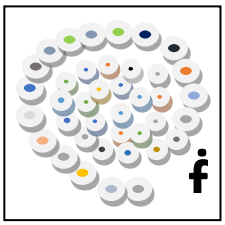

Journal of the Nigerian Society for Mathematical Biology

Volume 3, 2020

ISSN (Print): 2682 - 5694
ISSN (Online): 2682 - 5708

Journal of the Nigerian Society for Mathematical Biology
Volume 3 (2020), pp. 21 - 33

Mathematical model for the introduction of Wolbachia-infected mosquitoes to stop the spread of Yellow Fever

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Abstract

In this paper, we model the use of wolbachia-infected aedes aegypti mosquitoes to control the spread of yellow fever. Yellow fever is spread through bites of infected and uninfected aedes aegypti mosquitoes. The model, which is a system of non-linear ordinary differential equations, describes the transmission dynamics of the disease in the human population, natural aedes aegypti mosquitoes population and wolbachia-infected mosquitoes used for control. The expression for the control reproduction number of the disease is derived through the next generation matrix approach. In the stability analysis, the Gershgorin's theorem is used to obtain the condition under which the disease-free equilibrium is locally asymptotically stable. Also, in the absence of wolbachia-infected mosquitoes, the disease-free equilibrium is locally asymptotically stable if the basic offspring number and the basic reproduction number are less than one. The presented numerical results show that the population of the wolbachia-free aedes aegypti mosquitoes diminishes over time as compared to the population of the wolbachia-infected mosquitoes. These results confirm that the use of wolbachia can be effective in combating the spread of yellow fever.

Keywords: yellow fever; aedes aegypti; wolbachia; offspring number

1 Introduction

Yellow fever, a hemorrhagic fever caused by Flavivirus, family Flaviviridae is primarily transmitted to human through the bite of an infected female aedes aegypti. This mosquito also transmits dengue, chikungunya and zika[8, 9]. The origin of the disease is Africa, from where it spreads to South America through the slave trade in the 17th century[12, 14]. The yellow fever was the first human virus discovered and its family comprises approximately 70 viruses[9, 7], most of which are transmitted through arthropod insects. For those infected, the disease incubates in the first 3-6 days of onset, after which there is abrupt " period of infection " of the intense viremia lasting for 2-4 days (fever, weakness, headache, nausea, muscle pain)[7]. This is followed by a period of remission in which the symptoms reduce and settle and most infected individuals recover at this stage. Thus some 85% of yellow fever infections are asymptomatic and then 15% of patients relapse and move to a "period of intoxication "characterized by abdominal pain, vomiting, jaundice (yellow skin and eyes) and often culminating in death. Recent developments in epidemiological studies have shown that mathematical modeling played a significant role in the fight against infectious diseases and incessant disease outbreaks [6]. However, the control of these diseases can be achieved by acting on the mosquito population and in absence of vaccine or curative treatment, control turns out to be an important tool in the mission of reducing

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transmission. However, the traditional use of insecticides is often excessively expensive and environmentally undesirable and could lead to its resistance [20, 17].
In this work, we model the use of wolbachia bacterium which is a novel, natural and self- sustaining approach to reduce arboviral diseases such as Dengue, zika virus disease, etc, transmitted by aedes aegypti mosquitoes[4]. The symbolic Wolbachia is found naturally in over 60% of insect species, but not in aedes aegypti, which lives in the testes and ovaries of their hosts and is passed from one generation to the next through the eggs of mosquitoes[19]. Thus, they can interfere with the reproductive process of mosquitoes causing phenomena such as cytoplasmic incompatibility (C.I), parthenogenesis and fertilization of genetic males[4]. Appearances of these phenotypes depend on the host species and Wolbachia types. C.I causes uninfected Wolbachia females that mate with the infected Wolbachia males to rarely produce fertile eggs, while infected Wolbachia females are not affected. This gives the infected Wolbachia females an advantage and helps the bacteria to spread quickly through the mosquito population, which effectively block the reproduction of the vector mosquitoes[2].

2 Model Formulation

The mosquito population is made up of the wild(or wolbachia-free) (N) and wolbachia-infected aedes aegypti mosquitoes(W), with the classes Eggs(E_j), adult male mosquitoes(M_i), adult female mosquitoes that are not pregnant(F_i), and pregnant mosquitoes, which are either susceptible mosquitoes, (S_i),the exposed mosquitoes, (E_i) or infectious mosquitoes,(I_i), where $i = N, W$ and $j = 1, 2$. We assume that only the pregnant female mosquitoes bite humans since they need the blood to nourish their eggs after mating. Let $T_i = S_i + E_i + I_i$, be the total female pregnant mosquitoes. We assume that these pregnant mosquitoes lay eggs at the rate α, to produce the quantity of eggs, $\alpha F_i(1 - \frac{E_1+E_2}{K})$, where K is the carrying capacity of the environment. The laid eggs mature to either adult males (M_N) or adult females (F_N) in the numbers, $\epsilon m(1-c)E_1$ and $\epsilon(1-m)(1-c)E_1$, respectively, for wolbachia-free mosquitoes and $\epsilon m E_2$ and $\epsilon(1-m)E_2$, respectively, for adult male and female wolbachia-carrier mosquitoes, where ϵ is the rate of maturity of eggs into adult mosquitoes, m is the proportion of eggs that mature into adult males and c is the proportion of the eggs that are affected by cytoplasmic incompatibility(CI), hence, $(1 - c)$ is the proportion of the eggs that are not affected by CI. We take $c = 0$ for the case of wolbachia-infected mosquitoes, since their eggs are not affected by cytoplasmic incompatibility. The eggs are assumed to die at the rate,μ_0. The adult female mosquitoes comprise the female mosquitoes that have matured from eggs and the ones that migrated into the area at the recruitment level,π_1. The adult uninfected female mosquitoes become susceptible after mating with males of both species of mosquitoes. The process of mating and becoming pregnant is modeled through the expression $\rho F_i \frac{M_N+M_W}{M_N+M_W+M_\Theta}$, where ρ is the mating rate, and M_Θ is the number of male mosquitoes other than aedes aegypti. These male mosquitoes are assumed to interfere in the mating of aedes aegypti mosquitoes. The term $\frac{M_N+M_W}{M_N+M_W+M_\Theta}$ can be regarded as the probability of mating with wild male mosquitoes,M_N or wolbachia-infected males mosquitoes,M_W. Therefore, in the analysis and implementation of the model, we take $\frac{M_N}{M_N+M_W+M_\Theta} = p$ and $\frac{M_W}{M_N+M_W+M_\Theta} = q$ so that $\frac{M_N+M_W}{M_N+M_W+M_\Theta} = p+q$. The susceptible mosquitoes get exposed to the virus when they bite infectious humans at the rates, $b_1\alpha_{HN}$ and $b_1\alpha_{HW}$, respectively for wolbachia-free and wolbachia-carrier mosquitoes, respectively, where b_1 and b_2 are the biting rates of wolbachia-free and wolbachia-carrier mosquitoes, respectively, and α_{HN} and α_{HW} are the transmission probabilities of the virus from infected humans to wolbachia-free and wolbachia-carrier mosquitoes, respectively. The susceptible mosquitoes are also recruited through migration at the rate, π_3. The mosques become infectious at the incubation rates, β_N and β_W for wolbachia-free and wolbachia-carrier mosquitoes, respectively, where, $\beta_W \ll \beta_N$. The infectious mosquitoes remain so until they die naturally at the rate, μ_1. The susceptible class in the human population increases due to recruitment at the level, π_4, and those who

