

Malaria Transmission and Biological Control with Human Related Activities: A Mathematical Modeling Approach

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Abstract: In this paper, a nonlinear mathematical model for the control of vector borne diseases, like malaria is proposed and analyzed. In the modeling process it is assumed that the mosquito population is controlled by using Larvivorous fish, which partially depends on the larva of mosquito population. It is further assumed that the mosquito population grows logistically in the environment and its intrinsic growth rate is also affected by the human related activities. The equilibria of the model are obtained and their stability is discussed by using stability theory of differential equations. The threshold for the eradication of the disease, i.e. basic reproduction number is obtained. The analysis of the model shows that the growth rate in mosquito population due to human related activities has destabilizing effect on the system. Further numerical simulation is performed to verify the analytically obtained results.

Keywords: Mathematical model, human population, mosquito population, Larvivorous fish population.

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1. Introduction

Vector transmitted diseases are known to induce major behavioural and economic changes in tropical and subtropical region, in which mosquito-transmitted diseases are most prevalent illness and are responsible for many life- threatening diseases, e.g. malaria, yellow fever, dengue fever, and chikungunya, etc^{1- 6}. Out of these mosquitos borne serious illness, the

malaria is a highly complex disease in humans caused by several species of mosquito-borne parasite (*Plasmodium falciparum*, *vivax*, *malariae*, *knowlesi* and *ovale*) and it is endemic in many parts of the World, infecting between 350-500 million people per year^{7, 8}. Malaria is transmitted exclusively by Genus *Anopheles*. In the last several years so many efforts have been made to reduce the incidence of malaria focusing on reducing the number of mosquitoes and preventing mosquito bites^{9, 10}. However, most of these efforts, especially the ones that use pesticides, have been banned by the environmental protection organizations as they have an adverse effect on non-targeted population^{11, 12}. Despite more than hundred years of serious efforts for its control, malaria still ranks as one of the most widespread and prevalent vector borne diseases¹³⁻¹⁷. Also due to continuous application of pesticides, mosquitoes have developed resistance to these chemicals and now these chemicals are not so effective. This suggests us that looking for an alternative methods of control of mosquitoes and biological control seems to be environmental friendly method to control mosquito population. Biological control means introduction or manipulation of organisms to subdue vector population. Biological control, particularly using Larvivorous fish plays a very positive role in controlling mosquitoes¹⁸⁻²³. The method of control of mosquito using Larvivorous fish is not new; it has been implemented since 1937 in many parts of the world. But control of mosquitoes using pesticides was fast, so it suppressed the conventional method of control of mosquitoes. Now again this method of larval control is accepted and successfully implemented in many parts of the world²³⁻²⁵. Although there are lots of experimental studies to evaluate the efficiency of this method of control but not many researchers have explored mathematical modeling of this method of control.

2. The Mathematical Model

$N(t)$ be the total human population in the region under consideration at any time t , which is divided into susceptible class $X(t)$ and infective class $Y(t)$. Let $M_s(t)$ and $M_I(t)$ be the density of susceptible mosquitoes, the density of infective mosquitoes respectively and $B(t)$ be the population density of Larvivorous fish at time t . Let us denote the immigration rate, the transmission rate of susceptible to infective class, the natural death rate, the recovery rate and disease induced death rate by constants A , β , d , ν and α respectively. If the growth rate, the death rate, the depletion rate due to predator fish, the transmission rate, the growth rate due to human related activities of mosquito population, the natural growth rate of Larvivorous fish, the growth rate of fish due to uptake of larva of mosquitoes are denoted

by σ , θ_0 , θ_1 , λ , r_1 , γ , γ_0 and γ_1 respectively, then we propose the following model

$$(1) \quad \begin{cases} \frac{dX}{dt} = A - \beta X M_I - dX + Y \\ \frac{dY}{dt} = \beta X M_I - (d + \nu + \alpha)Y \\ \frac{dM_s}{dt} = \sigma M - \frac{\theta M^2}{L} - \theta_1 B M - \theta_0 M_s - \lambda M_s Y + r_1 N M \\ \frac{dM_I}{dt} = \lambda M_s Y - \theta_0 M_I \\ \frac{dB}{dt} = \gamma B - \frac{\gamma_0 B^2}{K} + \gamma_1 M B, \end{cases}$$

