \rho_{NN} \epsilon_N, \qquad b = \mu_{FN} \epsilon_N \gamma_N, \qquad c = \delta \mu_{MN} \mu_{FN}, \qquad d = \mu_{NA} + \gamma_N.$$

See Section 8 in Appendix for the proof of the theorem.

Note: Due to the complexity of the problem the stability of equilibrium E_2 could not be analyzed mathematically. However, in the next section (Figs. 3 and 6) it is shown using numerical simulations that the model also supports an equilibrium $E_3 = (A_N^*, M_N^*, F_N^*, A_W^*, M_W^*, F_W^*)$ in which both Wolbaquia infected and non-infected mosquitoes coexist, and the stability of E_2 is closely related to the existence of this coexistence equilibrium.

Theorem 3 (Perfect CI and vertical transmission without mating interference)**.** *Let $\alpha_W = 1$, $\rho_{NW} = 0$, and $\delta = 0$, then the system (1) has an equilibrium ($E_1 = (0, 0, 0, A_W^*, M_W^*, F_W^*)$) in which only Wolbachia infected mosquitoes persist in the population. This equilibrium will always exist and be locally stable under these conditions.*

See Section 8 in Appendix for the proof of the theorem.

Note: In the next section (Figs. 7–9) the existence of a coexistence equilibrium is shown numerically.

Parameter Estimation

In this section, we describe our parameter estimation. To obtain each baseline value, we utilized information found in laboratory experiments. In some cases, we assumed parameter values based on existing mathematical models available in the literature. The parameter definitions and estimates are summarized in Table 7.

To estimate the parameters pertaining to the aquatic life stages, we sourced the parameters from [11], where estimates were made based on several experimental data sets on the maturation and survival rates of the eggs, larvae, and pupae of *Aedes aegypti*. Hence, the death rate, $\mu_{Ai} = \frac{1}{7.78}$, and maturation rate, $\gamma_i = \frac{1}{6.67}$, per day for the aquatic mosquito population were obtained from [11]. While the birth sex ratio of mosquitoes may be closer to a 1:1 ratio, death rates between males and females result in a skewed ratio of adults, which are relevant to the model as they participate in mating. The parameter representing the proportion of adults that are male (ϵ_i) was determined after identifying the operational sex ratio (OSR) of adult mosquitoes. We found that the OSR for *Aedes aegypti* was a 5:3 male to female ratio in [8]. Hence, based on this biological reasoning the OSR was estimated at $\epsilon_i = 0.625$.

The per capita death rates of all adult mosquito compartments were all sourced from [9], which preformed longevity experiments on adult male and female mosquitoes, denoted with subscripts M and F respectively, of the following four infection statuses: non-Wolbachia infected (μ_{FN} and μ_{MN}), wMel-infected (μ_{FwMel} and μ_{MwMel}), wAlbB-infected (μ_{FwAlbB} and μ_{MwAlbB}), and wMelwAlbB-infected which is referred to as wSuper ($\mu_{FwSuper}$ and $\mu_{MwSuper}$). Specific values of these parameters are shown in Table 5.

Table 5: Adult Per Capita Death Rates [9]

Parameter	**Description**	**Value**	**Unit**
μ_{FN}	Non-Wolbachia adult female per capita death rate	$\frac{1}{43.5}$	day^{-1}
μ_{MN}	Non-Wolbachia adult male per capita death rate	$\frac{1}{42}$	day^{-1}
μ_{FwMel}	wMel infected adult female per capita death rate	$\frac{1}{47.5}$	day^{-1}
μ_{MwMel}	wMel infected adult male death rate	$\frac{1}{34}$	day^{-1}
μ_{FwAlbB}	wAlbB infected adult female per capita death rate	$\frac{1}{50.5}$	day^{-1}
μ_{MwAlbB}	wAlbB infected adult male per capita death rate	$\frac{1}{48}$	day^{-1}
$\mu_{FwSuper}$	Super-infected adult female per capita death rate	$\frac{1}{38}$	day^{-1}
$\mu_{MwSuper}$	Super-infected adult male per capita death rate	$\frac{1}{37}$	day^{-1}

The parameter, α_W, representing the vertical or maternal transmission of Wolbachia infection status was estimated on the basis that 97% of offspring were born with Wolbachia, based on the observations made on three generations within the wMel-infected strains found in [9]. Hence, α_W was assumed to be 0.97 for both wAlbB and wSuper, despite perfect transmission being observed in three generations of wAlbB to prevent the loss of significant portions of our model in simulations.

The aquatic mosquito carrying capacity (K) was set to the stable population of larvae found in the largest viable habitat labeled in [16]. This density is considered to be the population of aquatic mosquitoes per viable habitat, or breeding site.

In order to portray the World Mosquito Program's Wolbachia release strategy [7], a recruitment term (Λ) was added to the model. This represents a direct, continuous addition to the Wolbachia adult populations with an artificial 1:1 male to female ratio derived from ideal lab conditions. This parameter was varied in the analyses to determine the impact of the recruitment of new mosquitoes on the dynamics of the Wolbachia infected and non-infected mosquito population.

The reproductive rates of each mating cross were derived as a product of three variables including: the probability of successful mating (m_{ij}), the standard egg laying rate of the *Aedes aegypti* (e_{ij}), and the viability of eggs produced by a mating cross (v_{ij}) which represents the probability that an egg will hatch. Hence, the reproductive rate is defined as $\rho_{ij} = m_{ij} \cdot e_{ij} \cdot v_{ij}$, where m_{ij} is varied, e_{ij} is held constant, and v_{ij} is shown in Table 6.

Since m_{ij} is an unknown probability it will range between 0 and 1. In order to incorporate mating preference, the mating preferences with respect to females must sum to 1, so $m_{NN} + m_{NW} = 1$ and $m_{WN} + m_{WW}$, thus they are defined to be $m_{NN} = p$, $m_{NW} = 1 - p$, $m_{WN} = 1 - q$, $m_{WW} = q$, with both p and q ranging from 0 to 1 and $p = q = 0.5$ representing no preferential mating.

The rate e_{ij} was estimated based on the average number of eggs laid by an uninfected female over the average lifespan of a female mosquito. This was found by dividing the number of eggs (500) by the average lifespan of an uninfected female *Aedes aegypti* to get the full egg laying rate. The number of eggs and lifespan of uninfected female mosquitoes were used as they were more widely studied in the literature, though the egg laying rate has been found to have insignificant differences between Wolbachia and non-Wolbachia mosquitoes.

Then v_{ij}, which represents the viability of eggs produced by a mating cross also represents a probability which ranges between 0 and 1. Parameter in Table 6 were taken from [9] in which they were obtained experimentally via observed hatch rates. The hatch rates were obtained by counting the larvae hatched within 24-48 hrs of mating crosses of 50 males and 50 virgin females of specific crosses that were allowed to mate for 3-5 days before the females were blood fed. For same infection status crosses, four crosses were made per combination, for different infection status crosses, ten crosses were made per combination.

Table 6: Mating Cross Viability (v_{ij}) [9]

	M_N	M_{wMel}	M_{wAlbB}	M_{wSuper}
F_N	0.951	0.000	0.000	0.001
F_{wMel}	0.623	0.775	0.000	0.030
F_{wAlbB}	0.778	0.000	0.720	0.051
F_{wSuper}	0.824	0.589	0.678	0.668

Table 7: Model Parameters Estimates

Parameter	**Description**	**Value**	**Unit**
μ_{AN}, μ_{AW}	Aquatic mosquito death rate	$\frac{1}{7.78}$ [11]	day^{-1}
γ_N, γ_W	Aquatic mosquito maturation rate	$\frac{1}{6.67}$ [11]	day^{-1}
$\epsilon_N, \epsilon_W, \epsilon_{NW}$	Proportion of adults that are male	0.625 [8]	N/A
δ	Density of Interfering species	.001 (Estimated)	$pop./pool$
μ_{FN}, μ_{MN} μ_{FW}, μ_{MW}	Adult per capita death rate	Table 5	day^{-1}
α_W	Maternal transmission	0.97 [9]	N/A
K	Aquatic mosquito carrying capacity	1500 [16]	$pop./pool$
Λ	Recruitment of Wolbachia mosquitoes	(Varies)	$(pop./pool)day^{-1}$
ρ_{ij}	Reproductive rate of ($F_i \cdot M_j$)	$m_{ij} \cdot v_{ij} \cdot e_{ij}$	day^{-1}
m_{ij}	Mating probability of ($F_i \cdot M_j$)	(Varies)	N/A
e_{ij}	Egg laying rate of ($F_i \cdot M_j$)	$\frac{500}{43.5}$ (Estimated)	day^{-1}
v_{ij}	Viability of eggs from ($F_i \cdot M_j$)	Table 6	N/A

The parameters are separated into those needed to simulate different strains of Wolbachia in Tables 8–10.

