A Mathematical Model on the Biological Control of Malaria Transmission using Wolbachia

Netochukwu Onyiaji[1], Sunday I. Onah[2], Godwin C.E. Mbah[3].

ABSTRACT - This study shows that the transmission of malaria via mosquitoes to humans can be interrupted by injecting a strain of the bacteria, Wolbachia in the insects. Wolbachia acts as a vaccine of sorts for mosquitoes that would protect them from malaria parasites.

The analysis of the model was carried and disease free and endemic equilibrium points calculated. Using the method of the next generation matrix, the basic reproduction number of the disease was derived. To illustrate our theoretical analysis, some numerical simulations were carried out using MATLAB and recommendations given based on the results gotten. The mathematical model incorporating these results from the analysis predicts that infection with these endosymbionts will reduce malaria prevalence in human populations.

Index Terms—Wolbachia, Reproduction number, Stability, Numerical simulation, Malaria

1. INTRODUCTION

Malaria is a mosquito-borne infectious disease affecting humans and other animals caused by parasitic protozoans (a group of single-celled microorganisms) belonging to the *Plasmodium* type. Malaria causes symptoms that typically include fever, tiredness, vomiting, and headaches. In severe cases it can cause yellow skin, seizures, coma, or death.

Symptoms usually begin ten to fifteen days after being bitten by mosquito and the plasmodium transferred to the person. If not properly treated, people may have recurrences of the disease months later (Malaria Factsheet, 2014). In those who have recently survived an infection, reinfection usually causes milder symptoms. This partial resistance disappears over months to years if the person has no continuing exposure to malaria (Caraballo, 2014).

2. LITERATURE REVIEW

Mathematical modeling of malaria began with Ronald Ross, soon after his demonstration that malaria is transmitted by mosquitoes. The major advantage in Ross' model was his ability to provide a suitable control strategy through the transmission threshold criterion which is based on the reproductive capacity of the parasite which is referred to as basic reproduction number (R_0) (McKenzie, 2000).

Ross' model was extended by his researchers considering other factors such as latent period of infection in mosquitoes and humans, age related differential susceptibility to malaria in human population, acquired immunity and genetic heterogeneity or host parasite.

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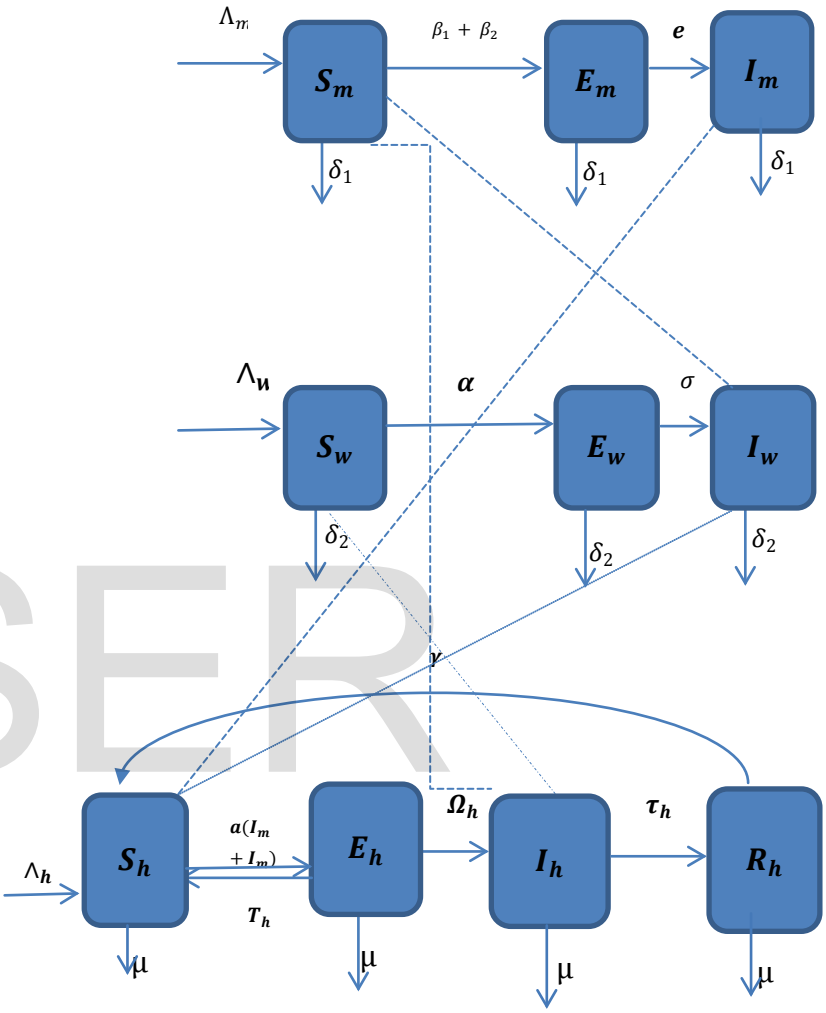
One of major mathematical modeling contribution to malaria transmission dynamics was by Dietz et al. (1974) and entailed the inclusion, into the basic Ross–Macdonald framework, of a kind of slowly-acquired immunity that results in a non-infectious parasitemia following inoculation that is cleared relatively rapidly. Non-immune hosts are assumed to manifest infectious clinical disease that transitions to a non-infectious parasitemia that is cleared slowly (Eikenberry, S. E., & Gumel, A. B. 2018).