have recovered from the illness at the rate, η. This class decreases due to natural death of humans at the rate, μ_2 and when they are infected with yellow fever through the bites of infected wolbachia-free and wolbachia-carrier mosquitoes at the rates, $b_1\alpha_{NH}$ and $b_2\alpha_{WH}$, respectively, where α_{NH} and α_{WH} are the transmission probabilities of the virus from infected wolbachia-free and wolbachia-carrier mosquitoes, respectively to humans such trhat $\alpha_{WH} \lll \alpha_{NH}$. After contracting the virus, humans become infectious at the expiration of the incubation period, $\frac{1}{\beta_H}$, where, β_H is the incubation rate of the virus in humans. The infected humans are assumed to recover from the disease at the rate, γ. while the disease-induced death occurs at the rate, δ. The associated system of ordinary differential equations based on the interactions amongst the three populations is given by

$$\begin{aligned}
\frac{dE_1}{dt} &= \alpha T_N\left(1-\frac{E_1+E_2}{K}\right)-\epsilon(1-c)(1-m)E_1-\epsilon m(1-c)E_1-\mu_0E_1\\
\frac{dM_N}{dt} &= \epsilon m(1-c)E_1-\mu_1M_N\\
\frac{F_N}{dt} &= \pi_1+\epsilon(1-c)(1-m)E_1-\rho F_N\frac{M_N+M_w}{M_N+M_w+M_\theta}-\mu_1F_N\\
\frac{dS_N}{dt} &= \pi_2+\rho F_N\frac{M_N+M_w}{M_N+M_w+M_\theta}-b_1\alpha_{HN}S_NI_H-\mu_1S_N\\
\frac{dE_N}{dt} &= b_1\alpha_{HN}S_NI_H-(\beta_N+\mu_1)E_N\\
\frac{dI_N}{dt} &= \beta_NE_N-\mu_1I_N\\
\frac{dE_2}{dt} &= \alpha T_W\left(1-\frac{E_1+E_2}{K}\right)-\epsilon(1-m)E_2-\epsilon mE_2-\mu_1E_2\\
\frac{dM_W}{dt} &= \epsilon mE_2-\mu_1M_W\\
\frac{F_W}{dt} &= \pi_3+\epsilon(1-m)E_2-\rho F_N\frac{M_N+M_w}{M_N+M_w+M_\theta}-\mu_1F_W\\
\frac{dS_W}{dt} &= \rho F_W\frac{M_N+M_w}{M_N+M_w+M_\theta}-b_2\alpha_{HW}S_WI_H-\mu_1S_W\\
\frac{dE_W}{dt} &= b_2\alpha_{HW}S_WI_H-(\beta_W+\mu_1)E_W\\
\frac{dI_W}{dt} &= \beta_WE_W-\mu_1I_W\\
\frac{dS_H}{dt} &= \pi_4+\eta R_H-b_1\alpha_{NH}S_HI_N-b_2\alpha_{WH}S_HI_W-\mu_2S_H\\
\frac{dE_H}{dt} &= b_1\alpha_{NH}S_HI_N+b_2\alpha_{WH}S_HI_W-(\beta_H+\mu_2)E_H\\
\frac{dI_H}{dt} &= \beta_HE_H-(\gamma+\delta+\mu_2)I_H\\
\frac{dR_H}{dt} &= \gamma I_H-(\eta+\mu_2)R_H
\end{aligned} \tag{1}$$

with the initial condition $X_0 = (E_1^0, M_N^0, F_N^0, S_N^0, E_N^0, I_N^0, E_2^0, M_W^0, F_W^0, S_W^0, E_W^0, I_W^0, S_H^0, E_H^0, I_H^0, R_H^0)$ which are all nonnegative quantities. The domain of existence of solution to the IVP can be described as $\mathcal{D} = \mathcal{D}_1 \cup \mathcal{D}_2 \cup \mathcal{D}_3$, where

$$\mathcal{D}_1 = \{(E_1, M_N, F_N, S_N, E_N, I_N) \in \mathbb{R}_+^6 | E_1 + M_N + F_N + S_N + E_N + I_N \leq T_1\}$$

$$\mathcal{D}_2 = \{(E_2, M_W, F_W, S_W, E_W, I_W) \in \mathbb{R}_+^6 | E_2 + M_W + F_W + S_W + E_W + I_W \leq T_2\}$$

$$\mathcal{D}_3 = \{(S_H, E_H, I_H, R_H) \in \mathbb{R}_+^4 | S_H + E_H + I_H + R_H \leq T_3\}$$

where $T_1(t), T_2(t)$ and $T_3(t)$ are respectively, the total population of normal mosquitoes, wolbachia-infected mosquitoes and humans, at any time t.