where L and K are the carrying capacities of mosquitoes and Larvivorous fish respectively. Using $N = X + Y$, $M = M_s + M_I$ and $\sigma - \theta_0 = \theta$, the reduced model is

$$(2) \quad \begin{cases} \frac{dY}{dt} = \beta(N - Y)M_I - (d + \alpha + \nu)Y, \\ \frac{dN}{dt} = A - dN - \alpha Y, \\ \frac{dM_I}{dt} = \lambda(M - M_I)Y - \theta_0 M_I, \\ \frac{dM}{dt} = \theta M \left(1 - \frac{M}{L}\right) - \theta_1 B M + r_1 N M, \\ \frac{dB}{dt} = \gamma B - \frac{\gamma_0 B^2}{K} + \gamma_1 M B. \end{cases}$$

It suffices to study the model system (2). The region of attraction for all solutions initiating in the positive orthant is given by

$$\Omega := \left\{ (Y, N, M_I, M, B) : 0 \leq Y \leq N \leq \frac{A}{d}, 0 \leq M_I \leq M \leq M_m, 0 \leq B \leq B_m \right\}$$

where $M_m = \frac{L}{\theta} \left(\sigma + \frac{r_1 A}{d} \right)$ and $B_m = \frac{K}{\gamma_0} \left\{ \gamma + \frac{\gamma_1 L}{\theta} \left(\sigma + \frac{r_1 A}{d} \right) \right\}$.

3. Equilibrium Analysis

The model system (2) has the following six non-negative equilibria:

- Mosquito and disease free equilibrium $E_0\left(0, \frac{A}{d}, 0, 0, 0\right)$ which always exists,
- $E_1\left(0, \frac{A}{d}, 0, \left(L + \frac{r_1 AL}{\theta d}\right), 0\right)$ which always exists,
- $E_2\left(0, \frac{A}{d}, 0, 0, \frac{K\gamma}{\gamma_0}\right)$ which always exists,
- $E_3\left(0, \frac{A}{d}, 0, M_3, B_3\right)$ exists provided

$$(3) \quad \theta - \frac{\theta_1 K \gamma}{\gamma_0} + \frac{r_1 A}{d} > 0,$$

- $E_4(Y_4, N_4, M_{I4}, M_4, 0)$ exists provided

$$(4) \quad \frac{\beta A L \lambda \left(\theta + \frac{r_1 A}{d}\right)}{d \theta \theta_0 (d + \nu + \alpha)} > 1,$$

- $E^*(Y^*, N^*, M_I^*, M^*, B^*)$ exists provided

$$(5) \quad \frac{\beta A L \left[\theta - \frac{\theta_1 K \gamma}{\gamma_0} + \frac{r_1 A}{d}\right]}{d \theta_0 (d + \nu + \alpha) \left(\frac{\theta}{L} + \frac{\theta_1 K \gamma_1}{\gamma_0}\right)} > 1,$$

$$(6) \quad \theta - \frac{\theta_1 K \gamma}{\gamma_0} + \frac{r_1 (A - \alpha Y^*)}{d} > 0.$$

It is sufficient to show the existence of equilibria E_4 and E^* .

3.1 Existence of E_4 : In the equilibrium $E_4(Y_4, N_4, M_{I4}, M_4, 0)$, the values of Y_4, B_4, M_{I4} and M_4 may be obtained by solving the algebraic equations