Chitnis et al (2006) developed an SEIR model. The human population was divided into Susceptible, Exposed, Infected and Recovered class. In their work they analyzed an ordinary differential equation model for transmission of malaria with four classes for humans and three classes for mosquitoes. They showed that there exists a domain where the model is epidemiologically and mathematically well-posed. They proved the existence of an equilibrium point with no disease. They defined a reproductive number, R_0, that is epidemiologically accurate since it provides the expected number of new infections (in mosquitoes and humans) from one infectious individual (human or mosquito) over the duration of the infectious period, given that all other members of the population are susceptible. They showed that if $R_0 < 1$, then the disease free equilibrium point, is locally asymptotically stable and if $R_0 > 1$, then the disease free equilibrium is unstable. They also proved that an endemic equilibrium point exists for all $R_0 > 1$ with a trans-critical bifurcation at $R_0 = 1$.

W. Robert Shaw (2016) in their mathematical model on spread of malaria predicts that infection of *Anopheles* mosquitoes with Wolbachia may reduce malaria prevalence in human populations.

3. The Model

The flow diagram of the model is given in the figure below:



We take the probability of vertical transmission as 1. Other mechanisms of transmission are so rare that they may be neglected. When a *Wolbachia*-infected male mosquito fertilises an uninfected egg, whether it is uninfected because its mother was uninfected or because its mother was infected but vertical transmission failed, there is a certain probability that the zygote dies through cytoplasmic incompatibility (CI). We take the transmission probability as 1. *Wolbachia* can alter the fertility, longevity and plasmodium transmission potential of its host.

The model is given by

$$\frac{dS_m}{dt} = \wedge_m - \beta_1 S_m - \beta_2 S_m - \delta_1 S_m$$

$$\frac{dE_m}{dt} = \beta_1 S_m + \beta_2 S_m - eE_m - \delta_1 E_m$$

$$\frac{dI_m}{dt} = eE_m - \delta_1 I_m$$

Wobachia-free mosquitoes

$$\frac{dS_w}{dt} = \wedge_w - \alpha S_w - \delta_2 S_w$$

$$\frac{dE_w}{dt} = \alpha S_w - \sigma E_w - \delta_2 E_w$$

$$\frac{dI_w}{dt} = \sigma E_w - \delta_2 I_w$$

Wolbachia infected mosquitoes

$$\frac{dS_h}{dt} = \wedge_h + \gamma R_h + T_h E_h - \psi S_h - \mu S_h$$

$$\frac{dE_h}{dt} = \psi S_h - \Omega_h E_h - T_h E_h - \mu E_h$$

$$\frac{dI_h}{dt} = \Omega_h E_h - \tau_h I_h - \mu I_h - \delta_3 I_h$$

$$\frac{dR_h}{dt} = \tau_h I_h - \gamma R_h - \mu R_h$$

Human compartment

…… (1)

Here, $\wedge_m$ and $\wedge_w$ represent the basic recruitment rate of *Wolbachia*-free and *Wolbachia*-infected adults respectively.

$$\beta_1 = \frac{\lambda_1 I_h}{N_h}, \ \beta_2 = \frac{\lambda_2 I_w}{N_w}, \alpha = \frac{\lambda_3 I_h}{N_h}, \ \psi = \frac{\lambda_1 I_m + \lambda_3 I_w}{N_h}$$

4. Stability Analysis of the Model

Disease Free Equilibrium

Considering the Wolbachia free mosquitoes, Wolbachia-infected mosquitoes and the Human compartment, the steady state of equation (1) is given by $(S_m^+, E_m^+, I_m^+, S_w^+, E_w^+, I_w^+, S_h^+, E_h^+, I_h^+, R_h^+)$.

The disease free equilibrium state of the model equation (1) is given by:

$$(S_m^{t_0}, E_m^{t_0}, I_m^{t_0}, S_w^{t_0}, E_w^{t_0}, I_w^{t_0}, S_h^{t_0}, E_h^{t_0}, I_h^{t_0}, R_h^{t_0}) =$$

$$(\frac{\wedge_m}{\delta_1}, 0, 0, \frac{\wedge_w}{\delta_2}, 0, 0, \frac{\wedge_h}{\mu}, 0, 0, 0)$$

Equation (2) represents the rate in which there is no infection in the society.