2.1 Model Properties

2.1.1 Existence and Uniqueness of Model Solution

All functions in the right-hand of the model equation (1) have continuous partial derivatives with respect to the state variables on $\mathcal{D}$. Therefore, the model IVP possesses a unique solution.

2.1.2 Positivity of Model Solution and positive invariance

Here, we follow the method described in [5] to show that all the components of the solution are nonnegative $\forall t > 0$, and that all the trajectories enter and remain in $\mathcal{D}$ at all times, $t \geq 0$. Let $(E_1^*(t), M_N^*(t) \cdots, R_H^*(t))$ be a fixed solution to the IVP(1) through the initial solution, X_0, on $[0, \tau)$, for a real τ. By continuity of the solution on $[0, \tau)$, there exists a τ_1, $0 < \tau_1 < \tau$, such that $E_1^*(t') > 0, M_N^*(t') > 0 \cdots, R_H^*(t') > 0$ for any $t' \in [0, \tau_1]$. So on $[0, \tau_1]$, we have
$\frac{dE_1^*(t)}{dt} > -(\epsilon(1-c)+\mu_0)E_1^*(t) \implies E_1^*(t) > E_1(0)e^{-(\epsilon(1-c)+\mu_0)t} > 0$,
$\frac{dM_N^*(t)}{dt} > -\mu_1 M_N^*(t) \implies M_N^*(t) > M_N(0)e^{-\mu_1 t} > 0$. In this manner, all other components of the solution can be shown to be positive on $[0, \tau_1]$. Since the solution is continuous on $[0, \tau)$, we have that the solution is positive on $[0, \tau)$. So all the components of the solution are bounded below by a positive number on $[0, \tau)$. So, $\lim_{t \to \tau^-}(E_1^*(t), M_N^*(t) \cdots, R_H^*(t)) > 0$. This shows that all the solution components can be continuously extended to $[0, \tau]$, and $\mathcal{D}$ is invariant with respect to the semi-flow defined by the model system on $[0, \tau]$. Consequently, $[0, \infty)$ is the maximal interval of existence of the solution[11]. Hence, the solution is nonnegative at all times, and $\mathcal{D}$ is positively invariant.

3 Effective Reproduction Number

The effective reproduction number of a disease infection gives on average, the number of secondary infections that would be recorded when an index case is introduced in a purely susceptible population in the presence of any control measure applied to stop the spread of the disease. The control measure is effective if the effective reproduction number is less than one. Otherwise, the control measure is ineffective, and should be discarded. The method of determining the effective reproduction number, $\mathcal{R}_{eff}$ of the disease is based on the next generation matrix approach where the reproduction number is given by the spectral radius of the next generation matrix:$\mathcal{R}_{eff} = \rho(FV^{-1})$, where FV^{-1} is called the next generation matrix. Tthe matrices F and V are easily calculated from the model system as described in[1] and in other articles on infectious disease modeling.

Theorem 1 *Given the disease-free equilibrium* $\Gamma^0 = (E_1^*, M_N^*, F_N^*, S_N^*, 0, 0, E_2^*, M_W^*, F_W^*, 0, 0, 0, S_H^*, 0, 0, 0)$,
with $E_1^* = \frac{(K-E_2^*)\alpha S_N^*}{\alpha S_N^* + K\epsilon(1-c)(1-m)+\mu_0}$, $M_N^* = \frac{em(1-c)E_1^*}{\mu_1}$, $F_N^* = \frac{\pi_1+\epsilon(1-c)(1-m)E_1^*}{\rho(p+q)+\mu_1}$, $S_N^* = \frac{\pi_2+\rho(p+q)F_N^*}{\mu_1}$
$E_2^* = \frac{(K-E_1^*)\alpha S_W^*}{\alpha S_W^* + K\epsilon(1-m)+\mu_e}$, $M_W^* = \frac{\epsilon m E_2^*}{\mu_1}$, $F_W^* = \frac{\pi_3+\epsilon(1-m)E_2^*}{\rho(p+q)+\mu_2}$, $S_W^* = \frac{\rho(p+q)F_W^*}{\mu_1}, S_H^* = \frac{\pi_4}{\mu_2}$,
the model has a next generation matrix of the form

$$\mathcal{K} = \begin{pmatrix} 0 & \mathcal{K}_{NH} & \mathcal{K}_{WH} \\ \mathcal{K}_{HN} & 0 & 0 \\ \mathcal{K}_{HW} & 0 & 0 \end{pmatrix}, \tag{2}$$

and the effective reproduction number is

$$\mathcal{R}_{eff}^2 = \mathcal{K}_{NH}\mathcal{K}_{HN} + \mathcal{K}_{WH}\mathcal{K}_{HW} \tag{3}$$

where $\mathcal{K}_{NH} = \frac{\beta_N b_1 \alpha_{NH} S_H^*}{\mu_1(\beta_N+\mu_1)}$, $\mathcal{K}_{WH} = \frac{\beta_W b_2 \alpha_{WH} S_H^*}{\mu_1(\beta_W+\mu_1)}$, $\mathcal{K}_{HN} = \frac{\beta_H b_1 \alpha_{HN} S_N^*}{(\gamma+\delta+\mu_2)(\beta_H+\mu_2)}$, $\mathcal{K}_{HW} = \frac{\beta_H b_2 \alpha_{HW} S_W^*}{(\gamma+\delta+\mu_2)(\beta_H+\mu_2)}$

