Chapter 7

Mathematical Model as a Tool for the Control of Vector-Borne Diseases: *Wolbachia* Example

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Additional information is available at the end of the chapter

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Abstract

Dengue is a vector-borne disease that risks two-thirds of the world's population particularly in tropical and subtropical regions. Strategies have been implemented, but they are only effective in the short term. A new innovative and promising strategy against dengue is by the use of *Wolbachia* bacterium. This requires that *Wolbachia*-carrying mosquitoes should persist in the population. To assess the persistence of *Wolbachia*-carrying mosquitoes and its effects on dengue, a number of mathematical models have been formulated and analysed. In this chapter, we review the existing mathematical models of *Wolbachia*-carrying mosquito population dynamics and dengue with *Wolbachia* intervention and provide examples of the mathematical models. Simulations of the models are presented to illustrate the model's solutions.

Keywords: Wolbachia, dengue, mathematical model

1. Introduction

Dengue is a vector-borne disease caused by four distinct serotypes (DEN1–DEN4), and is endemic in most countries particularly in tropical and subtropical areas [1]. It is estimated that around 390 million cases happen each year [2]. Individuals obtain lifelong immunity to the serotype that they are infected with, but have a higher chance to get the most severe form of dengue in the subsequent infection [1]. It is estimated that around 500,000 individuals get severe dengue and require hospitalisation. Of these, about 2.5% die [3]. Without a proper treatment, the fatality rate can reach 20% [3]. Dengue is also a substantial public health and economic burden [4].

A number of strategies have been implemented, but they are generally effective in the short term. Although some progresses have been made for dengue antiviral treatment, dengue control strategies still depend on vector control [5]. One of the strategies against dengue is by the use of *Wolbachia* bacterium. There are two *Wolbachia* strains used in the experiments: *WMelPop* and *WMel*. *WMelPop* strain can reduce the mosquito lifespan of more than 50% and almost 20% reduction in fecundity [6]. *WMel* strain reduces the lifespan of around 10% and only small reduction in fecundity [6]. *Wolbachia* can reduce the level of virus in the salivary glands. *Wolbachia* gives reproductive advantage for *Wolbachia*-carrying female mosquitoes known as cytoplasmic incompatibility (CI). The *Wolbachia*-carrying female mosquitoes can reproduce when mating with both non-*Wolbachia* and *Wolbachia*-carrying male mosquitoes. Non-*Wolbachia* female mosquitoes can reproduce when mating with non-*Wolbachia* males [7]. Field experiments showed that *Wolbachia*-carrying mosquitoes have established and dominated the population [8]. When *Wolbachia*-carrying mosquitoes persist in the field, the *Wolbachia* intervention can be implemented. The question that arises is that to what extend this intervention can reduce dengue transmission? To answer the above question, a number of mathematical models have been formulated and analysed. Mathematical model is a useful tool to understand complex phenomena. This can be used to understand population dynamics [9], disease transmission dynamics [10, 11], and others [12, 13]. A number of mathematical models have been developed to examine the persistence and spread of *Wolbachia*-carrying mosquitoes and its effects on dengue transmission dynamics. In this chapter, we review the existing mathematical models of *Wolbachia*-carrying mosquito population dynamics and dengue with *Wolbachia* intervention, give examples of the mathematical models, and show several numerical simulations to illustrate the model's solutions.

2. Mathematical modelling

This section presents background on mathematical modelling of infectious diseases. Mathematical modelling is a useful tool to understand complex phenomena including disease transmission dynamics and their control strategies. There are several types of modelling that are generally used: deterministic, stochastic, statistical, agent-based modelling, and the others. A deterministic model is mostly used because it is easily solved and can include many parameters or variables. The model is in the form of system of differential equations.

Many mathematical models have been developed to investigate disease transmission dynamics including vector-borne diseases [14]. The model is based on a standard SIR model where the human population is divided into susceptible (S), infected (I), and recovered (R) [15]. The susceptible individuals become exposed after being contacted with infected individuals at a rate β. They then recover at a rate γ. The model is written in the following system of differential equations:

$$\frac{dS}{dt} = -\beta \frac{SI}{N}, \quad \frac{dI}{dt} = \beta \frac{SI}{N} - \gamma I, \quad \frac{dR}{dt} = \gamma I. \tag{1}$$

The model can then be extended to include other compartments and parameters depending on the characteristics of diseases. For example, if the disease has long incubation period, we can add exposed compartment. If the disease is transmitted via vector, we can add another system of equations describing vector dynamics. When one aims to investigate the effects of vaccination, vaccinated compartment can be included. The important principles in modelling are to know characteristics of studied phenomena and the purpose of the research. The principles have been applied when we formulate mathematical models for *Wolbachia*-carrying mosquito population dynamics and dengue with *Wolbachia*.

3. Overview of mathematical models of *Wolbachia* and dengue

In this section, we review existing mathematical model of *Wolbachia*-carrying mosquito population dynamics and dengue with *Wolbachia* intervention.

