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# ON STABILITY OF THE IN-HUMAN HOST AND IN-MOSQUITO DYNAMICS OF MALARIA PARASITE

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Abstract. Stability analysis of dynamical system is basic requirement for its application in real-life settings. However, investigation for local stability is simpler than that for global stability, though the latter is more preferable. In this study, we perform stability analysis of mathematical model for in-human host and in-mosquito dynamics of malaria parasites, and establish the existence of two types of equilibrium: malaria-free equilibrium (MFE) and malaria-infection equilibrium (MIE). Using linearization of system, MFE is proved to be locally asymptotically stable. By Metzler matrix theory, the MFE is reported to be globally asymptotically stable provided $\mathcal{R}_0 < 1$. By applying Lyapunov functional method and LaSalle's invariance theory, we established that MIE is globally asymptotically stable, if $\mathcal{R}_0 > 1$. Numerical simulations are presented to confirm the analytical solutions.

## 1. Introduction

Mathematical models play a remarkable role in undestanding the dynamics of infectious diseases and suggest the control strategies. In the study of dynamical systems such as epidemiological models, the main focus is not on finding detailed solutions, but to investigate some characteristics of the system such as existence and stability of equilibrium points (Lungu *et al.*, 2007). A vector $\mathbf{x}^*$ is an equilibrium point of a dynamical system

$$\dot{\mathbf{x}} = f(\mathbf{x}, \mathbf{t}) \text{ if } f(\mathbf{x}^*, \mathbf{t}) = 0, \quad \forall t > 0.$$

An equilibrium $\mathbf{x}^*$ is said to be *stable* if an arbitrary point $\mathbf{x_0}$ of the system that starts near $\mathbf{x} = \mathbf{x}^*$ remains near it, and *unstable* if $\mathbf{x_0}$ moves away from $\mathbf{x}^*$. An equilibrium is said to be *locally stable* if for all initial values, $\mathbf{x_0}$ that are in a neighborhood $\mathcal{N}(\mathbf{x}^*)$ of $\mathbf{x}^*$, solution of the system remain near $\mathbf{x}^*$ for all values of $t$. $\mathbf{x}^*$ is said to be *globally stable*, if it is stable for all initial values $\mathbf{x_0} \in \mathbb{R}^n$.

Moreover, $\mathbf{x}^*$ is *asymptotically stable* if it is stable and for an arbitrary initial value $\mathbf{x}_0$, the solution of the system converges to $\mathbf{x}^*$ as time tends to infinity. It is *locally asymptotically stable* if it is locally stable and all solutions that start in neighborhood of $\mathbf{x}^*$ converge to $\mathbf{x}^*$ as $t \to \infty$. The $\mathbf{x}^*$ is *globally asymptotically stable*, if it is globally

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stable and for all initial values $\mathbf{x_0} \in \mathbb{R}^n$, the solution of the system tends to $\mathbf{x}^*$ as $t \to \infty$. Investigation of local stability is simpler than that of global stability, though the latter is more preferable (Cull, 1981). Stability of system is basic requirement for its applicability in real-life settings, since stability justify the convergence of solutions of system towards a particular equilibrium point of the system (Chen, 2004). This tells us how the system behaves if it a solution started relatively near, but not exactly at equilibrium point.

A number of techniques have been proposed in investigation of stability of equilibrium points of epidemiological models (Mpeshe *et al.*, 2014). Linearization (Mpeshe *et al.*, 2014; Li *et al.*, 2011; Tumwiine *et al.*, 2007*a*) is used on proving local stability, and Metzler matrix theory is used for global stability of disease free equilibrium (Mpeshe *et al.*, 2014; Wang and Liao, 2012; Dumont *et al.*, 2008; Kamgang and Sallet, 2008). Lyapunov fuctions has been useful tool on the study of global stability of endemic equilibrium (Kajiwara *et al.*, 2015; Korobeinikov and Maini, 2004). Morever, some models are complex in such a way that existence and stability of equilibria cannot be investigated explicitly. Instead numerical simulations have been used to facilitate the purpose (Chiyaka *et al.*, 2008).