Local Stability Of Disease Free Equilibrium

Invoking Theorem 2 in van den Driessche and Watmouh (2002), the DFE is locally asymptotically stable (LAS) whenever $R_0 < 1$ but unstable if $R_0 > 1$.

Basic Reproduction Number

The basic reproduction number (sometimes called basic reproductive ratio, and denoted R_0, *r nought*) of an infection can be thought of as the number of cases one case generates on average over the course of its infectious period, in an otherwise uninfected population

It has become common practice in the analysis of the simplest models to consider next the associated generation process and to define the basic reproduction ratio as the expected number of secondary cases produced, in a completely susceptible population, by a typical infected individual during its entire period of infectiousness. The famous threshold criterion then states: the disease can invade if R0 > 1, whereas it cannot if Ro < 1 (Diekmann, O., Heesterbeek, J., & Metz, J., 1990)

Using the next generation matrix the basic reproduction number was derived, which is given by:

$$R_0 = \left(\left(\frac{k^2 * p^2 * r^2}{4} - \left(\frac{m * r}{3} + \frac{p * t}{3}\right)^3\right)^{\frac{1}{2}} + \frac{k * p * r}{2}\right)^{\frac{1}{3}} + \frac{\frac{m * r}{3} + \frac{p * t}{3}}{\left(\left(\frac{k^2 * p^2 * r^2}{4} - \left(\frac{m * r}{3} + \frac{p * t}{3}\right)^3\right)^{\frac{1}{2}} + \frac{k * p * r}{2}\right)^{\frac{1}{3}}}$$

Where k $= \frac{\lambda_2 \wedge_m}{\delta_1 N_w} \frac{\sigma}{(\sigma+\delta_2)\delta_2}$, l $= \frac{\lambda_2 \wedge_m}{\delta_1 N_w} \frac{1}{\delta_2}$, m$= \frac{\lambda_1 \wedge_m}{\delta_1 N_h} \frac{\Omega_h}{(\Omega_h + T_h + \mu)(\tau_h + \mu + \delta_3)}$, n$= \frac{\lambda_1 \wedge_m}{\delta_1 N_h} \frac{1}{\tau_h + \mu + \delta_3}$,

p$= \frac{\lambda_1 \wedge_m}{\delta_1 N_h} \frac{1}{\tau_h + \mu + \delta_3}$, q$= \frac{\lambda_3 \wedge_w}{\delta_2 N_h} \frac{1}{\tau_h + \mu + \delta_3}$, r$= \lambda_1 \frac{e}{(e + \delta_1)\delta_1}$, s$= \frac{\lambda_1}{\delta_1}$, t$= \frac{\lambda_1}{\delta_1}$, u$= \frac{\lambda_3}{\delta_2}$

Endemic Equilibrium

The endemic equilibrium of the model equation (1) is given by,

EEP=$(\boldsymbol{S_m^e, E_m^e, I_{m,}^e S_w^e, E_w^e, I_w^e, S_h^e, E_h^e, I_h^e, R_h^e})$,

where $\left(\boldsymbol{S_m^e, E_m^e, I_{m,}^e S_w^e, E_w^e, I_w^e, S_h^e, E_h^e, I_h^e, R_h^e}\right) > 0$

We have,

S_h^e

$$= \frac{(\boldsymbol{\Omega_h + T_h} + \mu)(\boldsymbol{\tau_h} + \mu + \boldsymbol{\delta_3})\boldsymbol{N_h^2 \delta_1}(\boldsymbol{e} + \boldsymbol{\delta_1})\left(\boldsymbol{\lambda_1 I_h^e N_w} + \frac{\boldsymbol{\lambda_2 \sigma \lambda_3 I_h^e \wedge_w N_h}}{\boldsymbol{\delta_2 N_h}(\sigma + \boldsymbol{\delta_2})\left(\frac{\boldsymbol{\lambda_3 I_h^e + N_h \delta_2}}{\boldsymbol{N_h}}\right)} + \boldsymbol{\delta_1 N_h N_w}\right)\boldsymbol{\delta_2}(\sigma + \boldsymbol{\delta_2})\left(\frac{\boldsymbol{\lambda_3 I_h^e + N_h \delta_2}}{\boldsymbol{N_h}}\right)}{\boldsymbol{\lambda_1 e} \wedge_m \left(\boldsymbol{\lambda_1 N_w} + \frac{\boldsymbol{\lambda_2 \lambda_3 \sigma} \wedge_w \boldsymbol{N_h}}{\boldsymbol{\delta_2 N_h}(\sigma + \boldsymbol{\delta_2})\left(\frac{\boldsymbol{\lambda_3 I_h^e + \delta_2 N_h}}{\boldsymbol{N_h}}\right)}\right)\boldsymbol{N_h \delta_2 N_h}(\sigma + \boldsymbol{\delta_2})\left(\frac{\boldsymbol{\lambda_3 I_h^e + \delta_2}}{\boldsymbol{N_h}}\right)\boldsymbol{\Omega_h} + \sigma \boldsymbol{\lambda_3^2} \wedge_w \boldsymbol{N_h \delta_1}(\boldsymbol{e} + \boldsymbol{\delta_1})\left(\boldsymbol{\lambda_1 I_h^e N_w} + \frac{\boldsymbol{\lambda_2 \sigma \lambda_3 I_h^e} \wedge_w \boldsymbol{N_h}}{\boldsymbol{\delta_2 N_h}(\sigma + \boldsymbol{\delta_2})\left(\frac{\boldsymbol{\lambda_3 I_h^e + N_h \delta_2}}{\boldsymbol{N_h}}\right)} + \boldsymbol{\delta_1 N_h N_w}\right)\boldsymbol{\Omega_h}}$$

