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Stochastic Dengue Mathematical Model in the Presence of *Wolbachia*: Exploring the Disease Extinction

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Abstract: A new strategy against dengue is proposed by the use of the *Wolbachia* bacterium. In this paper, we analyse the effects of *Wolbachia* on dengue transmission dynamics using deterministic and stochastic epidemic models. The reduction in the reproduction number is measured and the probability of disease extinction is determined. We found that *Wolbachia* can reduce the reproduction number by up to 64%. We also found that the probability of extinction is around 90%, although the reproduction number is slightly above one. However, if the reproduction number is too high, which indicates a higher transmission level, the probability of disease extinction is smaller. Consequently, an outbreak is likely to take off. The results suggest that *Wolbachia* can be effective to reduce dengue transmission, particularly in areas with low to moderate transmission level.

Keywords: *Wolbachia; mathematical model; dengue; stochastic; probability; extinction.*

Mathematics Subject Classification (2010): 93E03, 92B05, 37N25.

1 Introduction

Dengue is a vector-borne disease transmitted via the bite of mosquitoes. Over half of the world's population is at risk of dengue, particularly in tropical and subtropical areas. Around 390 million cases happen annually [1] and can result in a higher fatality rate when no proper treatment is conducted [2].

The traditional strategies such as insecticide have been found less effective and hence an innovative biological strategy by the use of the *Wolbachia* bacterium has been proposed [3–6]. *Wolbachia* reduces the level of dengue virus in salivary glands, which lower

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the transmission probability [3, 7]. It also reduces the mosquito's lifespan, and hence mosquitoes have less time to transmit dengue. Furthermore, *Wolbachia* reduces the reproductive rate [3] and causes an effect called the bendy proboscis which leads to a reduced biting rate [8]. Additionally, there is a reproductive advantage for female mosquitoes since *Wolbachia* gives the so-called cytoplasmic incompatibility (CI) [9, 10]. The CI causes the *Wolbachia*-carrying females to reproduce when mating with the non-*Wolbachia* or *Wolbachia*-carrying males. On the other hand, non-*Wolbachia* females can only reproduce when mating with non-*Wolbachia* males.

The field trials of releasing *Wolbachia*-carrying mosquitoes have been conducted in several places including Indonesia. The results show that *Wolbachia*-carrying mosquitoes can persist in the population [11]. This is align with the results from mathematical analysis [12, 13]. The next crucial step is to determine the effectiveness of the *Wolbachia* intervention when it is implemented in the field.

Mathematical models have been widely used to understand the life sciences and technology-related problems [14–17]. A number of mathematical models have been developed to measure the effectiveness of *Wolbachia* to reduce dengue transmission [18–22]. They showed that *Wolbachia* can reduce dengue transmission by up to 80% and is highly effective in areas with low to moderate transmission level. However, these models are deterministic and do not take into account the effects of stochasticity. For a small population size, a stochastic approach is more appropriate. In this paper, stochastic epidemic models in the absence and presence of *Wolbachia* have been developed to measure the effectiveness of the *Wolbachia* intervention. The models are based on the deterministic mathematical models formulated by Ndii *et al.* [19, 21]. Furthermore, the reproduction number and the probability of extinction are determined. This paper is organised as follows. Section 2 presents the deterministic and stochastic model in the absence of *Wolbachia* and derivation of the probability generating function. Section 3 presents deterministic and stochastic models in the presence of *Wolbachia* and considers the derivation of the probability generating function. Results are presented in Section 4. The discussion and conclusions are presented at the end of the paper.

2 Mathematical Model in the Absence of *Wolbachia*

The determinsitic and stochastic epidemic models in the absence of *Wolbachia* are presented. A deterministic model serves as a basis for the development of a stochastic epidemic model [23, 24].

2.1 Deterministic model

In this section, a deterministic model in the presence of *Wolbachia* is presented. The model is in the form of a system of differential equations which has been formulated by Ndii *et al.* [21]. The human population is divided into four subpopulations, namely, Susceptible (S_H), Exposed (E_H), Infectious (I_H) and Recovered (R_H). Furthermore, a constant human population size is assumed, and hence the human birth and death rates are assumed to be equal, that is, $B = \mu_H$ and $N_H = S_H + E_H + I_H + R_H$.

The mosquito population is divided into subpopulations of Aquatic (A_N) which consists of eggs, larvae and pupae, Susceptible (S_N), Exposed (E_N) and Infectious (I_N) mosquitoes. The total adult female mosquito population is $F_N = S_N + E_N + I_N$. The subscript N is used to denote the non-*Wolbachia* mosquitoes. We use this subscript here for consistency and to differentiate from the *Wolbachia*-carrying mosquitoes included in

the models in the later sections. We group eggs, larvae and pupae into one compartment as they are not involved in the transmission of dengue. No recovered class is required for mosquitoes as they remain infected for the rest of their lives.

