Mathemaical Model of Malaria Transmission Dynamics with Treatment

By

Getachew Fetene

A Thesis Submitted to

The Program of Applied Mathematics

School of Applied Natural Science

Presented in Partial Fulfillment of the Requirement for the Degree of Master's of Science in Applied Mathematics

Office of Graduate Studies

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Abstract

In this thesis, a sixth dimensional system of non-linear ordinary differential equation is formulated to describes the dynamics of malaria transmission with treatment. The model is analyzed for disease free and endemic equilibrium point. We define the reproduction number interms of parameters. It shows that if the reproduction number $R_0 < 1$*, then the disease free equilibrium point is locally asymptotically stable so that the disease dies out after some period of time. In addition we showed that if an appropriate treatment is given for infectious human at the condition of number of reproduction* $R_0 \leq \sqrt{\frac{q_1 q_2}{NM}}$*, where* q_1 *recruitment rate of human per death rate of human and* q_2 *is recruitment rate of mosquito per death rate of mosquito then the disease free equilibrium point is globally asymptotically stable so that disease dies out in short period of time. We also established that when* $R_0 > 1$*, then the endemic equilibrium point is locally asymptotically stable. We supplemented the analytical solution by numerical simulation using matlab code with appropriate and biologically meaningful parameter values.*

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Chapter 1

Introduction

1.1 Background of Study

In WHO(2013), malaria is an ancient disease having a huge social, economic, and health burden in world wide. It is predominantly present in tropical countries. Malaria is caused by five species of parasite of genus plasmodium that affect human. These are plasmodium falciparum, plasmodium vivax, plasmodium ovale, plasmodium malariea and plasmodium knowlesi. Malaria due to plasmodium falciparum is the most deadly form and it predominant in Africa. Plasmodium vivax is less dangerous but more spread, and other three species are found much less frequently. Malaria parasite are transmitted to humans by the bite of infected female anopheles mosquitoes.

The development of malaria parasites in human host commence in the liver cell where the malaria parasite under go asexual multiplication to produce merozoits that are eventually released into blood stream to invade red blood cells. The infected blood cell burst after 2-3 days to release merozoites and gametocytes into the blood stream. Anopheles mosquito become infected when they feed and ingest human blood that contain mature gametocytes. The gametocyte develop into male and female gametes that fertilize to become zygote in the mid-gut wall of the mosquito. The zeygote elongate become ookinete and penetrates the mid-gut epithelium that later develop and ultimately produce sporozoites which become infective when they migrate to salivary gland Okosun et al (2012)

The common symptom of malaria are headache, aching muscle, tummy ache, and weakness or lack of energy Males.S, et al (200). The body temperature may rise and the pacient may have:- a fever, shiver, mild chills severe headache, vomiting, diarrhea, and loss of appetite. How ever, it takes at least six days for symptom to appear. If the person gets infected with plasmoduim falciparum, malaria can progress to more severe form called complicated malaria. The following symptom may appear, low blood sugar level, severe anemia ,jaundice, fluid on ones lungs, acute respiratory, distress syndrome, kidney failure, spontaneous bleeding, and state of shock, paralysis and coma. Severe malaria can affect the patients brain and central nervous system and can be fetal. Malaria transmission rates can differ depending on local factors such as rain fall patterns (mosquitoes

breed in wet condition), the proximity of mosquito breeding site to people, and types of mosquitoes species in the area.

Falciparum malaria is medical emergency that should be treated in the hospital. The type of drug, method of administration and length of the treatment depend on where the malaria was contracted and how sick the patient. Except for falciparum, the treatment for malaria is usually Chloroquine (Aralen) taken by mouth for three days, strains of falciparum suscepted to be resist to chloroquine are usually treated with a combination of quine and tetracycline. In countries where quinine resistance is developing other treatment may include clindamycin (cloasin) Lariam or pyrimrthamine. Those who are very ill need intensive care and intravenous (IV) malaria treatment for the first three days. WHO(2006)

1.2 Statement of Problem

Malaria is a serious social, economic and health problem. The disease affects majority of labour forces especially the poor; therefore, the cost of treatment is directly transfered to government, because they can not afford. A lot of malaria control programs are going on in the countries, yet the disease seems to be still raging on. Hence,we develop mathematical model of malaria dynamics and its transmission with treatment.

This study is intended to answer the following basic questions.

- What are the basic assumptions to develop a mathematical model which describes the dynamics of malaria and its transmission with treatment?
- What are the mathematical model which describes the dynamics of malaria and its transmission with treatment?
- What are the biological interpretation of the solution of the proposed mathematical model?

1.3 Objective of Study

1.3.1 General Objective

The general objective of this study is to investigate the dynamics of malaria and transmission with treatment.

1.3.2 Specific Objective

The specific objective of this study is to

- Develop a mathematical model which describes the dynamics of malaria transmission with treatment.
- Investigate the effect system parameters on the dynamics of malaria transmission.

- Perform local and global stability analysis of the model.
- Interprate the biological implication of the solution of the proposed mathematical model.

1.4 Significance of Study

The important of this study is to convey a broad understanding of the current method of the model of malaria.
Hence this thesis provide:

- Understand deterministic model formulation and analysis for dynamics malaria and its transmission with treatment.
- Useful result and information for controlling malaria disease.
- It may serve as reference for those needs to conduct research on this area.

1.5 Methodology

We use system of non-linear ordinary differential equations to describe the dynamics of malaria and its transmission. We solve this non-linear ordinary differential equation numerically since it may not solvable analytically. We perform model analysis using standard mathematical techniques like local and global stability analysis by applying Jacobian matrix and Lyapunov function respectively. We supplement the analytical solution by numerical simulation using MATLAB with appropriate and biologically meaningful parameter values.

Chapter 2

Review of Literature

Ronald Ross in 1911 introduced the first deterministic differential equation model of malaria by dividing the human population into susceptible S_h and infected I_h compartments, with the infected class returning to susceptible class again leading to the SIS structure. The mosquito population also has only two compartments (S_m, I_m), but they do not recover from infection due to their short life span, and thereby follow the SI structure. Time evolution of the fraction of individuals in the infected classes (I_h, I_m) is studied using two differential equations, one each for the human and mosquito population.

The malaria parasite spends approximately 10 days inside a mosquito during its life cycle. The simple Ross model did not consider this latency period of the parasite in mosquitoes and their survival during that period. This resulted in the model predicting a rapid progress of the epidemic in human, and a higher equilibrium prevalence of infectious mosquitoes. MacDonald (1968) considered this latency period t_m, and introduced the exposed E_m class in the mosquitoes. Therefore, the mosquito population is divided into three compartments (susceptible, exposed, infected), and the model studies the time evolution of the exposed E_m and infected I_m classes in mosquito.

Ross et al (1991), considered the 21 days latency period of the parasite in humans, and introduced the Exposed E_h class in human population in their model . This divided the host population into three compartments (S_h, E_h, I_h), along with that in the mosquito population (S_m, E_m, I_m). This is a SEIS model for the human population, and the model consists of four differential equations describing the time evolution of both the exposed and infected classes for humans and mosquitoes (E_h, I_h, E_m, I_m) population.