Many (spatial and non-spatial) mathematical models have been formulated to analyse the persistence and spread or dispersal of *Wolbachia*-carrying mosquitoes in the populations [9, 16–29]. The general aim is to understand the underlying factors required for the persistence and spread of *Wolbachia*-carrying mosquitoes.

A number of nonspatial mathematical model for *Wolbachia*-carrying mosquito population dynamics have been developed. Ndii et al. [19] developed a mathematical model for *Wolbachia*-carrying mosquito population dynamics and assessed the persistence of *Wolbachia*-carrying mosquito populations. They found that *Wolbachia*-carrying mosquitoes persist in the population given that the death rate is not too high. Zhang et al. [30] formulated a mathematical model to assess the best strategies for releasing *Wolbachia*-carrying mosquitoes. They found that initial quantities of non-*Wolbachia* and *Wolbachia*-carrying mosquitoes and augmentation methods (timing, quantity, and order of frequency) determine the success of the *Wolbachia* intervention. They also formulated birth-pulse model with different density dependent death rate functions. They found that for condition with a strong density dependent death rate, the initial ratio of non-*Wolbachia* and *Wolbachia*-carrying mosquitoes should exceed a critical threshold for *Wolbachia*-carrying mosquitoes to dominate the population.

The spatial mathematical models have been developed to assess the *Wolbachia*-carrying mosquitoes' dispersal. Chan and Kim [9] used reaction diffusion approach and incorporated slow and fast dispersal mode to assess the dynamics of the *Wolbachia* spread. They found that temperature affects the wavespeed of the *Wolbachia*-carrying *Aedes aegypti*, that is, *Wolbachia* invasion for *Aedes aegypti* increases when the temperature decreases within the optimal temperature rate for mosquito survival. Hancock et al. [17] developed a metapopulation model to assess the spatial dynamics of *Wolbachia*. They found that spatial variation in the density-dependent competition experienced by juvenile host insects can influence the spread of *Wolbachia* into population. In their other paper [16], they found a new expression for the threshold which takes into account the main aspects of insects' life history. They showed that constant or pulsed immigrations affect the spread of *Wolbachia*-carrying mosquitoes.

Mathematical models for *Wolbachia*-carrying mosquitoes' populations consider several important aspects. They are cytoplasmic incompatibility (CI), the maternal transmission, *Wolbachia*-carrying mosquito death rate, release strategies of *Wolbachia*-carrying mosquitoes [9, 16–29, 31, 32]. These are expressed in the parameters, variables, or simulations.

A number of mathematical models have been developed to understand dengue transmission mathematical models [33, 34]. However, little mathematical models have been developed to investigate the efficacy of *Wolbachia*-intervention [35–40] in reducing dengue transmission. Hancock et al. [39] developed a mathematical model and investigated the strategies for releasing *Wolbachia*-carrying mosquitoes and its effects on dengue transmission dynamics. They found that male-biased releases can substantially reduce the dengue transmission. Furthermore, male-biased release can be an effective strategy that results in the persistence of *Wolbachia*-carrying mosquitoes. Ndii et al. [36, 41, 42] formulated single and two serotype dengue mathematical models to investigate the *Wolbachia* effectiveness in reducing dengue transmission. They found that *Wolbachia* can reduce primary and secondary dengue infections with higher reduction in secondary infections. Hughes and Britton [35] found that *Wolbachia* can reduce dengue transmission in areas where the basic reproduction number is not too high. This implies that *Wolbachia* can reduce dengue transmission in areas with low to moderate transmission settings, which is similar to that found Ndii et al. [36] and Ferguson et al. [37]. Supriatna et al. [40] showed that *Wolbachia* can reduce the value of basic reproduction number. In their other paper, they showed that the predatory and *Wolbachia* can reduce primary and secondary infections [43]. Furthermore, Supriatna et al. [44] investigated the use of vaccine and *Wolbachia* on dengue transmission dynamics [44] and showed that the optimal dengue control is determined by the epidemiological parameters and economic factors. Furthermore, they found that introducing too many *Wolbachia*-carrying mosquitoes would be counter-productive.

4. Examples and numerical simulations of mathematical models

In this section, we present examples of mathematical models of *Wolbachia*-carrying mosquito population dynamics and dengue with *Wolbachia* intervention and their numerical simulations.

4.1. Mathematical model of *Wolbachia*-carrying mosquito population dynamics and numerical simulations

4.1.1. Mathematical model of Wolbachia*-carrying mosquito population dynamics*

Here, we present an example of the mathematical model of the *Wolbachia*-carrying mosquito population dynamics. We present the model by Ndii et al. [19, 45] and show several numerical simulations. The mosquito population is divided into aquatic (A_N and A_W), male (M_N and M_W) and female (F_N and F_W) mosquitoes. Note that the aquatic compartment consists of eggs, larvae and pupae, which are grouped into one compartment. Furthermore, the subscripts M and W denote non-*Wolbachia* and *Wolbachia*-carrying mosquito population.

