MODELLING THE TRANSMISSION DYNAMICS OF MALARIA USING SEIRS MODEL

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Certification

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Dedication

This project is dedicated to the glory of Almighty God, THE FATHER, THE SON and THE HOLY SPIRIT, who has made this programme a success.

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Except the Lord builds the house, they labour in vain that build it..." Indeed without the involvement of the Almighty God - Omnipotent, Omniscient, Omnipresent, this work would not have been a success. *Great is thy faithfulness O Lord!.*

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Abstract

Several mathematical and statistical models have been used to describe the features involved in the transmission of malaria. However malaria still remains the most widespread and life-threatening disease among the known vector-borne diseases. In this work, an SEIR model is adapted to capture the basic features regarding the dynamics of malaria. We obtain the basic reproduction number ($\mathcal{R}_0$) and use it to establish the local stability of the disease-free equilibrium. The parameters most responsible for the disease transmission in the population are examined with respect to the basic reproduction number by sensitivity analysis. The disease-free equilibrium is found to be locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. Numerical simulations are carried out to validate the theoretical results and to further investigate the dynamics of the disease.

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Chapter 1

INTRODUCTION

Human beings are at constant risk of infectious diseases. No human can be exempted from the menace of an epidemic disease. Malaria, a common parasitic disease in sub-Saharan Africa, Asia and Latin America, is caused by the genus *Plasmodium*. There are several known species, however, humans are often affected through the bite of the female Anopheles mosquito vector. Global estimates of malaria show 80 percent cases from Africa, and malaria is responsible for more than a million annual death in affected developing countries(WHO, 2012). Among children under five years of age, malaria seems to be the leading cause of mortality, with similar incidence among pregnant women (WHO, 2012). In pregant women,severe malaria cases have been reported to cause maternal death, still birth, severe anaemia, congenital malformations and low birth weights (WHO, 2012).

1.1 History of malaria

Here, we give a brief account of the origin, causes and transmission of malaria disease. However, a full account of the discovery of malaria disease can be seen in Cox (2010) .

1.1.1 Malaria history

In 1880, a French physician, Charles Louis A. Laveran, while working in Algeria, made a landmark discovery of the main cause of the malaria disease that has

been affecting human lives for the long period. He discovered the presence of a parasitic protozoan *Plasmodium* in the blood of humans infected with malaria and was awarded the Nobel prize in 1907 as a result of the discovery. In other discovery, an experiment was conducted in 1897 by a British Physician, Ronald Ross, who showed for the first time that mosquito was responsible for transmission of the *Plasmodium* parasite that causes malaria in human population.

Not less than half of the world's population, distributed across 104 countries are at risk of malaria disease (WHO, 2012). Meanwhile, an initial report of 300 - 500 million persons have been observed to be infected annually, of which 1.5 - 2.7 million annual deaths have been estimated (Magombedze et al, 2011). Malaria is widely spread in tropical and subtropical regions, including Africa, Asia, Latin America, the middle East and some parts of Europe. However the most cases and deaths occur in sub-Saharan countries of Africa which account for 80 percent of the world's malaria cases and 90 percent of the global malaria deaths (WHO, 2012).

Death of an African child occurs in every 30 seconds, while global report of deaths from malaria exceeds 2000 among the youth. (Tumwiine et al, 2007; Okosun and Makinde, 2011). For example, in Nigeria, malaria accounts for 60 percent of outpatient visits and 30 percent of hospitalization with children under five years of age most severely affected (USE, 2011).

1.1.2 Malaria parasites and cycle

Malaria is a disease characterized by fever, pain, paroxysms of chills, headache, vomitting and pain. The disease is caused by protozoan parasite, known as *Plasmodium*. The commonest species that infect humans are; *Plasmodium vivax, P. ovale, P. falciparum, P. malariae* and *P. knowlesi*. The socioeconomic burden of malaria disease and its clinical signs include multi-organ failures such as lung, brain, liver and kidney (Tumwiine et al., 2007).

The life cycle of the *plasmodium* parasite can be divided into two phases: sexual and asexual phases, with the sexual phase taking place in the female

anopheles mosquito and asexual phase in the human host (Ibezim and Odo 2008). The infection subtly begins when an infectious mosquito pierces the human skin with its proboscis and injects parasite in the form of sporozoites into the human's bloodstream for blood circulation. In the process, the sporozoites enter the liver where each sporozoites undergoes asexual multiplication stage to produce cells called merozoites. This first asexual multiplication stage in human host is known as exoerythrocytic schizogony (Cox, 2010).

Following the rupture of the hepatocytes, merozites escape into circulatory system for asexual reproduction in the red cells, a stage called erythrocytic schizogony develops (Cox, 2010). At this stage, more merozoites are produced until the red blood cells burst and new merozoites are released to further infect other red blood cells while some merozoites developed into gametocytes (Cox, 2010). These geametocytes in the human's bloodstream can be taken up by a naive mosquito in the blood meal gametocytes and mature into male and female gametes in the mosquito's gut. Consequently, microgamete and macrogamete representing male and female gametes respectively, fuse salivary gland of the mosquito vector where they can be injected when the mosquito bites another human host to continue the cycle.

1.2 Modelling and its importance

Modelling has been an important part of describing reality. It has been in existence since the stone age when humans constructed caved paintings. Modelling became important in ancient Greek when symbols were used to represent increase in substance which are called numbers and they were the first models.

Three very important civilizations stood out in the knowledge of mathematics and they were Egypt, Babylon and India. Geometry was the first major part of mathematics that was used to model reality by Thales. In 585 B.C., he developed a system for calculating heights by estimating shadow lengths. A further improvement in modelling through mathematics came along when Diophantus of Alexandria around 250 A.D. in his text called Arithmetica developed the genesis of algebra centered on symbols and the concept of a variable.

Ptolemy, based on the existing concept of Pythagoras derived a mathematical model for planetary, sun and moon motion which was further developed by Johannes Kepler in 1619. Kepler's model was further improved by Isaac Newton and Albert Einstein and their models were in use till date. Mathematical models were utilized when handling real life problems and hence, were very essential for the improvement of the human society at that time. After the fall of the Greek civilization, the most notable mathematican was Fibonacci Leonardo da Pisa (1170-1240). He realized the practical advantageous use of indian numbers over roman figures which was still in use in that time. His mathematical text, Liber Abaci first released in 1202 made an introduction of Indian numbers (0,1,2,3,4,5,6,7,8,9). The book was detailed guide of arithmetic rules using numerical illustrations. Another man, Giotto (1267-1336) and Filipo Brunelleschi (1377-1446) were both accounted for the improvement of geometric principles. Many more very important principles were discovered in later centuries like the use of variables for representation which was developed by Vieta (1540-1603) but it was still difficult to completely comprehend until it was used to describe physical science and its application to real life situations and problems. The significance of mathematical modelling cannot be ignored as it has played a major role in the understanding and representation of problems in other fields of study namely; biology, chemistry, physics, economics, accounting, business administration etc. As previously stated, a mathematical model is a mathematical description of a realistic problem so that if the model can copy the behaviour of the real life problems then proper analysis of the created model can be done using suitable mathematical tools. It is important to properly understand the problem to be modelled so as concisely represent it. Mathematical modelling allows the mathematician to be economist, biologist, chemist, physicist depending on the problem been considered. Mathematical modelling helps the mathematician to perform experiments on the mathematical description of the realistic problem as opposed to performing experiments in real life. Though sometimes, not without limitations, the use of mathematical models has increased greatly over time.

1.2.1 Advantages of Mathematical modelling

Some of the advantages of mathematical modelling are:

(a) It gives better understanding of the problem to be modelled. When a problem is been modelled, it helps to clarify some problem statements.

(b) It can be used to perform experiments by analysis instead of actually performing the experiment in real life.

(c) Multiple solution pathways can be discovered from modelling a problem mathematically.

(d) It allows the mathematician to connect to different fields of study and think along the line of study without actually entering into the field of study.

1.2.2 Limitations of Mathematical Modelling

Over the years, mathematical modelling has been and still is one of the greatest discoveries for the application of mathematics in solving real-world problems. However there are still some limitations that occur in mathematical modelling. Some of these limitations are stated as follows:

(i) Mathematical models cannot represent real life problems 100 percent as there can be some errors or some very important factors left out.

(ii) Not all factors in literature and real life can be represented mathematically.

(iii) Mathematical models may not function properly because there may be unforeseen changes in the problems.

(iv) Mathematical models can become outdated over time so that it does not solve the problem anymore due to the addition of unrepresented factors.

1.3 SEIRS Model

Mathematical models in epidemology have been salient tools for analysis of infectious diseases. The SEIRS model is one of the various types of compartmental

models used to describe the transmission of an infectious disease over a period of time (Biswas et al,2014). The model divides the population into 4 compartments or classes - the susceptible class (S) i.e prone to catching the disease, exposed class (E) i.e have the disease but cannot infect others (infected but not yet infectious), infectious class (I) i.e have the disease and can transfer it to others and the recovered class (R) as a result of treatment or natural recovery. SEIR model has been used to represent many diseases such as malaria (Osman and Adu, 2017), cholera, COVID-19 (He et al,2020), tuberculosis etc. However,after a recovered human losses immunity,they can become susceptible again. In this work, we use the model to understand the dynamics behind the transmission of malaria between humans and mosquitoes.