***proof*:** the size and the elements of the next generation matrix (2) are due to the three populations involved in the yellow fever dynamics as assumed in the model. Moreover, for the model,

$$F = \begin{pmatrix} 0 & 0 & 0 & b_1\alpha_{NH}S_H^* & 0 & b_2\alpha_{WH}S_H^* \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b_1\alpha_{HN}S_N^* & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b_2\alpha_{HW}S_W^* & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} \beta_H + \mu_2 & 0 & 0 & 0 & 0 & 0 \\ -\beta_H & \gamma + \delta + \mu_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_N + \mu_1 & 0 & 0 & 0 \\ 0 & 0 & -\beta_N & \mu_1 & 0 & 0 \\ 0 & 0 & 0 & 0 & \beta_W + \mu_1 & 0 \\ 0 & 0 & 0 & 0 & -\beta_W & \mu_1 \end{pmatrix}$$

so that the next generation matrix becomes

$$\mathcal{K} = \begin{pmatrix} 0 & 0 & \frac{\beta_N b_1 \alpha_{NH} S_H^*}{\mu_1(\beta_N+\mu_1)} & \frac{b_1\alpha_{NH}S_H^*}{\mu_1} & \frac{\beta_W b_2 \alpha_{WH} S_H^*}{\mu_1(\beta_W+\mu_1)} & \frac{b_2\alpha_{WH}S_H^*}{\mu_1} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\beta_H b_1 \alpha_{HN} S_N^*}{(\gamma+\delta+\mu_2)(\beta_H+\mu_2)} & \frac{b_1\alpha_{HN}S_N^*}{(\gamma+\delta+\mu_2)} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\beta_H b_2 \alpha_{HW} S_W^*}{(\gamma+\delta+\mu_2)(\beta_H+\mu_2)} & \frac{b_2\alpha_{HW}S_W^*}{(\gamma+\delta+\mu_2)} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

The multiplication of the form $A^T\mathcal{K}A$, where $A = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \end{pmatrix}^T$ is an auxiliary matrix, gives the desired structure(2). The largest eigenvalue of (2) is the effective reproduction number (3) of the model.□

4 Stability Analysis

In this section, we discuss the local asymptotic stability of the disease-free equilibrium for the complete system and in the absence of wolbachia-infected mosquitoes.

4.1 Local Stability of Γ^0 for the Complete System

The local asymptotic stability of the disease-free equilibrium is determined by the eigenvalues of the Jacobian matrix of the right-hand side of (1), evaluated at the disease-free equilibrium, Γ_0. Let $J(\Gamma^0)$ be the Jacobian matrix of the right-hand side of (1), evaluated at the disease-free equilibrium, Γ^0. If all the eigenvalues of $J(\Gamma^0)$ are negative or have negative real part, then Γ^0 is locally asymptotically stable. The disease-free equilibrium, Γ^0 is unstable if at least one eigenvalue of $J(\Gamma)$ is positive or have positive real part. From (1). we have that

$$J(\Gamma^0)=\begin{pmatrix}
-a_1 & 0 & 0 & a_2 & a_3 & a_4 & -a_5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
a_6 & -a_7 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
c_1 & 0 & -c_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & d_1 & -d_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -d_3 & 0\\
0 & 0 & 0 & 0 & -e_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & e_2 & 0\\
0 & 0 & 0 & 0 & f_1 & -f_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
-g_1 & 0 & 0 & 0 & 0 & 0 & -g_2 & 0 & 0 & g_3 & g_4 & g_5 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & h_1 & -h_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & k_1 & 0 & -k_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -m_1 & -m_2 & 0 & 0 & 0 & 0 & -m_3 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -n_1 & 0 & 0 & 0 & -n_2 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & -q_1 & 0 & 0 & 0 & 0 & -p_2 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & -q_1 & 0 & 0 & 0 & 0 & 0 & -q_2 & -q_3 & 0 & 0 & q_4\\
0 & 0 & 0 & 0 & 0 & s_1 & 0 & 0 & 0 & 0 & 0 & s_2 & 0 & -s_3 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & t_1 & -t_2 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & u_1 & -u_2
\end{pmatrix}$$

where $a_1=\frac{\alpha S_N^*}{K}+e(1-c)(1-m)+\mu_0),\ a_2=a_3=a_4=\alpha\left(1-\frac{E_1^*+E_2^*}{K}\right),\ a_5=\frac{\alpha S_N^*}{K}$
$c_1=e(1-c)(1-m),\ c_2=\rho(p+q)+\mu_1,\ d_1=\rho(p+q),\ d_2=\mu_1,\ d_3=b_1\alpha_{HN}S_N^*,\ e_1=\beta_N+\mu_1$
$e_2=b_1\alpha_{HN}S_N^*,\ f_1=\beta_N,\ f_2=\mu_1,\ g_1=\frac{\alpha S_W^*}{K},\ g_2=\frac{\alpha S_W^*}{K}+e(1-m)+\mu_0,$
$g_3=g_4=g_5=\alpha\left(1-\frac{E_1^*+E_2^*}{K}\right),\ h_1=em,\ e_2=\mu_1,\ k_1=e(1-m),\ k_2=\rho(p+q)+\mu_0,$
$m_1=\rho(p+q),\ m_2=\mu_1,\ m_3=b_2\alpha_{HW}S_W^*,\ n_1=\beta_W+\mu_1,\ n_2=b_2\alpha_{HW}S_W^*,\ p_1=\beta_W,$
$p_2=\mu_1,\ q_1=b_1\alpha_{NH}S_H^*,\ q_2=b_2\alpha_{WH}S_H^*,\ q_3=\mu_2,\ q_4=\eta,\ s_1=b_1\alpha_{NH}S_H^*,$
$s_2=b_2\alpha_{WH}S_H^*,\ s_3=\beta_H+\mu_2,\ t_1=\beta_N,\ t_2=(\gamma+\delta+\mu_2),\ u_1=\gamma,\ u_2=\eta+\mu_2.$
The eigenvalues of $J(\Gamma^0)$ are $a_7<0,\ h_2<0,\ q_3<0,\ u_2<0$ and the eigenvalues of the submatrix

$$J'(\Gamma^0)=\begin{pmatrix}
-a_1 & 0 & a_2 & a_3 & a_4 & -a_5 & 0 & 0 & 0 & 0 & 0 & 0\\
c_1 & -c_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & d_1 & -d_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -d_3\\
0 & 0 & 0 & -e_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & e_2\\
0 & 0 & 0 & f_1 & -f_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
-g_1 & 0 & 0 & 0 & 0 & -g_2 & 0 & g_3 & g_4 & g_5 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & k_1 & -k_2 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & -m_1 & -m_2 & 0 & 0 & 0 & -m_3\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -n_1 & 0 & 0 & -n_2\\
0 & 0 & 0 & 0 & 0 & -q_1 & 0 & 0 & 0 & -p_2 & 0 & 0\\
0 & 0 & 0 & 0 & s_1 & 0 & 0 & 0 & 0 & s_2 & -s_3 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & t_1 & -t_2
\end{pmatrix} \tag{4}$$

The theorem below gives the condition under which all the eigenvalues of $J'(\Gamma^0)$ are negative.