The deterministic mathematical model for dengue in the absence of *Wolbachia* is governed by the following system of differential equations:

$$\frac{dS_H}{dt} = BN_H - \frac{b_N T_N I_N}{N_H} S_H - \mu_H S_H, \tag{1}$$

$$\frac{dE_H}{dt} = \frac{b_N T_N I_N}{N_H} S_H - \gamma_H E_H - \mu_H E_H, \tag{2}$$

$$\frac{dI_H}{dt} = \gamma_H E_H - \sigma I_H - \mu_H I_H, \tag{3}$$

$$\frac{dR_H}{dt} = \sigma I_H - \mu_H R_H, \tag{4}$$

$$\frac{dA_N}{dt} = \rho_N \frac{F_N}{2}\left(1 - \frac{A_N}{K}\right) - (\tau_N + \mu_{NA})\, A_N, \tag{5}$$

$$\frac{dS_N}{dt} = \tau_N \frac{A_N}{2} - \left(\frac{b_N T_N I_H}{N_H} + \mu_N(t)\right) S_N, \tag{6}$$

$$\frac{dE_N}{dt} = \left(\frac{b_N T_N I_H}{N_H}\right) S_N - (\gamma_N + \mu_N(t))\, E_N, \tag{7}$$

$$\frac{dI_N}{dt} = \gamma_N E_N - \mu_N(t) I_N. \tag{8}$$

The description of parameters is given in Table 2.

When bitten by the infectious mosquitoes, humans have a chance to be exposed to dengue at rate of $b_N T_N I_N / N_H$ (equations (1) and (2)). The parameter b_N is the successful biting rate and T_N is the transmission probability from non-*Wolbachia* mosquitoes to humans and reverse. The exposed humans move to an infectious class at rate of γ_H and recover from dengue at rate of σ.

The aquatic population increases as the male and female mosquitoes mate and breed, but the population growth is limited by the carrying capacity K through a logistic term

$$\rho_N \frac{F_N M_N}{M_N + F_N}\left(1 - \frac{A_N}{K}\right).$$

Since there are equal numbers of male and female mosquitoes, $M_N = F_N$, this becomes $\rho_N F_N (1 - A_N/K)/2$ (equation (5)). The aquatic mosquito population dies at rate of μ_{NA} and mature into susceptible female mosquitoes at rate of τ_N, where only half of the maturing aquatics are female. Susceptible mosquitoes progress to the exposed class after biting infectious humans at rate of $b_N T_N I_H / N_H$. They then become infectious at rate of γ_N (equation (8)), where $1/\gamma_N$ is the extrinsic incubation period.

The reproduction number is obtained by creating the next generation matrix and finding the maximum eigenvalues of that matrix. The reproduction number of that model is given by

$$\mathcal{R}_0^2 = \frac{b_N^2 T_N^2 \gamma_H \gamma_N S_N}{N_H \mu_N \left(\gamma_H + \mu_H\right)\left(\sigma + \mu_H\right)\left(\gamma_N + \mu_N\right)}. \tag{9}$$

2.2 Stochastic model

We developed a stochastic version of deterministic model using a continous-time Markov chain (CTMC) model, where time is continous and the states are discrete. Let

$$X(t) = (S_H(t), E_H(t), I_H(t), A_N(t), S_N(t), E_N(t), I_N(t))$$

denote the discrete-valued random variables. It is assumed that the number of infections produced by an individual type i is independent of the number of infections produced by any other type. The individuals of type i have the same probability generating function (pgf). Let $\{X_{ji}\}_{j=1}^{n}$ be the offspring random variables for type i, where X_{ji} is the number of infected individuals of type j produced by the individuals of type i. The probability that one individual of type i produces x_j infected individuals of type j is given by

$$P_i(x_1, x_2, ..., x_n) = Prob\left\{X_{1i} = x_1, ..., X_{ni} = x_n\right\}. \tag{10}$$

The corresponding transition probabilities for the model in the absence of *Wolbachia* are

$$\begin{aligned}
\text{Prob}\{\Delta S_H = 1|X)\} &= BN_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_H, \Delta E_H) = (-1,+1)\} &= b_N T_N S_H I_N/N_H \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_H, \Delta I_H) = (-1,+1)\} &= \gamma_H E_H \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta I_H, \Delta R_H) = (-1,+1)\} &= \sigma I_H \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_H) = -1\} &= \mu_H S_H \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_H) = -1\} &= \mu_H E_H \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta I_H) = -1\} &= \mu_H I_H \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta R_H) = -1\} &= \mu_H R_H \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_N) = -1\} &= \mu_N E_N \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta I_N) = -1\} &= \mu_N I_N \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta A_N) = 1\} &= (\rho_N F_N/2)(1 - A_N/K)\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta A_N, \Delta S_N) = (-1,+1)\} &= \tau_N/2 A_N \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_N, \Delta E_N) = (-1,+1)\} &= b_N T_N S_N I_H/N_H \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_N, \Delta I_N) = (-1,+1)\} &= \gamma_N E_N \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_N) = -1\} &= \mu_N S_N \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_N) = -1\} &= \mu_N E_N \Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta I_N) = -1\} &= \mu_N I_N \Delta t + \mathcal{O}(\Delta t).
\end{aligned} \tag{11}$$

2.3 Continous-time branching processes

We construct the branching process and probability of extinction. The offspring pgf for E_H, given $E_H(0) = 1$ and $I_H(0) = 0$, $E_N(0) = 0$, $I_N(0) = 0$, is

$$f_1(u_1, u_2, u_3, u_4) = \frac{\gamma_H u_2 + \mu_H}{\gamma_H + \mu_H}, \quad u_1, u_2, u_3, u_4 \in [0, 1].$$

The expression $\gamma_H/(\gamma_H + \mu_H)$ means the probability that an exposed individual becomes infectious. The expression $\mu_H/(\gamma_H + \mu_H)$ means the probability that an exposed individual leaves compartment due to death.