1.4 Basic definitions in model analysis

In mathematical modelling, long-term behaviour of solutions to models is a main point of interest and focus. Consider the following general system of ordinary differential equations.

$$\left.\begin{array}{rcl} \frac{dx_1}{dt} &=& f_1(x_1(t), x_2(t), ..., x_n(t)) \\ \frac{dx_2}{dt} &=& f_2(x_1(t), x_2(t), ..., x_n(t) \\ \vdots & & \\ \frac{dx_n}{dt} &=& f_n(x_1(t), x_2(t), ..., x_n(t) \end{array}\right\} \tag{1.4.1}$$

which can be expressed in matrix form as

$$\frac{d\mathbf{X}}{dt} = \mathbf{f}(\mathbf{X}(t)) \tag{1.4.2}$$

where

$$\mathbf{X} = \begin{pmatrix} x_1 \\ x_2 \\ \vdots \\ x_n \end{pmatrix} \quad \text{and} \quad \mathbf{f} = \begin{pmatrix} f_1 \\ f_2 \\ \vdots \\ f_n \end{pmatrix}.$$

1.4.1 Equilibrium points

Definition 1.4.1. *(Lungu, et al, 2007): An equilibrium point of the system of differential equations (1.4.1) is a steady state* $\bar{x}$ *satisfying* $\mathbf{f}(\bar{x}) = 0$ *for all time t. This definition means that points at which the system (1.4.2) is equal to zero are referred to as points of equilibrium or steady-state solutions. The two kinds of points of equilibrium in mathematical epidemiology are: disease-free and endemic points of equilibrium. The former stands for the non-trivial stable-state solution where all the infected compartments that occur in the system are zero while the later refers to the positive stable-state solution where the disease persists in the system.*

1.4.2 Simulation

Definition 1.4.2. *Simulation, according to Shannon (1975), is "the process of designing a model of a real system and conducting experiments with this model for the purpose either of understanding the behaviour of the system or of evaluating various strategies (within the limits imposed by a criterion or set of criteria) for the operation of the system.*

1.4.3 Stability

Definition 1.4.3. *Stability properties characterize how a system behaves if its state is initiated close to, but not precisely at a given equilibrium point.*

An equilibrium point is stable whenever the system state is initiated near that point, the state remains near it, perhaps even tending towards the equilibrium point as time increases.

1.4.4 Basic reproduction number

For epidemiological models, a quantity of R_0 is derived to assess the stability of disease free equilibrium. The basic reproduction number, R_0, represent the number of secondary cases that are caused by a single infectious case introduced into a completely susceptible population (Anderson and May, 1991). When

$R_0 < 1$ if a disease is introduced, there are insufficient new cases per case and the disease cannot invade the population. When $R_0 > 1$, the disease will become endemic. To obtain R_0 for epidemiological model involving more than one infected class, a technique due to Diekmann et al (1990) is suitable. This technique, known as the *next generation matrix*, was explicitly studied by Van den Driessche and Watmough (2002) and summarized below.

1.4.5 The next generation matrix

Following the idea of Diekmann et al (1990), FV^{-1} is called the next generation matrix.

$$\mathbf{F} = \left[\frac{\partial \mathcal{F}_i}{\partial x_i}(\bar{x})\right] \quad \text{and} \quad \mathbf{V} = \left[\frac{\partial \mathcal{V}_i}{\partial x_i}(\bar{x})\right]$$

. Therefore, the basic reproduction number, R_0, is given by

$$R_0 = \rho(\mathbf{FV^{-1}}) \tag{1.4.3}$$

where ρ is the maximum eigenvalue of the product, $\mathbf{FV^{-1}}$ known as the next generation matrix; $\mathbf{F}$ is the rate of new infection in each infected compartment and $\mathbf{V}$ is the rate of transfer in infected compartment.

1.4.6 Lyapunov function

Definition 1.4.4. *(Derrick and Grossman, 1976): A function V defined on a region Ω of the state space and containing $\bar{x}$ is a Lyapunov function if it satisfies the following:*
(i) V is continuously differentiable,
(ii) V is positive definite, and
(iii) the derivative of V along the solution of the system (1.4.2) is defined by

$$\dot{V} = \frac{\partial V}{\partial x_1}\frac{dx_1}{dt} + \frac{\partial V}{\partial x_2}\frac{dx_2}{dt} + ... + \frac{\partial V}{\partial x_n}\frac{dx_n}{dt} = \frac{\partial V}{\partial x_i}f_i.$$

It is should be noted that the construction of these types of functions is an art rather than a rule, since there are no clear formulae for providing them. However, whenever such a function is found, satisfying specific properties, many stability results can be obtained (Ayoola, 2012).

1.4.7 Stability theorem

Theorem 1.4.5. *(Derrick and Grossman, 1976): Given the system $\dot{x} = Ax$ where A is the matrix of the linearised nonlinear system (1.4.2). Then,*
(i) the equilibrium point, $\bar{x}$, is stable if all the eigenvalues of A have only imaginary parts.
(ii) the equilibrium point, $\bar{x}$, is asymptotically stable if all the eigenvalues of A have negative real parts.
(iii) the equilibrium point is unstable in all other cases.

1.4.8 Lyapunov stability theorem

Theorem 1.4.6. *(Lungu et al, 2007): If there exists a Lyapunov function $\dot{V}(\bar{x})$ and such that $\dot{V} \leq 0$, then the equilibrium point $\bar{x}$ is stable. If, furthermore, the function $\dot{V}$ is strictly negative for every point then the stability is asymptotic.*

1.4.9 Lasalle's invariance principle

Theorem 1.4.7. *(Lasalle, 1976): Given a Lyapunov function $V(x)$ such that $\dot{V} \leq 0$ on a positive invariant set Ω and if the largest invariant set within $\{x \in \Omega : \dot{V}(x) = 0\}$ is $\{\bar{x}\}$. Then $\bar{x}$ is globally asymptotically stable in Ω.*

1.5 Aim and Objectives of this Work

The aim of the work is to investigate the transmission dynamics of malaria in an endemic setting using a mathematical model. The objectives of the work are:

(i) to model the transmission dynamics of malaria between humans and mosquitoes using a system of ordinary differential equations;

(ii) to investigate the local stability of the disease-free equilibrium point;

(iii) to determine the influence of some parameters on the basic reproduction number.

The rest of this work is organised as follows: in Chapter 2, we review some articles relevant to the mathematical modelling of malaria. Chapter 3 is devoted to model formulation and analysis. The theoretical results are validated numerically in Chapter 4 while conclusion is made in Chapter 5.

Chapter 2

LITERATURE REVIEW

Mathematical modelling of malaria began in 1911 with Ronald Ross(1911) who discovered the role of mosquitoes as an intermediate vector in the transmission of the pathogenic malaria parasite. He introduced the first deterministic model of the form

$$\begin{aligned} \frac{dI_h}{dt} &= b\beta_h m(1-I_h)I_m - rI_h, \\ \frac{dI_m}{dt} &= b\beta_m(1-I_m)I_h - \mu I_m. \end{aligned} \quad .$$

with variable I_h representing the fraction of infectious humans and I_m representing the fraction of infectious mosquitoes; b is the mosquito biting rate; β_h is the proportion of bites that produce infection in human; m is the fraction of number of mosquitoes to that of humans; r is the human recovery rate; β_m is the proportion of bites that produce infection in mosquitoes; and μ is the per capita rate of mosquitoes mortality. This model revealed that eradication of malaria could be made possible by decreasing vector (mosquitoes) biting rate and increasing the mosquitoes death rate resulting to reduction of threshold parameter given

$$R_0 = \frac{mb^2\beta_h\beta_m}{r\mu}$$

Macdonald (1957) presented the modification of the Ross model by incorporating the latency period of parasite in mosquitoes with an introduction of the

exposed class. The result revealed a decrease in the basic reproduction number with an increase in the latency period. A mathematical model was formulated by Ira and Smith (1983), the model stimulates permanent immunity and stability analysed. The findings of the study concluded that environmental factor could perturb the dynamical state from one subharmonic to another.

Macdonalds model was further extended by Anderson and May (1991) as they introduced new exposed class into the human population. The long term prevalence of both the infected humans and mosquitoes was decreased further by this improvement.

The three basic models discussed above are the building-ground for literature on malaria models. Since then, different factors have been incorporated in order to make the models epidemiologically more realistic. One such factor is the inclusion of recovered class into the human population on the idea that continuous exposure to reinfection could lead to acquired immunity in human. A deterministic model that incorporated human and mosquito populations with standard incidence function was developed by Nwga and shu (2000). The model formulated was

$$\begin{aligned}
\frac{dS_h}{dt} &= \lambda_h N_h + r_h I_h - f_h(N_h)S_h - \left(\frac{C_v a_v I_v}{N_h} S_h\right), \\
\frac{dI_h}{dt} &= \left(\frac{C_v a_v I_v}{N_h} S_h\right) - (r_h + f_h(N_h))I_h, \\
\frac{dS_v}{dt} &= \lambda_v N_v - f_v(N_v)S_v - \left(\frac{C_v a_v I_h}{N_h} S_v\right), \\
\frac{dE_v}{dt} &= \left(\frac{C_v a_v I_h}{N_h} S_v\right) - v_v + f_v(N_v)E_v, \\
\frac{dI_v}{dt} &= v_v E_v - f_v(N_v)I_v.
\end{aligned}$$

Their model made an exploration of the structure in which an infectious human recovers with temporary immunity to become a recovered human before entering the susceptible compartment again. Their conclusion unraveled that there is persistence in the disease whenever the threshold parameter R_0 exceeds one and that the disease-free equilibrium is globally asymptotically stable when

R_0 is below one.

Factors such as: environmental effects, mosquitoes resistance to insecticides, resistance of some parasite strains to anti-malaria drugs and the use of optimal control methods have been integrated into the models so as to gain more insight on the behaviour of the disease. Yang and Ferreira (2000), using bilinear incidence, studied malaria transmission model by incorporating socio-economic structure. From the model analysis, they showed how the basic reproduction number changes with global warming and local social and economic conditions.