$$E_h^e = \frac{(\tau_h + \mu + \delta_3)I_h^e}{\Omega_h}$$

$$I_h^e = I_h^e$$

$$R_h^e = \frac{\tau_h I_h^e}{\gamma + \mu}$$

$$S_m^e = \frac{\wedge_{m N_h N_w}}{\boldsymbol{\lambda_1 I_h^e N_w} + \boldsymbol{\lambda_2} \frac{\sigma \frac{\boldsymbol{\lambda_3 I_h^e}}{\boldsymbol{N_h}} \wedge_w}{\boldsymbol{\delta_2}(\sigma + \boldsymbol{\delta_2})(\frac{\boldsymbol{\lambda_3 I_h^e}}{\boldsymbol{N_h}} + \boldsymbol{\delta_2})} \boldsymbol{N_h} + \boldsymbol{\delta_1 N_h N_w}}$$

$$E_m^e = \frac{\boldsymbol{\lambda_1} I_h^e}{\boldsymbol{N_h}(\boldsymbol{e} + \boldsymbol{\delta_1})} \frac{\wedge_{\boldsymbol{mN_hN_w}}}{\boldsymbol{\lambda_1} I_h^e \boldsymbol{N_w} + \boldsymbol{\lambda_2} \frac{\sigma \frac{\boldsymbol{\lambda_3} I_h^e}{\boldsymbol{N_h}} \wedge_{\boldsymbol{w}}}{\boldsymbol{\delta_2}(\sigma + \boldsymbol{\delta_2})(\frac{\boldsymbol{\lambda_3} I_h^e}{\boldsymbol{N_h}} + \boldsymbol{\delta_2})} \boldsymbol{N_h} + \boldsymbol{\delta_1 N_h N_w}}$$

$$+ \frac{\boldsymbol{\lambda_2} \frac{\sigma \frac{\boldsymbol{\lambda_3} I_h^e}{\boldsymbol{N_h}} \wedge_{\boldsymbol{w}}}{\boldsymbol{\delta_2}(\sigma + \boldsymbol{\delta_2})(\frac{\boldsymbol{\lambda_3} I_h^e}{\boldsymbol{N_h}} + \boldsymbol{\delta_2})}}{N_w(e + \delta_1)} \frac{\wedge_{\boldsymbol{mN_hN_w}}}{\boldsymbol{\lambda_1} I_h^e \boldsymbol{N_w} + \boldsymbol{\lambda_2} \frac{\sigma \frac{\boldsymbol{\lambda_3} I_h^e}{\boldsymbol{N_h}} \wedge_{\boldsymbol{w}}}{\boldsymbol{\delta_2}(\sigma + \boldsymbol{\delta_2})(\frac{\boldsymbol{\lambda_3} I_h^e}{\boldsymbol{N_h}} + \boldsymbol{\delta_2})} \boldsymbol{N_h} + \boldsymbol{\delta_1 N_h N_w}}$$

$$I_m^e = \frac{e\boldsymbol{\lambda_1} I_h^e \wedge_{\boldsymbol{mN_hN_w}}}{\boldsymbol{\delta_1}(e+\boldsymbol{\delta_1})N_h(\boldsymbol{\lambda_1} I_h^e N_w + \boldsymbol{\lambda_2} \frac{\sigma \frac{\boldsymbol{\lambda_3} I_h^e}{N_h} \wedge_{\boldsymbol{w}}}{\boldsymbol{\delta_2}(\sigma+\boldsymbol{\delta_2})(\frac{\boldsymbol{\lambda_3} I_h^e}{N_h}+\boldsymbol{\delta_2})} N_h + \boldsymbol{\delta_1} N_h N_w)} + \frac{e\boldsymbol{\lambda_2} \frac{\sigma \frac{\boldsymbol{\lambda_3} I_h^e}{N_h} \wedge_{\boldsymbol{w}}}{\boldsymbol{\delta_2}(\sigma+\boldsymbol{\delta_2})(\frac{\boldsymbol{\lambda_3} I_h^e}{N_h}+\boldsymbol{\delta_2})} \wedge_{\boldsymbol{mN_hN_w}}}{\boldsymbol{\delta_1}(e+\boldsymbol{\delta_1})N_w \boldsymbol{\lambda_1} I_h^e N_w + \boldsymbol{\lambda_2} \frac{\sigma \frac{\boldsymbol{\lambda_3} I_h^e}{N_h} \wedge_{\boldsymbol{w}}}{\boldsymbol{\delta_2}(\sigma+\boldsymbol{\delta_2})(\frac{\boldsymbol{\lambda_3} I_h^e}{N_h}+\boldsymbol{\delta_2})} N_h + \boldsymbol{\delta_1} N_h N_w}$$