Sandip Mandal et al, (2011) carried out a survey work, in their article, starting from the basic Ross model, the key mathematical models and their underlying features, based on their specific contributions in the understanding of spread and transmission of malaria were discussed. The first aim of their article is to develop, starting from the basic models, a hierarchical structure of a range of deterministic models of different levels of complexity. The second objective is to elaborate, using some of the representative mathematical models, the evolution of modelling strategies to describe malaria incidence by including the critical features of host-vector-parasite interactions. They laid more emphasis on the

evolution of the deterministic differential equation based epidemiological compartment models with a brief discussion on data based statistical models. In their comprehensive survey, the approach has been to summarize the modelling activity in this area so that it helps reach a wider range of researchers working on epidemiology, transmission, and other aspects of malaria.

F.T. Oduro, et al (2012) developed a mathematical model to study the transmission of malaria; they showed from the study that the model has unique disease-free and endemic equilibria in the application of treatment and preventive measures. They analyzed the existence and stability of disease-free and endemic malaria equilibria. Key to their study is the definition of a reproductive number R_0 which is the number of the new infections caused by one individual in an otherwise fully susceptible population, through the duration of the infectious period. The disease-free equilibrium is locally asymptotically stable, if $R_0 < 1$ and that the endemic equilibrium exist provided $R_0 > 1$. In fact, their study showed clearly that effective treatment offered to about fifty percent of the infected population together with about fifty percent prevention rate is all that is required to eliminate the disease.

Now we investigate the mathematical model for transmission dynamics of malaria disease with treatment which is sixth dimensional system of non-linear ordinary differential equation. In this study we perform global stability analysis using lyapumov function.

Chapter 3

Model Formulation and Analysis

3.1 Model Formulation

Recently, S.Oloniyi (2013) proposed an ordinary differential equation compartmental model for malaria transmission dynamics with susceptible-exposed-infectious-recovered-susceptible (SEIRS) patterns for humans and a susceptible-exposed-infectious (SEI) patterns for mosquitoes. In this theses we reformulate the S.Oloniyi, et al (2013) model.

The new model (as shown Figure 3.1) divides the human population into four classes: susceptible, S_h; exposed, I_{h1}; infectious, I_{h2} and recovered(immune), R_h. People inter the susceptible class either through birth or immigration. When an infectious mosquito bites a susceptible human, there is some interaction rate that the parasite (in form of sporozoites) will be passed on to the human and that person will move to the exposed class. The parasite then travels to the liver where it develops into next stage. After certain period of time, the parasite (in form of meroziotes) enters the blood stream, usually onset of malaria. Next from the exposed class enter the infectious class at the rate reciprocal of the latent period. After some time, by using clinical treatment, the infectious humans recover and move to the recovered class. The recovered human have some immunity to the disease, but after some period of time, they lose their immunity and return to susceptible class.

The total population of human denoted by N is given as

$$N = S_h(t) + I_{h1}(t) + I_{h2}(t) + R_h(t).$$

Unlike human population, we divide mosquito population into two classes: susceptible, $S_m(t)$ and infectious mosquito, $I_m(t)$. Female mosquitoes(we denote include male mosquito in our model because the only female mosquitoes bites human for blood meal) enter susceptible class through birth. The parasite (in the form of gametocyte) enters the mosquito with some interaction rate when the mosquito bites an infectious human, and the mosquitoes moves the susceptible to infectious class. Since the latency period of mosquoito is short their is no an exposed class. The mosquito remains infectious for life and has not recovered class. Mosquitoes leave population through a per capita density dependent natural death rate.

The total population of mosquito denoted by M is given as

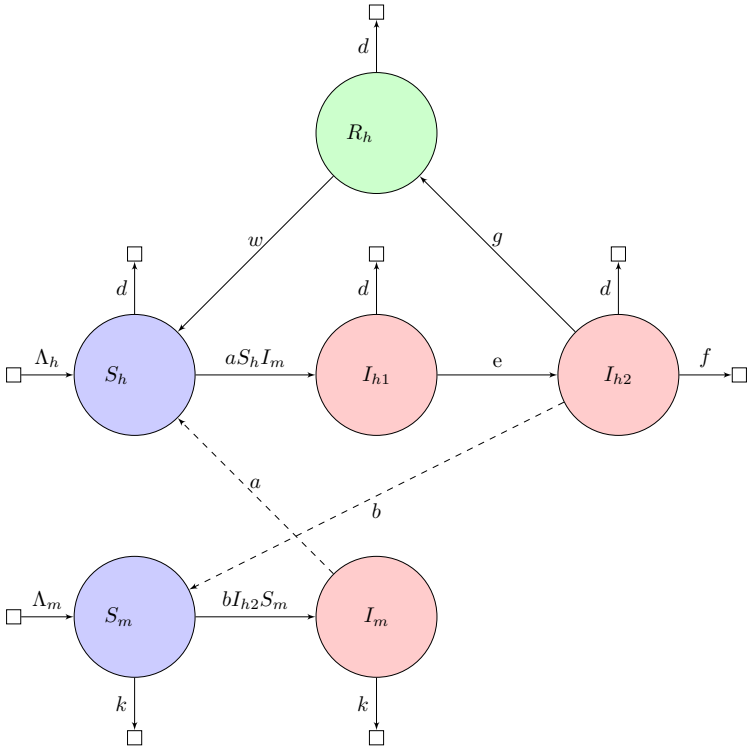

Figure 3.1: Schematic diagram of mathematical model for dynamics of malaria transmission. Susceptible humans, S_h , can be infected when they are bitten by infectious mosquitoes. Then they progress through the exposed, I_{h1} , infectious, I_{h2} , and recovered, R_h, classes, before re- entering the susceptible class. Susceptible mosquitoes, S_m , become infected when they bite infectious humans. Then the susceptible mosquitoes move to infectious, I_m , classes.

$$M(t) = S_m(t) + I_m(t).$$

From the schematic diagram (as shown figure 3.1) we obtain sixth dimensional system of non-linear ordinary differential equations which describes the transmission of malaria.

$$\frac{dS_h}{dt} = \Lambda_h - aS_hI_m - dS_h + wR_h, \tag{3.1.1}$$

$$\frac{dI_{h1}}{dt} = aS_hI_m - (d+e)I_{h1}, \tag{3.1.2}$$

$$\frac{dI_{h2}}{dt} = eI_{h1} - (d+f+g)I_{h2}, \tag{3.1.3}$$

$$\frac{dR_h}{dt} = gI_{h2} - (w+d)R_h, \tag{3.1.4}$$

$$\frac{dS_m}{dt} = \Lambda_m - bI_{h2}S_m - kS_m, \tag{3.1.5}$$

$$\frac{dI_m}{dt} = bI_{h2}S_m - kI_m \tag{3.1.6}$$

with positive initial value $S_h(0)$, $I_{h1}(0)$, $I_{h2}(0)$, $R_h(0)$, $S_m(0)$ and $I_m(0)$.

Defined variables and parameters in Table (3.1) and (3.2).