$$(7) \quad \beta(N - Y)M_I - (d + \nu + \alpha)Y = 0,$$

$$(8) \quad A - dN - \alpha Y = 0,$$

$$(9) \quad \lambda(M - M_I)Y - \theta_0 M_I = 0$$

and

$$(10) \quad \theta \left(1 - \frac{M}{L}\right) + r_1 N = 0.$$

From equation (8), we have

$$(11) \quad N = \frac{A - \alpha Y}{d}.$$

From equation (9), we have

$$(12) \quad M_I = \frac{\lambda M Y}{\theta_0 + \lambda Y}.$$

From equation (10), we have

$$(13) \quad M = L \left[1 + \frac{r_1(A - \alpha Y)}{\theta d}\right].$$

Using (11) and (12) in (7), we get

$$(14) \quad \beta \left[\frac{A - (\alpha + d)Y}{d} \right] \left[\frac{\lambda L Y}{\theta(\theta_0 + \lambda Y)} \right] \left[\theta + \frac{r_1(A - \alpha Y)}{d} \right] - (\nu + \alpha + d)Y = 0.$$

Let $Y \neq 0$. Then we have

$$(15) \quad f(Y) = \beta \left[\frac{A - (\alpha + d)Y}{d} \right] \left[\frac{\lambda L}{\theta(\theta_0 + \lambda Y)} \right] \left[\theta + \frac{r_1(A - \alpha Y)}{d} \right] - (\nu + \alpha + d) = 0.$$

From equation (15), we note the following:

(i) $f(0) > 0$ provided condition (4) is satisfied.

(ii) $f\left(\frac{A}{\alpha + d}\right) < 0$.

(iii) $f'(Y) < 0$.

Thus, there exists a unique positive root, say Y_2^* of equation (15) in the interval $\left(0, \frac{A}{\alpha + d}\right)$. Using the value of Y_4 in equations (11)-(13), we can get the values of N_4, Y_4, M_{I4} and M_4 respectively. Thus the equilibrium $E_4(Y_4, N_4, M_{I4}, M_4, 0)$ exists if condition (4) holds.

3.2 Existence of E^* : The equilibrium E^* may be obtained by solving the following set of algebraic equations:

$$(16) \quad \beta(N - Y)M_I - (d + \nu + \alpha)Y = 0,$$

$$(17) \quad A - dN - \alpha Y = 0,$$

$$(18) \quad \lambda(M - M_I)Y - \theta_0 M_I = 0,$$

$$(19) \quad \theta \left(1 - \frac{M}{L}\right) - \theta_1 B + r_1 N = 0,$$

$$(20) \quad \gamma - \frac{\gamma_0 B}{K} + \gamma_1 M = 0.$$

From equation (17), we have

$$(21) \quad N = \frac{A - \alpha Y}{d}.$$

From equation (18), we have

$$(22) \quad M_I = \frac{\lambda M Y}{\theta_0 + \lambda Y}.$$

From equation (20), we have

$$(23) \quad B = \frac{K}{\gamma_0} (\gamma + \gamma_1 M).$$

From equation (19), we have

$$(24) \quad M = \frac{\left[\theta - \frac{\theta_1 K \gamma}{\gamma_0} + \frac{r_1 (A - \alpha Y)}{d} \right]}{\frac{\theta}{L} + \frac{\theta_1 K \gamma_1}{\gamma_0}}.$$

From equation (16), we have

$$(25) \quad \beta \left[\frac{A - (\alpha + d)Y}{d} \right] \left[\frac{\lambda Y}{(\theta_0 + \lambda Y)} \right] \left[\frac{\theta - \frac{\theta_1 K \gamma}{\gamma_0} + \frac{r_1(A - \alpha Y)}{d}}{\frac{\theta}{L} + \frac{\theta_1 K \gamma_1}{\gamma_0}} \right] - (\nu + \alpha + d)Y = 0.$$

Now we assume $Y \neq 0$, then we have

$$(26) \quad F(Y) = \beta \left[\frac{A - (\alpha + d)Y}{d} \right] \left[\frac{\lambda}{(\theta_0 + \lambda Y)} \right] \left[\frac{\theta - \frac{\theta_1 K \gamma}{\gamma_0} + \frac{r_1(A - \alpha Y)}{d}}{\frac{\theta}{L} + \frac{\theta_1 K \gamma_1}{\gamma_0}} \right] - (\nu + \alpha + d) = 0.$$

From equation (26), we note the following:

(i) $F(0) > 0$ provided condition (4) is satisfied,

(ii) $F\left(\frac{A}{\alpha + d}\right) < 0$,

(iii) $F'(Y) < 0$.