Table 8: Parameters for wMel [9]

Parameter	Value
μ_{FwMel}	$\frac{1}{47.5}$
μ_{MwMel}	$\frac{1}{34}$
$v_{N,N}$	0.951
$v_{N,wMel}$	0.000
$v_{wMel,N}$	0.623
$v_{wMel,wMel}$	0.775

Table 9: Parameters for wAlbB [9]

Parameter	Value
μ_{FwAlbB}	$\frac{1}{50.5}$
μ_{MwAlbB}	$\frac{1}{48}$
$v_{N,N}$	0.951
$v_{N,wAlbB}$	0.000
$v_{wAlbB,N}$	0.778
$v_{wAlbB,wAlbB}$	0.720

Table 10: Parameters for wSuper [9]

Parameter	Value
$\mu_{FwSuper}$	$\frac{1}{38}$
$\mu_{MwSuper}$	$\frac{1}{37}$
$v_{N,N}$	0.951
$v_{N,wSuper}$	0.001
$v_{wSuper,N}$	0.824
$v_{wSuper,wSuper}$	0.668

4 Results

Bifurcation

This section is devoted to the bifurcation diagrams of both special cases. These diagrams show the possible proportion of the the super strain Wolbachia-infected aquatic mosquitoes over all aquatic mosquitoes equilibrium with respect to Λ, p, and q.

Case 1: No release of laboratory infected mosquitoes ($\Lambda = 0$ and $\delta \neq 0$)

In the absence of Wolbachia-infected female mating preference ($q = 0.5$) and without continuous release beyond the initial invasion ($\Lambda = 0$), there are two dynamic results:

1. Two stable equilibria and one unstable equilibrium.
2. A stable equilibrium and an unstable equilibrium.

When the non-infected female mating preference is below a certain value, the critical non-infected mating preference, the proportion of the Wolbachia-infected mosquitoes will always be able to dominate the population. When the non-infected female mating preference exceeds the critical non-infected mating preference, the stability depends on the initial conditions. The proportion of the invading Wolbachia-infected population must exceed a certain ratio (the unstable equilibrium in red) in order to dominate the population, otherwise the Wolbachia-infected mosquitoes will fail to invade.

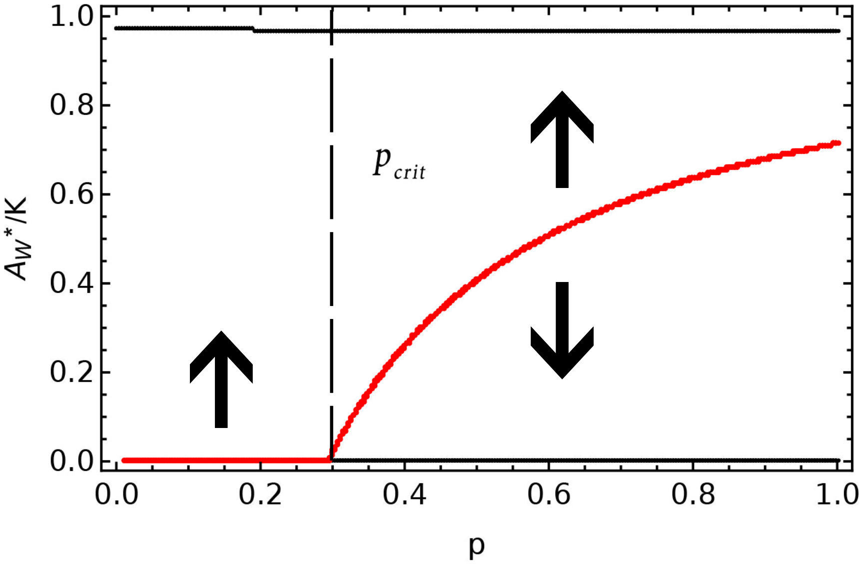


Figure 3: One parameter bifurcation of A_W^*/K on p with $\Lambda = 0$, $q = 0.5$. Black lines imply stable equilibria and red lines imply unstable equilibria.

From Fig. 3 there is a certain value p labeled as our p_{crit}. After this value of p rather than only being able to have two equilibrium we have 3 equilibrium. The top black line represents the equilibrium where Wolbachia-infected mosquitoes dominate the total population. While the bottom line represents where Wolbachia-infected mosquitoes are unable to persist and go extinct. The red line represents an unstable coexistent equilibrium. It is important to notice that the population tends to either of the two stable equilibrium depending on the initial invasion population.

A simpler picture of the equilibrium is shown in Figs. 2 and 5. The first diagram is displays the equilibrium points for the cases where p is less than the p_{crit} found from the the bifurcation diagram above. When $p < p_{crit}$ special case 1 can have 3 different equilibrium. There is the unstable equilibrium which are the extinction equilibrium and the case where only non-infected mosquitoes persist. The only stable equilibrium is a coexistence equilibrium where the Wolbachia-infected mosquitoes are able to dominate the non-infected population. This case is the one of interest since the higher density of Wolbachia-infected mosquitoes means a decrease of dengue infections.

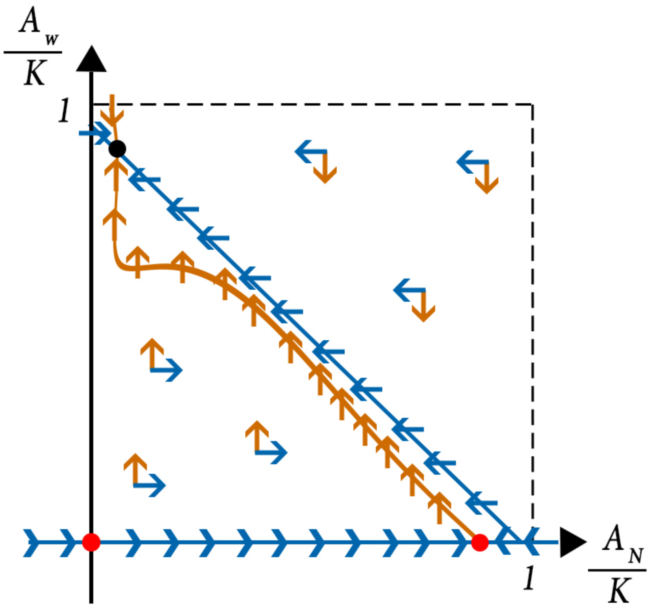


Figure 4: $p < p_{crit}$

When $p > p_{crit}$ there is a total of 4 equilibrium points as shown in Fig. 5. There are 2 unstable points one representing extinction of all mosquitoes. The other unstable point is a coexistent equilibrium where there Wolbachia-infected mosquitoes are not able to dominate the population but make up about 50% of the total population. There is also to stable equilibrium one which represents the extinction of the Wolbachia-infected population. The other equilibrium is the one of interest as it represent where Wolbachia-infected population are able to persist and dominate the total population.

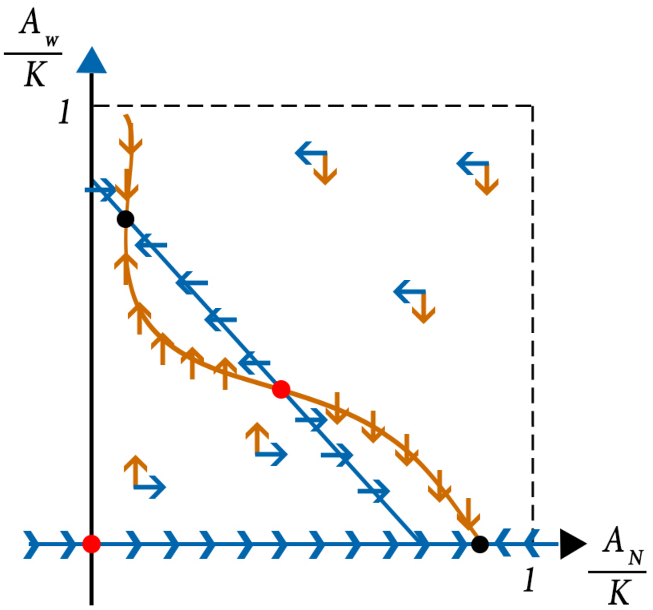


Figure 5: $p > p_{crit}$

In the absence of non-infected female mating preference ($p = 0.5$) and without continuous release beyond the initial invasion ($\Lambda = 0$), there are two results for the bifurcation of A_W^*/K on q:

1. Two unstable equilibria.
2. Two stable equilibria and one unstable equilibrium.

When the Wolbachia-infected female mating preference is below a certain value, the critical Wolbachia-infected mating preference, there are no stable equilibria. When the Wolbachia-infected female mating preference exceeds the critical Wolbachia-infected mating preference, the stability depends on the initial conditions. The proportion of the invading Wolbachia-infected population must exceed a certain ratio (the unstable equilibrium in red) in order to dominate the population, otherwise the Wolbachia-infected mosquitoes will fail to invade.