In this study, we investigated the existance and stability equilibrium points of mathematical model for the in-human host and in-mosquito dynamics of malaria parasites. We applied linearization technique to establish the local stability of MFE. We used Metzler theory to establish global stability of MFE. Global stability of MIE is established using Lyapunov function in combination with LaSalle's invariance principle. Moreover, we performed numerical simulations to prove the existence and stability of MIE.

This paper is organized as follows: Mathematical description and formulation of the model for in-human host and in-mosquito dynamics of malaria parasites is presented in Section 2. In Section 3, we present analysis of the formulated model, whereby existence and stability of equilibrium points are discussed. In Section 4, numerical simulations are presented to prove the analytical solutions. Lastly, conclusion and direction for the future works is presented in Section 5.

## 2. Model Formulation

The model formulated in this study describes the in-human host and in-mosquito dynamics of malaria parasites. During the blood meal infected mosquito injects sporozoites $S_h$, into human at rate $ab\nu$, which then attack hepatocytic liver cells (HLCs) $H$, at a rate $\beta_1 S_h H$, and die at rate $\mu_{sh}$ where $\beta_1$ is infection rate of sporozoites on HLCs. The infected HLCs $I_h$, progress to hepatic-schizont $T_h$, at a rate $\alpha_1 I_h$, which eventually burst at rate $\delta_1 T_h$, to release merozoites, $M$. The released merozoites, then attack the healthy red blood cells (RBCs), $R$ at rate $\beta_2 RM$, where $\beta_2$ is infection rate of merozoites on RBCs. The parasitized RBCs $I_r$, progress to erythrocytic-schizonts $T_r$, at rate $\alpha_2 I_r$. The $T_r$ burst to release either new merozoites at rate $p\delta_2 T_r$ that attack other healthy RBCs or gametocytes $G_b$, at a rate $(1-p)\delta_2 T_r$. When uninfected mosquito bites an infected human

ingests the gametocytes, $G_b$, which develop into gametes, $G_m$, at the rate $\rho q \omega G_b$, where $\rho$ is number of bites a mosquito made during its lifetime, $\omega$ is number of gametocytes ingested per bite and $q$ is probability that a mosquito bite is infective to mosquito while $G_b$ is number of gametocytes in blood stream. In the mosquito's midgut the microgametes fuse with macrogametes, to develop into Oocysts $C$, at a rate $\alpha_3 G_m$. Then, $C$ burst to release sporozoites $S_m$, at a rate $\delta_3 C$, which migrates to salivary glands ready to infect a new host. Death rates for $H$, $I_h$ and $T_h$ are $\mu_h$, $\mu_{ih}$ and $\mu_{th}$ respectively. Death rates of $R$, $I_r$ and $T_r$ are $\mu_r$, $\mu_{ir}$ and $\mu_{tr}$ respectively. $S_h$, $S_m$ and $M$ die at rates $\mu_{sh}$, $\mu_{sm}$ and $\mu_m$ respectively. The HLCs and RBCs are recruited from bone marrow at constant rates $\Lambda_h$ and $\Lambda_r$ respectively. The variables of the model are presented in Table 1.

**Table 1.** List of state variables

| **Variable** | **Descrption** |
|---|---|
| $S_h$ : | number of sporozoites in human |
| $H$ : | number of uninfected HLCs |
| $I_h$ : | number of infected HLCs |
| $T_h$ : | number of liver schizonts |
| $T_r$ : | number of blood schizonts |
| $M$ : | number of merozoites |
| $R$ : | number of uninfected RBCs |
| $I_r$ : | number of infected RBCs |
| $G_b$ : | number of gametocytes |
| $G_m$ : | number of gametes |
| $C$ : | number of Oocysts |
| $S_m$ : | number of sporozoites in mosquito |

In formulation of this model, we make the following assumptions. A cycle starts by a bite of infected mosquito onto uninfected human and we neglect a bite of infected mosquito onto an infected human host. The HLCs and RBCs recruited at constant rates from bone marrow and they are infected depending on their densities. Mosquito-human infection is does not depend sporozoites' density in salivary gland, while human-mosquito infection dependent of density of gametocytes in blood stream (Da *et al.*, 2015). We also assume that death rates of infected cells is higher than that of uninfected ones. Also, it has been assumed that each of injected sporozoite and released merozoite either die or successfully infect HLCs and RBCs respectively. Similarly, ingested gametocytes either die or successfully fuse.