Thus there exists a unique positive root Y^* of the equation (26), if condition (5) is satisfied. Using this value of Y^* in equation (24), we get positive value of M (say M^*) if the condition (6) is satisfied. From equation (21)-(23) we can get positive values of N^*, M_I^* and B^* . Thus the equilibrium $E^*(Y^*, N^*, M_I^*, M^*, B^*)$ exists if conditions (5) and (6) are satisfied.

4. Stability Analysis

4.1 Local Stability: In this section, we investigate the local stability of the equilibria E_0, E_1, E_2, E_3, E_4 and E^* by determining the sign of the eigenvalues of Jacobian matrix corresponding to each equilibria. The Jacobian matrix for the model (2) is

$$J = \begin{pmatrix} -a_{11} & \beta M_i & \beta(N-Y) & 0 & 0 \\ -\alpha & -d & 0 & 0 & 0 \\ \lambda(M-M_i) & 0 & -a_{33} & \lambda Y & 0 \\ 0 & r_1 M & 0 & a_{44} & -\theta_1 M \\ 0 & 0 & 0 & \gamma_1 B & a_{55} \end{pmatrix}$$

where

$$a_{11} = \beta M_i + (d + \nu + \alpha), \quad a_{33} = \lambda Y + \theta_0, \quad a_{44} = \theta - \frac{2\theta M}{L} - \theta_1 B + r_1 N$$

and

$$a_{55} = \gamma - \frac{2\gamma_0 B}{K} + \gamma_1 M.$$

Let J_0, J_1, J_2, J_3, J_4 and J^* be the variational matrices evaluated at E_0, E_1, E_2, E_3, E_4 and E^* respectively.

Theorem 1: *The inequalities*

$$(27) \quad \beta^2 \lambda^2 (N^* - Y^*)^2 (M^* - M_i^*)^2 < \frac{4}{9} (\lambda Y^* + \theta_0)^2 (\beta M_i^* + d + \nu + \alpha)^2,$$

and

$$(28) \quad 3\alpha k_2 (\lambda^2 L^2 r_1^2 Y^{*2}) < 4d\beta M_i^* \theta^2 (\lambda Y^* + \theta_0)$$

imply that E^* is locally asymptotically stable.

Proof : To prove this theorem we use Liapunov Linearization Method. Let

$$Y = Y^* + y, \quad N = N^* + n, \quad M_i = M_i^* + m_i, \quad M = M^* + m \quad \text{and} \quad B = B^* + b,$$

where y, n, m_i, m and b are small perturbations around the equilibrium E^* . Using the following positive definite function

$$(29) \quad V = \frac{1}{2} y^2 + \frac{k_1}{2} n^2 + \frac{k_2}{2} m_i^2 + \frac{k_3}{2M^*} m^2 + \frac{k_4}{2B^*} b^2,$$

where $k_i (i=1,2,3,4)$ are positive constants to be chosen appropriately. Differentiating (29) with respect to 't' and using the linearized system corresponding to E^* we get

$$(30) \quad \dot{V} = -(\beta M_i^* + d + \nu + \alpha)y^2 - k_1 dn^2 - k_2(\lambda Y^* + \theta_0)m_i^2 - \frac{k_3\theta}{L}m^2 - \frac{k_4\gamma_0}{K}b^2 + [\beta M_i^* - k_1\alpha]yn + [\beta(N^* - Y^*) + \lambda(M^* - M_i^*)k_2]ym_i + k_2\lambda Y^*mm_i + k_3r_1nm + [k_4\gamma_1 - k_3\theta_1]bm.$$