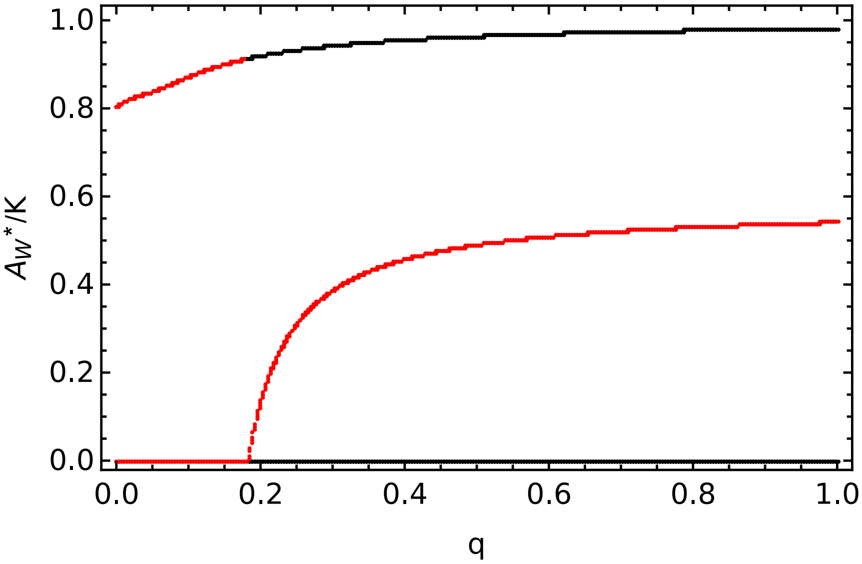


Figure 6: Bifurcation of A_W^*/K on q when $\Lambda = 0$, $p = 0.5$. Black lines imply stable equilibria and red lines imply unstable equilibria.

Case 2: Perfect CI and vertical transmission without mating interference ($\alpha_w = 1$, $\rho_{NW} = 0$, and $\delta = 0$)

In the absence of mating preferences ($p = q = 0.5$) there are two results for the bifurcation of A_W^*/K on Λ:

1. Two stable equilibria and an unstable equilibrium
2. A stable equilibrium

When the release rate is below a certain value, the critical release rate, the stability depends on the initial conditions. The proportion of the invading Wolbachia-infected population must exceed a certain ratio (the unstable equilibrium in red) in order to dominate the population, otherwise the Wolbachia-infected mosquitoes will settle to a lower proportion. When the release rate exceeds the critical release rate, the Wolbachia-infected mosquitoes will always be able to dominate the population.

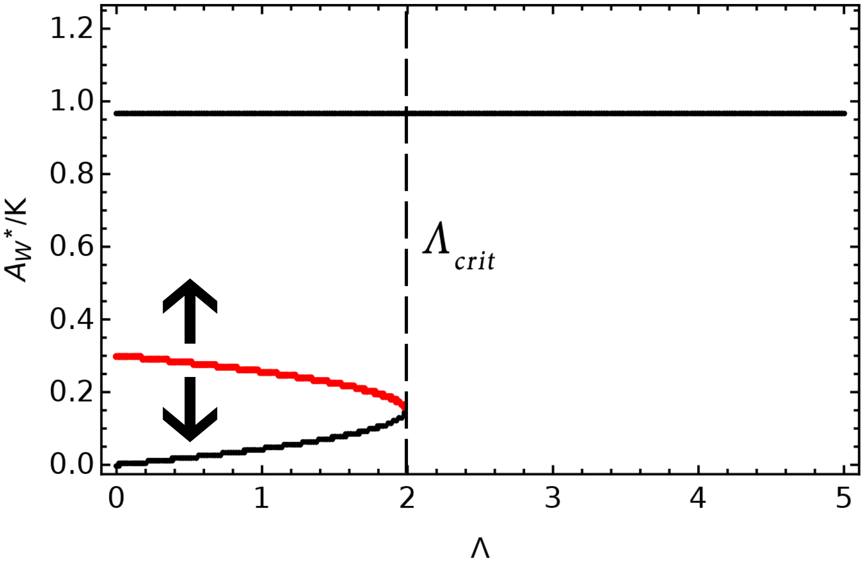


Figure 7: Bifurcation of A_W^*/K on Λ at: $p = 0.5$, $q = 0.5$. Black lines imply stable equilibria and red lines imply unstable equilibria.

In the absence of Wolbachia-infected female mating preference $q = 0.5$ and without continuous release beyond the initial invasion, there are two results for the bifurcation of A_W^*/K on p:

1. A stable equilibrium
2. Two stable equilibria and an unstable equilibrium

When the non-infected female mating preference is below a certain value, the critical non-infected mating preference, the proportion of the Wolbachia-infected mosquitoes will always be able to dominate the population. When the non-infected female mating preference exceeds the critical non-infected mating preference, the stability depends on the initial conditions. The proportion of the invading Wolbachia-infected population must exceed a certain ratio (the unstable equilibrium in red) in order to dominate the population, otherwise the Wolbachia-infected mosquitoes will settle to a lower proportion.

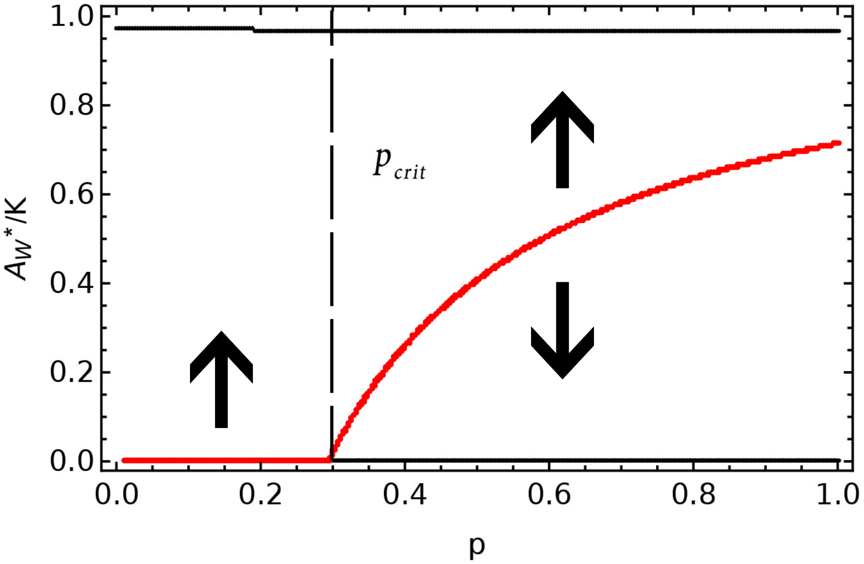


Figure 8: Bifurcation of A_W^*/K on p at: $\Lambda = 0$, $q = 0.5$. Black lines imply stable equilibria and red lines imply unstable equilibria.

In the absence of non-infected female mating preference $p = 0.5$ and without continuous release beyond the initial invasion, there are two results for the bifurcation of A_W^*/K on q:

1. A stable equilibrium
2. Two stable equilibria and an unstable equilibrium

When the Wolbachia-infected female mating preference is below a certain value, the critical Wolbachia-infected mating preference, the proportion of the Wolbachia-infected mosquitoes may be able to dominate the population. However, when the Wolbachia-infected females strongly prefer non-Wolbachia males, and often reject Wolbachia-infected males when contact is made. In this case, due to cytoplasmic incompatibility causing non-viable eggs for non-Wolbachia females and due to rejection causing a lack of eggs for Wolbachia females, the contributions to the overall population are minimal. The primary contributors to the overall population are a the fraction of crossings between non-Wolbachia mosquitoes and Wolbachia infected mosquitoes. When the Wolbachia-infected female mating preference exceeds the critical non-infected mating preference, the stability depends on the initial conditions. The proportion of the invading Wolbachia-infected population must exceed a certain ratio (the unstable equilibrium in red) in order to dominate the population, as the contribution of the Wolbachia-infected female and W@olbachia-infected male crossing will contribute significantly to the Wolbachia-infected population, otherwise the Wolbachia-infected mosquitoes will settle to a lower proportion, as the Wolbachia-infected females are too selective and reject the more common non-Wolbachia infected males when crosses with any type of male would produce Wolbachia-infected offspring.

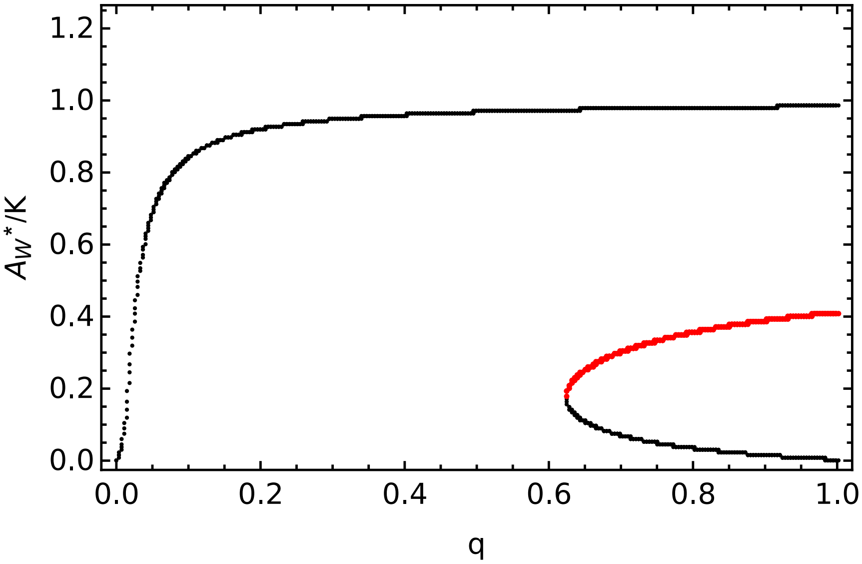


Figure 9: Bifurcation of A_W^*/K on q at: $\Lambda = 0$, $p = 0.5$. Black lines imply stable equilibria and red lines imply unstable equilibria.