$S_h(t)$	Susceptible Human per unit time
$I_{h1}(t)$	Exposed Humans per unit time
$I_{h2}(t)$	Infected Humans per unit time
$R_h(t)$	Number of recovered (immune) humans at time t
$S_m(t)$	Number of susceptible mosquitoes at time t
$I_m(t)$	Number of infectious mosquitoes at time t

Table 3.1: Variable of the model

a	Interaction rate between an infectious mosquito and a susceptible human.
b	Interaction rate between an infectious human and susceptible mosquito.
g	Clinical treatment-recovery rate of humans from the infectious state to the recovered state.
d	Natural death rate for humans.
e	Transmission rate from an exposed human to infectious human.
k	Natural death rate for mosquito.
f	Induced death rate of human.
w	Rate of loss immunity for humans.
Λ_h	Recruitment term of the susceptible humans.
Λ_m	Recruitment term of the susceptible mosquitoes.

Table 3.2: Parameter of the model

3.1.1 Basic Properties of Model

Theorem 1: If $S_h(0)$, $I_{h1}(0)$, $I_{h1}(0)$, $R_h(0)$, $S_m(0)$ and $I_m(0)$ are non-negative, then so are $S_h(t)$, $I_{h1}(t)$, $I_{h2}(t)$, $R_h(t)$, $S_m(t)$ and $I_m(t)$ for all $t > 0$.

Proof: Assume that T=sup$\{t > 0 : S_h(0) > 0, I_{h1}(0) > 0, I_{h2}, R_h(0) > 0, S_m(0) > 0$ and $I_m(0) > 0\}$. Since $S_h(0) > 0, I_{h1}(0) > 0, I_{h2}(0) > 0, R_h(0) > 0, S_m(0) > 0$ and $I_m(0) > 0$, then $T > 0$.

By rearranging equation (3.1.1) we have

$$\frac{dS_h}{dt} + (aI_m + d)S_h = \Lambda_h + iR_h \tag{3.1.7}$$

The integrating factor of (3.1.7) is $exp((a + I_m)t)$ and we obtain

$$S_h(t) = exp(-(a + I_m)t)(\int (\Lambda_h + wR_h)exp((a + I_m)t)dt + S_h(0)) > 0.$$

Hence, $S_h(t) > 0$.

Again by rearranging equation (3.1.2) we have

$$\frac{dI_{h1}}{dt} + (d + e)I_1 = aS_hI_m \tag{3.1.8}$$

The integrating factor of (3.1.8) is $exp((d + e)t)$ and we obtain

$$I_{h1} = exp(-(d + e)t)(a \int S_hI_mexp((d + e)t)dt + I_{h1}(0)) > 0$$

Hence, $I_{h1} > 0$.

In similar manner, by rearranging and solving equation (3.1.3), (3.1.4), (3.1.5) and (3.1.6) we obtain

$I_{h2}(t) > 0$, $R_h(t) > 0$, $S_m(t) > 0$ and $I_m(t) > 0$.

Therefore, all solution of equation (3.1.1-3.1.6) are non-negative.

Theorem 2 There exist a domain $D = D_h \times D_m$ in which the solution set $\{S_h, I_{h1}, I_{h2}, R_h, S_m, I_m\}$ of the system of equation (3.1.1-3.1.6) is bounded. Where $D_h = \{S_h, I_{h1}, I_{h2}, R_h\}$ and $D_m = \{S_m, I_m\}$.

Proof: Given the solution set $\{S_h, I_{h1}, I_{h2}, R_h, S_m, I_m\}$ with positive initial condition, we let

$$P(S_h, I_{h1}, I_{h2}, R_h) = S_h + I_{h1} + I_{h2} + R_h \text{ and}$$

$$Q(S_m, I_m) = S_m + I_m.$$

Then the time derivative of P along the solution of system of equation (3.1.1-3.1.4) for human population is given by

$$\frac{dP}{dt} = \frac{\partial P}{\partial S_h}\frac{dS_h}{dt} + \frac{\partial P}{\partial I_{h1}}\frac{dI_{h1}}{dt} + \frac{\partial P}{\partial I_{h2}}\frac{dI_{h2}}{dt} + \frac{\partial P}{\partial R_h}\frac{dR_h}{dt}$$

$$= \Lambda_h - dI_{h1} - (d+f)I_{h2} - dR_h - dS_h$$

$$\leq \Lambda_h - dP$$

$$\frac{dP}{dt} + dP \leq \Lambda_h.$$

$$\frac{d(Pe^{dt})}{dt} \leq \Lambda_h e^{dt}$$

$$\int_0^{t*} d(Pe^{dt}) \leq \Lambda_h \int_0^{t^*} e^d t$$

$$Pe^{dt^*} - P(S_h(0), I_{h1}(0), I_{h2}(0), R_h(0)) \leq \frac{\Lambda_h}{d}e^{t^*} - \frac{\Lambda_h}{d}$$

$$P \leq \frac{\Lambda_h}{d}(1 - e^{-dt^*}) + P(s_h(0), I_{h1}(0), I_{h2}(0), R_h(0))e^{-dt^*} \tag{3.1.9}$$

Similarly,

$$\frac{dQ}{dt} = \frac{\partial Q}{\partial S_m}\frac{dS_m}{dt} + \frac{\partial Q}{\partial I_m}\frac{dI_m}{dt}$$

$$= \frac{dS_m}{dt} + \frac{dI_m}{dt}$$

$$= \Lambda_m - kQ$$

$$\frac{dQ}{dt} + kQ = \Lambda_m$$

$$\frac{d(Qe^{kt})}{dt} = \Lambda_m e^{kt}$$

$$\int_0^{t^*} d(Qe^{kt}) = \Lambda_m \int_0^{t^*} e^{kt} dt$$

$$Q = \frac{\Lambda_m}{k}(1 - e^{-kt^*})) + Q(S_m(0), I_m(0))e^{-kt^*}. \tag{3.1.10}$$

Consequently, taking the limits as $t^* \longrightarrow \infty$ for equation(3.1.9) and (3.1.10) gives $p \leqslant \frac{\Lambda_h}{d}$ and $Q = \frac{\Lambda_m}{k}$. Thus, all solutions of the humans and mosquito population are bounded in D_h and D_m respectively.

Therefore, the system of equation (3.1.1-3.1.6) is bounded.

3.2 Model Analysis

3.2.1 Disease free equilibrium point

The disease free equilibrium point is a solution of the system of equation

$$\begin{cases} \Lambda_h - aS_h^* I_m^* - dS_h^* + wR_h^* = 0 \\ aS_h I_m^* - (d+e)I_{h1}^* = 0 \\ eI_{h1}^* - (d+f+g)I_{h2}^* = 0 \\ gI_{h2}^* - (w+d)R_h^* = 0 \\ \Lambda_m - bI_{h2}^* S_m^* - kS_m^* = 0 \\ bI_{h2}^* S_m^* - kI_m^* = 0 \end{cases} \tag{3.2.1}$$

where $I_{h1}^* = I_{h2}^* = I_m^* = 0$.

Then the disease free equilibrium point is $E_0 = (q_1, 0, 0, 0, q_2, 0)$, where $q_1 = \frac{\Lambda_h}{d}$ and $q_2 = \frac{\Lambda_m}{k}$.

This is disease free equilibrium point of (3.1.1-3.1.6) which represents the state at which there is no infection in the population.