The offspring pgf for I_H, given $I_H(0) = 1, E_H(0) = E_N(0) = I_N(0) = 0$, is

$$f_2(u_1, u_2, u_3, u_4) = \frac{(b_N T_N S_N/N_H)u_2 u_3 + \sigma + \mu_H}{(b_N T_N S_N/N_H) + \sigma + \mu_H}, \quad u_1, u_2, u_3, u_4 \in [0, 1].$$

The expression $b_N T_N S_N/N_H/(b_N T_N S_N/N_H + \sigma + \mu_H)$ means the probability that an infectious individual results in a new exposed mosquito. The expression $(\sigma + \mu_H)/(b_N T_N S_N/N_H + \sigma + \mu_H)$ means the probability that an infectious individual leaves the compartment due to recovery or death.

The offspring pgf for E_N, given $E_N(0) = 1$, $E_H(0) = I_H(0) = I_N(0) = 0$, is

$$f_3(u_1, u_2, u_3, u_4) = \frac{\gamma_N u_4 + \mu_N}{\gamma_N + \mu_N}, \quad u_1, u_2, u_3, u_4 \in [0, 1].$$

The expression $\gamma_N/(\gamma_N + \mu_N)$ means the probability that an exposed mosquito becomes infectious. The expression $\mu_N/(\gamma_N + \mu_N)$ means the probability that an exposed individual leaves compartment due to death.

The probability generating function for I_N, given $I_N(0) = 1, E_N(0) = 0$, $E_H(0) = 0, I_H(0) = 0$, is

$$f_4(u_1, u_2, u_3, u_4) = \frac{b_N T_N u_1 u_4 + \mu_N}{b_N T_N + \mu_N}, \quad u_1, u_2, u_3, u_4 \in [0, 1].$$

The expression $b_N T_N/(b_N T_N + \mu_N)$ is the probability that an infectious mosquito results in a new exposed individual. The expression $\mu_N/(b_N T_N + \mu_N)$ is the probability that an infectious mosquito leaves the compartment due to death.

The expectation matrix $M_c = [M_{ji}]$ of the pgf is an $n \times n$ non-negative matrix where the elements of that matrix (m_{ij}) are the expected number of offsprings of group j produced by an individual in group i:

$$m_{ji} = \frac{df_i}{du_j}|_{u_1=\ldots=u_n=1} < \infty. \tag{12}$$

The extinction threshold is the spectral radius of the expectation matrix, denoted by $\rho(M)$. The elements of the expectation matrix are found using (12).

The expectation matrix of the model is as follows:

$$\mathbb{M} = \begin{bmatrix} 0 & 0 & 0 & \frac{b_N T_N}{b_N T_N + \mu_N} \\ \frac{\gamma_H}{\gamma_H + \mu_H} & \frac{b_N T_N S_N/N_H}{b_N T_N S_N/N_H + \sigma + \mu_H} & 0 & 0 \\ 0 & \frac{b_N T_N S_N/N_H}{b_N T_N S_N/N_H + \sigma + \mu_H} & 0 & 0 \\ 0 & 0 & \frac{\gamma_N}{\gamma_N + \mu_N} & \frac{b_N T_N}{b_N T_N + \mu_N} \end{bmatrix}.$$

The eigenvalues of the expectation matrix are the roots of the characteristic equations

$$\lambda^4 + (A + C)\lambda^3 + CA\lambda^2 - ABCD = 0, \tag{13}$$

where

$$A = \frac{b_N T_N}{b_N T_N + \mu_N}, \quad B = \frac{\gamma_N}{\gamma_N + \mu_N}, \quad C = \frac{b_N T_N S_N / N_H}{b_N T_N S_N / N_H + \sigma + \mu_N}, \quad D = \frac{\gamma_N}{\gamma_N + \mu_N}.$$

Allen and Driessche [25] showed the general relationship between $\mathcal{R}_0$ and $\rho(\mathbb{M})$ as follows:

$$\mathcal{R}_0 < 1 (= 1, > 1) \quad \text{if and only if} \quad \rho(\mathbb{M}) < 1 (= 1, > 1).$$

3 Mathematical Model in the Presence of *Wolbachia*

This section presents a dengue mathematical model in the presence of *Wolbachia*. The model has been formulated by Ndii *et al.* [19, 21]. The model serves as a basis for the development of a stochastic model in the presence of *Wolbachia*.

3.1 Deterministic model

A deterministic model in the presence of *Wolbachia* is governed by the following system of differential equations. We include the model for *Wolbachia*-carrying mosquitoes. The population is divided into Susceptible (S), Exposed (E), Infectious (I) and Recovered (R) compartments. For the mosquito population, there is an aquatic compartment (A). The subscripts H, N, and W represent the human, non-*Wolbachia* and *Wolbachia*-carrying mosquitoes.

In this model, the exposed rate is different to that in the absence of *Wolbachia*. In this model, a susceptible human has been exposed to dengue after being bitten by non-*Wolbachia* or *Wolbachia*-carrying infectious mosquitoes at rate of $b_N T_N I_N / N_H$ or $b_W T_{HW} I_W / N_H$, respectively (see equations (17) and (18)). Here b_W is the biting rate for *Wolbachia*-carrying mosquitoes and T_{HW} is the transmission probability from *Wolbachia*-carrying mosquitoes to humans. Note that the transmission probability from humans to *Wolbachia*-carrying mosquitoes is assumed to be equal to that from humans to non-*Wolbachia* mosquitoes, so $T_{WH} = T_N$. By contrast, there are differences in the transmission probabilities of dengue from mosquitoes to humans for *Wolbachia* and non-*Wolbachia* mosquitoes.