$$S_w^e = \frac{\wedge_w}{\frac{\lambda_3 I_h^e}{N_h} + \delta_2}$$

$$E_w^e = \frac{\alpha}{\sigma + \boldsymbol{\delta_2}} \frac{\wedge_w}{\frac{\lambda_3 I_h^e}{N_h} + \delta_2}$$

$$I_w^e = \frac{\sigma \frac{\boldsymbol{\lambda_3} I_h^e}{\boldsymbol{N_h}} \wedge_{\boldsymbol{w}}}{\boldsymbol{\delta_2}(\sigma + \boldsymbol{\delta_2})(\frac{\boldsymbol{\lambda_3} I_h^e}{\boldsymbol{N_h}} + \boldsymbol{\delta_2})}$$

\

Local Stability of Endemic Equilibrium

We have that

J

$$= \begin{pmatrix} \frac{\partial S_m}{\partial S_m} & \frac{\partial S_m}{\partial E_m}\frac{\partial S_m}{\partial I_m} & \frac{\partial S_m}{\partial S_w}\frac{\partial S_m}{\partial E_w} & \frac{\partial S_m}{\partial I_w}\frac{\partial S_m}{\partial S_h} & \frac{\partial S_m}{\partial E_h}\frac{\partial S_m}{\partial I_h} & \frac{\partial S_m}{\partial R_h} \\ \frac{\partial E_m}{\partial S_m} & \frac{\partial E_m}{\partial E_m}\frac{\partial E_m}{\partial I_m} & \frac{\partial E_m}{\partial S_w}\frac{\partial E_m}{\partial E_w} & \frac{\partial E_m}{\partial I_w}\frac{\partial E_m}{\partial S_h} & \frac{\partial E_m}{\partial E_h}\frac{\partial E_m}{\partial I_h} & \frac{\partial E_m}{\partial R_h} \\ \frac{\partial I_m}{\partial S_m} & \frac{\partial I_m}{\partial E_m}\frac{\partial I_m}{\partial I_m} & \frac{\partial I_m}{\partial S_w}\frac{\partial I_m}{\partial E_w} & \frac{\partial I_m}{\partial I_w}\frac{\partial I_m}{\partial S_h} & \frac{\partial I_m}{\partial E_h}\frac{\partial I_m}{\partial I_h} & \frac{\partial I_m}{\partial R_h} \\ \frac{\partial S_w}{\partial S_m} & \frac{\partial S_w}{\partial E_m}\frac{\partial S_w}{\partial I_m} & \frac{\partial S_w}{\partial S_w}\frac{\partial S_w}{\partial E_w} & \frac{\partial S_w}{\partial I_w}\frac{\partial S_w}{\partial S_h} & \frac{\partial S_w}{\partial E_h}\frac{\partial S_w}{\partial I_h} & \frac{\partial S_w}{\partial R_h} \\ \frac{\partial E_w}{\partial S_m} & \frac{\partial E_w}{\partial E_m}\frac{\partial E_w}{\partial I_m} & \frac{\partial E_w}{\partial S_w}\frac{\partial E_w}{\partial E_w} & \frac{\partial E_w}{\partial I_w}\frac{\partial E_w}{\partial S_h} & \frac{\partial E_w}{\partial E_h}\frac{\partial E_w}{\partial I_h} & \frac{\partial E_w}{\partial R_h} \\ \frac{\partial I_w}{\partial S_m} & \frac{\partial I_w}{\partial E_m}\frac{\partial I_w}{\partial I_m} & \frac{\partial I_w}{\partial S_w}\frac{\partial I_w}{\partial E_w} & \frac{\partial I_w}{\partial I_w}\frac{\partial I_w}{\partial S_h} & \frac{\partial I_w}{\partial E_h}\frac{\partial I_w}{\partial I_h} & \frac{\partial I_w}{\partial R_h} \\ \frac{\partial S_h}{\partial S_m} & \frac{\partial S_h}{\partial E_m}\frac{\partial S_h}{\partial I_m} & \frac{\partial S_h}{\partial S_w}\frac{\partial S_h}{\partial E_w} & \frac{\partial S_h}{\partial I_w}\frac{\partial S_h}{\partial S_h} & \frac{\partial S_h}{\partial E_h}\frac{\partial S_h}{\partial I_h} & \frac{\partial S_h}{\partial R_h} \\ \frac{\partial E_h}{\partial S_m} & \frac{\partial E_h}{\partial E_m}\frac{\partial E_h}{\partial I_m} & \frac{\partial E_h}{\partial S_w}\frac{\partial E_h}{\partial E_w} & \frac{\partial E_h}{\partial I_w}\frac{\partial E_h}{\partial S_h} & \frac{\partial E_h}{\partial E_h}\frac{\partial E_h}{\partial I_h} & \frac{\partial E_h}{\partial R_h} \\ \frac{\partial I_h}{\partial S_m} & \frac{\partial I_h}{\partial E_m}\frac{\partial I_h}{\partial I_m} & \frac{\partial I_h}{\partial S_w}\frac{\partial I_h}{\partial E_w} & \frac{\partial I_h}{\partial I_w}\frac{\partial I_h}{\partial S_h} & \frac{\partial I_h}{\partial E_h}\frac{\partial I_h}{\partial I_h} & \frac{\partial I_h}{\partial R_h} \\ \frac{\partial R_h}{\partial S_m} & \frac{\partial R_h}{\partial E_m}\frac{\partial R_h}{\partial I_m} & \frac{\partial R_h}{\partial S_w}\frac{\partial R_h}{\partial E_w} & \frac{\partial R_h}{\partial I_w}\frac{\partial R_h}{\partial S_h} & \frac{\partial R_h}{\partial E_h}\frac{\partial R_h}{\partial I_h} & \frac{\partial R_h}{\partial R_h} \end{pmatrix}$$