In addition, Iddi et al (2002) used deterministic model with standard incidence function to study the impact of infectious immigrants on vector-borne disease with direct transmission. The research work was analyzed qualitatively, the computation of the basic reproduction number using the next generation matrix method and the conditions for the stability of the equilibra were determined. It was revealed through numerical simulation that increment in the number of immigrants tends to result to an increment in the number of infected population which leads to the persistence of the disease in the population.

Koella and Anita (2003) developed a model in order to understand the epidemiology of anti-malaria resistance and to assess approaches to decrease resistance spread. The model developed is shown as follows:

$$\begin{aligned} \frac{dx}{dt} &= \delta - \delta x - hx + pz, \\ \frac{dy}{dt} &= hx - (r+\delta)y, \\ \frac{dz}{dt} &= ry - (p+\delta)z. \end{aligned}$$

.

Their analyses showed that resistance to treatment does not spread if the fraction of infected individuals treated is less than a threshold value and if the drug treatment exceeds this value, then resistance to drug eventually becomes fixed in the population.

Chitnis et al (2006) presented a malaria model that incorporated human

immigration and disease-induced death rates. This model was based on Nwga and Shu model. The basic reproduction number was obtained to investigate the stability of disease-free equilibrium point using the next generation operator approach. It was further depicted through numerical examples that backward bifurcation is possible for some positive values of disease-induced death rate.

In another development, Tumwiine et al (2007) developed a five dimensional model with standard incidence for the dynamics of malaria in the human hosts and vectors. The model considered is as follows:

$$\begin{aligned}
\frac{dS_H}{dt} &= \lambda_h N_H - \frac{abS_H I_V}{N_H} + vI_H + \gamma R_H - \mu_h S_H, \\
\frac{dI_H}{dt} &= \frac{abS_H I_V}{N_H} - vI_H - rI_H - \delta I_H - \mu_h I_H, \\
\frac{dR_H}{dt} &= rI_H - \gamma R_H - \mu_h R_H, \\
\frac{dS_V}{dt} &= \lambda_v N_V - \frac{acS_V I_H}{N_H} - \mu_v S_V, \\
\frac{dI_V}{dt} &= \frac{acS_V I_H}{N_H} - \mu_v I_V.
\end{aligned}$$

. In this model, the reservoir of the susceptible human was refilled by immunity loss to the disease and newborns. The stability of the system was analysed for the existence of disease-free and endemic equilibra. However, it was shown that the basic reproduction number is independent of the rate of loss of immunity.

Schaffer and Bronnikova (2007), from another perspective, discussed the bifurcation structure of epidemic model subject to seasonality. The model that was discussed is as follows:

$$\begin{aligned}
\frac{ds}{dt} &= m(N - s) - \beta(t)SI + \gamma R, \\
\frac{dE}{dt} &= \beta(t)SI - (m + a)E, \\
\frac{dI}{dt} &= aE - (m + g)I, \\
\frac{dR}{dt} &= gE - (m + \gamma)R.
\end{aligned}$$

. The combination of phenomenological equation (Regression analysis in Statistical model) which admits to mathematical analysis and detailed simulation was suggested in their result as a proof and recipe for progress.

In addition, Chitnis et al (2008) carried out a sensitivity analysis of malaria model with human immigration factor and disease-induced death rate in order to determine the relative importance of model parameters to the disease transmission and prevalence. A computation of sensitivity indices of the basic reproduction number to parameters at the baseline values was done. It was found out that the basic reproduction number is most sensitive to the mosquito biting rate.

Labadin et al (2009) formulated and analysed a deterministic model with standard incidence function. The model that was considered is shown below,

$$\begin{aligned}
\frac{dS_H}{dt} &= m + bN_h + cR_H - \left(\beta_M H \frac{I_M}{N_H} S_H\right) + rI_H - (D_1 + D_2 N_H) S_H, \\
\frac{dE_H}{dt} &= \left(\beta_M H \frac{I_M}{N_H} S_H\right) - LE_H - (D_1 + D_2 N_H) S_H, \\
\frac{dI_H}{dt} &= LE_H - \left(\frac{qr}{q+r} I_H\right) - rI_H - dI_H - (D_1 + D_2 N_H) S_H, \\
\frac{dR_H}{dt} &= \left(\frac{qr}{q+r} I_H\right) - cR_H - (D_1 + D_2 N_H) S_H, \\
\frac{dS_M}{dt} &= BN_M - \left(\beta_H M \frac{I_H}{N_H} S_M\right) - \left(\beta_H M \frac{R_H}{N_H} S_M\right) - (\delta_1 + \delta_2 N_M) E_M, \\
\frac{dE_M}{dt} &= \left(\beta_H M \frac{I_H}{N_H} S_M\right) + \left(\beta_H M \frac{R_H}{N_H} S_M\right) - uE_M - (\delta_1 + \delta_2 N_M) E_M, \\
\frac{dI_M}{dt} &= uE_M - (\delta_1 + \delta_2 N_M) E_M.
\end{aligned}$$

.

In this model, a consideration of the recovered population with and without immunity and the impact of the different values of the average duration to build effective immunity on infectious humans were investigated numerically. The findings of their research showed that if the ability to build an effective immunity is fast for those who recovered from the disease, then the number of cases could be reduced.

One of the contributory factors to the spread of malaria is proven to be the movement of human from one environment to another. In the light of this, Arino et al (2011) came up with a metapopulation model for malaria where interaction between humans in rural and urban area was investigated. They brought to the light that the basic reproduction number governed the stability of the disease-free steady state. Also, the unrestricted movement of infected humans could lead to the persistence of the disease in the population. Again, the class of infectious individuals with drug resistance symptoms was incorporated in the standard incidence function deterministic model that was formulated and analysed by Okosun and Makinde (2011). The model which was considered as follows;

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + kR_h - \beta_m S_h - \mu_h S_h, \\
\frac{dE_h}{dt} &= \beta_m S_h - (a_1 + \mu_h)E_h, \\
\frac{dI_h}{dt} &= a_1 E_h - (b + \tau u_2(t) + \psi + \mu_h)I_h, \\
\frac{dI_d h}{dt} &= u_2(t)(1-\rho)\tau I_h - (\mu + \psi + \sigma)I_d h, \\
\frac{dR_h}{dt} &= u_2(t)\rho\tau I_h + \sigma I_d h - (k + \mu_h)R_h, \\
\frac{dS_v}{dt} &= \Lambda_v - \lambda_v S_v - \mu_v S_v, \\
\frac{dE_v}{dt} &= \lambda_v S_v - (a_2 + \mu_v)E_v, \\
\frac{dI_v}{dt} &= a_2 E_v - \mu_v I_v.
\end{aligned}$$

. The model was shown to exhibit backward bifurcation and by the basic reproduction number, the existence and stability of equilibria were established. Pontryagin maximum principle was used to obtain conditions for optimal control of the disease and their numerical results showed that effective control of the proportion of individuals with drug resistance has a positive impact in reducing the spread of the disease.

Magombedze et al (2011) developed an intra-host mathematical model of malaria that described the interaction of immune system with the blood stage

malaria merozoites. The model which was considered is as follows;

$$\begin{aligned}
\frac{dX(t)}{dt} &= \Lambda_x + \sigma Y(t) - \beta\frac{X(t)M(t)}{1+c_0A(t)} - \mu_x X(t) - wX(t)M(t)B(t), \\
\frac{dY(t)}{dt} &= \beta\frac{X(t)M(t)}{1+c_0A(t)} - u_y Y(t) - k_y B(t)Y(t), \\
\frac{dM(t)}{dt} &= \frac{ru_yY(t)}{1+c_1B(t)} - \mu_m M(t) - k_m B(t)M(t) - \beta\frac{X(t)M(t)}{1+c_0A(t)}.
\end{aligned}$$

.

Optimal control strategy was used in this analysis. This led to a suggestion in their result that a malaria therapy that seeks to minimize merozoites population was beneficial to patients as this will lead to the reduction of infected red blood cells. Also, a seven-dimensional compartmental model of malaria that incorporated three control functions such as: the prevention of host-vector contacts, treatment of hosts and reduction of mosquito population was studied by Lashari et al (2012). In the analyses by the model, necessary conditions for optimal control of malaria were obtained. The numerical simulation of the model revealed that the combination of the control efforts has a very desirable effect on the population in reducing the number of infected individuals.

The influence of seasonal forcing system when the dynamical system which is unforced have either stable, monotonic or oscillatory cycle was examined by Rachel (2012). Their results revealed that the degree of oscillation in the unforced system has a larger effect on the range of behaviour when the system is seasonally forced.

Moreover, Gouhei and Kazuyuki (2013) investigated the influence of seasonal structure on disease transmission dynamics. In their result, it was suggested that accurately estimated seasonal fluctuation is necessary to have good knowledge on disease transmission.

Furthermore, Olaniyi and Obabiyi (2013) formulated a mathematical model that incorporated antibodies to curtail transmission of parasite that causes

malaria in both human and mosquito. The model formulated is as follows;

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - \frac{b\beta_h S_h(t) I_m}{1 + v_h I_m(t)} - \mu_h S_h(t) + \omega R_h(t), \\
\frac{dE_h}{dt} &= \frac{b\beta_h S_h(t) I_m}{1 + v_h I_m(t)} - \alpha_h E_h(t) - \mu_h E_h(t), \\
\frac{dI_h}{dt} &= \alpha_h E_h(t) - (\gamma + \mu_h + \delta_h) I_h(t), \\
\frac{dR_h}{dt} &= \gamma I_h(t) - (\mu_h + \omega) R_h(t), \\
\frac{dS_m}{dt} &= \Lambda_m - \frac{b\beta_m S_m(t) I_h}{1 + v_m I_h(t)} - \mu_m S_m(t), \\
\frac{dE_m}{dt} &= \frac{b\beta_m S_m(t) I_h}{1 + v_m I_h(t)} - (\alpha_m + \mu_m) E_m(t), \\
\frac{di_m}{dt} &= \alpha_m E_m(t) - (\mu_m + \delta_m) I_h(t).
\end{aligned}$$

.