The effects of the cytoplasmic incompatibility and imperfect maternal transmission on the mosquito populations are included in this model. The effect of the CI is incorporated by differences in the mating functions. The non-*Wolbachia* female mosquitoes reproduce when mating with the *Wolbachia* male mosquitoes, and hence it gives

$$\frac{\rho_N F_N M_N}{P}, \tag{14}$$

where $P = F_N + M_N + F_W + M_W$. It is assumed that the ratio of male to female mosquitoes is 1:1, and therefore the equation is reduced to $\rho_N F_N^2 / (2(F_N + F_W))$ (see equation (21)). The aquatic *Wolbachia* mosquitoes are produced when *Wolbachia*-carrying female mosquitoes mate with either non-*Wolbachia* or *Wolbachia* males, giving the term

$$\frac{\rho_W F_W (M_N + M_W)}{P}, \tag{15}$$

where $P = F_N + M_N + F_W + M_W$, which simplifies to $\rho_W F_W/2$ (equation (25)). The growth of aquatic mosquitoes is limited by the carrying capacity K, so that each mating function is multiplied by

$$\frac{A_N + A_W}{K}. \tag{16}$$

The *Wolbachia*-carrying aquatic mosquitoes mature to be the *Wolbachia*-carrying adult mosquitoes at rate of τ_W. To capture the imperfect maternal transmission of *Wolbachia* [3, 26], it is assumed that a proportion α of them become *Wolbachia*-carrying adults and the rest $(1-\alpha)$ become non-*Wolbachia* adults (see equations (22) and (26)).

The mathematical model in the presence of *Wolbachia* is governed by the following system of differential equations:

$$\frac{dS_H}{dt} = BN_H - \frac{b_N T_N I_N}{N_H} S_H - \frac{b_W T_{HW} I_W}{N_H} S_H - \mu_H S_H, \tag{17}$$

$$\frac{dE_H}{dt} = \frac{b_N T_N I_N}{N_H} S_H + \frac{b_W T_{HW} I_W}{N_H} S_H - \gamma_H E_H - \mu_H E_H, \tag{18}$$

$$\frac{dI_H}{dt} = \gamma_H E_H - \sigma I_H - \mu_H I_H, \tag{19}$$

$$\frac{dR_H}{dt} = \sigma I_H - \mu_H R_H, \tag{20}$$

$$\frac{dA_N}{dt} = \rho_N \frac{F_N^2}{2(F_N + F_W)} \left(1 - \frac{(A_N + A_W)}{K}\right) - (\tau_N + \mu_{NA})\, A_N, \tag{21}$$

$$\frac{dS_N}{dt} = \tau_N \frac{A_N}{2} + (1-\alpha)\, \tau_W \frac{A_W}{2} - \left(\frac{b_N T_N I_H}{N_H} + \mu_N(t)\right) S_N, \tag{22}$$

$$\frac{dE_N}{dt} = \frac{b_N T_N I_H}{N_H} S_N - (\gamma_N + \mu_N(t))\, E_N, \tag{23}$$

$$\frac{dI_N}{dt} = \gamma_N E_N - \mu_N(t) I_N, \tag{24}$$

$$\frac{dA_W}{dt} = \rho_W \frac{F_W}{2} \left(1 - \frac{(A_N + A_W)}{K}\right) - (\tau_W + \mu_{WA})\, A_W, \tag{25}$$

$$\frac{dS_W}{dt} = \tau_W \alpha \frac{A_W}{2} - \left(\frac{b_W T_N I_H}{N_H} + \mu_W(t)\right) S_W, \tag{26}$$

$$\frac{dE_W}{dt} = \frac{b_W T_N I_H}{N_H} S_W - (\gamma_W + \mu_W(t))\, E_W, \tag{27}$$

$$\frac{dI_W}{dt} = \gamma_W E_W - \mu_W(t) I_W. \tag{28}$$

By using the concept of the next generation matrix, we obtain the reproduction number of the model in the presence of *Wolbachia* as

$$\mathbb{R}_0 = \frac{b_N^2 T_N^2 \gamma_N \gamma_H S_N}{(\gamma_N + \mu_N)\mu_N(\gamma_H + \mu_H)(\sigma + \mu_H) N_H} + \frac{b_W^2 T_{HW} \gamma_W T_N \gamma_H S_W}{(\gamma_W + \mu_W)\mu_W(\sigma + \mu_H)(\gamma_H + \mu_H) N_H}. \tag{29}$$

3.2 Stochastic model

A stochastic model in the presence of *Wolbachia* is presented. The model is a corresponding model of the deterministic model as presented in Ndii *et al.* [19].

Let $X(t) = (S_H(t), E_H(t), I_H(t), R_H(t), S_N(t), E_N(t), I_N(t), S_W(t), E_W(t), I_W(t))$. The corresponding transition probabilities are