The effect of CI is captured by the following expression. The non-*Wolbachia* female mosquitoes reproduce when mating with non-*Wolbachia* males, which is governed by the following equations:

$$\rho_N \frac{M_N F_N}{M_N + F_N + M_W + F_W} \tag{2}$$

and the *Wolbachia*-carrying females reproduce when mating with non-*Wolbachia* and *Wolbachia*-carrying males, which is governed by the following equations:

$$\rho_W \frac{F_W(M_N + M_W)}{M_N + F_N + M_W + F_W} \tag{3}$$

Note that the population growth is limited by carrying capacity K. The maternal transmission is not perfect [46]. This means that not all *Wolbachia*-carrying aquatic mature to be *Wolbachia*-carrying adult. There is a proportion of $(1-\alpha)$ that mature to be non-*Wolbachia* adults that is $\epsilon_{NW}(1-\alpha)$. Note that the ratio of male and female mosquitoes is denoted by ϵ ($\epsilon_N, \epsilon_W, \epsilon_{NW}$). The model is governed by the following systems of differential equations:

$$\begin{aligned}
\frac{dA_N}{dt} &= \rho_N \frac{M_N F_N}{P}\left(1 - \frac{(A_N + A_W)}{K}\right) - \mu_{NA} A_N - \gamma_N A_N,\\
\frac{dM_N}{dt} &= \epsilon_N \gamma_N A_N - \mu_N M_N + \epsilon_{NW}(1-\alpha_W)\gamma_W A_W,\\
\frac{dF_N}{dt} &= (1-\epsilon_N)\gamma_N A_N - \mu_N F_N + (1-\epsilon_{NW})(1-\alpha_W)\gamma_W A_W,\\
\frac{dA_W}{dt} &= \rho_W \frac{F_W(M_W + M_N)}{P}\left(1 - \frac{(A_N + A_W)}{K}\right) - \mu_{WA} A_W - \gamma_W A_W,\\
\frac{dM_W}{dt} &= \epsilon_W \alpha_W \gamma_W A_W - \mu_W M_W,\\
\frac{dF_W}{dt} &= (1-\epsilon_W)\alpha_W \gamma_W A_W - \mu_W F_W.
\end{aligned} \tag{4}$$

where $P = M_N + F_N + M_W + F_W$ is the total population.

4.1.2. Numerical simulations

In this section, numerical simulations are conducted to illustrate the solutions of the model. The parameter values used are given in **Table 1**. The initial conditions are $A_{N0} = 0$, $F_{N0} = M_{N0} = 7253$, $A_{W0} = 0$, and $M_{W0} = F_{W0} = 14200$.

Figure 1 shows the numerical solutions of the model using the parameter values given in **Table 1**, but the *Wolbachia* adult mosquito death rate is $2 \times \mu_N$. This reflects the *WMelPop Wolbachia* strain which reduces the mosquito lifespan by a half. **Figure 1** shows that the non-*Wolbachia* mosquitoes dominate the population. This means that this strain cannot be used as a strategy to reduce dengue transmission. **Figure 2** shows the numerical solutions of the model

Symbol	Description	Value	Unit	Source
ρ_N	Non-*Wolbachia* reproductive rate	1.25	day^{-1}	[19]
μ_{NA}	Non-*Wolbachia* aquatic death rate	1/7.78	day^{-1}	[47]
γ_N	Non-*Wolbachia* maturation rate	1/6.67	day^{-1}	[48]
ϵ_N	The proportion of non-*Wolbachia* adult male offspring	0.5	Proportion	[49]
μ_N	Non-*Wolbachia* adult death rate	1/14	day^{-1}	[47]
μ_{WA}	*Wolbachia* aquatic death rate	1/7.78	day^{-1}	[47]
μ_W	*Wolbachia* adult death rate	1/7	day^{-1}	[46]
ρ_W	*Wolbachia* reproductive rate	$0.95\rho_N$	day^{-1}	[19]
γ_W	*Wolbachia* maturation rate	1/6.67	day^{-1}	[46]
ϵ_W	The proportion of *Wolbachia*-infected male adults	0.5	N/A	Assumed
ϵ_{NW}	The rate of uninfected males hatched from a *Wolbachia*-infected mother	0.5	N/A	Assumed
α_W	The proportion of *Wolbachia*-infected offspring from a *Wolbachia*-infected mother	0.9	N/A	[7, 46, 50, 51]
K	Carrying capacity	300,000		[48]

Table 1. Parameters, description, values and sources for the model of *Wolbachia*-carrying mosquitoes.