Theorem 2 (Gershgorin) *Let $A=a_{ij}$ be a complex $n\times n$ matrix with eigenvalues, λ. For $i\in n$, let $R_i=\sum_{j\neq i}|a_{ij}|$ be the sum of the absolute values of the non-diagonal entries in the i^{th} row. Let $D(a_{ii},R_i):=|\lambda-a_{ii}|\leq R_i$ be a closed disc centered at a_{ii} with radius R_i. Then, the eigenvalues of A belong to the union of the discs, $D(a_{ii},R_i)$.*

From the Gershgorin's theorem, we have that all the eigenvalues, λ of $J'(\Gamma^0)$ lie in the union of the closed disc $|\lambda - a_{ii}| \leq \sum_{j\neq i} |a_{ij}|$, $i, j = 1, 2, 3 \cdots 12$. Hence, we have

$$\begin{gathered}
-(a_1 + a_2 + 3a_3) \leq \lambda \leq a_2 + 3a_3 - a_1, \\
-(c_1 + c_2) \leq \lambda \leq c_1 - c_2, \\
-(d_1 + d_2 + d_3) \leq \lambda \leq d_1 + d_3 - d_2, \\
-(e_1 + e_2) \leq \lambda \leq e_2 - e_1, \\
-(f_1 + f_2) \leq \lambda \leq f_1 - f_2, \\
-(g_1 + g_2 + 3g_3) \leq \lambda \leq g_1 + 3g_3 - g_2 \\
-(k_1 + k_2) \leq \lambda \leq k_1 - k_2, \\
-(m_1 + m_2 + m_3) \leq \lambda \leq m_1 + m_3 - m_2, \\
-(n_1 + n_2) \leq \lambda \leq n_2 - n_1, \\
-(p_1 + p_2) \leq \lambda \leq p_1 - p_2, \\
-(s_1 + s_2 + s_3) \leq \lambda \leq s_1 + s_2 - s_3, \\
-(t_1 + t_2) \leq \lambda \leq t_1 - t_2
\end{gathered} \tag{5}$$

Therefore, if $J'(\Gamma^0)$ is strictly diagonally dominant, then Gershgorin's theorem ensures that $\lambda \in [-\Theta_1, -\Theta_2]$, where $-\Theta_1$ and $-\Theta_2$ are respectively, the minimum and maximum of the left-hand and right-hand sides of the inequalities in (5). Therefore, the disease-free equilibrium Γ^0 is locally asymptotically stable if $J'(\Gamma^0)$ is strictly diagonally dominant(SDD).

4.2 Local Stability of Γ^0 in the wolbachia-free mosquito system

We consider the stability of Γ^0 when the wolbachia-infected mosquitoes have not been introduced in the population. In this case, the disease-free equilibrium is $(E_1^*, M_N^*, F_N^*, S_N^*, E_N^*, I_N^*, S_H^*, E_H^*, I_H^*, R_H^*)$, and the associated Jacobian matrix is

$$J''(\Gamma^0) = \begin{pmatrix}
-a_1 & 0 & 0 & a_2 & a_3 & a_4 & 0 & 0 & 0 & 0 \\
a_6 & -a_7 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
c_1 & 0 & -c_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & d_1 & -d_2 & 0 & 0 & 0 & 0 & -d_3 & 0 \\
0 & 0 & 0 & 0 & -e_1 & 0 & 0 & 0 & e_2 & 0 \\
0 & 0 & 0 & 0 & f_1 & -f_2 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & q_1 & -q_2 & 0 & 0 & q_3 \\
0 & 0 & 0 & 0 & 0 & s_1 & 0 & -s_2 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & t_1 & -t_2 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & u_1 & -u_2
\end{pmatrix} \tag{6}$$

Eliminating the rows and columns containing the entries $a_7 < 0, q_2 < 0, u_2 < 0$, and transforming the remaining submatrix to an upper traingular matrix, we find that all the eigenvalues of $J''(\Gamma^0)$ are negative if

$$K_{offN} < 1 \quad \text{and} \quad \mathcal{R}_0^2 < 1$$

where

$$K_{offN} = \frac{\alpha\left(1 - \frac{E_1^*}{K}\right)\epsilon(1-c)(1-m)\rho p}{\left(\frac{\alpha S_N^*}{K} + \epsilon(1-c)(1-m) + \mu_0\right)(\rho p + \mu_1)\mu_1}$$

is the basic offspring number of the mosquito, and

$$\mathcal{R}_0^2 = \frac{b_1\beta_H\alpha_{HN}S_N^*}{(\beta_H + \mu_2)(\gamma + \delta + \mu_2)} \frac{\beta_N b_1 \alpha_{NH} S_H^*}{\mu_1(\beta_N + \mu_1)}$$

is the basic reproduction number of the disease in the absence of wolbachia-infected mosquitoes used for control, Therefore, the disease-free equilibrium in the absence of wolbachia-infected mosquitoes is locally asymptotically stable if $K_{offN} < 1$ and $\mathcal{R}_0 < 1$, simultaneously. This shows that ther disease-free equilibrium is locally asymptotically stable if the average number of mosquito offspring produced by each adult female mosquito is less than one, and if the average number of persons infected by a single index case of yellow fever in a purely susceptible human and mosquito population is less than one.

5 Numerical Simulations

The simulation of the model is carried out with the following initial solution and the parameter values in Table 1. $E_1^0 = 1000, M_N^0 = 1000, F_N^0 = 1200, S_N^0 = 10000, E_N^0 = 1000, I_N^0 = 12000, E_2^0 = 0, M_W^0 = 100, F_W^0 = 1000, S_W = 10000, E_W^0 = 0, I_N^0 = 0, S_H = 10000, E_H^0 = 1300, I_H^0 = 1500, R_H^0 = 50, \Pi_1 = 150, \pi_2 = 150, \pi_3 = 10000, \pi_4 = 100, K = 20000$.In table 1, we chose parameters of the wolbachia-infected mosquitoes based on the parameters of the normal mosquitoes. For example, the incubation period of yellow fever virus in the normal mosquitoes is 12 days. Hence, we choose the incubation period of the virus in the wolbachia-infected mosquito to be double that of the normal mosquito, which is 24 days.This is because wolbachia increases the incubation period of the virus in its host mosquito. Also, the probability of transmission α_{WH} of the virus from wolbachia-infected mosquitoes is chosen so that it is much smaller than that of the normal mosquitoes, since wolbachia reduces the ability of the mosquitoes to transmit the virus to humans. The result of the numerical experiment is given in Figures 1-6. In the graphs, 'N' represents normal aedes aegypti mosquitoes, while 'W' represents wolbachia-infected aedes aegypti mosquitoes.