$$\begin{aligned}
\text{Prob}\{\Delta S_H = 1|X)\} &= BN_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_H, \Delta E_H) = (-1,+1)\} &= b_N T_N S_H I_N/N_H\Delta t + b_W T_{HW} S_H I_W/N_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_H, \Delta I_H) = (-1,+1)\} &= \gamma_H E_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta I_H, \Delta R_H) = (-1,+1)\} &= \sigma I_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_H) = -1\} &= \mu_H S_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_H) = -1\} &= \mu_H E_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta I_H) = -1\} &= \mu_H I_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta R_H) = -1\} &= \mu_H R_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta A_N) = 1\} &= (\rho_N F_N^2/2(F_N+F_W))(1-(A_N+A_W)/K)\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta A_N, \Delta S_N) = (-1,+1)\} &= \tau_N/2A_N\Delta t + (1-\alpha)\tau_W A_W/2\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_N, \Delta E_N) = (-1,+1)\} &= b_N T_N S_N I_H/N_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_N, \Delta I_N) = (-1,+1)\} &= \gamma_N E_N\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_N) = -1\} &= \mu_N S_N\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_N) = -1\} &= \mu_N E_N\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta I_N) = -1\} &= \mu_N I_N\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta A_W) = 1\} &= (\rho_W F_W/2)(1-(A_N+A_W)/K)\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta A_W, \Delta S_W) = (-1,+1)\} &= \tau_W\alpha/2A_W\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_W, \Delta E_W) = (-1,+1)\} &= b_W T_N S_W I_H/N_H\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_W, \Delta I_W) = (-1,+1)\} &= \gamma_W E_W\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta A_W) = -1\} &= \mu_{WA} A_W\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta S_W) = -1\} &= \mu_W S_W\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta E_W) = -1\} &= \mu_W E_W\Delta t + \mathcal{O}(\Delta t),\\
\text{Prob}\{(\Delta I_W) = -1\} &= \mu_N I_N\Delta t + \mathcal{O}(\Delta t).
\end{aligned} \tag{30}$$

3.3 Continous-time branching processes

This section presents the probability generating function (pgf) of the model in the presence of *Wolbachia*. The probability generating function for E_H, given $E_H(0) = 1$, $E_N(0) = E_W(0) = I_H(0) = I_N(0) = I_W(0) = 0$, is

$$\phi_1(u_1, u_2, u_3, u_4, u_5, u_6) = \frac{\gamma_H u_2 + \mu_H}{\gamma_H + \mu_H}, \quad u_1, ..., u_6 \in [0, 1].$$

The offspring probability generating function for I_H, given $I_H(0) = 1$, $E_N(0) = E_W(0) = E_H(0) = I_N(0) = I_W(0) = 0$, is

$$\phi_2(u_1, u_2, u_3, u_4, u_5, u_6) = \frac{b_N T_N S_N/N_H u_2 u_3 + b_W T_N S_W/N_H u_2 u_5 + \sigma + \mu_H}{b_N T_N S_N/N_H + b_W T_N S_W/N_H + \sigma + \mu_H},$$

where $u_1, ..., u_6 \in [0, 1]$. The offspring probability generating function for E_N, given $E_N(0) = 1$, $E_H(0) = E_W(0) = I_H(0) = I_N(0) = I_W(0) = 0$, is

$$\phi_3(u_1, u_2, u_3, u_4, u_5, u_6) = \frac{\gamma_N u_4 + \mu_N}{\gamma_N + \mu_N}, \quad u_1, ..., u_6 \in [0, 1].$$

The probability generating function for I_N, given $I_N(0) = 1$, $E_H(0) = E_W(0) = E_N(0) = I_H(0) = I_W(0) = 0$, is

$$\phi_4(u_1, u_2, u_3, u_4, u_5, u_6) = \frac{b_N T_N u_1 u_4 + \mu_N}{b_N T_N + \mu_N}, \quad u_1, ..., u_6 \in [0, 1].$$

The probability generating function for E_W , given $E_W(0) = 1$, $E_H(0) = E_N(0) = I_N(0) = I_H(0) = I_W(0) = 0$, is

$$\phi_5(u_1, u_2, u_3, u_4, u_5, u_6) = \frac{\gamma_W u_6 + \mu_W}{\gamma_W + \mu_W}, \quad u_1, ..., u_6 \in [0, 1].$$

The probability generating function for I_W, given $I_W(0) = 1$, $E_H(0) = E_W(0) = E_N(0) = I_N(0) = I_H(0)$, is

$$\phi_6(u_1, u_2, u_3, u_4, u_5, u_6) = \frac{b_W T_{HW} u_1 u_6 + \mu_W}{b_W T_{HW} + \mu_W}, \quad u_1, ..., u_6 \in [0, 1].$$

Using the procedure given in equation (12), we obtain the expectation matrix. The expectation matrix is

$\mathbb{M} =$

$$\begin{bmatrix} 0 & 0 & 0 & \frac{b_N T_N}{b_N T_N + \mu_N} & 0 & \frac{b_W T_{HW}}{b_W T_{HW} + \mu_W} \\ \frac{\gamma_H}{\gamma_H + \mu_H} & \frac{b_N T_N S_N/N_H + b_W T_N S_W/N_H}{b_N T_N S_N/N_H + b_W T_N S_W/N_H + \sigma + \mu_H} & 0 & 0 & 0 & 0 \\ 0 & \frac{b_N T_N S_N/N_H}{b_N T_N S_N/N_H + b_W T_N S_W/N_H + \sigma + \mu_H} & 0 & 0 & 0 & \\ 0 & 0 & \frac{\gamma_N}{\gamma_N + \mu_N} & \frac{b_N T_N}{b_N T_N + \mu_N} & 0 & 0 \\ 0 & \frac{b_W T_N S_W/N_H}{b_N T_N S_N/N_H + b_W T_N S_W/N_H + \sigma + \mu_H} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{\gamma_W}{\gamma_W + \mu_W} & \frac{b_W T_{HW}}{b_W T_{HW} + \mu_W} \end{bmatrix}.$$

The spectral radius of the matrix $\mathbb{M}$ determines whether the system is sub critical, critical or supercritical.

4 Results

This section presents the reproduction number and the probability of disease extinction.