Choosing $k_1 = \frac{\beta M_i^*}{\alpha}$ and $k_4 = \frac{\theta_1 k_3}{\gamma_1}$, we have the linearized system corresponding to E^* as

$$(31) \quad \dot{V} = -(\beta M_i^* + d + \nu + \alpha)y^2 - \frac{\beta M_i^* d}{\alpha}n^2 - k_2(\lambda Y^* + \theta_0)m_i^2 - \frac{k_3\theta}{L}m^2 - \frac{k_3\theta_1\gamma_0}{\gamma_1 K}b^2 + \beta(N^* - Y^*)ym_i + k_2\lambda(M^* - M_i^*)ym_i + k_2\lambda Y^*m_i m + k_3r_1nm.$$

$\dot{V}$ will be negative definite if the following conditions are satisfied

$$(32a) \quad \beta^2(N^* - Y^*)^2 < \frac{2}{3}k_2(\lambda Y^* + \theta_0)(\beta M_i^* + d + \nu + \alpha),$$

$$(32b) \quad k_2\lambda^2(M^* - M_i^*)^2 < \frac{2}{3}(\lambda Y^* + \theta_0)(\beta Y^* + d + \nu + \alpha),$$

$$(32c) \quad k_2\lambda^2Y^{*2} < \frac{2k_3\theta}{3L}(\lambda Y^* + \theta_0),$$

$$(32d) \quad k_3r_1^2 < \frac{2d\theta\beta M_i^*}{\alpha L}.$$

From inequalities (32a) and (32b), we can get a positive value of k_2 provided the condition (27) holds. Further from the inequalities (32c) and (32d), we can get a positive value of k_3 , provided the condition (28) holds.

4.2 Global Stability: To establish the non-linear stability of the equilibrium E^* we employ Liapunov's stability theory and obtain the following results regarding the global stability of equilibrium E^* .

Theorem 2: *The equilibrium E^* if exists, is globally asymptotically stable in Ω , provided*

$$(33) \quad \beta^2\lambda^2(N^* - Y^*)^2(M^* - M_i^*)^2 < \frac{4}{9}\theta_0^2(d + \nu + \alpha)^2,$$

and

$$(34) \quad m_2(\lambda L r_1 A)^2 < \frac{4}{3} \frac{\beta M_i^*}{\alpha} d^3 \theta_0 \theta^2.$$

Proof : Let us consider the positive definite function

$$(35) \quad W = \frac{1}{2}(Y - Y^*)^2 + \frac{m_1}{2}(N - N^*)^2 + \frac{m_2}{2}(M_I - M_I^*)^2 \\ + m_3 \left(M - M^* - M^* \ln \frac{M}{M^*} \right) + m_4 \left(B - B^* - B^* \ln \frac{B}{B^*} \right),$$

where $m_i (i = 1, 2, 3, 4)$ are positive constants to be chosen appropriately.

Differentiating W with respect to t along the solution of model (2), we get

$$(36) \quad \dot{W} = -[\beta M_i + d + \alpha + \nu](Y - Y^*)^2 - m_1 d(N - N^*) - m_2(\theta_0 + \lambda Y)(M_I - M_I^*)^2 \\ - \frac{m_3 \theta}{L}(M - M^*)^2 - \frac{m_4 \gamma_0}{K}(B - B^*)^2 + \beta(N - Y^*)(Y - Y^*)(M_I - M_I^*) \\ + m_2 \lambda(M - M_I^*)(Y - Y^*)(M_I - M_I^*) + m_2 \lambda Y(M - M^*)(M_I - M_I^*) \\ + [\beta M_i - m_1 \alpha](Y - Y^*)(N - N^*) + m_3 r(N - N^*)(M - M^*) \\ + [m_4 \gamma_1 - m_3 \theta_1](M - M^*)(B - B^*).$$

Choosing $m_1 = \frac{\beta M_i^*}{\alpha}$ and $m_4 = \frac{m_3 \theta_1}{\gamma_1}$, $\dot{W}$ can be made negative definite

inside the region of attraction Ω if the following conditions are satisfied

$$(37a) \quad \beta^2(N^* - Y^*)^2 < \frac{2m_2}{3} \theta_0(d + \nu + \alpha),$$

$$(37b) \quad m_2 \lambda^2 (M^* - M_I^*)^2 < \frac{2}{3} \theta_0(d + \nu + \alpha),$$

$$(37c) \quad m_2 \lambda^2 \frac{A^2}{d^2} < \frac{2}{3L} m_3 \theta \theta_0 [\lambda Y^* + \theta_0 + \theta_1 C_h^* + d_m],$$

$$(37d) \quad m_3 r_1^2 < \frac{2}{L} m_1 d \theta.$$

From inequalities (37a) and (37b), we can get a positive value of m_2 provided the condition (33) holds. Further, from the inequality (37c) and (37d), we can get the positive value of m_3 provided (34) holds.