Within each replication in erythrocytic cycle a constant proportion of asexual parasites switches to gametocytes. Finally, we assumed that existence of mosquito depends on human blood to develop their eggs. Based on the dynamics and assumptions stated above, the in-human host and in-mosquito dynamics on malaria are presented in Figure 1.

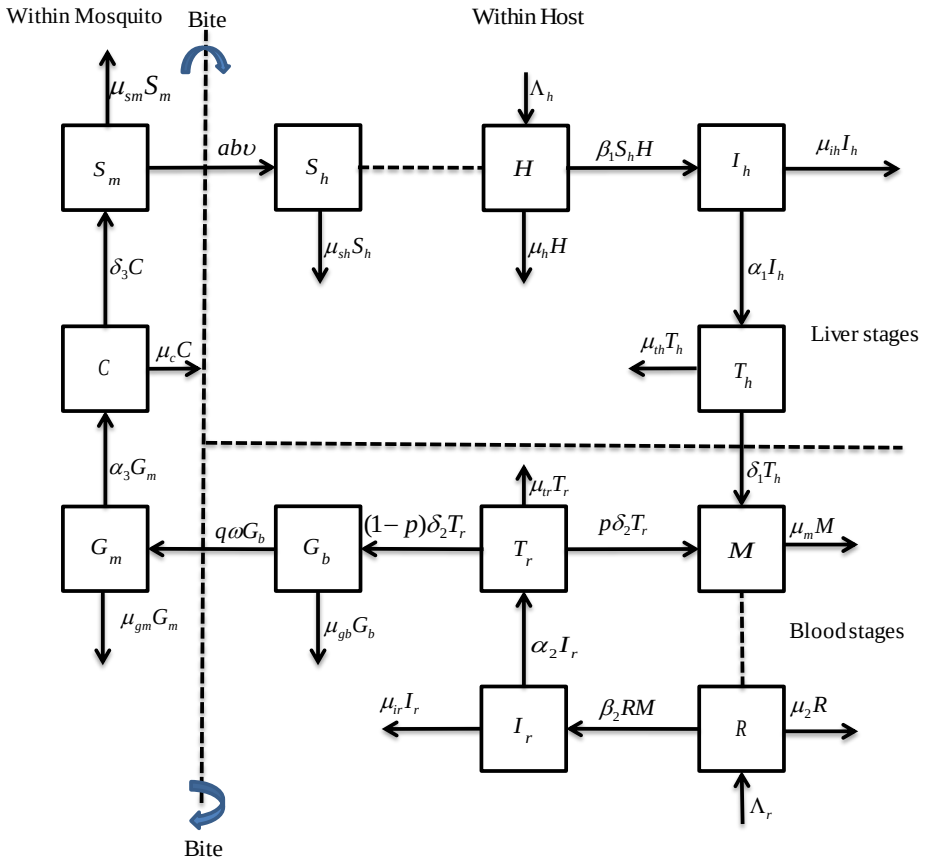



**Figure 1.** Model compartmental diagram for in-human host and in-mosquito dynamics of malaria parasites

The detailed biological descriptions of parameters are as presented in Table 2.