The stability of the model analyzed through threshold parameter (R_0). The results of their analyses showed that the disease will not persist in the population whenever R_0 is below unity. However, the system become unstable whenever R_0 is above unity. In a related work, a non- autonomous model that incorporated multiple control measures was developed by Olaniyi et al (2018) to investigate the dynamics of malaria transmission in both human and mosquito populations. The model considered is as follows;

$$\begin{aligned}
\frac{dS_h}{dt} &= (1-\tau)\Lambda_h - (1-u_1(t)) b\beta_h S_h(t) I_m(t) - \mu_h S_h(t), \\
\frac{dE_h}{dt} &= (1-u_1(t)) b\beta_h S_h(t) I_m(t) - (\alpha_h + \mu_h) E_h(t), \\
\frac{dI_h}{dt} &= (1-u_2(t))\alpha_h E_h(t) - (u_3(t)\gamma + \mu_h) I_h(t), \\
\frac{dV_h}{dt} &= \tau\Lambda_h + u_2(t)\alpha_h E_h(t) + u_3(t)\gamma I_h(t) - \mu_h V_h(t), \\
\frac{dS_m}{dt} &= (1-u_4(t))\Lambda_m - (1-u_1(t)) b\beta_m S_m(t) I_h(t) - (\mu_m + u_4(t) r) S_m(t), \\
\frac{dE_m}{dt} &= (1-u_1(t)) b\beta_m S_m(t) I_h(t) - (\alpha_m + \mu_m + u_4(t) r) E_m(t), \\
\frac{dI_m}{dt} &= \alpha_m E_m(t) - (\mu_m + u_4(t) r) I_m(t).
\end{aligned}$$

. With the aid of suitable Lyapunov functions, the stability of both disease-free and endemic equilibra was established. A suggestion is made in the result of their analysis that combination of multiple control at a time by human traveler will help to eliminate the spread of malaria in the population.

Chapter 3

MODEL FORMULATION AND ANALYSIS

3.1 Model description

To study the transmission and spread of malaria in two interacting populations of humans (the host) and mosquitoes (the vector), we formulate a model which subdivides the total human population size at time t into susceptible humans, $S_h(t)$, exposed humans, $E_h(t)$, infectious humans, $I_h(t)$ and recovered humans, $R_h(t)$. Hence, we have $N_h(t) = S_h(t)+E_h(t)+I_h(t)+R_h(t)$. We denote β_h and ω, as the Probability that a bite by an infectious mosquito results in transmission of disease to human at time t and loss of immunity. Similarly, we divide the adult mosquito population into two subclasses: susceptible mosquitoes $S_m(t)$ and infectious mosquitoes $I_m(t)$. The mosquito population has no recovered class as the mosquitoes remain infectious for life (Lashari et al, 2012; Chitnis et al, 2008). Thus, the total size of the mosquito population at any time t is denoted by $N_m(t) = S_m(t) + I_m(t)$.

Susceptible individuals are recruited into the human population by input rate Λ_h. Following the concept of parasite transmission as described in Cox (2010), an infectious female anopheles mosquito, I_m, usually attacks susceptible human S_h by piercing and sucking using its proboscis, with which it introduces an enzyme from the saliva into human's bloodstream in order to inhibit blood clotting while sucking. In the process, sporozoites are injected into the blood and the susceptible human moves to the exposed class $E_h(t)$. Exposed humans are those who have parasites in them and the parasites are in asexual stages. They are without gametocytes and are not capable of transmitting the disease

to the susceptible mosquitoes. Generally, individuals are asymptomatic for 7-30 days since the incubation period depends on the parasite species (CDC, 2015).

From the blood of the exposed human, the parasite goes into the liver for cell division and multiplication before being released into the blood again as merozoites. At this stage, the exposed human becomes infectious $I_h(t)$. After treatment, the infectious human recovers and moves to the recovered class $R_h(t)$. Every class of human population is decreased by natural death except for the infectious class which has a per capita disease-induced death rate δ_h in addition. α_h represents progression rate of exposed human to infectious human. Humans leave the population through natural death rate μ_h. When a susceptible mosquito $S_m(t)$ bites an infectious human, the parasite (in the form of a gametocytes) enters the mosquito with some probability, β_m, and the mosquito moves from the susceptible then becomes infectious and enters the class $I_m(t)$. Mosquitoes leave the population through natural death rate μ_m.

The compartmental model which shows the mode of transmission of malaria between the two interacting populations is depicted in the Figure 3.1. Based on the above assumptions, we have the following system of ordinary differential equations:

$$\begin{cases} \frac{dS_h}{dt} &= \Lambda_h - \beta_h S_h(t) I_m(t) + \omega R_h(t) - \mu_h S_h(t) \\ \frac{dE_h}{dt} &= \beta_h S_h(t) I_m(t) - (\alpha_h + \mu_h) E_h(t) \\ \frac{dI_h}{dt} &= \alpha_h E_h(t) - (\gamma_h + \mu_h + \delta_h) I_h(t) \\ \frac{dR_h}{dt} &= \gamma_h I_h - (\omega + \mu_h) R_h(t) \\ \frac{dS_m}{dt} &= \Lambda_m - \beta_m S_m(t) I_h(t) - \mu_m S_m(t) \\ \frac{dI_m}{dt} &= \beta_m S_m(t) I_h(t) - \mu_m I_m \end{cases} \tag{3.1.1}$$

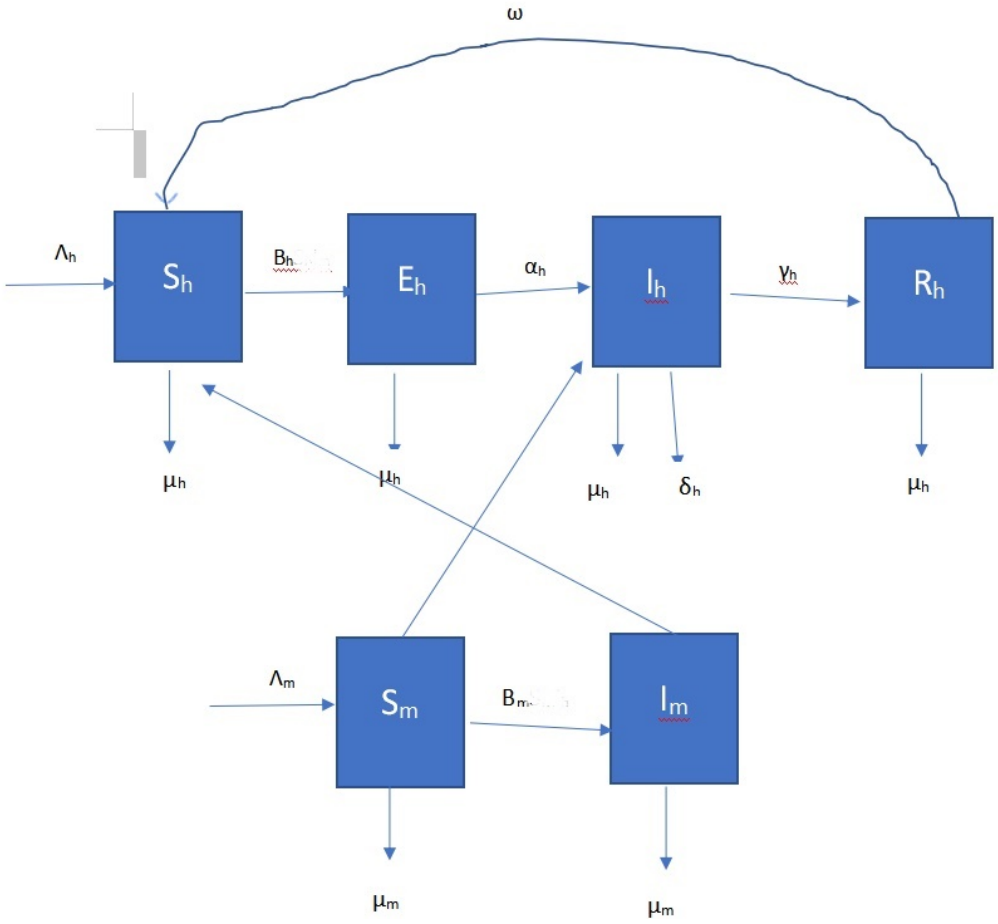

Figure 3.1: Schematic diagram showing the transmission dynamics of malaria

Table 3.1: Description of parameters.