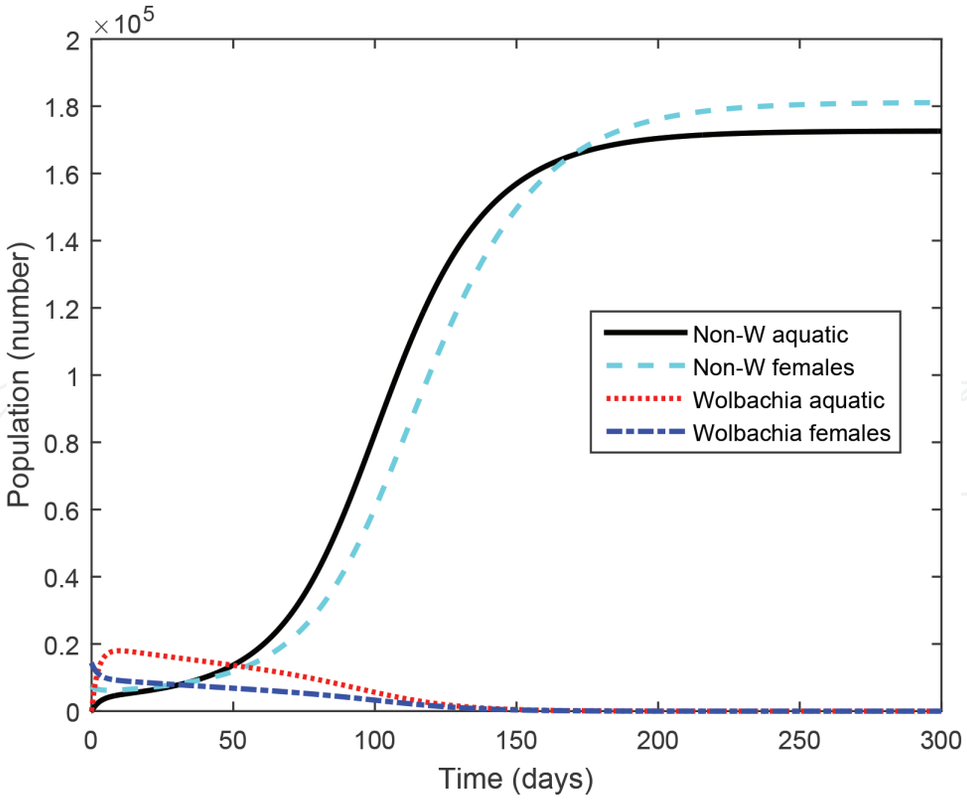

Figure 1. Numerical simulations of the Model (4). The parameter values used are given in **Table 1**, but the parameter μ_W is $2 \times \mu_N$ to reflect the *WMelPop Wolbachia* strain.

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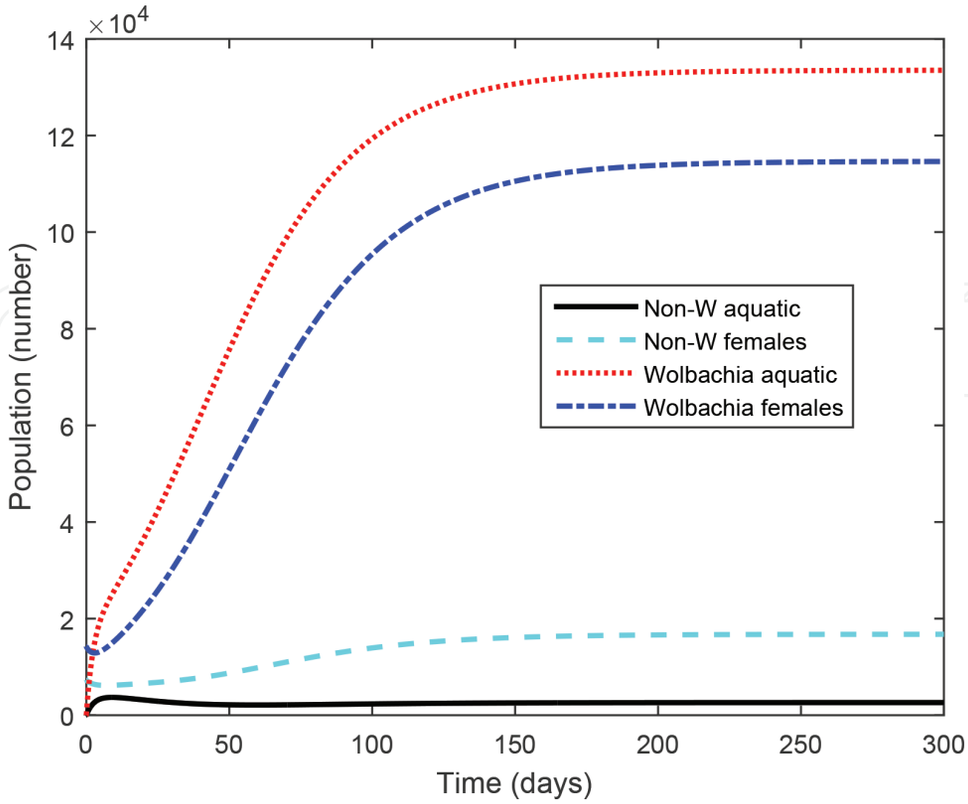