Mating preference on proportion of aquatic Wolbachia-infected mosquito populations

This section shows the effect of mating preferences on population dynamics by plotting heat maps of the proportion of a compartment to the total aquatic population, at stability, observing that Wolbachia tends to dominate with low values for (p) and low values for (q), but with (p) often needing to be much lower then (q). In order to compare the effect of preferential mating, the set of preferences needed to achieve a 1:1 ratio of Wolbachia-infected to non-infected mosquitoes are referred to as the preferential mating threshold of a simulation.

Within the preferential mating thresholds, describe the parameter values at which the initial invasion level is the critical population size needed for Wolbachia-infected mosquitoes to dominate the population.

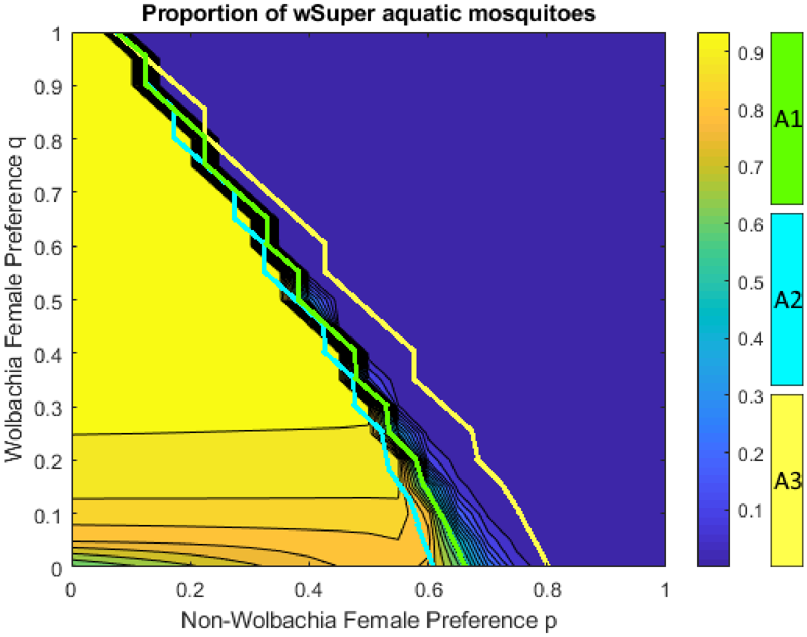
The preference of non-infected females for non-infected males (p) has an adverse effect on the proportion of Wolbachia-infected mosquitoes as it increases. When non-infected females mate with non-infected males, they are able to produce viable non-infected eggs, which decreases the overall proportion of Wolbachia-infected offspring. Conversely, when non-infected females mate with Wolbachia-infected males, they produce non-viable eggs, which increases the proportion of Wolbachia-infected offspring.

This study shows that the preference of Wolbachia-infected females for Wolbachia-infected males (q) has a beneficial effect on the proportion of Wolbachia-infected mosquitoes as it increases when it is low, but a value of (q) that is too high can cause a drastically adverse effect. If Wolbachia-infected females are too selective for Wolbachia-infected males, then it may not be possible to reach a stable equilibrium at which Wolbachia-infected mosquitoes dominate unless the population is flooded with a vast amount of Wolbachia-infected mosquito invaders.

These patterns are clearly common to mating preferences on multiple strains of Wolbachia-infected *Aedes aegypti*, as we can observe these patterns in graphs developed from parameters based on wMel, wAlbB, and wSuper.

Strains

These preferential mating thresholds depict the sensitivity of the different Wolbachia strains towards preferential mating at an initial Wolbachia-infected mosquito invasion population that comprises 10% of the total population. The strains wSuper and wMel are more sensitive to preferential mating, than wAlbB. They are unable to dominate in the absence of preferential mating and othe combinations of preferential mating values that are within the preferential mating threshold of wAlbB.



A1: 10% wSuper Invasion

A2: 10% wMel Invasion

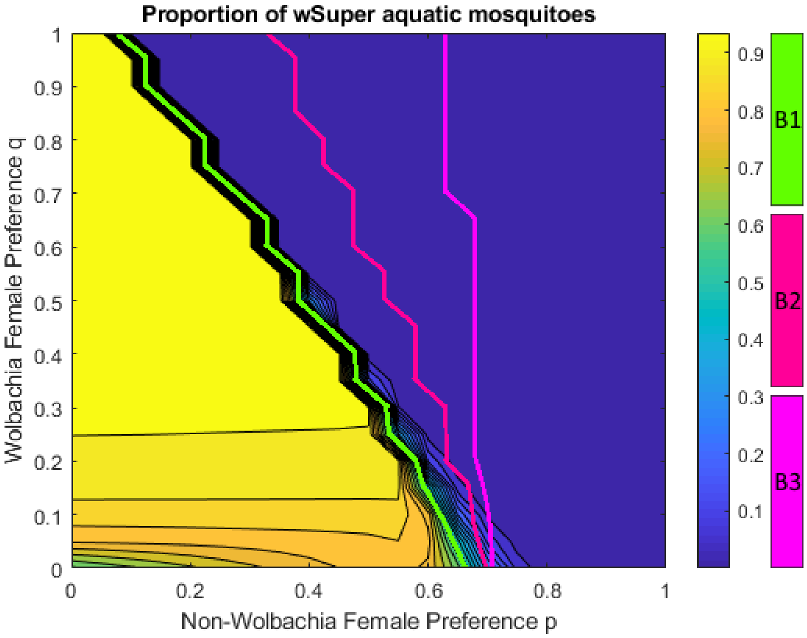
A3: 10% wAlbB Invasion

Strains {wSuper, wMel, wAlbB}
A1 = wSuper($A_N = A_W = 0,\ F_N = M_N = 900,\ F_W = M_W = 100,\ \Lambda = 0$)
A2 = wMel($A_N = A_W = 0,\ F_N = M_N = 900,\ F_W = M_W = 100,\ \Lambda = 0$)
A3 = wAlbB($A_N = A_W = 0,\ F_N = M_N = 900,\ F_W = M_W = 100,\ \Lambda = 0$)

Figure 10: Effect on critical preferential mating threshold by Wolbachia strains

Initial Invasion Proportions

In the case of different invasion levels only the wSuper strain was modeled. The Wolbachia-infected invasion proportions of 10%, 35%, and 50% without constant release were modeled to show how preferential mating influences changed based on invasion size. At 10% invasion, without mating preferences, Wolbachia-infected mosquitoes could not dominate. At 35% invasion, Wolbachia-infected mosquitoes could dominate without mating preferencces, but not with weak same status mating preferences. At 50% invasion, Wolbachia-infected mosquitoes could dominate with weak same status mating preferences. The negative effect of same status mating preference on the ability for Wolbachia-infected mosquitoes to dominate diminishes as the proportion of Wolbachia-infected mosquitoes increases.



B1: 10% wSuper Invasion

B2: 35% wSuper Invasion

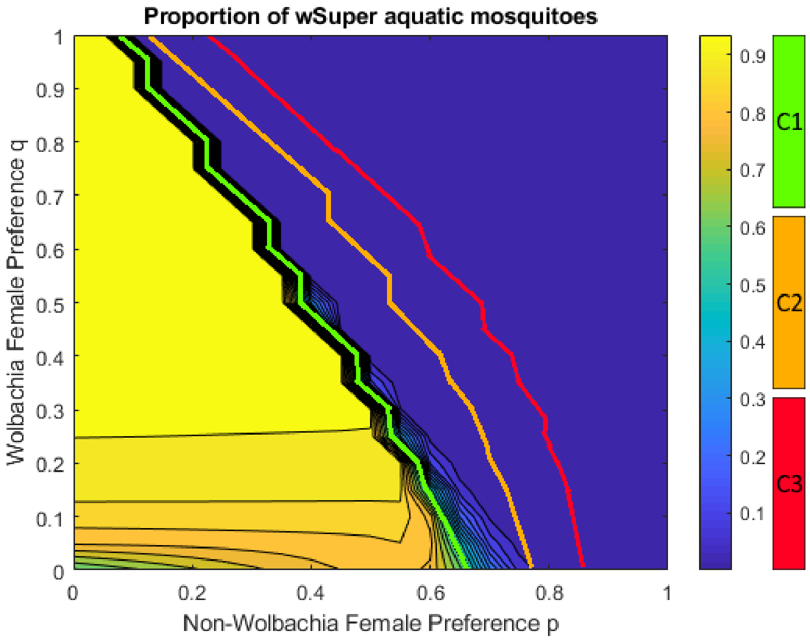
B3: 50% wSuper Invasion

Initial Invasion Proportions {10%, 35%, 50%}
B1 = wSuper($A_N = A_W = 0,\ F_N = M_N = 900,\ F_W = M_W = 100,\ \Lambda = 0$)
B2 = wSuper($A_N = A_W = 0,\ F_N = M_N = 650,\ F_W = M_W = 350,\ \Lambda = 0$)
B3 = wSuper($A_N = A_W = 0,\ F_N = M_N = 500,\ F_W = M_W = 500,\ \Lambda = 0$)