Definition	Symbols	Value	Source
Recruitment rate of humans	Λ_h	0.05	(Assumed)
Effective Infection Rate of Humans	β_h	0.005	(Assumed)
Natural death rate of humans	μ_h	0.0000548	(Lashari et al,2012)
Loss of immunity	ω	0.01	(Assumed)
Progression rate of exposed Humans	α_h	0.0588235294	(Blayneh et al,2009)
Recovery Rate of Infectious Humans	γ_h	0.05	(Assumed)
Disease Induced Death rate	δ_h	0.001	(Okosun and Makinde,2011)
Recruitment Rate of the Mosquito population	Λ_m	100	(Assumed)
Effective Infection Rate of Mosquitoes by the Parasite.	β_m	0.004	(Assumed)
Natural Death Rate of Mosquitoes	μ_m	0.0666667	(Lashari et al,2012)

3.2 Positivity of solutions

Here, we provide the following results which guarantee that the malaria model governed by system (3.1.1) is mathematically well-posed in a feasible region $\mathcal{D}$

Theorem 3.2.1. *There exists a domain $\mathcal{D}$ in which the solution set $\{S_h, E_h, I_h, R_h, S_m, I_m\}$ of model (3.1.1) is contained and bounded.*

Proof. If the total human population size is given by $N_h = S_h + E_h + I_h + R_h$, and the total size of mosquito population is $N_m = S_m(t) + I_m(t)$. From model (3.1.1) we have that,

$$\begin{aligned}\frac{dN_h}{dt} &= \Lambda_h - \beta S_h I_m + \gamma R_h - \mu_h S_h + \beta S_h I_m - \alpha_h E_h - \mu_h E_h \\ &\quad + \alpha_h E_h - \mu_h I_h - \delta I - \gamma R_h \\ &= \Lambda - \mu[S_h + E_h + I_h + R_h] - \delta_h I_h. \end{aligned} \tag{3.2.1}$$

Equation (3.2.1) becomes,

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h - \delta_h I_h. \tag{3.2.2}$$

ignoring the term $\delta_h I_h$, we have,

$$\frac{dN_h}{dt} \leq \Lambda_h - \mu N_h \tag{3.2.3}$$

solving equation (3.2.3), We have

$$\frac{\mathrm{d}N_h(t)}{\mathrm{d}t} + \mu N_h(t) \leq \Lambda_h$$

Using the integration factor I.F$= e^{\int \mu \mathrm{d}t} = e^{\mu_h t}$

$$\frac{\mathrm{d}}{\mathrm{d}t}(e^{\mu_h t}N(t)) = \Lambda_h$$
$$\frac{\mathrm{d}N(t)}{\mathrm{d}t} = \Lambda_h e^{\mu_h t}$$

Integrating both sides, we have

$$N(t) = \int \Lambda_h e^{-\mu t}\mathrm{d}t$$
$$N(t) = \int_0^t \Lambda_h e^{-\mu t}\mathrm{d}t$$
$$N(t) = -\frac{\Lambda_h}{\mu}e^{-\mu x}|_0^t$$
$$N(t) = -\frac{\Lambda_h}{\mu}e^{-\mu t} - \left(-\frac{\Lambda_h}{\mu}e^{-\mu_h(0)}\right)$$
$$N(t) = -\frac{\Lambda_h}{\mu}e^{-\mu t} + \frac{\Lambda_h}{\mu_h},$$

as $t \to \infty$ we have

$$\lim_{t\to\infty} N(t) \leq -\frac{\Lambda_h}{\mu}e^{-\mu(\infty)} + \frac{\Lambda_h}{\mu_h}$$
$$N(t) \leq \frac{\Lambda_h}{\mu_h}.$$

Therefore,

$$\mathcal{D} = \left\{ N(t) \leq \frac{\Lambda_h}{\mu_h}, S_h > 0, E_h \geq 0, I_h \geq 0, R_h \geq 0 \right\}.$$

.

3.3 Local stability of disease-free equilibrium

Now, we obtain the disease free equilibrium, E_0. At the steady state the first derivatives $\frac{dS_h}{dt} = \frac{dE_h}{dt} = \frac{dI_h}{dt} = \frac{dR_h}{dt} = \frac{dS_m}{dt} = \frac{dI_m}{dt} = 0$, we then set all the disease classes E_h, I_h, I_m to zero. Solving the resulting solutions, we obtain the disease

free equilibrium

$$E_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, \frac{\Lambda_m}{\mu_m}, 0\right).$$

Now, we obtain the basic reproduction number usually denoted by ($\mathcal{R}_0$) using next generation matrix technique. Detailed explanation of this approach is contained in Section 1.3.5. Following the idea of Dikmann, 1990 we obtain $\mathcal{R}_0$ as follows:

$$F(x) = \begin{pmatrix} \beta_h S_h I_m \\ 0 \\ \beta_h S_m I_h \end{pmatrix}, \qquad V(x) = \begin{pmatrix} (\alpha_h + \mu_h)E_h \\ -\alpha_h E_h + (\gamma_h + \delta_h + \mu_h)I_h \\ \mu_m I_m \end{pmatrix}$$

Taking the Jacobian matrix of $F(x)$ and $V(x)$ we have

$$J_F = \begin{pmatrix} 0 & 0 & \beta_h S_h \\ 0 & 0 & 0 \\ 0 & \beta_m S_m & 0 \end{pmatrix}$$

$$J_V = \begin{pmatrix} \alpha_h + \mu_h & 0 & 0 \\ -\alpha_h & \gamma_h + \delta_h + \mu_h & 0 \\ 0 & 0 & \mu_m \end{pmatrix}$$

At the disease free equilibrium, E_0

$$J_F E_0 = \begin{pmatrix} 0 & 0 & \frac{\beta_h \Lambda_h}{\mu_h} \\ 0 & 0 & 0 \\ 0 & \frac{\beta_m \Lambda_m}{\mu_m} & 0 \end{pmatrix}$$

$$J_V E_0 = \begin{pmatrix} \alpha_h + \mu_h & 0 & 0 \\ -\alpha_h & \gamma_h + \delta_h + \mu_h & 0 \\ 0 & 0 & \mu_m \end{pmatrix}$$

Now we compute the inverse of $J_V E_0$ as,

$$J_V(E_0)^{-1} = \begin{pmatrix} \frac{1}{\alpha_h + \mu_h} & 0 & 0 \\ \frac{\alpha}{(\gamma_h + \delta_h + \mu_h)(\alpha_h + \mu_h)} & \frac{1}{\gamma_h + \delta_h + \mu_h} & 0 \\ 0 & 0 & \frac{1}{\mu_m} \end{pmatrix}$$

$$
\begin{aligned}
&J_F(E_0) \times J_V(E_0)^{-1} \\
&= \begin{pmatrix} 0 & 0 & \dfrac{\beta_h \Lambda_h}{\mu_h} \\ 0 & 0 & 0 \\ 0 & \dfrac{\beta_m \Lambda_m}{\mu_m} & 0 \end{pmatrix} \begin{pmatrix} \dfrac{1}{\alpha_h + \mu_h} & 0 & 0 \\ \dfrac{\alpha}{(\gamma_h + \delta_h + \mu_h)(\alpha_h + \mu_h)} & \dfrac{1}{\gamma_h + \delta_h + \mu_h} & 0 \\ 0 & 0 & \dfrac{1}{\mu_m} \end{pmatrix} \\
&= \begin{pmatrix} 0 & 0 & \dfrac{\beta_h \Lambda_h}{\mu_h \mu_m} \\ 0 & 0 & 0 \\ \dfrac{\beta_m \Lambda_m \alpha_h}{\mu_m (\delta_h + \mu_h)(\gamma_h + \delta_h)} & \dfrac{\beta_m \Lambda_m}{\mu_m (\gamma_h + \delta_h + \mu_h)} & 0 \end{pmatrix}. \qquad (3.3.1)
\end{aligned}
$$

The basic reproduction number is the spectral radius of (3.3.1) and is given as

$$\mathcal{R}_0 = \frac{\Lambda_h \Lambda_m \alpha_h \beta_h \beta_m}{(\alpha_h + \mu_h)(\gamma_h + \delta_h + \mu_h)\mu_m^2 \mu_h}.$$

Theorem 3.3.1. *The disease-free equilibrium, E_0, of* (3.1.1) *is locally asymptotically stable in $\mathcal{D}$ if $\mathcal{R}_0 < 1$.*

Proof. Taking the Jacobian matrix of the malaria model (3.1.1) we have

$$
J = \begin{pmatrix} -\beta_h I_m - \mu_h & 0 & 0 & \omega & 0 & -\beta_h S_h \\ \beta_h I_m & -\alpha_h - \mu_h & 0 & 0 & 0 & \beta_h S_h \\ 0 & -\alpha_h & -\gamma_h - \mu_h - \delta_h & 0 & 0 & 0 \\ 0 & 0 & \gamma_h & -\omega - \mu_h & 0 & 0 \\ 0 & 0 & -\beta_m S_m & 0 & -\beta_m I_h - \mu_m & 0 \\ 0 & 0 & \beta_m S_m & 0 & \beta_m I_h & -\mu_m \end{pmatrix}.
$$

At the disease free equilibrium point E_0, J becomes,

$$J(E_0) = \begin{pmatrix} -\mu_h & 0 & 0 & \omega & 0 & -\frac{\beta_h \Lambda_h}{\mu_h} \\ 0 & -\alpha_h - \mu_h & 0 & 0 & 0 & \frac{\beta_h \Lambda_h}{\mu_h} \\ 0 & \alpha_h & -\gamma_h - \mu_h - \delta_h & 0 & 0 & 0 \\ 0 & 0 & \gamma_h & -\omega - \mu_h & 0 & 0 \\ 0 & 0 & -\frac{\beta_m \Lambda_m}{\mu_m} & 0 & -\mu_m & 0 \\ 0 & 0 & \frac{\beta_m \Lambda_m}{\mu_m} & 0 & 0 & -\mu_m \end{pmatrix}.$$