Figure 2. Numerical simulations of the Model (4). The parameter values used are given in **Table 1**. The parameter values reflect the *WMel Wolbachia* strain.

using the parameter values given in **Table 1**. The *Wolbachia* mosquito death rate is $1.1 \times \mu_N$ which reflects the *WMel Wolbachia* strain. This strain reduces the mosquito lifespan by around 10%. It shows that the *Wolbachia*-carrying mosquitoes dominate the population. This means that *WMel* strain can be used in the *Wolbachia* intervention. **Figure 3** shows the simulation results using *WMel* parameter values with initial conditions of $A_{N0} = 0$, $F_{N0} = M_{N0} = 7253$, $A_{W0} = 0$, and $M_{W0} = F_{W0} = 145$. It shows that the non-*Wolbachia* mosquitoes dominate the populations. It implies that the initial conditions also affects the persistence of *Wolbachia*-carrying mosquitoes.

4.2. Dengue mathematical model and numerical simulations

4.2.1. Dengue mathematical model in the presence of Wolbachia

In this section, we give example of two-serotype dengue mathematical model. We present the model by Ndii et al. [42]. The model consists of human, non-*Wolbachia* and *Wolbachia*-carrying mosquito population. The human population is divided into susceptible (S_H), exposed to serotype i (E_H^i), infected to serotype i (I_H^i), temporary immunity to the serotype i (X_H^i), recovered class (R_H), susceptible, exposed and infected to j strain (S_H^{ji}, E_H^{ji}, I_H^{ji}, respectively). The superscript ji means individuals that were previously infected by serotype i and currently infected by serotype j. The mosquito population is divided into susceptible (S_N and S_W),

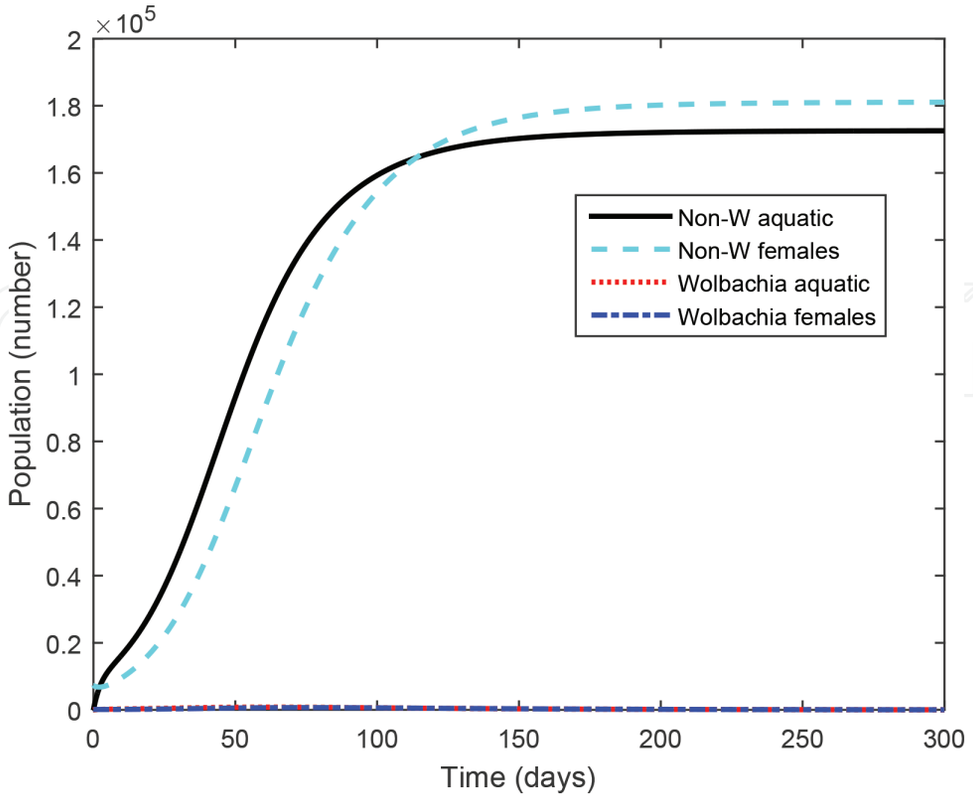

Figure 3. Numerical simulations of the Model (4). The parameter values used are given in **Table 1**. The parameter values reflect the *WMel Wolbachia* strain but different initial conditions. The initial conditions are $A_{N0} = 0$, $F_{N0} = M_{N0} = 7253$, $A_{W0} = 0$, and $M_{W0} = F_{W0} = 145$.

exposed to serotype i (E_N^i and E_W^i) and infected to serotype i (I_N^i and I_W^i). The subscript N and W is for non-*Wolbachia* and *Wolbachia*-carrying mosquitoes.