4.1 Reproduction number

We compare the reproduction number of the model in the absence and presence of *Wolbachia*. Therefore, the aims to assess the reduction in the reproduction number and hence the effectiveness of the *Wolbachia* intervention can be determined. The expressions for the reproduction number in the absence and presence of *Wolbachia* are given in equations (9) and (29), respectively. The parameter values for the models are given in Table 2.

The reproduction number for the model in the absence and presence of *Wolbachia* is 3.31 and 1.17, respectively. This shows that there is around 64.65% reduction in the reproduction number. An epidemic would not take off when $\mathcal{R}_0 < 1$, otherwise it will take off. The result implies that the *Wolbachia* intervention can stop dengue transmission in areas with the reproduction number being at most around 3, which indicates a moderate transmission level. This is because the *Wolbachia* intervention can reduce the basic reproduction number below one. When the reproduction number is higher than three, *Wolbachia* can still reduce dengue transmission though the epidemic still takes off. The numerical simulation is presented in Figure 1.

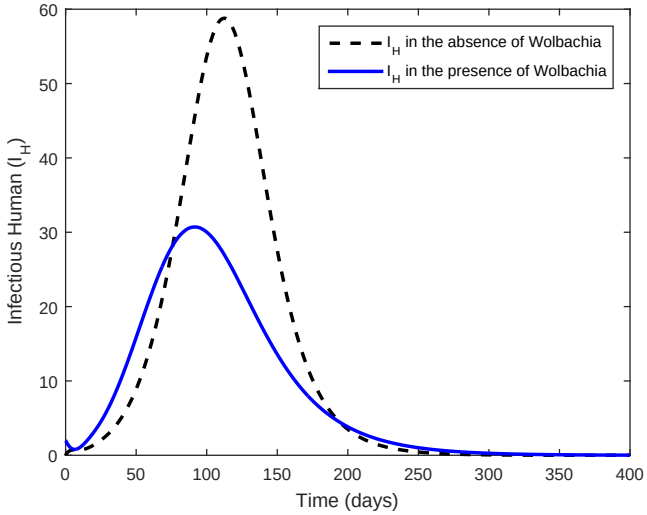

Figure 1: The number of infectious individuals in the absence and presence of *Wolbachia*.

Figure 1 shows that the peak of an outbreak is reduced in the presence of *Wolbachia*. An epidemic peak happens on around the 100^{th} day. Furthermore, the number of infectious individuals at the peak time is around 60. It declines when the *Wolbachia* intervention is implemented. Nevertheless, the end time of epidemic is relatively similar. This indicates that the *Wolbachia* intervention is effective in reducing dengue transmission.

4.2 Probability of extinction

This section presents the probability of extinction ($\mathbb{P}_0$) in the absence and presence of *Wolbachia*. This aims to measure the performance of *Wolbachia* in reducing dengue transmission. When the basic reproduction number is less than one, the probability of extinction is one. Therefore, we investigate the scenario where the reproduction number is greater than one and determine the probability of disease extinction.

The fixed point of the probability generating function is used to determine the probability of extinction

$$\mathbb{P}_0 = \lim_{t\to\infty} \text{Prop}\{I(t) = P(t) = 0\} = \begin{cases} 1, & \text{if } \rho(M) \leq 1, \\ q_k^{i_0^k}, & \text{if } \rho(M) > 1, \end{cases}$$

where q_k is the fixed point of the probability generating function and i_0^k denotes the initial conditions of the infectious individuals of type k.

Table 1: The initial conditions and the probability of extinction in the absence and presence of *Wolbachia*. The initial conditions are for E_H, I_H, E_N, I_N, E_W, I_W. Here W stands for *Wolbachia*.

Initial conditions						$\mathbb{P}_0$ non-W	$\mathbb{P}_0$ with-W
1	0	0	0	0	0	0.6622	0.9470
1	1	0	0	0	0	0.4384	0.8969
2	0	0	0	0	0	0.4385	0.8969
0	2	0	0	0	0	0.4385	0.8969
5	5	0	0	0	0	0.0162	0.5803

The results show that the probability of extinction for the model in the presence of *Wolbachia* is higher than that in the absence of *Wolbachia*. Furthermore, it is found that the probability of extinction declines when the initial number of infected individuals increases. In the absence of *Wolbachia*, the probability of extinction is around 0.6622. It becomes 0.9470 when *Wolbachia*-carrying mosquitoes are introduced into the population. Furthermore, the probability of extinction is close to 60% when there are 10 initially infected individuals in the population. However, the probability of extinction is close to zero for the same initial condition without the *Wolbachia* intervention.

5 Discussion and Conclusion

In this paper, we formulated stochastic models for dengue in the presence of *Wolbachia*. This research aims to measure the effectiveness of the *Wolbachia* intervention to reduce dengue transmission. We determine the proportion of reduction in the basic reproduction number and also the probability of extinction. The result shows that there is around 64% reduction in the basic reproduction number in the presence of *Wolbachia*. This is relatively similar to the result found by Ferguson *et al.* [18]. They found a reduction of 65-75% in the basic reproduction number when the *Wolbachia* intervention is implemented. Furthermore, when the reproduction number is significantly high, the reduction in the reproduction number is not sufficient to end dengue transmission. This is similar to the result obtained by Hughes and Britton [27]. The results imply that the *Wolbachia* intervention may be effective in regions with moderate transmission level.