Taking the eigenvalues of $J(E_0)$, the following results are obtained

$$\begin{vmatrix} -\mu_h - \lambda & 0 & 0 & \omega & 0 & -\frac{\beta_h \Lambda_h}{\mu_h} \\ 0 & -A - \lambda & 0 & 0 & 0 & \frac{\beta_h \Lambda_h}{\mu_h} \\ 0 & \alpha_h & -B - \lambda & 0 & 0 & 0 \\ 0 & 0 & \gamma_h & -\omega - \mu_h - \lambda & 0 & 0 \\ 0 & 0 & -\frac{\beta_m \Lambda_m}{\mu_m} & 0 & -\mu_m - \lambda & 0 \\ 0 & 0 & \frac{\beta_m \Lambda_m}{\mu_m} & 0 & 0 & -\mu_m - \lambda \end{vmatrix} = 0, \tag{3.3.2}$$

where $A = \alpha_h + \mu_h$ and $B = \gamma_h + \mu_h + \delta_h$. Reducing (3.3.2), we have;

$$(-\mu_h - \lambda) \begin{vmatrix} -A - \lambda & 0 & 0 & 0 & \frac{\beta_h \Lambda_h}{\mu_h} \\ \alpha & -B - \lambda & 0 & 0 & 0 \\ 0 & \gamma_h & -\omega - \mu_h - \lambda & 0 & 0 \\ 0 & -\frac{\beta_m \Lambda_m}{\mu_m} & 0 & -\mu_m - \lambda & 0 \\ 0 & \frac{\beta_m \Lambda_m}{\mu_m} & 0 & 0 & -\mu_m - \lambda \end{vmatrix} = 0. \tag{3.3.3}$$

Now reducing (3.3.3), we have

$$(-\mu_h-\lambda)(-\mu_m-\lambda)\begin{vmatrix} -A-\lambda & 0 & 0 & \frac{\beta_h\Lambda_h}{\mu_h} \\ \alpha_h & -B-\lambda & 0 & 0 \\ 0 & \gamma_h & -\omega-\mu_h-\lambda & 0 \\ 0 & \frac{\beta_m\Lambda}{\mu_m} & 0 & -\mu_m-\lambda \end{vmatrix} = 0, \tag{3.3.4}$$

Now,reducing (3.3.4)

$$(-\mu_h-\lambda)(-\mu_m-\lambda)(-\omega-\mu_h-\lambda)\begin{vmatrix} -A-\lambda & 0 & \frac{\beta_h\Lambda_h}{\mu_h} \\ \alpha_h & -B-\lambda & 0 \\ 0 & \frac{\beta_m\Lambda_m}{\mu_m} & -\mu_m-\lambda \end{vmatrix} = 0.$$

It is therefore obvious that $-\mu_h$, $-\mu_m$ and $-\omega-\mu_h$ are negative eigenvalues. To obtain the remaining eigenvalues, we solve for the determinant,

$$\begin{vmatrix} -A-\lambda & 0 & \frac{\beta_h\Lambda_h}{\mu_h} \\ \alpha_h & -B-\lambda & 0 \\ 0 & \frac{\beta_m\Lambda_m}{\mu_m} & -\mu_m-\lambda \end{vmatrix} = 0$$

whose characteristic equation is obtained as

$$\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0, \tag{3.3.5}$$

where

$$\begin{aligned} a_2 &= A + B + \mu_m \\ a_1 &= A\mu_m + B\mu_m + AB \\ a_0 &= AB\mu_m - \frac{\alpha_h\beta_h\beta_m\Lambda_h\Lambda_m}{\mu_m\mu_h}. \end{aligned}$$

Next, we use Routh-Hurwitz criterion to establish that all roots of (3.2.8) have negative real part. By Routh-Hurwitz criterion, the roots of (3.2.8) have negative real parts if and only if a_0, a_2 are positive and $a_2a_1 > a_0$.

Obviously, $a_1 > 0$, $a_2 > 0$, and

$$\begin{aligned} a_0 &= AB\mu_m - \frac{\alpha_h\beta_h\beta_m\Lambda_h\Lambda_m}{\mu_m\mu_h} \\ &= AB\mu_m - \left(\frac{\alpha_h\beta_h\beta_m\Lambda_h\Lambda_m}{AB\mu_m^2\mu_h}\right) AB\mu_m \\ &= AB\mu_m - \mathcal{R}_0 AB\mu_m \\ &= (1-\mathcal{R}_0)AB\mu_m \ > 0 \qquad \text{provided} \quad \mathcal{R}_0 < 1. \end{aligned}$$

Next, we check for $a_2a_1 > a_0$.

$$\begin{aligned} a_2a_1 - a_0 &= (A+B+\mu_m)(A\mu_m + B\mu_m + AB) - (1-R_0)AB\mu_m \\ &= A^2(B+\mu_m) + B^2(A+\mu_m) + 3AB\mu_m + \mu_m^2(A+B) \\ &\quad + (2+R_0)AB\mu_m > 0. \end{aligned}$$

Thus, the Routh-Hurwitz criterion is satisfied provided $\mathcal{R}_0 < 1$. Implying that all the eigenvalues have negative real parts when $\mathcal{R}_0 < 1$. Therefore, the disease-free equilibrium point E_0 is locally asymptotically stable when $\mathcal{R}_0 < 1$. The biological implication of this is that the disease will completely die out of the population whenever the basic reproduction number, $\mathcal{R}_0$ is below unity.

3.4 Sensitivity Analysis

In order to determine the parameters or factors most essential in the transmission dynamics and spread of malaria, we perform a sensitivity analysis of the formulated model (3.2.1) in the sense of Chitnis et al (2008).

Definition 3.4.1. *The normalized forward sensitivity analysis index, of a variable, v to a parameter p denoted by Υ_p^v, is denoted as a ratio of the relative change in the variable to the relative change in the parameter*

$$\Upsilon_p^v = \frac{\partial v}{\partial p} \times \frac{p}{v}.$$

The detailed sensitivity indices of $\mathcal{R}_0$, using the parameter values provided in Table 1 are computed thus

$$\begin{aligned} \Upsilon_{\alpha_h}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial \alpha_h} \times \frac{\alpha_h}{\mathcal{R}_0} \\ &= \left[\frac{C_1}{\alpha_h+\mu_h} - \frac{C_1\alpha_h}{(\alpha_h+\mu_h)^2}\right] \times \frac{\alpha_h}{\frac{\alpha_h}{\alpha_h+\mu_h}C_1} \qquad \text{where} \quad C_1 = \frac{\Lambda_h\Lambda_m\beta_h\beta_m}{(\gamma_h+\delta_h+\mu_h)\mu_m^2\mu_h} \\ &= \left[\frac{1}{\alpha_h+\mu_h} - \frac{\alpha_h}{(\alpha_h+\mu_h)^2}\right](\alpha_h+\mu_h) \\ &= 1 - \frac{\alpha_h}{\alpha_h+\mu_h} \\ &= 0.0009307 \end{aligned}$$

$$
\begin{aligned}
\Upsilon_{\beta_h}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial \beta_h} \times \frac{\beta_h}{\mathcal{R}_0} \\
&= C_2 \times \frac{\beta_h}{\beta_h C_2} \qquad \text{where} \quad C_2 = \frac{\Lambda_h \Lambda_m \alpha_h \beta_m}{(\alpha_h + \mu_h)(\gamma_h + \delta_h + \mu_h)\mu_m^2 \mu_h} \\
&= \frac{C_2 \beta_h}{\beta_h C_2} \\
&= 1
\end{aligned}
$$

$$
\begin{aligned}
\Upsilon_{\beta_m}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial \beta_m} \times \frac{\beta_m}{\mathcal{R}_0} \\
&= C_3 \times \frac{\beta_m}{\beta_m C_3} \qquad \text{where} \quad C_3 = \frac{\Lambda_h \Lambda_m \alpha_h \beta_h}{(\alpha_h + \mu_h)(\gamma_h + \delta_h + \mu_h)\mu_m^2 \mu_h} \\
&= \frac{C_3 \beta_m}{\beta_m C_3} \\
&= 1
\end{aligned}
$$

$$
\begin{aligned}
\Upsilon_{\gamma_h}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial \gamma_h} \times \frac{\gamma_h}{\mathcal{R}_0} \\
&= \left[-C_4(\gamma_h + \delta_h + \mu_h)^{-2}\right] \times \frac{\gamma_h}{(\gamma_h + \delta_h + \mu_h)^{-1} C_4} \qquad \text{where} \quad C_4 = \frac{\Lambda_h \Lambda_m \alpha_h \beta_h \beta_m}{(\alpha_h + \mu_h)\mu_m^2 \mu_h} \\
&= \frac{(-C_4(\gamma_h + \delta_h + \mu_h)^{-2})\gamma_h}{(\gamma_h + \delta_h + \mu_h)^{-1} C_4} \\
&= \frac{-\gamma_h}{\gamma_h + \delta_h + \mu_h} \\
&= -0.97934
\end{aligned}
$$

$$
\begin{aligned}
\Upsilon_{\delta_h}^{\mathcal{R}_0} &= \frac{\partial \mathcal{R}_0}{\partial \delta_h} \times \frac{\delta_h}{\mathcal{R}_0} \\
&= \left[-C_5(\gamma_h + \delta_h + \mu_h)^{-2}\right] \times \frac{\delta_h}{(\gamma_h + \delta_h + \mu_h)^{-1} C_5} \qquad \text{where} \quad C_5 = \frac{\Lambda_h \Lambda_m \alpha_h \beta_h \beta_m}{(\alpha_h + \mu_h)\mu_m^2 \mu_h} \\
&= \frac{(-C_5(\gamma_h + \delta_h + \mu_h)^{-2})\delta_h}{(\gamma_h + \delta_h + \mu_h)^{-1} C_5} \\
&= \frac{-\delta_h}{\gamma_h + \delta_h + \mu_h} \\
&= -0.0195867969.
\end{aligned}
$$

The sensitivity indices are summarized in Figure 3.2.