Parameter	*Value*	*Source*	*Parameter*	*Value*	*Source*
m	0.6	[3]	μ_2	3.5×10^{-5}	[13]
μ_0	0.0005	[10]	e	1/6.67	[10]
α_{HN}	0.175	[21]	γ	0.143	[13]
α_{HW}	0.175	[21]	α_{WH}	0.0005	assumed
μ_1	0.09	[13]	α_{NH}	0.175	[21]
β_H	1/5	[8]	q	0.25	assumed
b_1	0.004	assumed	η	0.015	assumed
b_2	0.7	[21]	p	0.58	assumed
β_N	1/12	[19]	δ	3.5×10^{-4}	[13]
β_W	1/24	$\frac{1}{2}$ of β_N	α	0.15	assumed
ρ	0.075	assumed	c	0.6	assumed

Table 1: Parameter Values used in this model

6 Results and Discussion

The graphs depict the impact of wolbachia-infected mosquitoes on the population of wolbachia-free mosquitoes. Figure 1 shows the quantity of eggs produced by the normal mosquitoes(N) and the wolbachia-infected mosquitoes(W) in a given period of time. From the graph, we see that the quantity of eggs produced by the normal mosquitoes rises slightly and begins to decrease as the eggs produced by the wolbachia-infected mosquitoes increase. The reduction in the quantity of eggs produced by the normal mosquitoes is attributed to cytoplasmic incompatibility, which prevents eggs produced by the normal female mosquitoes from hatching, when mated by