3.2.2 Reproduction number

We shall use the next generation operator approach as described by Diekmann, Heesterbeek and Metz (1990) to define basic reproduction number ,R_0, as the 'expected number of secondary case per primary case in a virgin population'.

From system of equation (3.1.1-3.1.6) the only disease states are I_{h1}, I_{h2} and I_m . The disease state F and the transfer state C are given by

$$\frac{dX}{dt} = C(X) - F(X) \tag{3.2.2}$$

where

$$C(X) = \begin{bmatrix} aS_hI_m \\ 0 \\ bI_{h2}s_m \end{bmatrix}, F(X) = \begin{bmatrix} (d+e)I_{h1} \\ (d+f+g)I_{h2} - eI_{h1} \\ kI_m \end{bmatrix} \tag{3.2.3}$$

The Jacobian matrices of C(X) and F(X) at the disease-free equilibrium E_0 are, respectively,

$$DC(E_0) = \begin{bmatrix} 0 & 0 & aq_1 \\ 0 & 0 & 0 \\ 0 & bq_2 & 0 \end{bmatrix}$$

and

$$DF(E_0) = \begin{bmatrix} d+e & 0 & 0 \\ -e & d+f+g & 0 \\ 0 & 0 & k \end{bmatrix}$$

Assume that $A = DC(E_0)$ and $B = DF(E_0)$.

Then

$$B^{-1} = \begin{bmatrix} \frac{1}{d+e} & 0 & 0 \\ \frac{e}{(d+e)(d+f+g)} & \frac{1}{d+f+g} & 0 \\ 0 & 0 & \frac{1}{k} \end{bmatrix},$$

$$AB^{-1} = \begin{bmatrix} 0 & 0 & aq_1 \\ 0 & 0 & 0 \\ 0 & bq_2 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{d+e} & 0 & 0 \\ \frac{e}{(d+e)(d+f+g)} & \frac{1}{d+f+g} & 0 \\ 0 & 0 & \frac{1}{k} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{aq_1}{k} \\ 0 & 0 & 0 \\ \frac{ebq_2}{(d+e)(d+f+g)} & \frac{bq_2}{d+f+g} & 0 \end{bmatrix},$$

Now we find the spectral radius of AB^{-1} which is given by

$det(AB^{-1} - \lambda I) = \lambda^3 - \frac{abeq_1q_2}{k(d+e)(d+f+g)}\lambda = 0$

Hence

$$\lambda = \sqrt{\frac{abeq_1q_2}{k(d+e)(d+f+g)}}$$

Therefore,

$$R_0 = \sqrt{\frac{abeq_1q_2}{k(d+e)(d+f+g)}} \tag{3.2.4}$$

Here R_0 is associated with disease transmission by infected humans as well as the infection of susceptible humans by infected mosquitoes.

3.2.3 Endemic Equilibrium Point

Theorem 3: If $R_0 > 1$, then the system of equation (3.1.1-3.1.6) has a unique endemic equilibrium point $E_e = (S_h^*, I_{h1}^*, I_{h1}^*, R_h^*, S_m^*, I_m^*)$

where

$$\begin{cases} S_h^* = \frac{(d+e)(beI_{h1}^*+k(d+f+g))}{abeq_1q_2}. \\ I_{h2}^* = \frac{eI_{h1}^*}{d+f+g}. \\ R_h^* = \frac{geI_{h1}^*}{(w+d)(d+f+g)}. \\ S_m^* = \frac{\Lambda_m(d+f+g)}{beI_{h1}^*+k(d+f+g)}. \\ I_m^* = \frac{beq_2I_{h1}^*}{beI_{h1}^*+k(d+f+g)}. \\ I_{h1}^* \geq \frac{kd(d+f+g)(R_0^2-1)}{be(d+aq_2)} \end{cases} \tag{3.2.5}$$

Proof: The endemic equilibrium point of the solution is the solution of the system of equations (3.2.1).

From system of equation (3.2.1) consider the third equation, then we obtained

$$I_{h2}^* = \frac{eI_{h1}^*}{d+f+g}. \tag{3.2.6}$$

Substitute (3.2.6) into fourth and fifth equation of (3.2.1), then we obtained

$$R_h^* = \frac{geI_{h1}^*}{(w+d)(d+f+g)}. \tag{3.2.7}$$

$$S_m^* = \frac{\Lambda_m(d+f+g)}{beI_{h1}^*+k(d+f+g)}. \tag{3.2.8}$$

Again substitute (3.2.8) into sixth equation of (3.2.1),then we obtained

$$I_m^* = \frac{beq_2I_{h1}^*}{beI_{h1}^*+k(d+f+g)}. \tag{3.2.9}$$

Similarly substitute (3.2.9) into the second equation of (3.2.1), then we obtained

$$S_h^* = \frac{(d+e)(beI_{h1}^* + k(d+f+g))}{abeq_2}. \tag{3.2.10}$$

Finally substitute (3.2.7), (3.2.9)and (3.2.10) into first equation of system (3.2.1) we have

$$\Lambda_h - aS_h^* I_m^* - dS_h^* + wR_h^* = 0.$$

$$\Lambda_h - (\tfrac{a(d+e)(beI_{h1}^*+k(d+f+g)}{abeq_2})(\tfrac{beq_2 I_{h1}^*}{beI_{h1}^+ k(d+f+g)}) - d(\tfrac{a(d+e)(beI_{h1}^*+k(d+f+g)}{abeq_2}) + \tfrac{wgeI_{h1}^*}{(w+d)(d+f+g)} = 0$$

$$\Lambda_h - (d+e)I_{h1}^* - \frac{d(d+e)I_{h1}^*}{aq_2} - \frac{dk(d+e)(d+f+g)}{abeq_2} + \frac{wgeI_{h1}^*}{(w+d)(d+f+g)} = 0 \tag{3.2.11}$$

$$q_1 - \tfrac{(d+e)I_{h1}^*}{d} - \tfrac{(d+e)I_{h1}^*}{aq_2} - \tfrac{k(d+e)(d+f+g)}{abeq_2} \leq 0$$

$$\tfrac{(d+e)(d+aq_2)I_{h1}^*}{d} \geq \tfrac{abeq_1q_2 - k(d+e)(d+f+g)}{be}$$

$$I_{h1}^* \geq \tfrac{-kd(d+e)(d+f+g)(1-R_0^2)}{be(d+e)(d+aq_2)}$$

$$I_{h1}^* \geq \tfrac{kd(d+f+g)(R_0^2-1)}{be(d+aq_2)}$$

Hence, I_{h1}^* is non-negative if and only if $R_0 \geq 1$ and all $S_h^*, I_{h2}^*, R_h^*, S_m^*, I_m^*$ are non-negative.