It is obvious that intervention strategies are best built around human-to-mosquito transmission rate (β_h), mosquito-to-human transmission rate (β_m) and recovery rate of humans (γ_h), therefore, the following could be adopted:

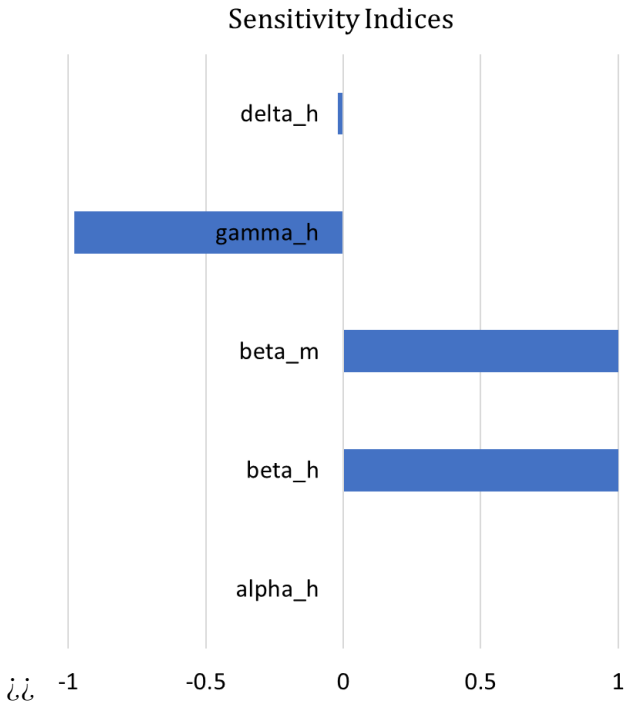

Figure 3.2: Sensitivity indices

(a) Public health sensitization of the population. The population should be informed to go for regular medical check-up and treatment where necessary. This will help to increase the knowledge in the populace about the disease, and also improve on the number of treated infectious individuals.

(b) Use of active insecticides to help eradicate mosquitoes in residential areas thereby decreasing mosquito-to-human transmission rate.

(c) Removal of breeding grounds (eg stagnant water) for mosquitoes. Removal of these breeding grounds leads to the reduction of mosquitoes and prevention of malaria.

(d) Use of effective antimalaria drugs. When malaria has been discovered in the system of a human, the right adminstration of the drugs help improve on the recovery from malaria.

(e) Use of treated mosquito nets. Mosquito nets are important in preventing the spread of malaria. Proper treatment of the mosquito nets help them stay effective against mosquitoes.

Chapter 4

SIMULATION AND DISCUSSION OF RESULTS

In this chapter, model (3.1.1) is solved numerically using fourth order Runge-Kutta method. All simulations were done using Maple 15 software (see Appendix for the codes). Using parameter values in Table 3.1, we solve model (3.1.1) to

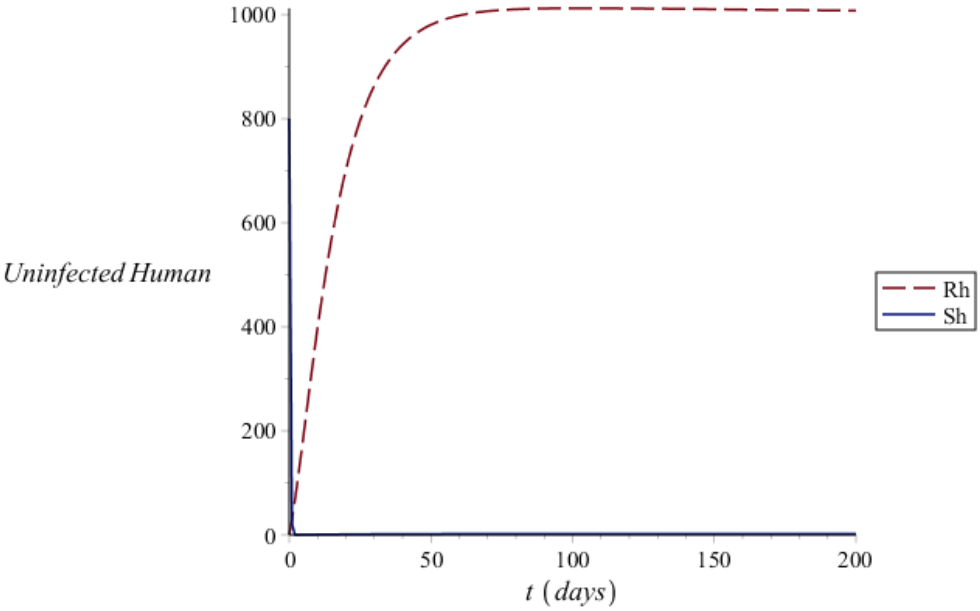

Figure 4.1: Time responses of S_h and R_h when $R_0 > 1$

obtain Figures 4.1−4.3. In this case, $\mathcal{R}_0 > 1$.

Figure 4.1 shows that susceptible class S_h decreases over time while the recovered class R_h increases over time. In Figure 4.2, the exposed class E_h decreases then appears constant over time and the infectious class I_h decreases and also appears constant over time. Figure 4.3 shows that both the populations of susceptible mosquitoes S_m and infectious mosquitoes I_m remain in the ecosystem

when $\mathcal{R}_0 > 1$. Figures 4.1−4.3 show that disease persists in the population when $\mathcal{R}_0 > 1$ and also suggest that the model has a stable endemic equilibrium point when $\mathcal{R}_0 > 1$.