The mathematical expression of the probability of extinction is derived. We found that the probability of extinction is higher in the presence of *Wolbachia*-carrying mosquitoes than that in the absence of *Wolbachia*. A 90% chance of disease extinction is obtained when the *Wolbachia* intervention is implemented. Around 60% chance of disease extinction is still obtained, although the number of the initially infected individuals is around ten. This implies that a *Wolbachia* intervention can be effective in reducing dengue transmission.

It can be concluded that the use of the *Wolbachia* bacterium can be an alternative strategy against dengue where the probability of disease extinction can reach 90%. Additionally, the use of the *Wolbachia* bacterium would be effective in reducing dengue transmission, particularly in areas with moderate transmission level. Therefore, the combination of the *Wolbachia* bacterium and the other strategy such as vaccination may be needed to optimise the delivery of the intervention.

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References

[1] S. Bhatt, P. W. Gething, O. J. Brady, J. P. Messina, A. W. Farlow, et al. The global distribution and burden of dengue. *Nature* **496** (2013) 1476–4687.

[2] World Health Organisation. Dengue and severe dengue Fact sheet No.117, http://www.who.int/mediacentre/factsheets/fs117/en/, [Online; accessed 03 March 2015] (February 2015).

[3] T. Walker, P. H. Johnson, L. A. Moreira, I. Iturbe-Ormaetxe, F. D. Frentiu, et al. The*WMel Wolbachia* strain blocks dengue and invades caged Aedes aegypti populations.*Nature* **476** (2011) 450–453.

[4] A. A. Hoffmann, B. L. Montgomery, J. Popovici, I. Iturbe-Ormaetxe, P. H. Johnson, et al. Successful establishment of *Wolbachia* in *Aedes* populations to suppress dengue transmission. *Nature* **476** (2011) 454–457.

[5] L. Lambrechts, N. M. Ferguson, E. Harris, E. C. Holmes, E. A. McGraw, S. L. O'Neill, E. E. Ooi, S. A. Ritchie, P. A. Ryan, T. W. Scott, C. P. Simmons, S. C. Weaver. Assessing the epidemiological effect of *Wolbachia* for dengue control. *The Lancet Infectious Diseases* **15** (2015) 862–866.

[6] Y. H. Ye, A. M. Carrasco, F. D. Frentiu, S. F. Chenoweth, N. W. Beebe, A. F. van den Hurk, C. P. Simmons, S. L. O'Neill, and E. A. McGraw. *Wolbachia* reduces the transmission potential of dengue-infected *Aedes aegypti*. *PLoS Neglected Tropical Diseases* **9** (2015) e0003894.

[7] F. D. Frentiu, T. Zakir, T.Walker, J. Popovici, A. T. Pyke, A. van den Hurk, E. A. McGraw, S. L. O'Neill. Limited dengue virus replication in field-collected *Aedes aegypti* mosquitoes infected with *Wolbachia*. *PLoS Negl Trop Dis.* **8** (2014) e2688.

[8] A. P. Turley, L. A. Moreira, S. L. O'Neill, E. A. McGraw. *Wolbachia* infection reduces blood-feeding success in the dengue fever mosquito, *Aedes aegypti*. *PLoS Neglected Tropical Diseases*. **3** (2009) e516.

[9] M. Turelli. Cytoplasmic incompatibility in populations with overlapping generations. *Evolution* **64** (2010) 232-241.

[10] H. L. Yeap, P. Mee, T.Walker, A. R.Weeks, S. L. O'Neill, et al., Dynamics of the "Popcorn" *Wolbachia* infection in outbred *Aedes aegypti* informs prospects for mosquito vector control. *Genetics* **187** (2011) 583-595.

[11] A. A. Hoffmann, I. Iturbe-Ormaetxe, A. G. Callahan, B. L. Phillips, K. Billington, J. K. Axford, B. Montgomery, A. P. Turley, and S. L. O'Neill, Stability of the *wMel Wolbachia* infection following invasion into *Aedes aegypti* populations. *PLoS Neglected Tropical Diseases* **8** (2014) e3115.

[12] M. Z. Ndii, R. I. Hickson, and G. N. Mercer, Modelling the introduction of *Wolbachia* into *Aedes aegypti* to reduce dengue transmission. *The ANZIAM Journal* **53** (2012) 213–227.

[13] A. K. Supriatna, N. Anggriani, Melanie, and H. Husniah, The optimal strategy of *Wolbachia*- infected mosquitoes release program: An application of control theory in controlling dengue disease. In: *Proc. International Conference on Instrumentation, Control and Automation (ICA)*. Bandung, Indonesia, 2016, 38–43.

[14] M. Z. Ndii, N. Anggriani, and A. K. Supriatna. Application of differential transformation method for solving dengue transmission mathematical model. In: *AIP Conference Proceedings*. Bandung, Indonesia, 2018, 020012.

[15] S. A. Alharbi, A. S. Rambely and A. O. Almatroud. Dynamic modelling of boosting the immune system and its functions by vitamins intervention. *Nonlinear Dynamics and System Theory* **19** (2) (2019) 263–273.

[16] B. Benaid, H. Bouzahir, C. Imzegouan, and F. E. Guezar. Stability analysis for stochastic neural networks with markovian switching and infinite delay in a phase space. *Nonlinear Dynamics and System Theory* **19** (3) (2019) 372–385.

[17] S. Boudiar, A. Ouannas, S. Bendoukha, and A. Zarair. Coexistence of different types of chaos synchronization between non-identical and different dimensional dynamical systems. *Nonlinear Dynamics and System Theory* **18** (2) (2018) 253–258.