The model is governed by the following system of differential equations:

$$\frac{dS_H}{dt} = BN_H - \sum_{i=1}^{2} \lambda_H^i S_H - \mu_H S_H, \tag{5}$$

$$\frac{dE_H^i}{dt} = \lambda_H^i S_H - \gamma_H E_H^i - \mu_H E_H^i, \tag{6}$$

$$\frac{dI_H^i}{dt} = \gamma_H E_H^i - \sigma I_H^i - \mu_H I_H^i, \tag{7}$$

$$\frac{dX_H^i}{dt} = \sigma I_H^i - \theta^i X_H^i - \mu_H X_H^i, \tag{8}$$

$$\frac{dS_H^{ji}}{dt} = \lambda_H^j S_H^{ji} - \mu_H S_H^{ji}, \tag{9}$$

$$\frac{dE_H^{ji}}{dt} = \lambda_H^j S_H^{ji} - \gamma_H E_H^{ji} - \mu_H E_H^{ji}, \tag{10}$$

$$\frac{dI_H^{ji}}{dt} = \gamma_H E_H^{ji} - \sigma I_H^{ji} - \left(\mu_H + d\right) I_H^{ji}, \tag{11}$$

$$\frac{dR_H}{dt} = \sum_{j=1,\, j\neq i}^{2} \sigma I_H^{ji} - \mu_H R_H, \tag{12}$$

Model for non-*Wolbachia* mosquito population

$$\frac{dA_N}{dt} = \frac{\rho_N F_N^2}{2(F_N + F_W)} \left(1 - \frac{A_N + A_W}{K}\right) - \tau_N A_N - \mu_{NA} A_N, \tag{13}$$

$$\frac{dS_N}{dt} = \frac{\tau_N A_N}{2} + \frac{(1-\alpha)\tau_W A_W}{2} - \sum_{i=1}^{2} \lambda_N^i S_N - \mu_N S_N, \tag{14}$$

$$\frac{dE_N^i}{dt} = \lambda_N^i S_N - \gamma_N E_N^i - \mu_N E_N^i, \tag{15}$$

$$\frac{dI_N^i}{dt} = \gamma_N E_N^i - \mu_N I_N^i. \tag{16}$$

Model for *Wolbachia*-carrying mosquito population

$$\frac{dA_W}{dt} = \frac{\rho_W F_W}{2} \left(1 - \frac{A_N + A_W}{K}\right) - \tau_W A_W - \mu_{WA} A_W, \tag{17}$$

$$\frac{dS_W}{dt} = \frac{\alpha \tau_W A_W}{2} - \sum_{i=1}^{2} \lambda_W^i S_W - \mu_W S_W, \tag{18}$$

$$\frac{dE_W^i}{dt} = \lambda_W^i S_W - \gamma_W E_W^i - \mu_W E_W^i, \tag{19}$$

$$\frac{dI_W}{dt} = \gamma_W E_W^i - \mu_W I_W^i, \tag{20}$$

where the force of infections are

$$\lambda_H^i = \frac{b_N T^i I_N^i}{N_H} + \frac{b_W T_{HW}^i I_W^i}{N_H}, \tag{21}$$

$$\lambda_N^i = \frac{b_N T^i I_H^i}{N_H} + \phi_i \frac{b_N T^i I_H^{ij}}{N_H}, \tag{22}$$

$$\lambda_W^i = \frac{b_W T^i I_H^i}{N_H} + \phi_i \frac{b_W T^i I_H^{ij}}{N_H}, \tag{23}$$

where ϕ_i is the antibody-dependent enhancement factor for serotype i. Note that the susceptible human becomes exposed to dengue after being bitten by non-*Wolbachia* and *Wolbachia*-infected