Therefore, for $R_0 \geq 1$ the system of equation (3.1.1-3.1.6) has a unique endemic equilibrium point $E_e = (S_h^*, I_{h1}^*, I_{h1}^*, R_h^*, S_m^*, I_m^*)$

Again from equation (3.2.11) we have

$$I_{h1}^* = \frac{(dk(d+e)(d+f+g) - abeq_2\lambda_h)(w+d)(d+f+g)}{be(mgeaq_2 - (d+e)(d+aq_2))(m+d)(d+f+g)} \tag{3.2.12}$$

Hence, by substituting equation (3.2.12) into equation (3.2.6), (3.2.7), (3.2.8), (3.2.9) and (3.2.10) we obtain an endemic equilibrium point

$$E_e = (\delta_1, \beta, \delta_2, \delta_3, \delta_4, \delta_5) \tag{3.2.13}$$

$$\begin{cases} \delta_1 = \frac{(d+e)(be\beta^*+k(d+f+g))}{abeq_2}. \\ \beta = \frac{(dk(d+e)(d+f+g)-abeq_2\lambda_h)(w+d)(d+f+g)}{be(mgeaq_2-(d+e)(d+aq_2))(m+d)(d+f+g)} \\ \delta_2 = I_{h2}^* = \frac{e\beta}{d+f+g} \\ \delta_3 = \frac{ge\beta}{(w+d)(d+f+g)} \\ \delta_4 = \frac{\Lambda_m(d+f+g)}{be\beta+k(d+f+g)} \\ \delta_5 = \frac{beq_2\beta}{beI_{h1}^*+k(d+f+g)} \end{cases} \tag{3.2.14}$$

3.2.4 Stability Analysis

Theorem 4: The disease free equilibrium point for system of equation (3.1.1-3.1.6) is locally asymptotically stable if $R_0 < 1$.

Proof:The Jacobian matrix J of the system of equation (3.1.1-3.1.6) evaluated at the disease free equilibrium point E_0 is given by

$$J(E_0) = \begin{bmatrix} -d & 0 & 0 & w & 0 & -aq_1 \\ 0 & -(d+e) & 0 & 0 & 0 & aq_1 \\ 0 & e & -(d+f+g) & 0 & 0 & 0 \\ 0 & 0 & g & -(w+d) & 0 & 0 \\ 0 & 0 & -bq_2 & 0 & -k & 0 \\ 0 & 0 & bq_2 & 0 & 0 & -\eta \end{bmatrix}$$

Then the characteristic equation of te Jacobian matrix is given by

$$(\lambda + d)(\lambda + w + d)(\lambda + k)((\lambda + d + e)(\lambda + d + f + g)(\lambda + k) + abeq_1q_2) = 0$$

Therefore, immediately we obtain an eigenvalue $\lambda_1 = -d$, $\lambda_2 = -(w + d)$, $\lambda_3 = -k$ and the other eigenvalues are the solution of equation

$$(\lambda + u_1)(\lambda + u_2)(\lambda + k) + abeq_1q_2 = 0. \tag{3.2.15}$$

where

$$\begin{cases} u_1 = d + e \\ u_2 = d + f + g \end{cases} \tag{3.2.16}$$

which is equivalent to

$$\lambda^3 + r_2\lambda^2 + r_1\lambda + r_0 = 0 \tag{3.2.17}$$

where

$$\begin{cases} r_2 = u_1 + u_2 + k \\ r_1 = u_1u_2 + u_1k + u_2k \\ r_0 = u_1u_2k + abeq_1q_2 \end{cases} \tag{3.2.18}$$

Using the Routh-Hurwitz Criteria, we can prove that all roots of the polynomial have negative real parts.

$$H_1 = u_1 + u_2 + k > 0.$$

Again

$$H_2 = r_1 r_2 - r_0.$$

$$= (u_1 + u_2 + k)(u_1u_2 + u_1k + u_2k) - u_1u_2k - abeq_1q_2.$$

$$= u_1^2(u_2 + k) + u_2^2(u_1 + k) + k(u_1u_2 + u_1k + u_2k) + u_1u_2k - abeq_1q_2.$$

$$= (u_1^2(u_2 + k) + u_2^2(u_1 + k) + k(u_1u_2 + u_1k + u_2k) + u_1u_2k)(1 - \frac{abeq_1q_2}{u_1^2(u_2+k)+u_2^2(u_1+k)+k(u_1u_2+u_1k+u_2k)+u_1u_2k})$$

$$\geq (u_1^2(u_2 + k) + u_2^2(u_1 + k) + k(u_1u_2 + u_1k + u_2k) + u_1u_2k)(1 - \frac{abeq_1q_2}{u_1u_2k})$$

$$= (u_1^2(u_2 + k) + u_2^2(u_1 + k) + k(u_1u_2 + u_1k + u_2k) + u_1u_2k)(1 - R_0^2)$$

Hence $H_2 > 0$ if and only if $R_0 < 1$.

Similarly

$$H_3 = a_0a_1a_2 - a_0^2.$$

$$= a_0(a_1a_2 - a_0) = a_0H_2. \tag{3.2.19}$$

Since $a_0 > 0$, we conclude that $H_3 > 0$ if and only if $R_0 < 1$.

Hence, Routh-Hurwitz Criteria is satisfied.

Therefore, the disease free equilibrium point of the system is locally asymptotically stable.

Theorem 5:- For system equation (3.1.1-3.1.6), the disease-free equilibrium E_0 globally asymptotically stable if $R_0 \leq \sqrt{\frac{q_1q_2}{NM}}$.

Proof: We introduce the following Lyapunov function

$$V(S_h, I_{h1}, I_{h2}, R_h, S_h, S_m, I_m) = \alpha_1 I_{h1} + \alpha_2 I_{h2} + \alpha_3 I_m \tag{3.2.20}$$

where

$$\begin{cases} \alpha_1 = \frac{ebq_1q_2}{N} \\ \alpha_2 = \frac{bq_1q_2(d+e)}{N} \\ \alpha_3 = \frac{q_1q_2(d+e)(d+f+g)}{MN}. \end{cases} \tag{3.2.21}$$

Hence $V > 0$ otherwise $V = 0$ at disease free equilibrium point $E_0 = (q_1, 0, 0, 0, q_2, 0)$.

The derivative of V is given by

$$\frac{dV}{dt} = \alpha_1 \frac{dI_{h1}}{dt} + \alpha_2 \frac{dI_{h2}}{dt} + \alpha_3 \frac{dI_m}{dt}$$

$$= \alpha_1(aS_hI_m - (d+e)I_{h1}) + \alpha_2(eI_{h1} - (d+f+g)I_{h2}) + \alpha_3(bI_{h2}S_m - kI_m).$$

$$= \alpha_1(a(N - I_{h1} - I_{h2} - R_h)I_m - (d+e)I_{h1}) + \alpha_2(eI_{h1} - (d+f+g)I_{h2}) + \alpha_3(bI_{h2}(M - I_m) - kI_m)$$

$$= -\alpha_1 a(I_{h1} + R_h)I_m - (\alpha_1 a + \alpha_3 b)I_{h2}I_m - (\alpha_1(e+d) - \alpha_2 e)I_{h1} + (\alpha_3 bM - \alpha_2(d+f+g))I_{h2} + (\alpha_1 aN - \alpha_3 k)I_m$$

Hence

$$\frac{dV}{dt} = -\alpha_1 a(I_{h1} + R_h)I_m - (\alpha_1 a + \alpha_3 b)I_{h2}I_m + (\alpha_1 aN - \alpha_3 k)I_m \tag{3.2.22}$$