5. Numerical Simulation

To confirm the analytically obtained results and to illustrate the dynamical behavior of the system, numerical simulation has been carried out using MATLAB 7.0.5. We have taken the following set of parameter values in model (2):

$$A=100, \beta=0.00002, d=0.01, \nu=0.1, \alpha=0.0001, \lambda=0.0001, \theta_0=0.6, \sigma=0.31, \\ \theta=0.1, L=10000, \theta_1=0.0001, r_1=0.0001, \gamma=0.01, K=10000, \gamma_0=0.1, \gamma_1=0.00001.$$

For the above set of parameter values it may be checked that the condition of existence of endemic equilibrium E^* is satisfied. The equilibrium components are found as follows:

$$Y^* = 2006.0605, N^* = 9979.9393, M_I^* = 1384.9424, M^* = 5527.2176, B^* = 6527.2176.$$

The eigenvalues of the Jacobian matrix corresponding to the equilibrium E^* for the model (2) are $-0.8886, -0.0497, -0.0101, -0.0602+0.1899i$ and $-0.0602-0.1899i$.

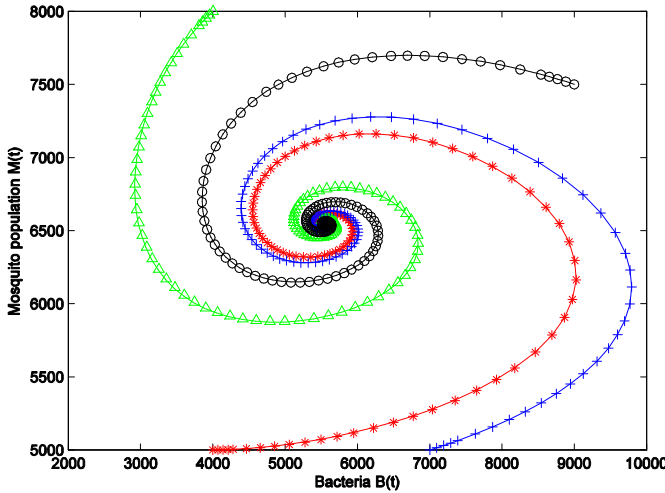


Figure 1: Nonlinear stability of (M^*, B^*) in $M - B$ plane.

We note that the three eigen values of J_{E^*} are negative and the other two eigen values have negative real parts. Hence, for the above set of parameter values the endemic equilibrium E^* is locally asymptotically stable. With these parameter values, the solution trajectories of the model (2) have been drawn in figure 1 with different initial starts. From this figure, we may see that all the trajectories initiating inside the region of attraction are approaching towards the equilibrium point (M^*, B^*) . This shows the non-linear stability behavior of the endemic equilibrium E^* in $M^* - B^*$ plane.

The variation of infective human population $Y(t)$ and infective mosquito population $M_i(t)$ with respect to time t for different values of rate of transmission of susceptible human population to infective human population β and the rate of transmission of susceptible mosquito population to infective mosquito population λ are shown in figures 2 and 3 respectively.