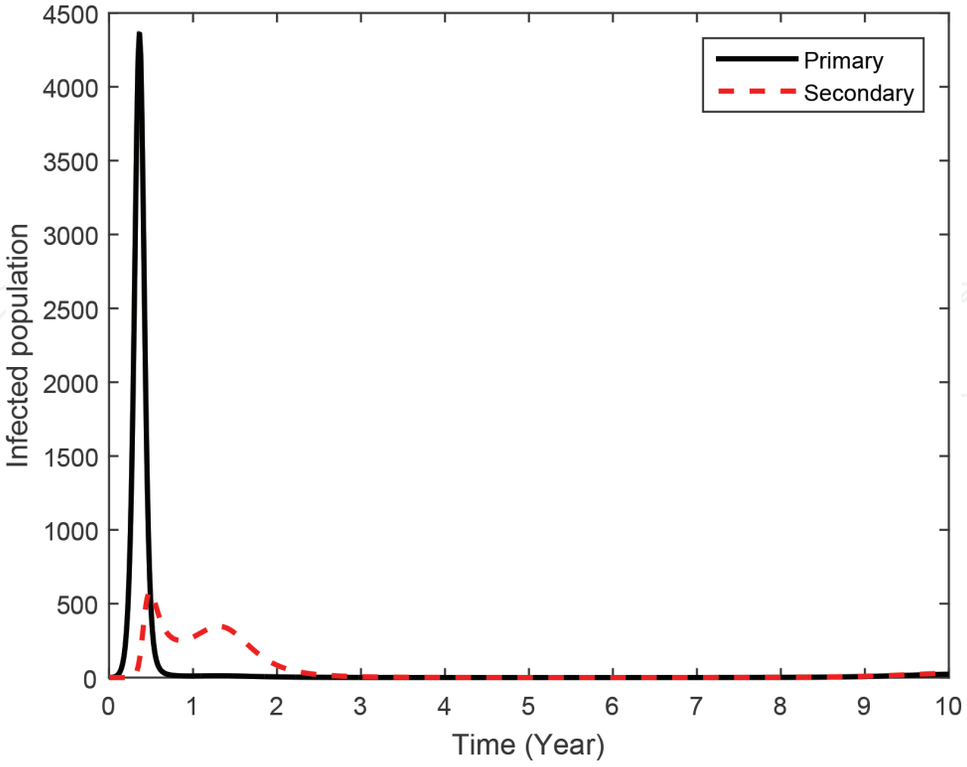

Figure 4. Numerical simulations of primary and secondary infections in the absence of *Wolbachia*-carrying mosquitoes. The parameters values used are given in **Table 2**. Initial conditions are $I_H^1(0) = I_H^2(0) = 1$ and $N_H = 10^5$. $A_N(0) = S_N(0) = 3 \times N_H$.

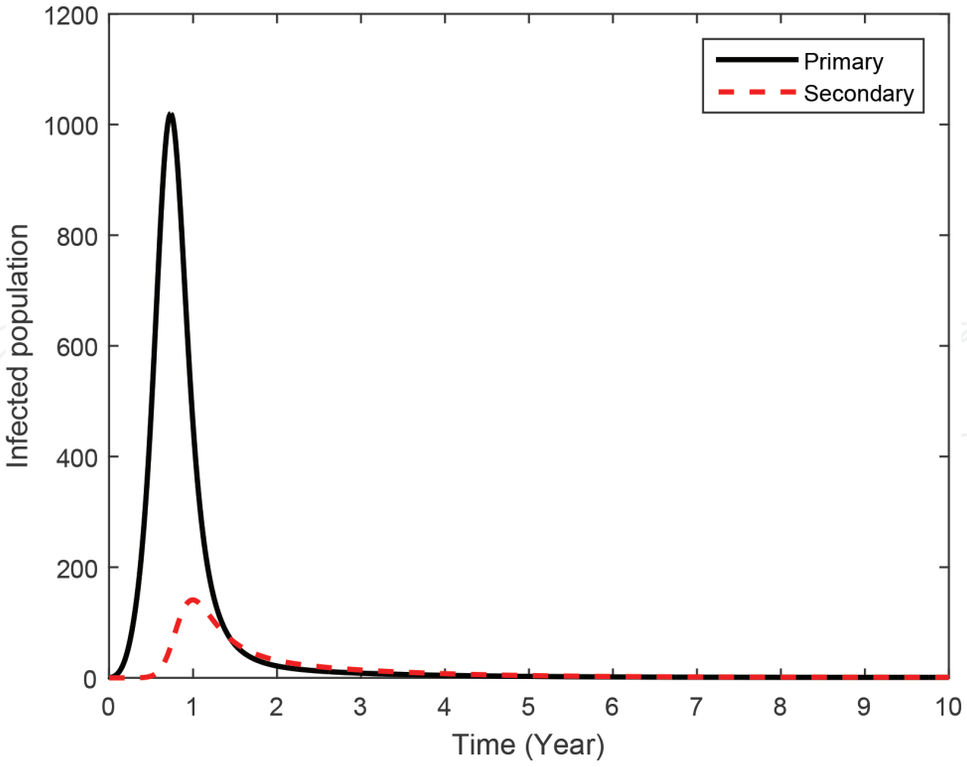

Figure 5. Numerical simulations of primary and secondary infections in the presence of *Wolbachia*-carrying mosquitoes. The parameters values used are given in **Table 2**. Initial conditions are $I_H^1(0) = I_H^2(0) = 1$ and $N_H = 10^5$. $A_N(0) = S_N(0) = A_W(0) = S_W(0) = 1.5 \times N_H$.

mosquitoes, which then becomes infected and have temporary immunity. After a certain period in temporary immunity class, they become susceptible to the other dengue serotype. They will have secondary infection after being bitten by infected mosquitoes carrying different dengue serotype to that they are previously infected.

4.2.2. Numerical simulations

This section presents numerical simulations of the model. **Figures 4** and **5** show the numerical simulations of primary and secondary infections in the absence and presence of *Wolbachia*, respectively.