Since

$$\begin{cases} \alpha_1(e+d) - \alpha_2 e = 0 \\ \alpha_3 bM - \alpha_2(d+f+g) = 0 \end{cases}$$

$$\frac{dV}{dt} = -\alpha_1 a(I_{h1} + R_h)I_m - (\alpha_1 a + \alpha_3 b)I_{h2}I_m + (abeq_1q_2 - k(e+d)(f+d)\frac{q_1q_2}{MN})I_m$$

$$= -\alpha_1 a(I_{h1} + R_h)I_m - (\alpha_1 a + \alpha_3 b)I_{h2}I_m - k(e+d)(f+d)(\frac{q_1q_2}{MN} - \frac{abeq_1q_2}{k(e+d)(f+d)})I_m$$

$$= -\alpha_1 a(I_{h1} + R_h)I_m - (\alpha_1 a + \alpha_3 b)I_{h2}I_m - k(e+d)(f+d)(\frac{q_1q_2}{MN} - R_0^2)I_m$$

Now we conclude that if $R_0 < \sqrt{\frac{q_1q_2}{MN}}$, we obtain

$$\frac{dV}{dt} < 0.$$

Further more, if we take $R_0 = \sqrt{\frac{q_1q_2}{MN}}$ then immediately we obtain $\frac{dV}{dt} = 0$.

Therefore, the point E_0 is globally asymptotically stable.

Theorem 6: The endemic equilibrium point for system of equation (3.1.1-3.1.6) is locally asymptotically stable if $R_0 > 1$.

Proof: The Jacobian matrix at the endemic equilibrium $E_e = (\delta_1, \beta, \delta_2, \delta_3, \delta_4, \delta_5)$ is given by

$$J(E_e) = \begin{bmatrix} -(a\delta_5 + d) & 0 & 0 & w & 0 & -a\delta_5 \\ a\delta_1 & -(d+e) & 0 & 0 & 0 & a\delta_1 \\ 0 & e & -(d+f+g) & 0 & 0 & 0 \\ 0 & 0 & g & -(w+d) & 0 & 0 \\ 0 & 0 & -(b\delta_4) & 0 & -(b\delta_2 + k) & 0 \\ 0 & 0 & b\delta_4 & 0 & b\delta_2 & -k \end{bmatrix}$$

.

Then the corresponding characteristic equation is given by

$$(\lambda+\gamma_1)(\lambda+\gamma_2)(\lambda+\gamma_3)(\lambda+\gamma_4)(\lambda+\gamma_5)(\lambda+k) - aemg\delta_5(\lambda+\gamma_5)(\lambda+k)$$

$$+a^2e\delta_1\delta_5(\lambda+\gamma_4)(b^2\delta_2\delta_4 + b\delta_4(\lambda+\gamma_5)) = 0$$

where

$$\begin{cases} \gamma_1 = a\delta_5 + d \\ \gamma_2 = d + e \\ \gamma_3 = d + f + g \\ \gamma_4 = w + d \\ \gamma_5 = b\delta_2 + k \end{cases} \tag{3.2.23}$$

which is equivalent to

$$\lambda^6 + \theta_5\lambda^5 + \theta_4\lambda^4 + \theta_3\lambda^3 + \theta_2\lambda^2 + \theta_1\lambda + \theta_0 = 0 \tag{3.2.24}$$

where

$$\begin{cases} \theta_5 = \gamma_1 + \gamma_2 + \gamma_3 + \gamma_4 + \gamma_5 + k \\ \theta_4 = \gamma_1\gamma_3 + \gamma_1\gamma_4 + \gamma_2\gamma_3 + \gamma_2\gamma_4 + \gamma_5 k \\ \theta_3 = k\gamma_5(\gamma_1 + \gamma_2 + \gamma_3 + \gamma_4) + (\gamma_5 + k)(\gamma_1\gamma_3 + \gamma_1\gamma_4 + \gamma_2\gamma_3 + \gamma_2\gamma_4) \\ \theta_2 = k\gamma_5(\gamma_1 + \gamma_2 + \gamma_3 + \gamma_4) + (k + \gamma_5)(\gamma_1\gamma_3\gamma_4 + \gamma_1\gamma_3\gamma_4 + \gamma_1\gamma_2\gamma_3 + \gamma_1\gamma_2\gamma_4) + a^2be\delta_1\delta_4\delta_5 - aemg\delta_5 \\ \theta_1 = \gamma_1\gamma_2\gamma_3\gamma_4(\gamma_5 + k) + \gamma_5 k(\gamma_1\gamma_3\gamma_4 + \gamma_2\gamma_3\gamma_4) + b^2\delta_2\delta_4 + b\delta_4\gamma_4 - aemg\delta_5(\gamma_5 + k) \\ \theta_0 = \gamma_1\gamma_2\gamma_3\gamma_4\gamma_5 k + b^2\delta_2\delta_4\gamma_4 + b\delta_2\gamma_4\gamma_5 - aemg\delta_5\gamma_5 k \end{cases} \tag{3.2.25}$$

Now it is difficult to solve the polynomial characteristic equation analytically so that we solve it numerically in chapter 4.

Chapter 4

Numerical Simulation

We carry out numerical simulation using a fourth order Runge-kutta method in ode45 matlab code. The aim is to verify some analytical results on the local and global stability of system equation (3.1.1-3.1.6). All parameter values are obtained from literature except treatment rate g that we estimated it.

Symbol	Value	Reference
Λ_h	0.0000215	S.Olaniyi (2013)
Λ_m	0.07	S.Olaniyi (2013)
a	0.1	S.Olaniyi (2013)
b	0.09	S.Olaniyi (2013)
e	0.0588	S.Olaniyi (2013)
f	0.001	S.Olaniyi (2013)
d	0.0000549	S.Olaniyi (2013)
k	0.066667	S.Olaniyi (2013)
g	estimated	

Table 4.1: parameter values

We find the eigenvalue for the characteristic equation (3.2.25) numerically by using treatment rate $g = 0.0421$ and all parameter value from table 4.1. Hence, we obtain that real part of all eigenvalue for Jacobian matrix $J(E_e)$ are negative so that the system of equation at an endemic equilibrium point $E_e = (0.1559, 0.00022238, 0.000592, .0087, 1.0491, 0.00017584)$ is locally asymptotically stable.

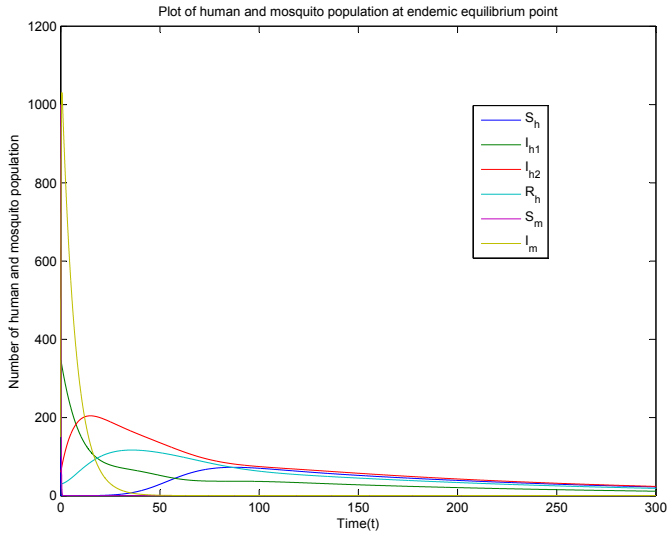

Figure 4.1: Simulation for system of equation (3.1.1-3.1.6) Showing that if the treatment rate $g = 0.0421$ and use parameter value of table 4.1 with initial value $S_h = 100$, $I_{h1} = 50$, $I_{h2} = 30$, $R_h = 0$, $S_m = 1000$ and $I_m = 30$ so that $R_0 = 1.5968 > 1$ which implies that a unique endemic equilibrium point $E_e = (0.1559, 0.00022238, 0.000592, .0087, 1.0491, 0.00017584)$ and also it is locally asymptotically stable.