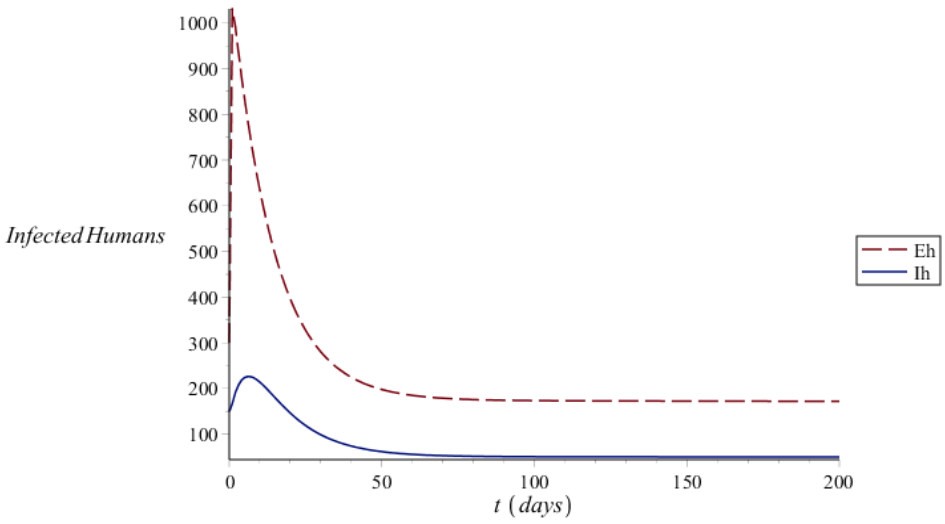

Figure 4.2: Time responses of E_h and I_h when $R_0 > 1$

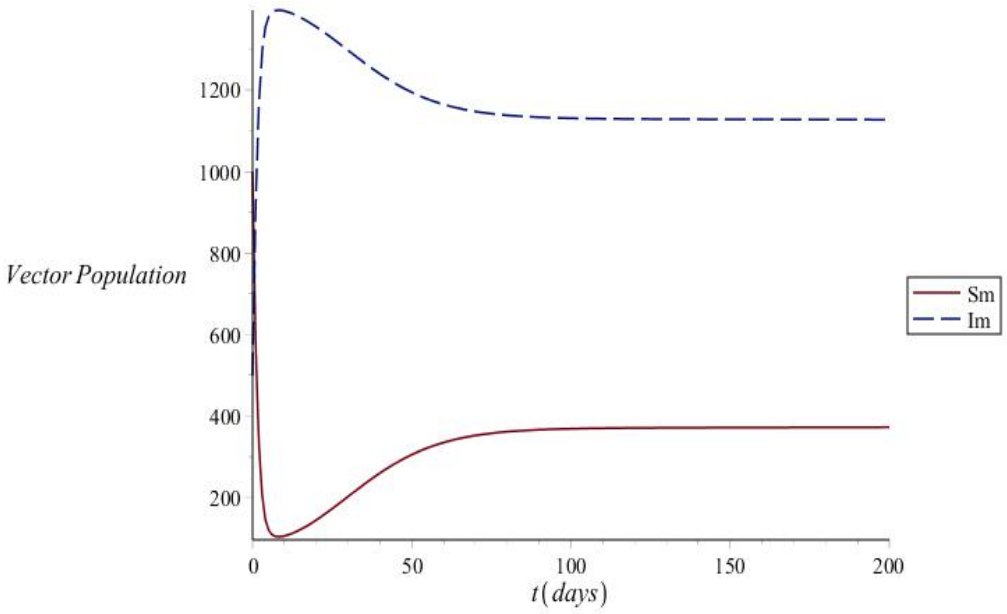

Figure 4.3: Time responses of S_m and I_m when $R_0 > 1$

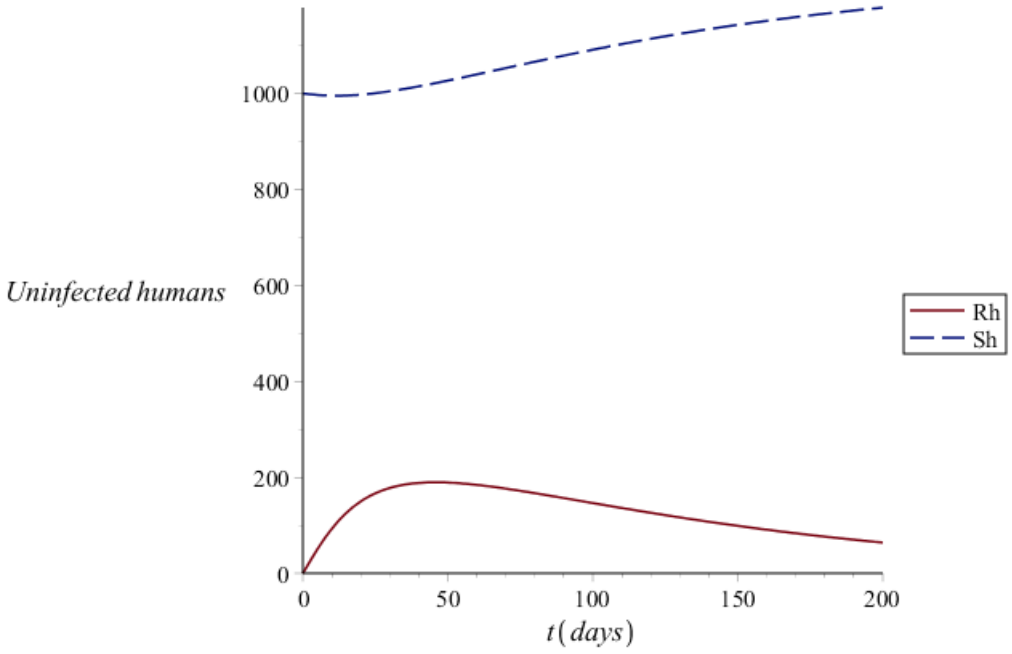

Figure 4.4: Time responses of S_h and R_h when $R_0 < 1$

It was noted in Theorem 3.3.1 that the disease-free equilibrium point is locally asymptotically stable when $\mathcal{R}_0 < 1$. Next we investigate this numerically. To arrive at the conditions that make $\mathcal{R}_0 < 1$, we refer to Section 3.4. The sensitivity analysis in Section 3.4 reveals that human-to-mosquito transmission rate (β_h), mosquito-to-human transmission rate (β_m) and recovery rate of humans (γ_h). It is therefore necessary to build controls around these parameters for quick elimination of the disease. For our simulation, we choose β_h such that $\mathcal{R}_0 < 1$. The effect of this is shown in Figures 4.4−4.6.

Figure 4.4 shows that there is an increase in the susceptible class S_h and and also shows a decrease in the recovered class.the decrease in the recovered class is as a result of decrease in the number of infection in the population and this also explains the increase in the number of susceptible individuals. .Figure 4.5 shows that there is a decrease in the infected class I_h and the exposed class E_h decreases over time. Figure 4.6 shows that there is an increase in the susceptible class of mosquitoes S_m leading to a decrease in the infectious mosquitoes I_m.

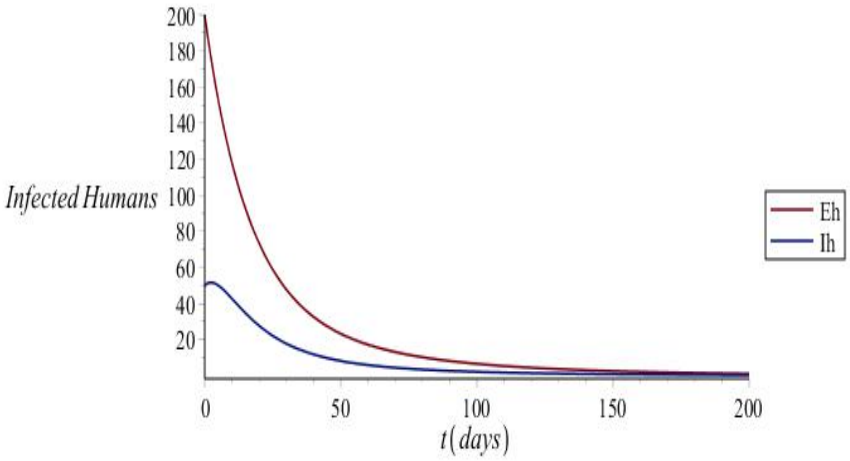

Figure 4.5: Time responses of E_h and I_h when $R_0 < 1$

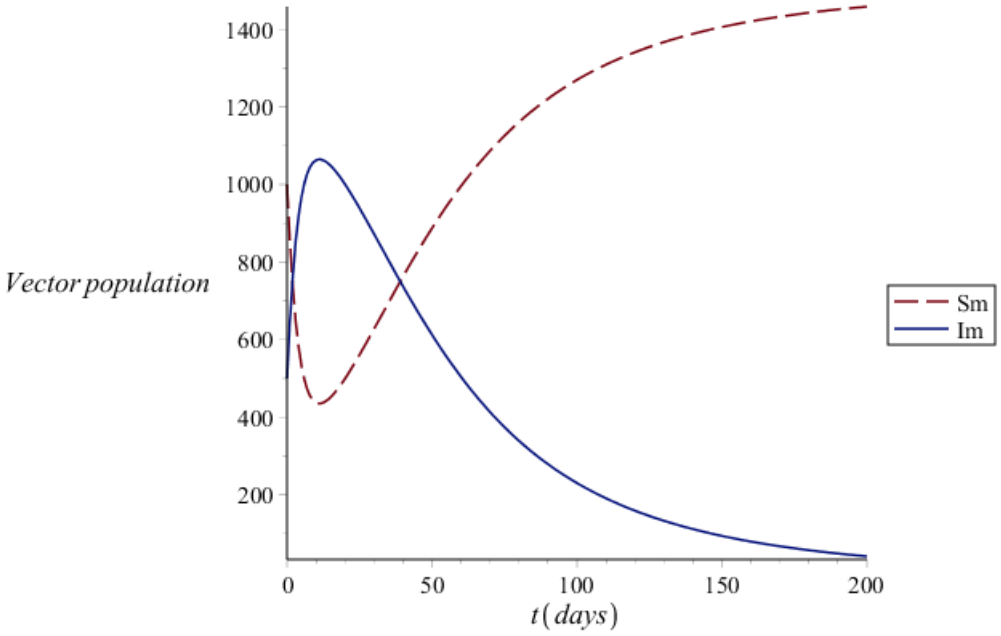

Figure 4.6: Time responses of S_m and I_m when $R_0 < 1$

Chapter 5
CONCLUSION

In this project, an SEIRS model is used to study the transmission dynamics between human and mosquito populations. Next generation matrix technique is used to obtain the basic reproduction number which is then used to establish the asymptotic stability of the disease-free equilibrium. The disease free equilibrium point is found to be locally asymptotically stable if the basic reproduction number $\mathcal{R}_0$ is less than one and unstable if $\mathcal{R}_0 > 1$.

Sensitivity analysis was carried out to understand the impact of some parameters in the transmission of malaria. It was discovered that human-to-mosquito transmission rate (β_h), mosquito-to-human transmission rate (β_m) and recovery rate of humans (γ_h) are most influential in the spread of the disease. The numerical simulations are done by fourth order Runge-Kutta method in Maple 15 environment. It was shown numerically that the disease persists in both human and mosquito populations when $\mathcal{R}_0 > 1$ but vanishes when $\mathcal{R}_0 < 1$. Our model suggests that if necessary control measures are built to reduce human-to-mosquito and mosquito-to-human transmission rates, the spread of the disease could be curtailed.

The results of this work should be interpreted with caution for the following reasons:

(i) consideration was not made for the case of drug resistant part of the population i.e people who do not recover from malaria by a single administration of drugs

(ii) the work does not include the case of a genetic resistant part of the popu-

lation i.e part of the population that is naturally not prone to the disease because of a natural immunity.

(iii) local stability does not imply global stability, therefore further investigation needs to be done on the global stability of the disease-free and endemic equilibrium points of the model.

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Appendix

Codes in Maple 15 that produced Figures 4.1−4.6

```
> restart :
> local gamma :
> local I :
                                        I
Warning, The imaginary unit, I, has been renamed _I
> beta[h] := 0.005 :
> Lambda[h] := 0.05 :
> alpha[h] := 0.0588235294 :
> mu[h] := 0.0000548 :
> omega := 0.01 :
> gamma[h] := 0.2 :
> delta[h] := 0.001 :
> Lambda[m] := 100 :
> beta[m] := 0.004 :
> mu[m] := 0.06667 :
>
> ODE := ([diff(S(t),t) = Lambda[h] - beta[h]*S(t)*Y(t) + omega*R(t) - mu[h]*S(t), diff(E(t),t) = beta[h]*S(t)
      *Y(t) - alpha[h]*E(t) - mu[h]*E(t), diff(I(t),t) = alpha[h]*E(t) - gamma[h]*I(t) - mu[h]*I(t)
      - delta[h]*I(t), diff(R(t),t) = gamma[h]*I(t) - omega*R(t) - mu[h]*R(t), diff(X(t),t) = Lambda[m]
      - beta[m]*X(t)*I(t) - mu[m]*X(t), diff(Y(t),t) = beta[m]*X(t)*I(t) - mu[m]*Y(t), S(0) = 800, E(0)
      = 300, I(0) = 150, R(0) = 0, X(0) = 1000, Y(0) = 500], numeric, range = 0..200) :
>
> solution := dsolve(ODE, numeric) :
> with(plots) :
> odeplot(solution, {[t, S(t)], [t, R(t)]}, 0..200)
> odeplot(solution, {[t, E(t)], [t, I(t)]}, 0..200)
> odeplot(solution, {[t, X(t)], [t, Y(t)]}, 0..200)
>
```