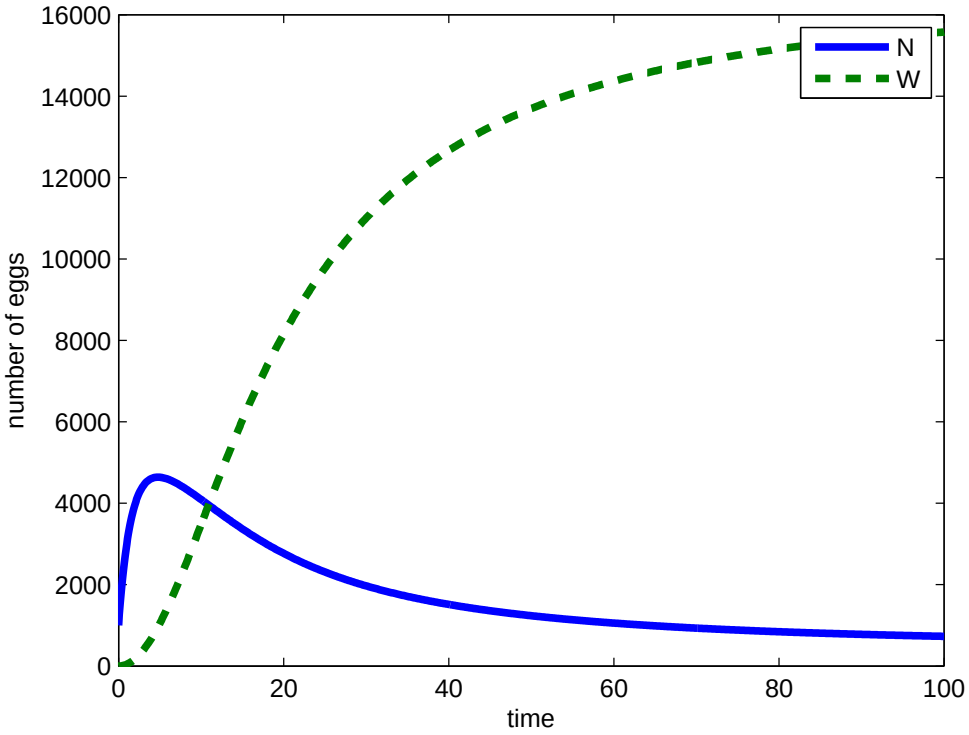

Figure 1: Quantity of Eggs produced by the mosquitoes

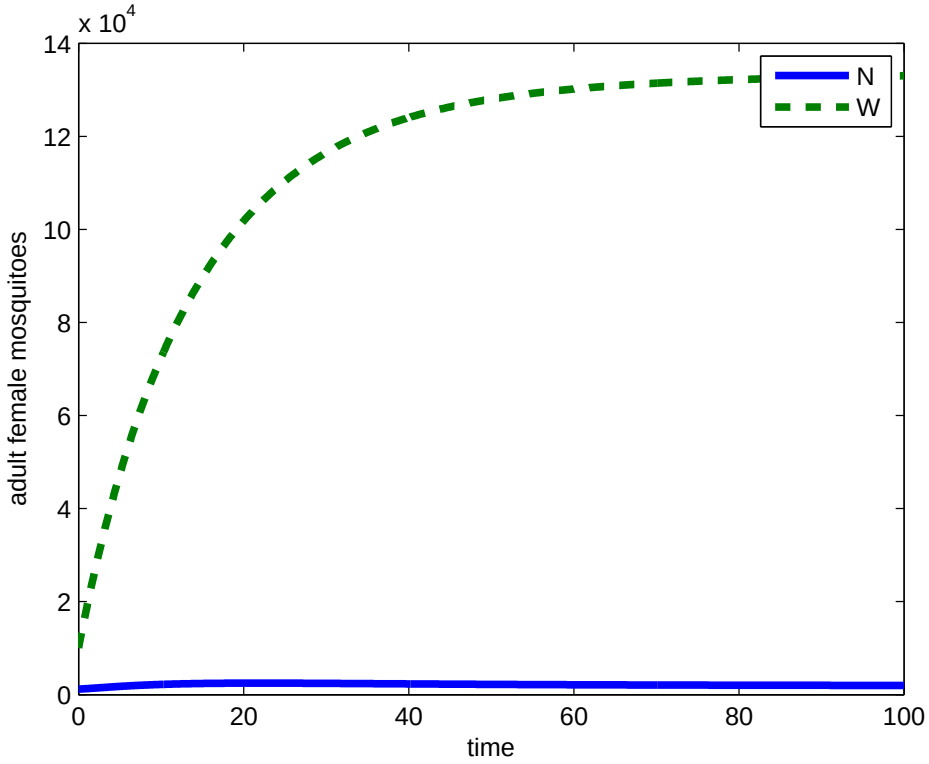

Figure 2: Number of adult female mosquitoes

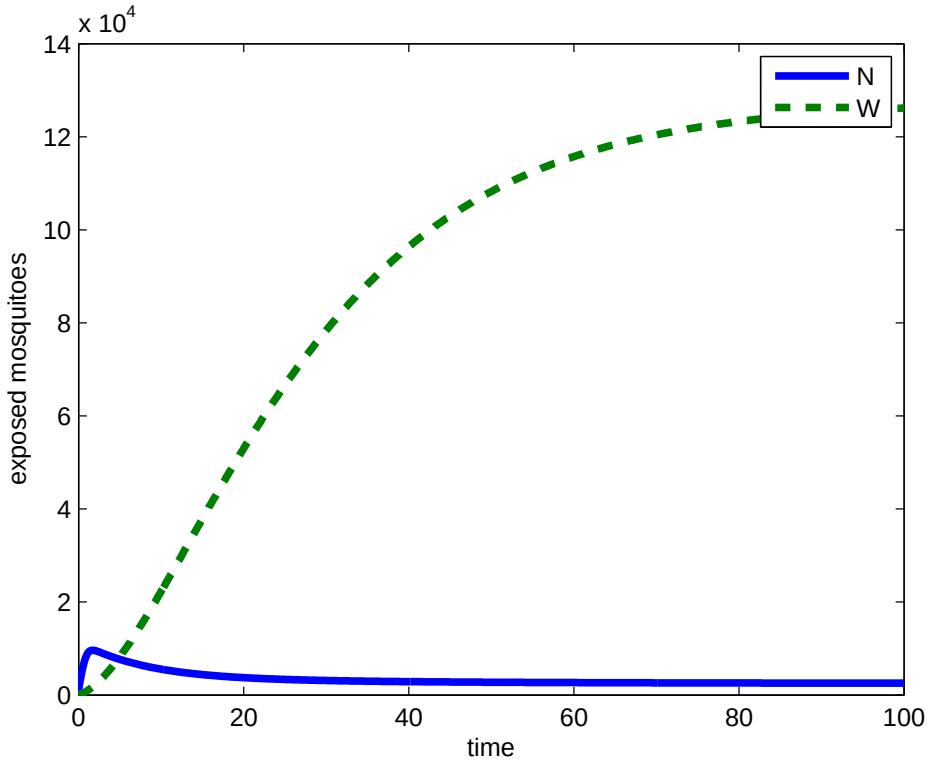

Figure 3: Number of exposed mosquitoes

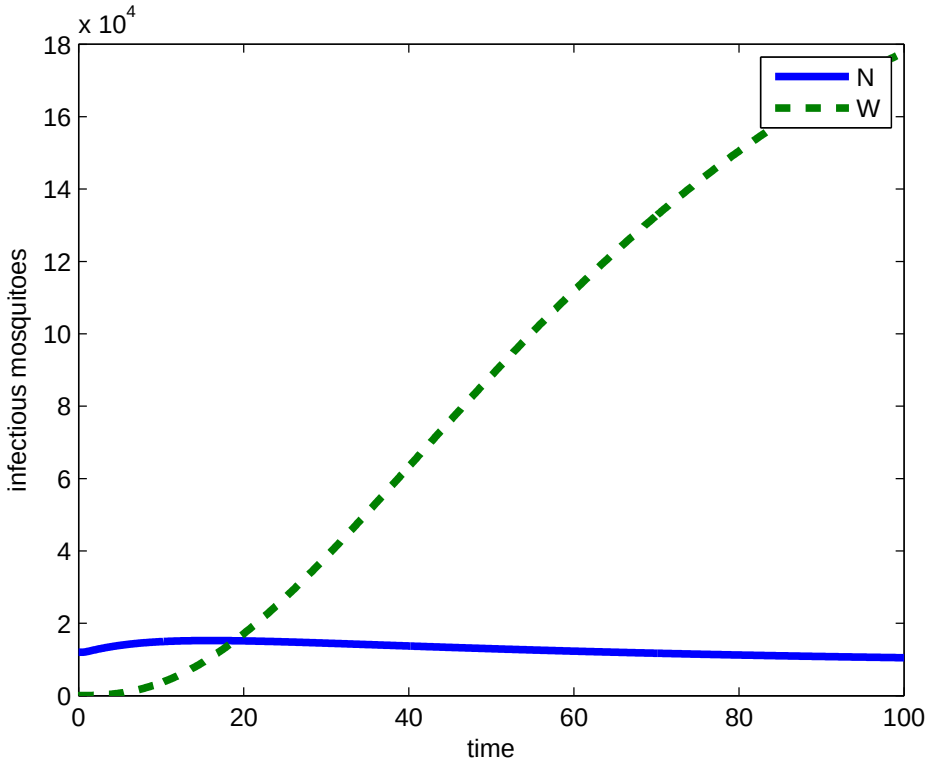

Figure 4: Number of infectious mosquitoes

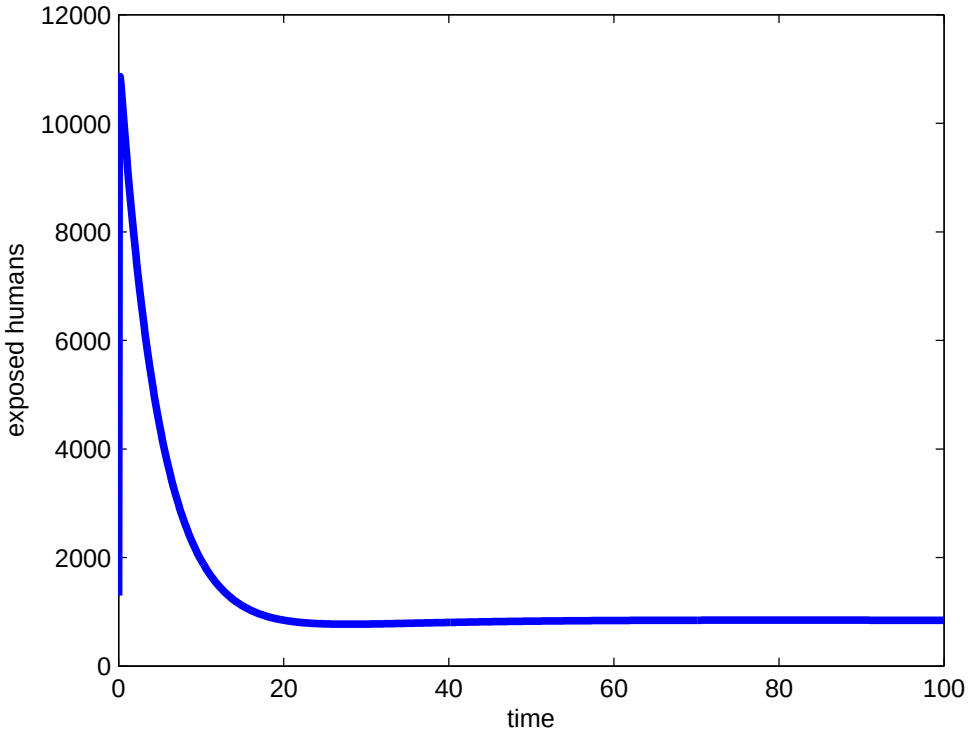

Figure 5: Number of exposed humans

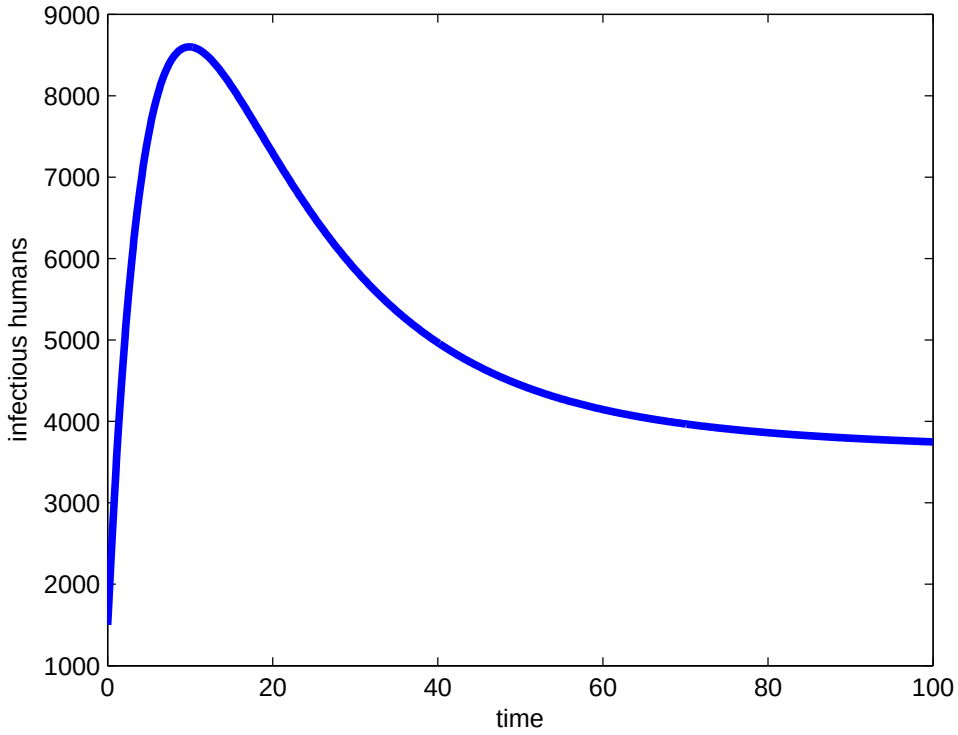

Figure 6: Number of infectious humans

wolbachia-infected male mosquitoes. The reduction in the number of eggs produced by the normal mosquitoes leads to reduction in the emerging normal adult female mosquitoes as shown in figure 2, figure 3 and figure 4. In figure 5 and figure 6, we notice an initial increase in the exposed and infectious human classes, which later decrease as time increases. The period of increase in the size of exposed and infectious humans can be regarded as the period when wolbachia-infected mosquitoes have not fully established in the population. In this case, more normal infectious mosquitoes are available to bite and infect humans with yellow fever.

7 Conclusion

We have modeled the introduction of wolbachia into aedes argypti mosquitoes in order to curb the spread of yellow fever. An application of Gershgorin's theorem gives the condition under which the disease-free equilibrium of the model is locally asymptotically stable. In the absence of the wolbachia-infected mosquitoes used for control, we derived that the disease-free equilibrium is locally asymptotically stable if the basic offspring number of the normal mosquitoes and the basic reproduction number of the disease are simultaneously less than one. This agrees with the use of wolbachia-infected mosquitoes as control since it reduces the basic offspring number of the wild mosquitoes through the action of cytoplasmic incompatibility and reduces the basic reproduction number through reduction in the incubation rate of the virus in the wolbachia-infected mosquitoes. Numerical simulations of the model also show that the population of the normal mosquitoes, including its eggs is reduced compared to the population of the wolbachia-infected mosquitoes which increases. This shows that the wolbachia-infected mosquitoes gradually replaces the normal mosquitoes in the area where yellow fever is endemic. In this case, less number of normal mosquitoes would be available to bite and transmit yellow fever virus to humans, and the more abundant wolbachia-infected mosquitoes would have less ability to transmit the disease to humans. We therefore conclude that releasing wolbachia-infected aedes aegypti mosquitoes in the area where yellow fever is endemic has the ability to prevent the disease from spreading in the population.

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