To get the Eigenvalues λ, we calculate the Jacobian J^* defined as,

$$|J - \lambda I| = 0$$

We have that $\lambda = -w, -i, -j, -k$,-p,-t,-q,

Where

$$k = \left(\frac{\lambda_1 I_h}{N_h} + \frac{\lambda_2 I_w}{N_w} + \delta_1\right),\ \mathrm{l} = \frac{\lambda_2 S_m}{N_w}, m = \frac{\lambda_1 S_m}{N_h}, n = \frac{\lambda_1 I_h}{N_h} + \frac{\lambda_2 I_w}{N_w},$$

$$p = (e + \delta_1), q = \left(\frac{\lambda_3 I_h}{N_h} + \delta_2\right),$$

$$r = \frac{\lambda_3 S_w}{N_h}, \qquad \ldots\ldots\ldots (4.4.1.2)$$

$$s = \frac{\lambda_3 I_h}{N_h},\ \ t = (\sigma + \delta_2), u = \frac{\lambda_1 S_h}{N_h}, v = \frac{\lambda_3 S_h}{N_h}, w = \frac{\lambda_1 I_m}{N_h} + \frac{\lambda_3 I_w}{N_h},$$

$$x = (\Omega_h + T_h + \mu), y = \tau_h + \mu + \delta_3, z = \gamma + \mu, i = \delta_1, j = \delta_2, a = \sigma, b = \gamma, c = T_h, d = \Omega_h, \mathrm{f} = \tau_h$$

and

$$\lambda^3 + \lambda^2(c + x + y + z) + \lambda(yz - cz - cy + xz + xy) + xyz - cyz + bdf = 0$$

5. Numerical Simulation

In this section we present a numerical analysis of the model. A numerical simulation of the model is conducted to find out the dynamics of the disease in the human population.

For Reproduction number, $R_0 < 1$
The initial conditions are:

$S_m = 80{,}000{,}000, E_m = 50{,}000{,}000,\ I_m = 20{,}000{,}000,$
$S_w = 15{,}000{,}000,\ E_w = 10{,}000{,}000, I_w = 5{,}000{,}000, S_h = 90{,}000{,}000,\quad E_h = 60{,}000{,}000,\ I_h = 30{,}000{,}000,\ R_h = 18{,}000{,}000,$

$$R_0 = 0.1650$$

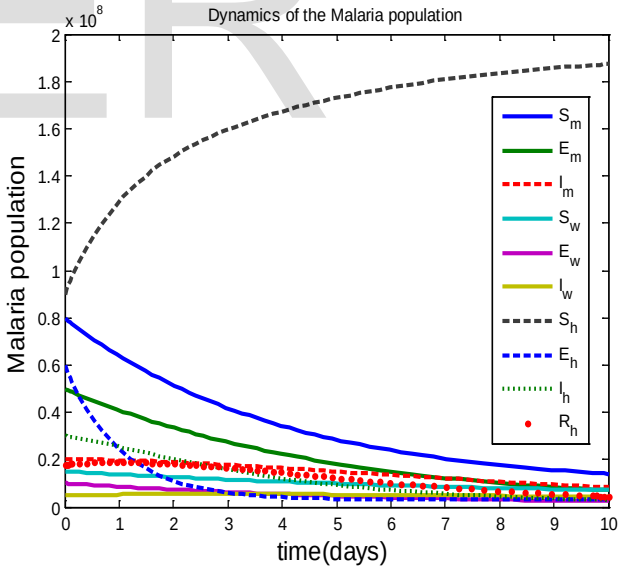


Fig 2: a numerical simulation representing the entire mosquito (Wolbachia-free and Wolbachia-infected) and human population.