**Table 2.** Parameters estimates for the model (1a)-(1l)

| Parameter | Description | Value | Reference |
|---|---|---|---|
| $a$ : | probability that a bite infects human | 0.75 | (Tumwiine *et al.*, 2007*b*) |
| $b$ : | number of mosquito bites per individual | $15day^{-1}$ | Estimated |
| $\nu$ : | number of sporozoites injected per bite | $10-20$ | (Nelson and Williams, 2014) |
| $\beta_1$ : | infection rate of HLCs by sporozoites | $0.001\ \mu lcell^{-1}day^{-1}$ | Estimated |
| $r_1$ : | number of merozoites per liver schizont | 10000 | (Tumwiine *et al.*, 2014) |
| $\alpha_1$ : | progression rate of infected HCLs to schizonts | $0.125\ day^{-1}$ | Estimated |
| $\delta_1$ : | rupture rate of liver schizonts | $0.0975\ day^{-1}$ | Estimated |
| $\Lambda_h$ : | the recruitmet rate of HLCs | $3000\ cellsday^{-1}\mu l^{-1}$ | Estimated |
| $\mu_h$ : | natural death rate of uninfected HLCs | $0.94\ day^{-1}$ | Estimated |
| $\mu_{ih}$ : | death rate of infected HLCs | $0.95\ day^{-1}$ | Estimated |
| $\mu_{th}$ : | death rate of liver-schizonts | $0.029\ day^{-1}$ | Estimated |
| $\beta_2$ : | infection rate of RBCs by merozoites | $2\times10^{-6}\ \mu lcell^{-1}day^{-1}$ | Estimated |
| $\delta_2$ : | rupture rate of blood schizonts | $0.115\ day^{-1}$ | Estimated |
| $\alpha_2$ : | progression rate of infected RBCs to schizonts | $0.145\ day^{-1}$ | Estimated |
| $r_2$ : | number of merozoites per blood schizont | 16 | (Dube *et al.*, 2010) |
| $q$ : | probability that a bite is infectious to mosquito | 0.09 | (Agusto *et al.*, 2012) |
| $\omega$ : | number of gametocytes ingested per bite | 10 | Estimated |
| $\rho$ : | number of bites made by mosquito in its lifetime | 3 | Estimated |
| $\Lambda_r$ : | the recruitmet rate of RBCs | $4.15\times10^4\ cells\mu l^{-1}day^{-1}$ | (Li *et al.*, 2011) |
| $\mu_r$ : | natural death rate of uninfected RBCs | $0.02\ day^{-1}$ | (Dube *et al.*, 2010) |
| $\mu_{ir}$ : | total death rate of uninfected RBCs | $0.025\ day^{-1}$ | (Diebner *et al.*, 2000) |
| $\mu_{tr}$ : | death rate of blood-schizonts | 0.185 | Estimated |
| $\mu_m$ : | death rate of merozoites | $48\ day^{-1}$ | (Li *et al.*, 2011) |
| $\mu_{gb}$ : | death rate of gametocytes in bloodstream | $6.25\times10^{-5}day^{-1}$ | Estimated |
| $\delta_3$ : | rupture rate of Oocysts | $0.05\ day^{-1}$ | Estimated |
| $r_3$ : | number of sporozoites per Oocyst | 1000 | (Nelson and Williams, 2014) |
| $\alpha_3$ : | progresion rate of gametes to Oocysts | $0.07\ day^{-1}$ | Estimated |
| $\mu_{gm}$ : | death rate of gametes in mosquito's midgut | $0.052\ day^{-1}$ | Estimated |
| $\mu_c$ : | death rate of Oocysts | $0.024\ day^{-1}$ | Estimated |
| $\mu_{sm}$ : | death rate of sporozoites in mosqouito | $40\ day^{-1}$ | Estimated |
| $\mu_{sh}$ : | death rate of sporozoites in human liver | $1.2\times10^{-11}\ day^{-1}$ | Estimated |
| $p$ : | proportion of asexual that differentiate to merozoites | 0.926 | Estimated |

From the compartmental diagram in Figure 1, the dynamics of the entire in-human and in-mosquito malaria cycle we derive the model which is governed by the following set of nonlinear ordinary differential equations:

$$\frac{\mathrm{d}H}{dt} = \Lambda_h - \beta_1 S_h H - \mu_h H \tag{1a}$$

$$\frac{\mathrm{d}I_h}{dt} = \beta_1 S_h H - (\alpha_1 + \mu_{ih}) I_h \tag{1b}$$

$$\frac{\mathrm{d}T_h}{dt} = \alpha_1 I_h - (\delta_1 + \mu_{th}) T_h \tag{1c}$$

$$\frac{\mathrm{d}M}{dt} = r_1\delta_1 T_h + pr_2\delta_2 T_r - \beta_2 RM - \mu_m M \tag{1d}$$