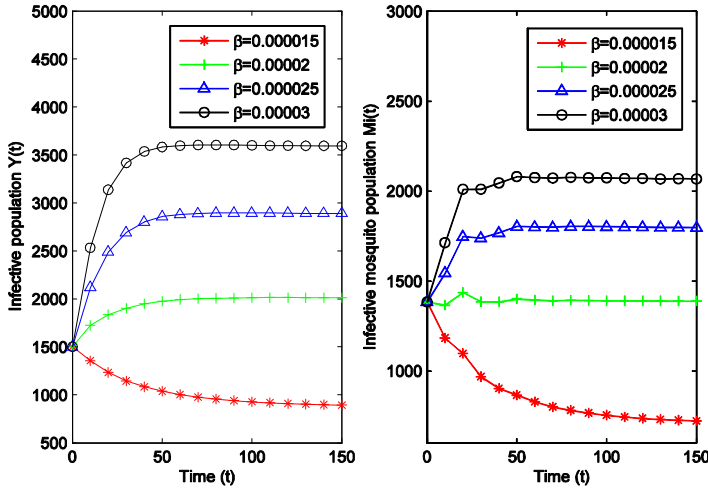


Figure 2: Variation of infected human population and infected mosquito population with time for different values of β .

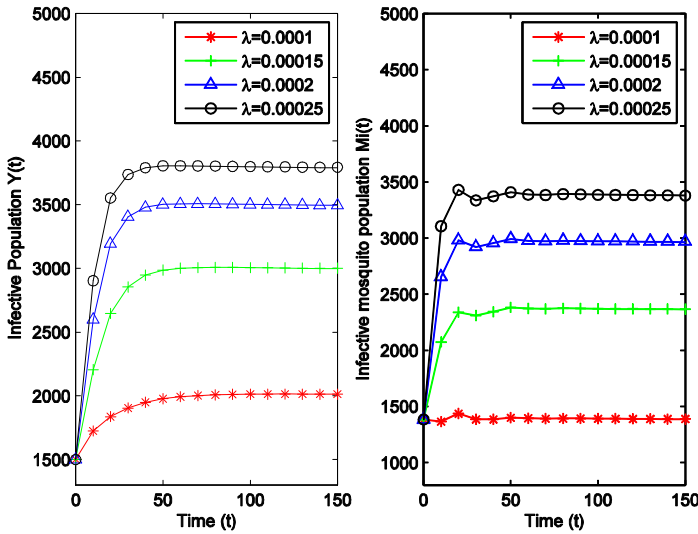


Figure 3: Variation of infected human population and infected mosquito population with time for different values of λ

These figures, illustrate that as the rate of transmission of susceptible human population to infective human population and the rate of transmission of susceptible mosquito population to infective mosquito population increase, infective human population $Y(t)$ and infective mosquito population $M_i(t)$ both increase.

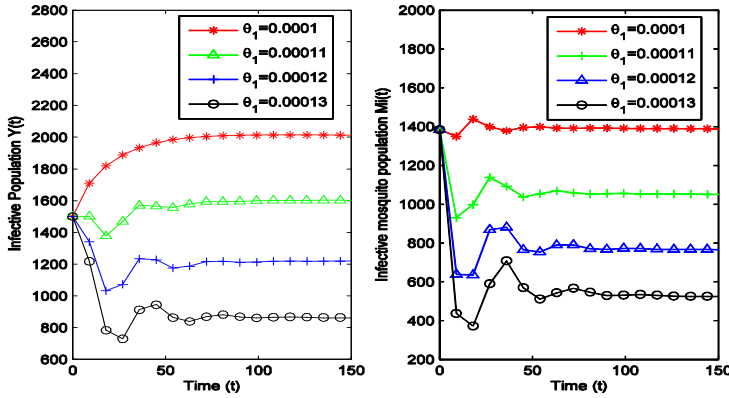


Figure 4: Variation of infected human population and infected mosquito population with time for different values of θ_1