The figure above shows the dynamics of the disease in a

disease free equilibrium state. The graph shows the susceptible individuals are increasing, but at disease free equilibrium, an infectious

mosquito infects less than one susceptible individual and vice versa, which leads to a decline in the exposed human and mosquito population, thus, lesser humans are infected and over time, the disease is eliminated in the society.

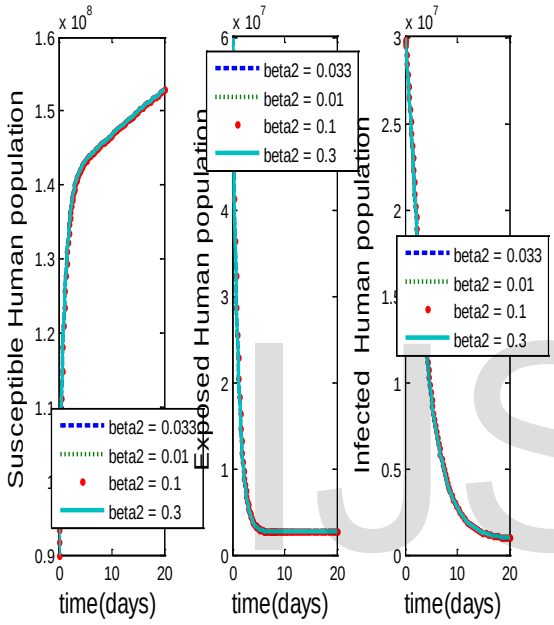


Fig 3: simulation of the Human population only with respect to the rate of cytoplasmic incompatibility, β_2.

At disease free equilibrium, we see that the susceptible human population increases as β_2 increases over time while the exposed and infected humans decrease as β_2 increases over time.

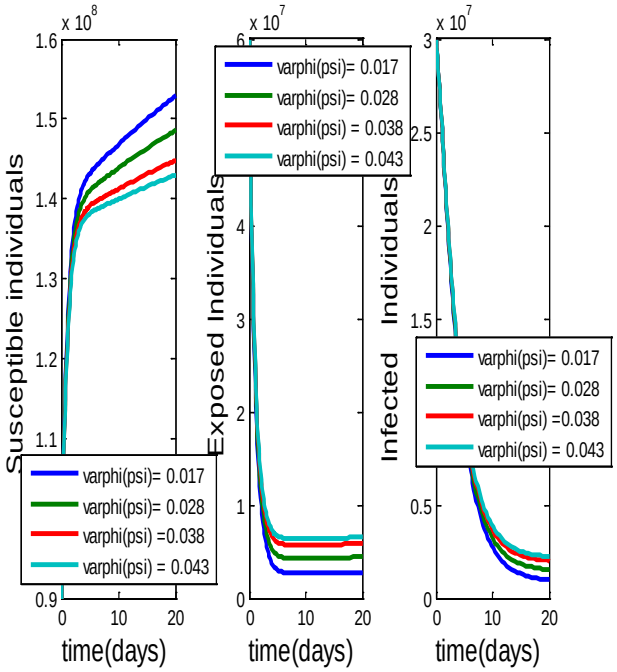


Fig 4: simulation of the Human population only with respect to the rate at which Humans move from the Susceptible to the Exposed class.

We see that the susceptible humans decrease as psi increases over time while the exposed and infected humans increase as psi increases over time.

Reproduction number $R_0 > 1$

$S_m = 65{,}000{,}000, E_m = 55{,}000{,}000, I_m = 30{,}000{,}000,$ $S_w = 15{,}000{,}000, E_w = 10{,}000{,}000, I_w = 5{,}000{,}000, S_h =$ $75{,}000{,}000, \quad E_h = 55{,}000{,}000, I_h = 45{,}000{,}000, R_h =$ $23{,}000{,}000, R_0 = 5.8752$