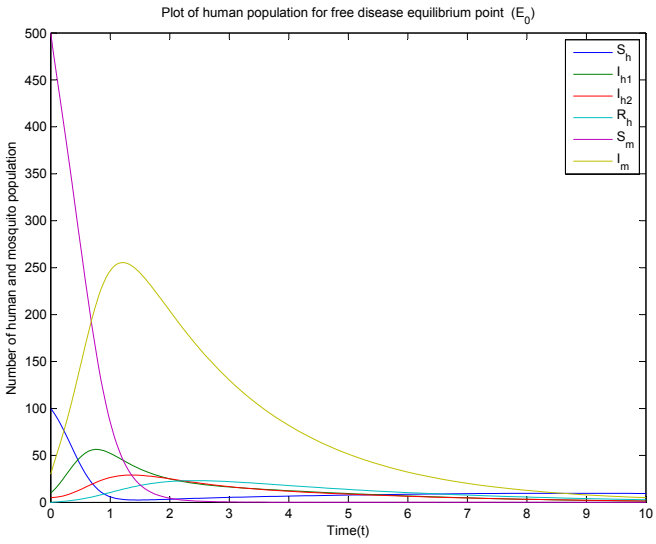

Figure 4.2: Simulation for system of equation (3.1.1-3.1.6) using parameter value in table 4.1 with treatment rate $g = 0.078$ and initial value $S_h = 100$, $I_{h1} = 20$, $I_{h2} = 10$, $R_h = 0$, $S_m = 500$ and $I_m = 30$ so that $R_0 = 0.8334 < 1$ and also the system of disease free equilibrium point $E_0 = (0.3916, 0, 0, 0, 1.05, 0)$ is locally asymptotically stable.

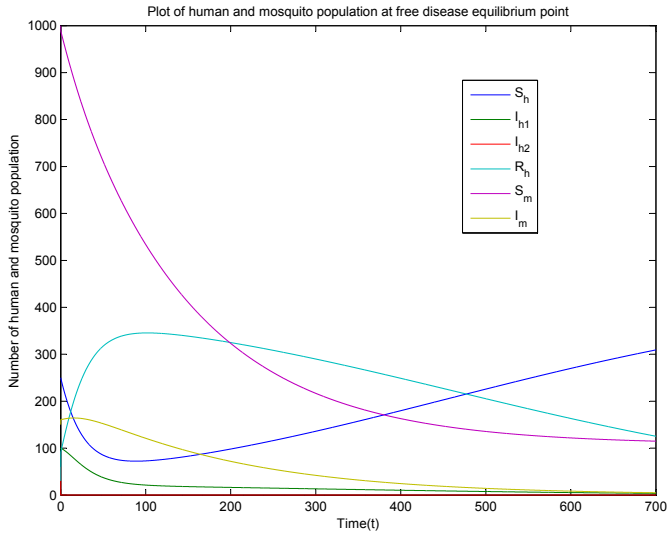

Figure 4.3: Simulation for system of equation (3.1.1-3.1.6) using parameter value in table 4.1 with treatment rate $g = 2.98$ and initial value $S_h = 250$, $I_{h1} = 100$, $I_{h2} = 50$, $R_h = 20$, $S_m = 1000$ and $I_m = 150$ so that $R_0 = 0.00137 < \sqrt{\frac{q_1 q_2}{NM}} = 0.0016$ and also the system of disease free equilibrium point $E_0 = (0.3916, 0, 0, 0, 1.05, 0)$ is globally asymptotically stable.

Chapter 5

Result and Discussion

5.1 Result

We formulated a mathematical model for dynamics of malaria transmission as a non-linear ordinary differential equation with treatment. From the determined basic reproduction number we established that, $R_0 < 1$, then the disease free equilibrium point is locally asymptotically stable so that the disease dies out after some period of time. In addition we showed that if the treatment rate is very high, $R_0 \leq \sqrt{\frac{q_1 q_2}{NM}}$, then the disease free equilibrium point is globally asymptotically stable so that disease dies out in short period of time. We also established that when $R_0 > 1$, then the endemic equilibrium point is exist and using parameter value and estimating treatment rate E_e locally asymptotically stable. From Figure (4.3) we conclude that if there is high treatment rate, then an infectious human is decreasing rapidly while immunity is increasing while for long period time the prevalence of infectious and recovered human is occur. .

5.2 Discussion

We used a system of non-linear ordinary differential equations to describe the dynamics of malaria and its transmission. The model was analyzed for the disease free equilibrium and endemic equilibrium point. We performed model analysis using standard mathematical techniques like local and global stability analysis by applying Jacobian matrix and constructing Lyapunov function respectively. We supplemented the analytical solutions by numerical simulation using matlab code with appropriate and biologically meaningful parameter values. Simulation for system of equation (3.1.1-3.1.6) Showing that if the treatment rate $g = 0.0421$ and use parameter value of table 4.1 with initial value $S_h = 100$, $I_{h1} = 50$, $I_{h2} = 30$, $R_h = 0$, $S_m = 1000$ and $I_m = 30$ so that $R_0 = 1.5968 > 1$ which implies that a unique endemic equilibrium point $E_e = (0.1559, 0.00022238, 0.000592, .0087, 1.0491, 0.00017584)$ and also it is locally asymptotically stable

Chapter 6

Conclusion and Recommendation

6.1 Conclusion

The mathematical model for malaria dynamics and its transmission with treatment is divides the human population into four classes: susceptible, S_h; exposed, I_{h1}; infectious, I_{h2} and recovered(immune), R_h while mosquito population into two classes: susceptible, S_m and infectious, I_m. The model is analyzed for disease free equilibrium point and endemic equilibrium point. By applying Jacobian matrix on system of equation (3.1.1-3.1.6) we obtain that if $R_0 < 1$, then the free disease equilibrium point, E_0 is locally asymptotically stable. Again by constructing Lyapunov function we obtain that if $R_0 \leq \sqrt{\frac{q_1 q_2}{NM}}$, then the free disease equilibrium point E_0 is globally asymptotically stable. Similarly, if $R_0 > 1$ then the endemic equilibrium point E_e is exist so that the model is persist. More over, by using parameter value of table 4.1, estimating treatment rate and we shown that the endemic equilibrium point is locally asymptotically stable. Generally, we remember that an appropriate clinical treatment is needed for infectious human to reduce malaria disease in society.