Figure 11: Effect on critical preferential mating threshold by invasion level

Release Rates

When releasing wSuper strain Wolbachia-infected mosquitoes the following graphs depict release rate of $\Lambda = 0$, $\Lambda = 5$, and $\Lambda = 10$ male and female mosquitoes per pool per day (for a total of 2Λ mosquitoes beging released per pool per day). When there is no constant release, i.e. $\Lambda = 0$, Wolbachia-infected mosquitoes will not be able to persist without preferential mating. For the next case $\Lambda = 5$ Wolbachia-infected mosquitoes are able to dominate without preferential mating, as well as weak preferential mating. When $\Lambda = 10$ the Wolbachia-infected mosquitoes are shown to dominate in the population unless there is a strong preference for same status mating



C1: 10% wSuper Invasion,
$\Lambda = 0$ Release

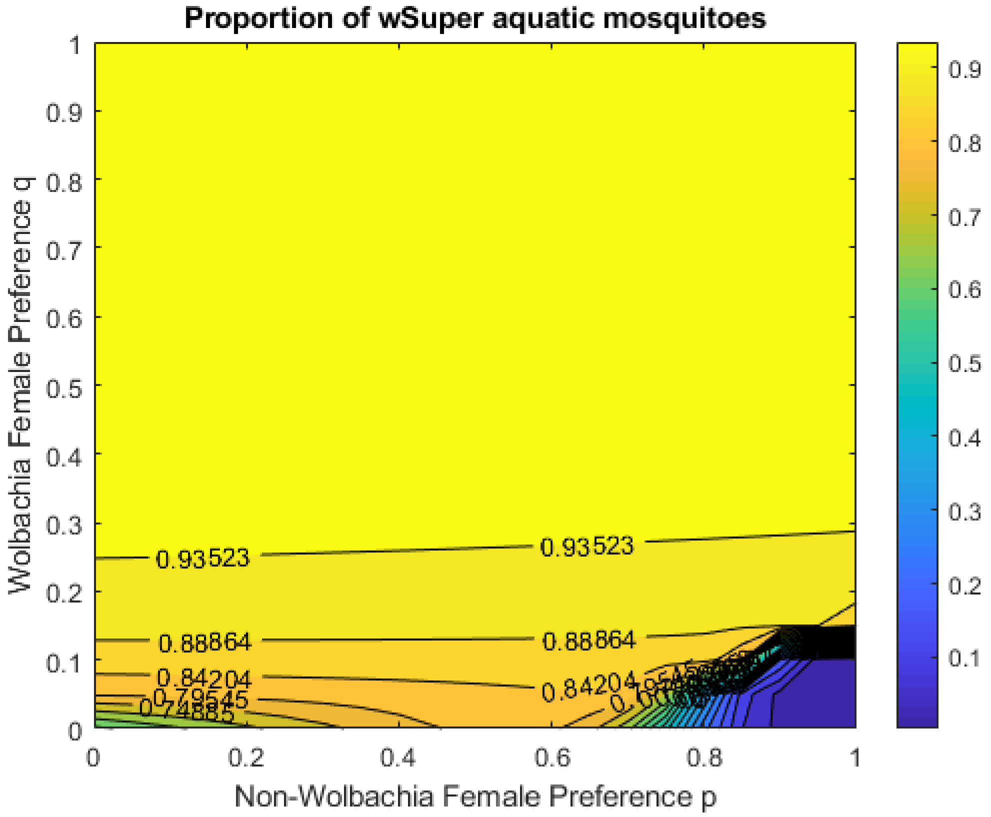
C2: 10% wSuper Invasion,
$\Lambda = 5$ Release

C3: 10% wSuper Invasion,
$\Lambda = 10$ Release

Release Rates $\{\Lambda = 0,\ \Lambda = 5,\ \Lambda = 10\}$
C1 = wSuper($A_N = A_W = 0,\ F_N = M_N = 900,\ F_W = M_W = 100,\ \Lambda = 0$)
C2 = wSuper($A_N = A_W = 0,\ F_N = M_N = 900,\ F_W = M_W = 100,\ \Lambda = 5$)
C3 = wSuper($A_N = A_W = 0,\ F_N = M_N = 900,\ F_W = M_W = 100,\ \Lambda = 10$)

Figure 12: Effect on critical preferential mating threshold by release rate

If the Wolbachia-infected popultion has taken over to a significant extent, then release can be stopped, as mating preferences do not have a large effect on the proportion of Wolbachia-infected mosquitoes at equilibrium. This can be inferred by the results of Fig. 11 and Fig. 12. That constant release can be stooped after the population has reached a dominating equilibrium is shown in Fig. 13, when the Wolbachia-infected mosquitoes make up 90% of the population, it is clear that only extreme mating preferences will prevent the Wolbachia-infected mosquitoes from maintaining dominance.



Initial Invasion Proportion {90%}
wSuper($A_N = A_W = 0$, $F_N = M_N = 100$, $F_W = M_W = 900$, $\Lambda = 0$)

Figure 13: Effect on critical preferential mating threshold by 90% invasion

5 Sensitivity Analysis

This section is focused on the sensitivity of the state variable A_W with respect to Λ, p, and q. It is important to observe how effective it will be in different situations.

Considering an initial population where Wolbachia-infected mosquitoes (aquatic & adult) are 50% of the total population. When preferential mating is not strong ($p < .65$) it had little to no effect on Wolbachia-infected population over time. At a higher recruitment rate Λ, p and q had less effect on the population. In Fig. 14 Λ=3, p=0.6, and q = 0.575 are the parameters being used. This case shows that the Wolbachia-infected are able to persist in the population.

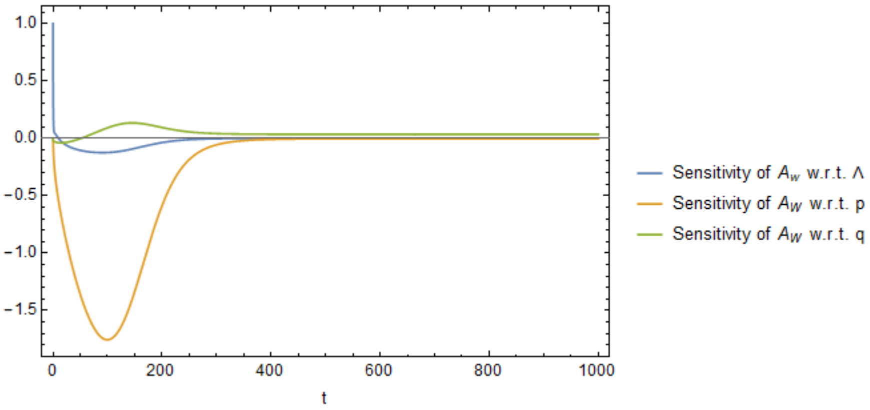


Figure 14: Sensitivity of A_W w.t.r to p, q, and Λ

In Fig. 15 Wolbachia-infected mosquitoes (aquatic & adult) are 50% of the total population, but there is an increase in mating preference. Taking the case where nn-infected mosquitoes prefer to mate with other non-infected mosquitoes, thus increasing the value of p. Ratio (p) is kept greater than .85 and q is kept at .575. Observing at different values for Λ there was insignificant change to the graph on the interval $0 < \Lambda < 5$. It seen that for preferential mating where non-infected mosquitoes want to mate with other non-infected mosquitoes, in a 1:1 population the Wolbachia-infected population is not able to dominate. Concluding that there is a need for a higher value for the recruitment rate Λ. Having a higher invasion level (initial pop. of Wolbachia-infected mosquitoes) also nullifies the effect of p on the Wolbachia-infected population

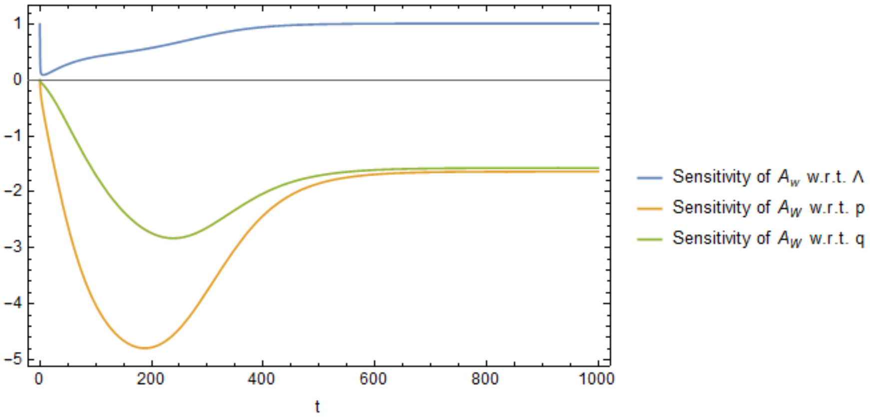


Figure 15: Sensitivity of A_W w.t.r to p, q, and Λ

6 Discussion

The release of Wolbachia-infected mosquitoes has become one of the most effective control strategies to lower the transmission of dengue. There have been successes in a few countries, and new countries, such as Brazil[15], are looking to try this method. Readings prompted the question if Wolbachia-infected mosquitoes could have an effect on mating preference in *Aedes aegypti* similar to the two-spotted spider mites. This lead to the question of what effects would such mating preferences would have on the effectiveness and sustainability of Wolbachia-infected mosquitoes in the overall population.