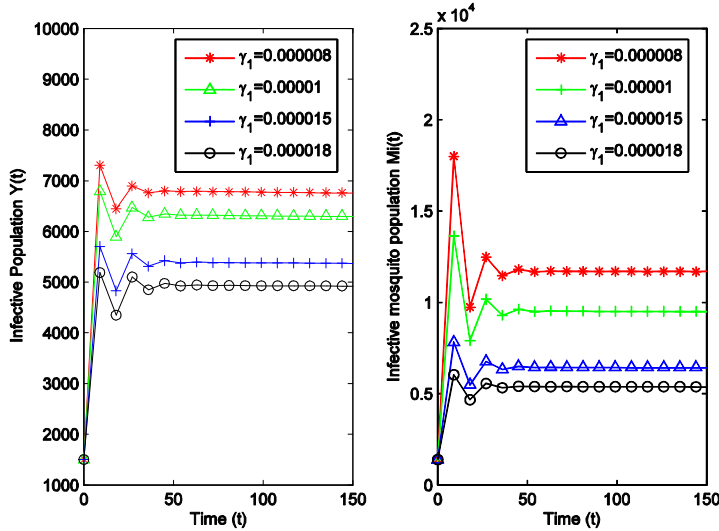


Figure 5: Variation of infected human population and infected mosquito population with time for different values of γ_1

The variations of infective human population $Y(t)$ and infective mosquito population $M_i(t)$ with respect to time t for different values of

growth rate coefficient of insecticides due to mosquito population ϕ and decay rate due to uptake by mosquito of the chemicals ϕ_1 are shown in figures 4 and 5 respectively. From these figures, it is apparent that as the depletion rate coefficient of mosquito population due to insecticides ϕ and growth rate coefficient of insecticides due to mosquito population ϕ_1 increase, infective human population $Y(t)$ and infective mosquito population $M_i(t)$ decrease.

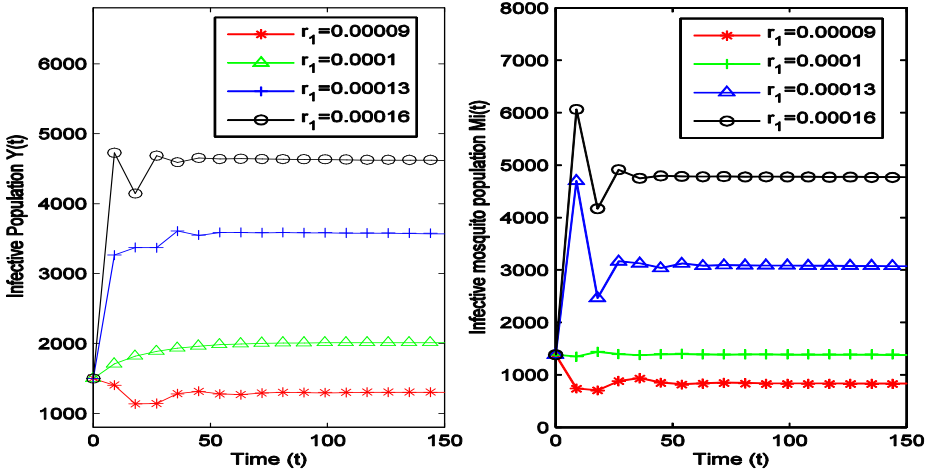


Figure 6: Variation of infected human population and infected mosquito population with time for different values of r_1

6. Conclusions

In this paper, a nonlinear mathematical model for malaria is proposed and analyzed. Equilibria of the model are found and stability behavior of these equilibria is discussed using variational matrix method. It is found that with the introduction of predatory fish, the equilibrium level of larva population decreases which causes the decrease in the population level of mosquito population and this decreases the basic reproduction number. Therefore the introduction of Larvivorous fish has positive impact in controlling the transmission of malaria. Further, numerical simulation is performed to demonstrate the analytical results. Finally this model is extended to include optimal control by introducing a time dependent control parameter corresponding to biological control. The optimality system is solved using Runge-Kutta fourth order method^{7, 8, 11, 16, 17}. Results of numerical

simulation are demonstrated using the control plots which reflects the decrease in vector as well as infected human population in the optimality system. We found that under some conditions the mosquito population may present in the atmosphere but the infected human population is zero. This suggests that under these conditions, the malaria can be eradicated from the community. It is also found that the number of infected individuals decreases as the rate of introduction of Larvivorous fish increases. Furthermore it is found that immigration rate of susceptible class makes disease more endemic. Numerical simulation is performed to demonstrate the analytical results.

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