6.2 Recommendation

The effect of malaria infection continuous to take its toll on individual and community so that the policy makers have to be informed about a research result. As a recommendation you should be consider that giving an appropriate clinical treatment on infectious human is an important to increase a recovered human population.

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Appendexes

Latex to Draw Schematic Diagram of the Malaria Transmission Dynamics

```
\documentclass{article}
\usepackage{amsmath}
\usepackage{amsfonts}
\usepackage{amssymb}
\usepackage[latin1]{inputenc}
\usepackage{tikz}
\usetikzlibrary{shapes,arrows}
\begin{document}
\pagestyle{empty}
% Define block styles
\tikzstyle{block} = [rectangle, draw, fill=red!20,text width=1cm,
node distance=4cm, text centered, rounded corners, minimum
height=2cm]

\tikzstyle{line} = [draw, node distance=4cm, -latex']
\tikzstyle{cloud} = [draw, rectangle, fill=green!20,
text width=1cm, node distance 3cm, minimum height=2cm]
\tikzstyle{yes} = [draw, line]
 \tikzstyle{waw} = [draw, rectangle, fill=blue!20, text width=1cm,
node distance=5cm, minimum height=2cm]

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

\begin{tikzpicture}[node distance = 10cm, auto]
    % Place nodes
    \node [block] (init) {$I_{h1}$};
    \node [waw, left of=init, node distance=4cm] (system) {$S_h$};
    \node [block, right of=init] (identify) {$I_{h2}$};
    \node [cloud, above of=init,node distance=4cm] (non){$R_h$};
    \node [block, below of=init] (evaluate) {$I_m$};
    \node [waw, left of=evaluate, node distance=4cm] (update) {$S_m$};
   \node [yes, left of=system, node distance=2cm] (step1) {};
   \node [yes, above of=system, node distance=2cm] (step2) {};
    \node [yes, above of=init, node distance=2cm] (step3) {};
    \node [yes, above of=identify, node distance=2cm] (step4) {};
    \node [yes, right of=identify, node distance=2cm] (step5) {};
    \node [yes, above of=non, node distance=2cm] (step6) {};
    \node [yes, below of=evaluate, node distance=2cm] (step7) {};
    \node [yes, below of=update, node distance=2cm] (step8) {};
    \node [yes, left of=update, node distance=2cm] (step9) {};
```

```
% Draw edges
   \path [line] (system) -- node[above, near $I_{h1}$]{$ aS_h I_m$}
(init);
   \path [line] (init) -- node[above, near $I_{h2}$]{e}(identify);
   \path [line] (identify) -- node[above, near $I_{h2}$]{$g$}(non);
   \path [line, dashed] (identify) -- node[below, near $I_{h2}$]{$b$}
(update);
   \path [line] (update) -- node[above, near$I_m$]{$bI_{h2}S_m$}
(evaluate);
   \path [line,dashed] (evaluate) --node[above, near $I_m$]{$a$}
(system);
   \path [line] (non) --node[above, near $I_m$]{$i$}(system);
   \path [line] (step1) -- node[above,near $S_h$]{$dN$}(system);
   \path [line] (system) --node[left, near$S_h$]{$d$} (step2);
   \path [line] (init) --node[left, near $I_{h1}$]{$d$} (step3);
  \path [line] (identify) -- node[left, near$I_{h2}$]{$d$}(step4);
  \path [line] (identify) --node[above, near $R_h$]{$f$} (step5);
  \path [line] (non) --node[left, near $R_h$]{$d$} (step6);
  \path [line] (evaluate) -- node[left, near[$I_m$]{$k$}(step7);
  \path [line] (update) -- node[left, near $S_m$]{$k$}(step8);
  \path [line] (step9) -- node[above, near $S_m$]{$kM$}(update);
  \end{tikzpicture}
 \end{document}
```

MATLAB Commands to Calculate Endemic Equilibrium point and Determine Local Stability

6/11/17 4:40 PM C:\Users\toshiba\Desktop\sm3.m 1 of 1

```
clear;
lamdah=0.000215;
lamdam=0.07;
a=0.1;
b=0.09;
d=0.0000549;
k=0.06667;
f=0.001;
e=0.0588;
i=0.00138;
g=0.021;
q1=0.3971;
q2=1.05;
x7=(a*b*e*q1*q2)./(k*(d+e)*(d+f+g));
x6=(k*d*(d+f+g)*(d+f+g)-a*b*e*q2*lamdah)*(i+d)*(d+f+g)./(i*g*e*a*q2-(d+e)*(d+a*q2)*(i+d)↙
*(d+f+g));
x1=((d+e)*(b*e*x6+k*(d+f+g))).(a*b*e*q2);
x2=(e*x6)./(d+f+g);
x3=(g*e*x6)./((i+d)*(d+f+g));
x4=(lamdam*(d+f+g))./(b*e*x6+k*(d+f+g));
x5=(b*e*q2*x6)./(b*e*q2+k*(d+f+g));
A=[-a*x5+d 0 0 i 0 -a*x1;
    a*x5 -(d+e) 0 0 0 a*x1;
    0 e -(d+f+g) 0 0 0 ;
    0 0 g -(i+d) 0 0;
    0 0 -b*x4 0 -b*x3-k 0;
    0 0 b*x4 0 b*x3 -k];
disp(x7)
disp(x1)
disp(x6)
disp(x2)
disp(x3)
disp(x4)
disp(x5)
disp(A)
eig(A)
```

```
    2.5497

    0.1559

  2.2238e-004

  5.9287e-004

    0.0087

    1.0491

  1.7584e-004

    0.0000         0         0    0.0014         0   -0.0156
    0.0000   -0.0589         0         0         0    0.0156
         0    0.0588   -0.0221         0         0         0
         0         0    0.0210   -0.0014         0         0
         0         0   -0.0944         0   -0.0675         0
         0         0    0.0944         0    0.0008   -0.0667


ans =

  -0.0741 + 0.0352i
  -0.0741 - 0.0352i
  -0.0001
  -0.0002
  -0.0013
  -0.0667

>>
```

MATLAB ode45 codes to Draw the Graph of Local Stability for Endemic Equilibrium Point


```
function ftr=ftr(t,y)
lamdah=0.000215;
lamdam=0.07;
a=0.1;
b=0.09;
d=0.0000549;
k=0.06667;
f=0.001;
e=0.0588;
z=0.00138;
g=0.0421;
ftr(1)=lamdah-a*y(1)*y(6)-d*y(1)+z*y(4);
ftr(2)=a*y(1)*y(6)-(d+e)*y(2);
ftr(3)=e*y(2)-(d+f+g)*y(3);
ftr(4)=g*y(3)-(z+d)*y(4);
ftr(5)=lamdam-b*y(3)*y(5)-k*y(5);
ftr(6)=b*y(3)*y(5)-k*y(6);
ftr=[ftr(1) ftr(2) ftr(3) ftr(4) ftr(5) ftr(6)]';
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
clear;
to=0;
tf=10;
yo=[100 10  5 0 1000 30];
[t y]=ode45('ftr',[to tf],yo);
plot(t,y(:,1),t,y(:,2),t,y(:,3),t,y(:,4));
```