In the presence of preferential mating it becomes difficult for the Wolbachia-infected mosquitoes to persist when ratio (p) is greater than .85 ,but increases in recruitment can nullify these effects. Also, Ratio (p) had less effect in different level of invasions. Meaning that it had insignificant when Wolbachia-infected mosquitoes made up more than half of the initial population.

Certain strains are more sensitive to preferential mating. In the absence of mating preferences, it is predicted that only the wAlbB strain of Wolbachia-infected mosquitoes can dominate the population when intially comprizing 10% of the population, while wMel and wSuper can not. There was greater tolerance to same infection status preferences by the wAlbB strain.

Invading Wolbachia-infected mosquitoes are more able to dominate the population when comprising greater initial proportions of the population. The impact of preferential mating has less of an impact when Wolbachia-infected mosquitoes comprise a larger proportion of the population.

As the number of Wolbachia-infected lab mosquitoes released increased, the lab mosquitoes represented more of the population. As the proportion of lab mosquitoes increases, the proportion of wild Wolbachia-infected mosquitoes produced by vertical transmission becomes less vital to the Wolbachia-infected domination of the population. So, as preferential mating only affects the dynamics of mosquitoes born, it has less of an effect when the release rates which bypass this comprise enough of the population. If large enough, the release rate can cause there to only be a single stable equilibrium at which Wolbachia-infected mosquitoes dominate.

Limitations

In the model, the release of lab raised mosquitoes was represented as a constant recruitment (Λ). This an unrealistic assumption. If this were the case, then a certain density of mosquitoes would be continuously per pool per day. When Wolbachia-infected mosquitoes are released, they are released via egg kits and van drops. Lambda could instead be represented by a discrete function that better reflects such strategies. In this model, Lambda was represented as the release of adult mosquitoes, but not as the release of aquatic mosquitoes. Lambda could be represented as a discrete function to better represent the release of mosquitoes from vans. Another term could also be added to represent the egg kit introduction of Wolbachia-infected mosquitoes.

The carrying capacity (K) was considered the population density as the population supported by a particular breeding site, or individuals per breeding site. This was not based on an average stable population supported by a breeding site, only but on the largest breeding site found.

The egg laying rate of the mosquito crosses were considered to be insignificantly different from one another in a single study, however, this information was not derived from a study that focused on the egg laying rates of mosquito crosses. It would be beneficial to confirm this information with more studies on the egg laying rates of various Wolbachia-infected mosquito crosses.

For Special case 2 where $\Lambda = 0$ and $\delta \neq 0$the existence and stability of the steady state (0,0,0,0,0,0) were found. Only the existence of the steady state $(A_N^*, M_N^*, F_N^*, 0, 0, 0)$ was found, and its stability was not found.

Issues

While analyzing our model the contact rate of adult mosquitoes needed to be modified. The term delta was added in order to include interference to the contact rate, mathematically, this prevents dividing by zero when solving for the extinction equilibrium. This was estimated to occur rarely, however, the incidence rate could not be found within the literature.

The model had complex non-linearities, which were difficult to analyze mathematically. Simulations were needed to analyze the effects of the parameters on the population dynamics.

Future Work

Future work could incorporate the parameters of other strains. While the parameter values for the wMel, wAlbB, and wSuper(wMelwAlbB) strains were found, there are many other strains, such as wAu and wRi, that could also be studied for the effects of mating preference.

Future work could also include adding temperature vector to a model. There are significant effects on the lifespan of mosquitoes and the survival of Wolbachia in higher temperatures. This has strong impacts on the reproductive rates of the crosses and transmission rates of Wolbachia. This can be interesting to explore the effectiveness and sustainability of this method to combat MBD's in different scenarios.

In the model the value of carrying capacity is constant, but in wild, this value influenced by many factors such as water temperature, human intervention, resource limitations, predation. Future work can make (K) more suitable for the model.

7 Acknowledgements

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References

[1] Irka E Bargielowski, L Philip Lounibos, and María Cristina Carrasquilla. “Evolution of resistance to satyrization through reproductive character displacement in populations of invasive dengue vectors”. In: *Proceedings of the National Academy of Sciences* 110.8 (2013), pp. 2888–2892.

[2] Ashley G Callahan, Perran A Ross, and Ary A Hoffmann. “Small females prefer small males: size assortative mating in *Aedes aegypti* mosquitoes”. In: *Parasites & vectors* 11.1 (2018), p. 445.

[3] J. E. Cogan. *Dengue and severe dengue*. Ed. by World Health Organization. URL: `https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue`.

[4] Emadeldin Y Fawaz et al. “Swarming mechanisms in the yellow fever mosquito: aggregation pheromones are involved in the mating behavior of *Aedes aegypti*”. In: *Journal of Vector Ecology* 39.2 (2014), pp. 347–354.

[5] Neil M Ferguson et al. “Modeling the impact on virus transmission of Wolbachia-mediated blocking of dengue virus infection of *Aedes aegypti*”. In: *Science translational medicine* 7.279 (2015), 279ra37–279ra37.

[6] Johanna E Fraser et al. “Novel Wolbachia-transinfected *Aedes aegypti* mosquitoes possess diverse fitness and vector competence phenotypes”. In: *PLoS pathogens* 13.12 (2017), e1006751.

[7] Daniel Gordon. *The city where children are learning to love mosquitoes*. Ed. by BBC News. 2019. URL: `https://www.bbc.com/news/av/stories-47854648/the-city-where-children-are-learning-to-love-mosquitoes`.

[8] William A Hickey and George B Craig Jr. “Genetic distortion of sex ratio in a mosquito, *Aedes aegypti*”. In: *Genetics* 53.6 (1966), p. 1177.

[9] D Albert Joubert et al. “Establishment of a Wolbachia superinfection in *Aedes aegypti* mosquitoes as a potential approach for future resistance management”. In: *PLoS pathogens* 12.2 (2016), e1005434.

[10] Conor J McMeniman et al. “Stable introduction of a life-shortening Wolbachia infection into the mosquito *Aedes aegypti*”. In: *Science* 323.5910 (2009), pp. 141–144.

[11] Meksianis Z Ndii, Roslyn I Hickson, and Geoffry N Mercer. “Modelling the introduction of Wolbachia into *Aedes aegypti* mosquitoes to reduce dengue transmission”. In: *The ANZIAM Journal* 53.3 (2012), pp. 213–227.

[12] Scott L O’Neill et al. “Scaled deployment of Wolbachia to protect the community from dengue and other Aedes transmitted arboviruses”. In: *Gates open research* 2 (2018).

[13] Perran A. Ross et al. “Loss of cytoplasmic incompatibility in Wolbachia-infected aegypti under field conditions”. In: *PLOS Neglected Tropical Diseases* 13.4 (Apr. 2019), pp. 1–20. DOI: `10.1371/journal.pntd.0007357`. URL: `https://doi.org/10.1371/journal.pntd.0007357`.

[14] Perran Ross and Jason Axford. *WOLBACHIA BACTERIA IN ACTION | How we're using naturally occurring bacteria to stop mosquitoes from spreading disease.* 2018. URL: `https://blogs.unimelb.edu.au/pearg/2018/04/13/wolbachia-bacteria-in-action-how-were-using-naturally-occurring-bacteria-to-stop-mosquitoes-from-spreading-disease/`.

[15] Kelly Servick. *Brazil will release billions of lab-grown mosquitoes to combat infectious disease. Will it work?* 2016. URL: `https://www.sciencemag.org/news/2016/10/brazil-will-release-billions-lab-grown-mosquitoes-combat-infectious-disease-will-it`.

[16] David L Smith et al. "Mosquito population regulation and larval source management in heterogeneous environments". In: *PLoS One* 8.8 (2013), e71247.

[17] Horst R Thieme. *Mathematics in population biology, Princeton Series in theoretical and computational biology.* Princeton University Press, Princeton, NJ, 2003.

[18] F Vala et al. "Wolbachia affects oviposition and mating behaviour of its spider mite host". In: *Journal of Evolutionary Biology* 17.3 (2004), pp. 692–700.

[19] Heng Lin Yeap, Nancy Margaret Endersby-Harshman, and Ary Anthony Hoffmann. "The effect of nonrandom mating on Wolbachia dynamics: implications for population replacement and sterile releases in Aedes mosquitoes". In: *The American journal of tropical medicine and hygiene* 99.3 (2018), pp. 608–617.

[20] Sofia Zabalou et al. "Wolbachia-induced cytoplasmic incompatibility as a means for insect pest population control". In: *Proceedings of the National Academy of Sciences* 101.42 (2004), pp. 15042–15045. ISSN: 0027-8424. DOI: `10.1073/pnas.0403853101`. eprint: `https://www.pnas.org/content/101/42/15042.full.pdf`. URL: `https://www.pnas.org/content/101/42/15042`.

[21] Guangmei Zhang et al. "Wolbachia uses a host microRNA to regulate transcripts of a methyltransferase, contributing to dengue virus inhibition in *Aedes aegypti*". In: *Proceedings of the National Academy of Sciences* 110.25 (2013), pp. 10276–10281.