Figures 4 and **5** show that *Wolbachia* can reduce dengue transmission. The number of infections in the presence of *Wolbachia*-carrying mosquitoes (see **Figure 5**) is smaller than that in the absence of *Wolbachia*-carrying mosquitoes (see **Figure 4**). This means that the *Wolbachia* can

Symbol	Description	Value	Unit	Source
α	Maternal transmission	0.9	N/A	[19, 46, 52]
B	Human birth rate	$1/(70 \times 365)$	day^{-1}	[3]
b_N	Biting rate of non-W mosquitoes	0.63	day^{-1}	[53]
b_W	Biting rate of W mosquitoes	$0.95\, b_N$	day^{-1}	[54]
γ_H	Progression rate from exposed to infectious	1/5.5	day^{-1}	[1]
γ_N	Progression from exposed to infectious class of non-W mosquitoes	1/10	day^{-1}	[55]
γ_W	Progression from exposed to infectious class of W mosquitoes	1/10	day^{-1}	[55]
K	Carrying capacity	$3 \times N_H$	N/A	[55]
λ	Force of infection	Eqs. (21)–(23)		
μ_N	Adult mosquito death rate (non-W)	1/14	day^{-1}	[47]
μ_H	Human death rate	$1/(70 \times 365)$	day^{-1}	[3]
μ_{NA}	Death rate of aquatic non-W mosquitoes	1/14	day^{-1}	[47]
μ_W	Adult aquatic death rate	$1.1\mu_N$	day^{-1}	[46, 51]
μ_{WA}	Death rate of W mosquitoes	1/14	day^{-1}	[47]
ϕ	ADE	1.1	N/A	[56]
ρ_N	Reproductive rate of non-W mosquitoes	1.25	day^{-1}	[19]
ρ_W	Reproductive rate of W-mosquitoes	$0.95\rho_N$	day^{-1}	[46]
σ	Recovery rate	1/5	day^{-1}	[1]
T_N	Transmission probability from non-W mosquitoes to human	0.5	N/A	[36]
T_{HW}	Transmission probability from W mosquitoes to human	$0.5T_N$	N/A	[36, 57]
θ	Progression rate from temporary immunity class to susceptible class	$1/(0.5 \times 365)$	day^{-1}	[58]
τ_N	Maturation rate of non-W mosquitoes	1/10	day^{-1}	[47]
τ_W	Maturation rate of W mosquitoes	1/10	day^{-1}	[47]

Table 2. Parameter descriptions, values, and sources. Note that W and N are used to indicate Wolbachia-carrying and non-Wolbachia mosquitoes in the parameter descriptions, respectively. $N_H = 10^5$.

potentially be used to break the cycle of dengue transmission. Note that the parameter values are largely uncertain. Therefore, large data set is needed to validate the model against data.

5. Discussion and conclusions

The use of *Wolbachia* bacterium has been proposed as a new innovative strategy against dengue. A lot of research have been conducted to look at the persistence of *Wolbachia*-carrying mosquitoes and the potential reduction in the number of dengue cases by the use of *Wolbachia* bacterium. One of the approaches is by the use of mathematical model. It can be seen that mathematical model can provide insights into the persistence and the effectiveness of the *Wolbachia* in reducing dengue transmission dynamics.

One of the important steps in modelling is model's validation. The model can be validated against the real data. Although several parameters can be obtained from literature, it is important to estimate the influential parameters such as transmission rate against the real data. Ferguson et al. [37] validated their model against the real data. Furthermore, most parameters are strongly uncertain, which indicate that sensitivity analysis is strongly required. This aims to find the most important parameters which can guide us in collecting appropriate data to be estimated.

Models presented in this work do not take into account the environmental factors such as temperature and rainfall. These may affect the dynamics of mosquito population and hence dengue transmission dynamics. Furthermore, in our work, the ratio of male and female mosquitoes is equal, which possibly affects the mosquito's population dynamics. It is important to consider sex-biased ratio to determine its effects on the persistence of *Wolbachia*-carrying mosquitoes and dengue reduction.

In this paper, we review existing mathematical models of *Wolbachia*-carrying mosquitoes' population dynamics and dengue with *Wolbachia*. Examples of the mathematical models are given. It shows that *Wolbachia*-carrying mosquitoes can persist in the population depending on the *Wolbachia* strains. Furthermore, the initial conditions also affect the persistence of *Wolbachia*-carrying mosquito populations. It is shown that *Wolbachia* can potentially reduce the primary and secondary infections with higher reduction in secondary infections. Results suggest that using *Wolbachia* can potentially reduce the transmission of dengue and hence minimise the public health and economic burden.

The results showed that the *Wolbachia* can persist in the population. When mosquitoes are infected with the *WMel* strain of *Wolbachia*. For dengue mathematical models with *Wolbachia*, it shows that the *Wolbachia* can potentially reduce the primary and secondary infections. This means that using *Wolbachia* can be an alternative strategy against dengue.

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