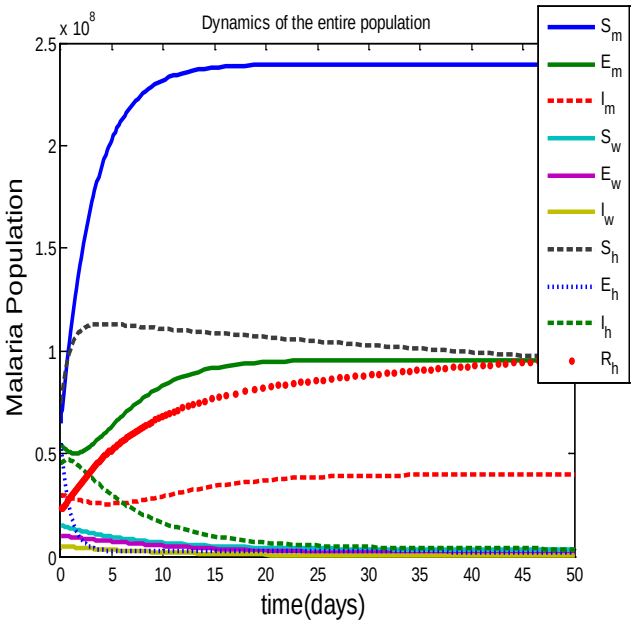


Fig 5: a numerical simulation representing the entire mosquito (Wolbachia-free and Wolbachia-infected) and human population.

The figure above shows the dynamics of the disease in an endemic equilibrium state. The graph shows the susceptible individuals are decreasing and in an endemic equilibrium state, infection persists in the environment, which leads to an increase in the exposed human and mosquito population, thus, more humans are infected and over time, the disease is endemic in the society.

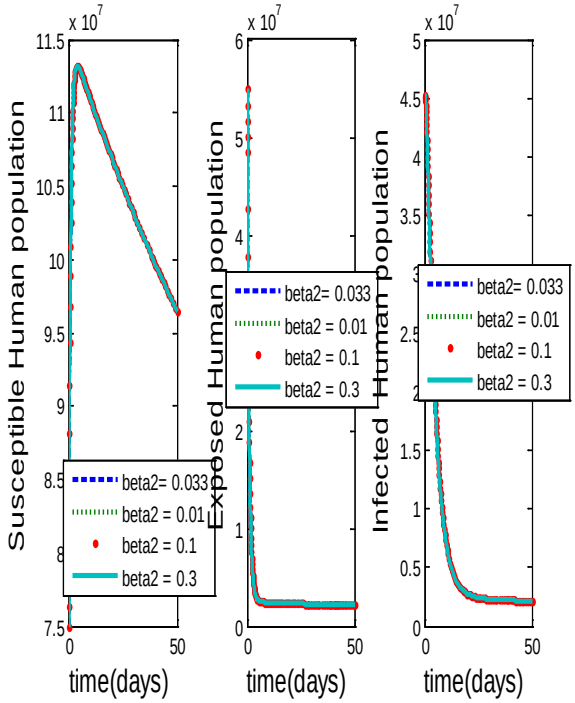


Figure 6: Simulation of the individual classes of the Human population over time with respect to β_2.

Here, we considered what happens in each class of the Human population alone over time as β_2 increases

The susceptible class, exposed and infected class of humans decreases over time as β_2, the rate of *Wolbachia*-infected male and uninfected female producing inviable offspring (CI) increases.

Finally, we see that from the analysis model predicts that infection with these endosymbionts will reduce malaria prevalence in human populations.

It shows that if the Wolbachia infected male mosquitoes mate at a high with the non-wolbachia infected female Anopheles mosquito which would result in cytoplasmic incompatibility- death of the embryo, the mosquito population would decline over time, leading to a decline in the population of the malaria vector. Hence the rate of malaria transmission will be reduced

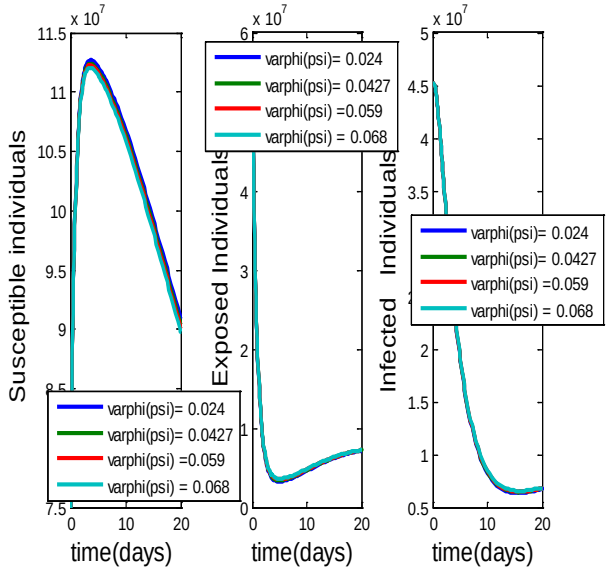


Figure 7: simulation of the Human population only with respect to psi.

Here, we considered what happens in the Human population alone. At the endemic equilibrium, we see that as we increase the rate at which humans move from the Susceptible to the Exposed class, φ, here is an increase in the susceptible class of the human population and a decrease in the exposed and infected classes of the human population as time increases.

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