8 Appendix

Proof of Theorem 1

Proof. Notice that

$$\begin{aligned}
\left.\frac{dA_N}{dt}\right|_{A_N=0} &= F_N\left(\frac{\rho_{NW}M_W+\rho_{NN}M_N}{M_W+M_N+\delta}\right)\left(1-\frac{A_W}{K}\right)\geq 0,\\
\left.\frac{dM_N}{dt}\right|_{M_N=0} &= \epsilon_N\gamma_N A_N+\epsilon_{NW}(1-\alpha_W)\gamma_W A_W\geq 0,\\
\left.\frac{dF_N}{dt}\right|_{F_N=0} &= (1-\epsilon_N)\gamma_N A_N+(1-\epsilon_{NW})(1-\alpha_W)\gamma_W A_W\geq 0,\\
\left.\frac{dA_W}{dt}\right|_{A_W=0} &= F_W\left(\frac{\rho_{WW}M_W+\rho_{WN}M_N}{M_W+M_N+\delta}\right)\left(1-\frac{A_N}{K}\right)\geq 0,\\
\left.\frac{dM_W}{dt}\right|_{M_W=0} &= \Lambda+\epsilon_W\alpha_W\gamma_W A_W\geq 0\\
\left.\frac{dF_W}{dt}\right|_{F_W=0} &= \Lambda+(1-\epsilon_W)\alpha_W\gamma_W A_W\geq 0
\end{aligned}$$

Thus, we can conclude that the model (1) is positive invariant in $\mathbb{R}^6_+$ by Theorem A.4 in [17]. □

Proof of Theorem 2

Proof. Letting $\Lambda=0$, it can be easily verified that the trivial equilibrium $E_1=(0,0,0,0,0,0)$ always exists. Now, in order to show that that $E_2=(A_N^*,M_N^*,F_N^*,0,0,0)$ is an equilibrium, we let $A_W=M_W=F_W=0$. This simplifies our system as follows:

$$0=F_N\frac{\rho_{NN}M_N}{M_N+\delta}\left(1-\frac{A_N}{K}\right)-(\mu_{AN}+\gamma_N)A_N \tag{4a}$$

$$0=\epsilon_N\gamma_N A_N-\mu_{MN}M_N \tag{4b}$$

$$0=(1-\epsilon_N)\gamma_N A_N-\mu_{FN}F_N \tag{4c}$$

From the above equations we solve for M_N and F_N in terms of A_N which yields,

$$M_N^*=\frac{\epsilon_N\gamma_N A_N^*}{\mu_{MN}},\qquad F_N^*=\frac{(1-\epsilon_N)\gamma_N A_N^*}{\mu_{FN}}$$

Upon substitution in Eq. (4a) and dividing by A_N^* one obtains the following equation for A_N^*:

$$\frac{(1-\epsilon_N)\gamma_N^2\rho_{NN}\epsilon_N A_N^*}{\mu_{FN}\epsilon_N\gamma_N A_N^*+\delta\mu_{MN}\mu_{FN}}\left(1-\frac{A_N^*}{K}\right)-(\mu_{AN}+\gamma_N)=0 \tag{5}$$

Let

$$a=(1-\epsilon_N)\gamma_N^2\rho_{NN}\epsilon_N,\qquad b=\mu_{FN}\epsilon_N\gamma_N,\qquad c=\delta\mu_{MN}\mu_{FN},\qquad d=\mu_{NA}+\gamma_N, \tag{6}$$

such that when plugged into Eq. (5), we simplify to get

$$-aA_N^{*2} + A_N^*(aK - bdK) - cdK = 0 \tag{7}$$

Next, from the above equation, we solve for A_N and obtain

$$A_N^* = \frac{aK - bKd + \sqrt{(aK - bKd)^2 - 4abcKd}}{2a} \tag{8}$$

which shows that there exists an equilibrium of the form $(A_N^*, M_N^*, F_N^*, 0, 0, 0)$, When

$$R_W = \frac{4abcd}{K(a - bd)^2} < 1 \tag{9}$$

Now, in order to determine the stability of system (1), we obtain the corresponding Jacobian matrix of the system:

$$J = \begin{bmatrix} -\mu_{AN} - \gamma_N - \frac{Q_N}{K}F_N & (\frac{\rho_{NN}}{P} - \frac{Q_N}{P})GF_N & GQ_N & -\frac{Q_N}{K}F_N & (\frac{\rho_{NW}}{P} - \frac{Q_N}{P})GF_N & 0 \\ \epsilon_N \gamma_N & -\mu_{MN} & 0 & \epsilon_{NW}(1-\alpha_W)\gamma_W & 0 & 0 \\ (1-\epsilon_N)\gamma_N & 0 & -\mu_{FN} & (1-\epsilon_{NW})(1-\alpha_W)\gamma_W & 0 & 0 \\ -\frac{Q_W}{K}F_W & (\frac{\rho_{WN}}{P} - \frac{Q_W}{P})GF_W & 0 & -\mu_{AW} - \gamma_W - \frac{Q_W}{K}F_W & (\frac{\rho_{WW}}{P} - \frac{Q_W}{P})GF_W & GQ_W \\ 0 & 0 & 0 & \epsilon_W \alpha_W \gamma_W & -\mu_{MW} & 0 \\ 0 & 0 & 0 & (1-\epsilon_W)\alpha_W \gamma_W & 0 & -\mu_{FW} \end{bmatrix} \tag{10}$$

where

$$P = M_N + M_W + \delta, \qquad G = \left(1 - \frac{A_N + A_W}{K}\right)$$

$$Q_N = \frac{\rho_{NW} M_W + \rho_{NN} M_N}{M_W + M_N + \delta} \qquad Q_W = \frac{\rho_{WW} M_W + \rho_{WN} M_N}{M_W + M_N + \delta}$$

The stability of the extinction equilibrium is obtained by evaluating the Jacobian (10) at $E_0 = (0, 0, 0, 0, 0, 0)$, in which we obtain

$$J = \begin{bmatrix} -\mu_{AN} - \gamma_N & 0 & 0 & 0 & 0 & 0 \\ \epsilon_N \gamma_N & -\mu_{MN} & 0 & \epsilon_{NW}(1-\alpha_W)\gamma_W & 0 & 0 \\ (1-\epsilon_N)\gamma_N & 0 & -\mu_{FN} & (1-\epsilon_{NW})(1-\alpha_W)\gamma_W & 0 & 0 \\ 0 & 0 & 0 & -\mu_{AW} - \gamma_W & 0 & 0 \\ 0 & 0 & 0 & \epsilon_W \alpha_W \gamma_W & -\mu_{MW} & 0 \\ 0 & 0 & 0 & (1-\epsilon_W)\alpha_W \gamma_W & 0 & -\mu_{FW} \end{bmatrix} \tag{11}$$

Notice that the eigenvalues for the above Jacobian are all negative:

$\lambda_1 = -(\gamma_N + \mu_{AN})$, $\lambda_2 = -\mu_{MN}$, $\lambda_3 = -\mu_{FN}$, $\lambda_4 = -(\gamma_W + \mu_{AW})$, $\lambda_5 = -\mu_{MW}$, $\lambda_6 = -\mu_{FW}$,

thus, the extinction equilibrium is locally asymptotically stable.

For the stability of the non-Wolbachia steady state, $E_2 = (A_N^*, M_N^*, F_N^*, 0, 0, 0)$, some stability conditions have been found, but not completed. The following is framework to find the stability conditions:

In the case of the Wolbachia-free equilibrium, the Jacobian is

$$J = \begin{bmatrix} -\mu_{AN}-\gamma_N-\frac{Q_N^*}{K}F_N^* & \frac{\delta\rho_{NN}}{P^{*2}}G^*F_N^* & G^*Q_N^* & -\frac{Q_N^*}{K}F_N^* & (\frac{\rho_{NW}}{P^*}-\frac{Q_N^*}{P^*})G^*F_N^* & 0 \\ \epsilon_N\gamma_N & -\mu_{MN} & 0 & \epsilon_{NW}(1-\alpha_W)\gamma_W & 0 & 0 \\ (1-\epsilon_N)\gamma_N & 0 & -\mu_{FN} & (1-\epsilon_{NW})(1-\alpha_W)\gamma_W & 0 & 0 \\ 0 & 0 & 0 & -\mu_{AW}-\gamma_W & 0 & G^*Q_W^* \\ 0 & 0 & 0 & \epsilon_W\alpha_W\gamma_W & -\mu_{MW} & 0 \\ 0 & 0 & 0 & (1-\epsilon_W)\alpha_W\gamma_W & 0 & -\mu_{FW} \end{bmatrix} \tag{12}$$

where

$$P^* = M_N^* + \delta, \qquad G^* = \Big(1 - \frac{A_N^*}{K}\Big), \qquad Q_N^* = \frac{\rho_{NN}M_N^*}{M_N^*+\delta}, \qquad Q_W^* = \frac{\rho_{WN}M_N^*}{M_N^*+\delta}$$