[18] N. M. Ferguson, D. T. Hue Kien, H. Clapham, R. Aguas, V. T. Trung, T. N. Bich Chau, J. Popovici, P. A. Ryan, S. L. O'Neill, E. A. McGraw, V. T. Long, L. T. Dui, H. L. Nguyen, N. V. Vinh Chau, B. Wills, and C. P. Simmons. Modeling the impact on virus transmission of *Wolbachia*-mediated blocking of dengue virus infection of *Aedes aegypti*. *Science Translational Medicine* **7** (2015) 279ra37.

[19] M. Z. Ndii, R. I. Hickson, D. Allingham, and G. N. Mercer, Modelling the transmission dynamics of dengue in the presence of *Wolbachia*. *Mathematical Biosciences* **262** (2015) 157–166.

[20] M. Z. Ndii, D. Allingham, R. I. Hickson, and K. Glass. The effect of *Wolbachia* on dengue dynamics in the presence of two serotypes of dengue: symmetric and asymmetric epidemiological characteristics. *Epidemiology and Infection* **144** (2016) 2874–2882.

[21] M. Z. Ndii, D. Allingham, R. Hickson, and K. Glass. The effect of *Wolbachia* on dengue outbreaks when dengue is repeatedly introduced. *Theoretical Population Biology* **111** (2016) 9–15.

[22] N. Anggriani, A. K. Supriatna, The effect of *Wolbachia* introduction and predatory in dengue disease transmission. *Advanced Science, Engineering and Medicine* **7** (2015) 864–868.

[23] L. J. S. Allen and L. Jr. Extinction thresholds in deterministic and stochastic epidemic models. *Journal of Biological Dynamics* **6** (2012) 590–611.

[24] M. Z. Ndii and A. Supriatna. Stochastic mathematical models in epidemiology. *Information* **20** (2017) 6185–6196.

[25] L. Allen and P. van den Driessche. Relations between deterministic and stochastic thresholds for disease extinction in continuous and discrete time infectious disease models. *Mathematical Biosciences* **243** (2013) 99–108.

[26] A. A. Hoffmann, M. Turelli, and L. G. Harshman. Factors affecting the distribution of cytoplasmic incompatibility in Drosophila simulans. *Genetics* **126** (1990) 933–948.

[27] H. Hughes and N. Britton. Modelling the use of *Wolbachia* to control dengue fever transmission. *Bulletin of Mathematical Biology* **75** (2013) 796-818.

[28] T. W. Scott, P. H. Amerasinghe, A. C. Morrison, L. H. Lorenz, G. G. Clark, D. Strickman, P. Kittayapong, and J. D. Edman. Longitudinal studies of *Aedes aegypti (Diptera: Culicidae)* in Thailand and Puerto Rico: Blood feeding frequency. *Journal of Medical Entomology* **37** (2000) 89–101.

[29] G. Bian, Y. Xu, P. L., Y. Xie, and Z. Xi. The endosymbiotic bacterium *Wolbachia* induces resistance to dengue virus in *Aedes aegypti*. *PLoS Pathogen* **6** (2010) e1000833.

[30] D. J. Gubler. Dengue and dengue hemorrhagic fever. *Clinical Microbiology Reviews* **11** (1998) 480–496.

[31] G. Chowel, P. Diaz-Duenas, J. C. Miller, A. A. Velazco, J. M. Hyman, P. W. Fenimore, and C. Castillo-Chaves. Estimation of the reproduction number of dengue fever from spatial epidemic data. *Mathematical Biosciences* **208** (2007) 571–589.

[32] H. M. Yang, M. L. G. Macoris, K. C. Galvani, M. T. M. Andrighetti, and D. M. V. Wanderley. Assessing the effects of temperature on the population of *Aedes aegypti*, the vector of dengue. *Epidemiology and Infection* **137** (2009) 1188–1202.

Appendix

Parameter Descriptions

The following table presents the parameter descriptions and values of the models.

Table 2: The description, values, units, and references of the parameters for the mathematical model. The letter W is to denote *Wolbachia*.

Symbol	Description	Value	Unit	Source
α	Maternal transmission	0.9	N/A	[3, 12, 26]
b_N	Biting rate	0.63	day^{-1}	[28]
ρ_W	Reproductive rate of *Wolbachia*-carrying mosquitoes	$0.95\rho_N$	N/A	[3]
T_{HW}	Transmission probability from *Wolbachia*-carrying mosquitoes to human	$0.5T_N$	N/A	[29]
μ_W	Death rate of *Wolbachia*	1.1 μ_N	N/A	[3, 10]
b_W	Biting rates of *Wolbachia*-carrying mosquitoes	0.95 b_N	N/A	[8]
γ_H	Progression rate from exposed to infectious human	1/5.5	day^{-1}	[30]
γ_N	Progression from exposed to infectious non-W	1/10	day^{-1}	[31]
γ_W	Progression rate from exposed to infectious	1/10	day^{-1}	[31]
μ_N	Adult mosquito death rate (non-W)	1/14	day^{-1}	[32]
μ_{NA}	Death rate of aquatic non-W	1/14	day^{-1}	[32]
μ_{WA}	Aquatic death rate	1/14	day^{-1}	[32]
ρ_N	Reproductive rate of non-W	1.25	day^{-1}	[12]
σ	Recovery rate	1/5	day^{-1}	[30]
T_N	Transmission probability	0.2614	N/A	[19]
τ_N	Maturation rate of non-W	1/10	day^{-1}	[32]
τ_W	Maturation rate of W	1/10	day^{-1}	[32]