Notice that J can be divided into four 3×3 matrices:

$$J = \begin{bmatrix} A & B \\ C & D \end{bmatrix} \tag{13}$$

Since element C is a 3×3 zero matrix, the eigenvalues of the Jacobian will be the eigenvalues of A and D. Since $-\mu_{MW}$ is an eigenvalue, it remains to find the eigenvalues of

$$A = \begin{bmatrix} -\mu_{AN} - \gamma_N - \frac{Q_N^*F_N^*}{K} & \frac{\delta\rho_{NN}}{P^{*2}}G^*F_N^* & G^*Q_N^* \\ \epsilon_N\gamma_N & -\mu_{MN} & 0 \\ (1-\epsilon_N)\gamma_N & 0 & -\mu_{FN} \end{bmatrix},$$

$$D' = \begin{bmatrix} -\mu_{AW} - \gamma_W & G^*Q_W^* \\ (1-\epsilon_W)\alpha_W\gamma_W & -\mu_{FW} \end{bmatrix}$$

According to the Routh-Hurwitz Criterion for third-degree characteristic polynomial of the form

$$\lambda^3 + \left[-\sum_{r=1}^{3}\lambda_i\right]\lambda^2 + \left[\sum_{r,s=1,r\neq s}^{3}\lambda_r\lambda_s\right]\lambda + \left(-\prod_{r=1}^{3}\lambda_r\right) = 0. \tag{14}$$

it is sufficient to show that its coefficients are all positive:

$$-\sum_{r=1}^{3}\lambda_i = \frac{F_N^*Q_N^* + K(\gamma_N + \mu_{AN} + \mu_{MN} + \mu_{FN})}{K} > 0$$

$$\begin{aligned} \sum_{r,s=1,r\neq s}^{3}\lambda_r\lambda_s &= \mu_{MN}\mu_{FN} + \gamma_N(\mu_{MN}+\mu_{FN}) + \mu_{AN}(\mu_{MN}+\mu_{FN}) \\ &\quad + \frac{F_N^*\left(Q_N^*(\mu_{MN}+\mu_{FN}) - \frac{(K-A_N^*)\delta\rho_{NN}\gamma_N\epsilon_N}{(M_N^*+\delta)^2}\right)}{K} - G^*Q_N^*\gamma_N(1-\epsilon_N) \\ -\prod_{r=1}^{3}\lambda_r &= \frac{\mu_{FN}\left(F_N^*Q_N^*\mu_{MN} + K(\gamma_N+\mu_{AN})\mu_{MN} - \frac{F_N^*(K-A_N^*)\delta\rho_{NN}\gamma_N\epsilon_N}{(M_N^*+\delta)^2}\right)}{K} \\ &\quad - G^*Q_N^*\gamma_N(1-\epsilon_N)\mu_{MN} \end{aligned}$$

For D', $tr(D') = -\gamma - \mu_{FN} - \mu_{AW} < 0$ and for the determinant to be positive, we need

$$\frac{G^* Q_W^* \alpha_W \gamma_W (1-\epsilon_W)}{(\gamma_W + \mu_{AW})\mu_{FW}} < 1$$

If these conditions are satisfied, then the Wolbachia-free equilibrium is locally asymptotically stable. □

Proof of Theorem 3

Proof. Let $\alpha_W = 1$, $\rho_{NW} = 0$, and $\delta = 0$. Then our system reduces to the following equations which we set equal to zero:

$$0 = F_N \frac{\rho_{NN} M_N}{M_W + M_N}\left(1 - \frac{A_N + A_W}{K}\right) - \mu_{AN} A_N - \gamma_N A_N \tag{15a}$$
$$0 = \epsilon_N \gamma_N A_N - \mu_{MN} M_N \tag{15b}$$
$$0 = (1-\epsilon_N)\gamma_N A_N - \mu_{FN} F_N \tag{15c}$$
$$0 = F_W \frac{\rho_{WW} M_W + \rho_{WN} M_N}{M_W + M_N}\left(1 - \frac{A_N + A_W}{K}\right) - \mu_{AW} A_W - \gamma_W A_W \tag{15d}$$
$$0 = \Lambda + \epsilon_W \gamma_W A_W - \mu_{MW} M_W \tag{15e}$$
$$0 = \Lambda + (1-\epsilon_W)\gamma_W A_W - \mu_{FW} F_W \tag{15f}$$

It is clear that under this special case, the extinction equilibrium does not exist. Therefore, we proceed to show the existence of the only Wolbachia-infected mosquitoes equilibrium. We let $A_N = M_N = F_N = 0$ getting:

$$0 = \rho_{WW} F_W^* \left(1 - \frac{A_W^*}{K}\right) - (\mu_{AW} + \gamma_W) A_W^* \tag{16a}$$
$$0 = \Lambda + \epsilon_W \gamma_W A_W^* - \mu_{MW} M_W^* \tag{16b}$$
$$0 = \Lambda + (1-\epsilon_W)\gamma_W A_W^* - \mu_{FW} F_W^* \tag{16c}$$

One can solve for M_W^* and F_W^* in Eqs. (16b) and (16c):

$$M_W^* = \frac{\Lambda + \epsilon_W \gamma_W A_W^*}{\mu_{MW}}, \qquad F_W^* = \frac{\Lambda + (1-\epsilon_W)\gamma_W A_W^*}{\mu_{FW}}$$

Then, substituting into Eq. (16a) gives the following equation for A_W^*:

$$\begin{aligned} 0 &= \frac{\rho_{WW}}{\mu_{FW}}\left(\Lambda + (1-\epsilon_W)\gamma_W A_W^*\right)\left(1 - \frac{A_W^*}{K}\right) - (\mu_{AW} + \gamma_W) A_W^* \\ &= a A_W^{*2} + b A_W^* + c \end{aligned}$$

with

$$\begin{aligned} a &= \frac{\rho_{WW}(1-\epsilon_W)\gamma_W}{\mu_{FW}K} \\ b &= \mu_{AW} + \gamma_W + \frac{\rho_{WW}\Lambda}{\mu_{FW}K} - \frac{\rho_{WW}(1-\epsilon_W)\gamma_W}{\mu_{FW}} \\ c &= -\frac{\rho_{WW}\Lambda}{\mu_{FW}} \end{aligned}$$

Since $ac > 0$, then $b^2 - 4ac > b^2 > 0$, hence

$$A_W^* = -\frac{b}{2a} + \sqrt{\left(\frac{b}{2a}\right)^2 - \frac{c}{a}}$$

is a biologically feasible equilibrium (positive). Notice that $A_W^* < K$ since otherwise Eq. (15d) would be negative and A_W^* would not be an equilibrium point. To asses the stability of this equilibrium one must plug-in these values into the Jacobian (10):

$$J = \begin{bmatrix} -\mu_{AN}-\gamma_N & 0 & 0 & 0 & 0 & 0 \\ \epsilon_N\gamma_N & -\mu_{MN} & 0 & 0 & 0 & 0 \\ (1-\epsilon_N)\gamma_N & 0 & -\mu_{NF} & 0 & 0 & 0 \\ -\frac{\rho_{WW}}{K}F_W^* & \frac{\rho_{WN}-\rho_{WW}}{M_W^*}G^*F_W^* & 0 & -\mu_{AW}-\gamma_W-\frac{\rho_{WW}}{K}F_W^* & 0 & \rho_{WW}G^* \\ 0 & 0 & 0 & \epsilon_W\gamma_W & -\mu_{MW} & 0 \\ 0 & 0 & 0 & (1-\epsilon_W)\gamma_W & 0 & -\mu_{FW} \end{bmatrix} \tag{17}$$

where

$$G^* = 1 - \frac{A_W^*}{K}$$

Thus, the Jacobian is divided into four 3×3 matrices:

$$J = \begin{bmatrix} A & C \\ B & D \end{bmatrix} \tag{18}$$

Since C is a 3×3 zero matrix this allows for the eigenvalues to be the diagonals of both A and D. We note that $-\mu_{AN} - \gamma_N$, $-\mu_{FN}$, $-\mu_{MN}$ and $-\mu_{MW}$ are eigenvalues of our Jacobian. Therefore the equilibrium will be stable if the eigenvalues of the matrix

$$D' = \begin{bmatrix} -\mu_{AW} - \gamma_W - \frac{\rho_{WW}}{K}F_W^* & \rho_{WW}G^* \\ (1-\epsilon_W)\gamma_W & -\mu_{FW} \end{bmatrix},$$

are all negative. Since the trace is negative, one only needs to check that the determinant is positive, hence the condition for stability is given by

$$0 < \Big(\mu_{AW} + \gamma_W + \frac{\rho_{WW}F_W^*}{K}\Big)\mu_{FW} - \rho_{WW}\gamma_W(1-\epsilon_W)\Big(1 - \frac{A_W^*}{K}\Big) \tag{19}$$

Upon substitution of F_W^* in Eq. (19) one obtains the following Equivalent condition

$$0 < \Lambda + \frac{(\mu_{AW} + \gamma_W) K \mu_{FW}}{\rho_{WW}} + \gamma_W (1 - \epsilon_W)(2A_W^* - K) \tag{20}$$

and solving for Λ after plugging-in the value of A_W^* gives the following condition

$$0 < \gamma_W (1 - \epsilon_W) \sqrt{\left(\frac{b}{a}\right)^2 - 4\frac{c}{a}} \tag{21}$$

which is always true, therefore the only-Wolbachia equilibrium will always exist and be locally stable as long as CI and vertical transmission are perfect. It is important to note that the stability of this equilibrium is only local unless Λ is large enough, as is shown in the numerical analysis. Thus for small recruitment rates the outcome will depend on the initial conditions. $\square$