$$\frac{\mathrm{d}R}{dt} = \Lambda_r - \beta_2 RM - \mu_r R \tag{1e}$$

$$\frac{\mathrm{d}I_r}{dt} = \beta_2 RM - (\alpha_2 + \mu_{ir}) I_r \tag{1f}$$

$$\frac{\mathrm{d}T_r}{dt} = \alpha_2 I_r - (\delta_2 + \mu_{tr}) T_r \tag{1g}$$

$$\frac{\mathrm{d}G_b}{dt} = (1-p) r_2\delta_2 T_r - (q\omega + \mu_{gb}) G_b \tag{1h}$$

$$\frac{\mathrm{d}G_m}{dt} = \rho q\omega G_b - (\alpha_3 + \mu_{gm}) G_m \tag{1i}$$

$$\frac{\mathrm{d}C}{dt} = \alpha_3 G_m - (\delta_3 + \mu_c) C \tag{1j}$$

$$\frac{\mathrm{d}S_m}{dt} = r_3\delta_3 C - (a\nu + \mu_{sm}) S_m \tag{1k}$$

$$\frac{\mathrm{d}S_h}{dt} = ab\nu - \beta_1 S_h H - \mu_{sh} S_h \tag{1l}$$

## 3. Analysis of the Model

In this section, we study the basic properties of the model system (1a)-(1l). For epidemiological implications, we prove that the model system (1a)-(1l) has the solution that is mathematically and biologically well-posed in the feasible region

$$\begin{aligned}\Omega = \Bigg\{ &(H, I_h, T_h, M, R, I_r, T_r, G_b, G_m, C, S_m, S_h) \in \mathbb{R}^{12}_+ : N_h(t) \le \max\left\{ N_h(0),\ \frac{\Lambda_h}{\mu_1} \right\}, \\ &N_r(t) \le \max\left\{ N_r(0),\ \frac{\Lambda_r}{\mu_2} \right\},\ M(t) \le \max\left\{ M(0),\ \frac{1}{\mu_m}\left[ r_1\delta_1\frac{\Lambda_h}{\mu_1} + pr_2\delta_2\frac{\Lambda_r}{\mu_2} \right] \right\}, \\ &G_b(t) \le \max\left\{ G_b(0),\ (1-p) r_2\delta_2\frac{\Lambda_r}{\mu_2} \right\},\ N_m(t) \le \max\left\{ N_m(0),\ \frac{q\rho\omega}{\mu_3}\left[ (1-p) r_2\delta_2\frac{\Lambda_r}{\mu_2} \right] \right\}, \\ &S_m \le \max\left\{ S_m(0),\ \frac{r_3\delta_3}{\mu_{sm}}\frac{q\rho\omega}{\mu_3}\left[ (1-p) r_2\delta_2\frac{\Lambda_r}{\mu_2} \right] \right\},\ S_h(t) \le \max\left\{ S_h(0),\ \frac{ab\nu}{\mu_{sh}} \right\} \Bigg\}\end{aligned}$$

where

$$\mu_1 = \min\{\mu_h,\ \mu_{th} + \delta_1\},\ \mu_2 = \min\{\mu_r,\ \mu_{tr} + \delta_2\},\ \mu_3 = \min\{\mu_{gm},\ \mu_c\},$$

$$N_h(t) = H(t) + I_h(t) + T_h(t),\ N_r(t) = R(t) + I_r(t) + T_r(t),\ N_m(t) = G_m(t) + C(t),$$

and $\mathbb{R}^{12}_+$ is non-negative orthant of $\mathbb{R}^{12}$.
Conditions for existence and stability of equilibra of the model in this region are discussed in next subsection.

### 3.1. Existence and Stability of Equilibra

In absence of infection, we obtain one equilibrium termed as malaria free equilibrium (MFE),

$$E^0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, \frac{\Lambda_r}{\mu_r}, 0, 0, 0, 0, 0, 0, 0, 0\right)$$

The stability of MFE is discussed in next subsection.

#### 3.1.1. Local and Global Stability of MFE

We establish the local stability of $E^0$ by investigating the signs of the real parts of the eigenvalues of the Jacobian matrix of the system at $E^0$. Jacobian matrix of system (1a)-(1l) at $E^0$ is given by

$$J(E^0) = \begin{bmatrix}
-\mu_h & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -z_1 \\
0 & -z_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & z_1 \\
0 & \alpha_1 & -z_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & r_1\delta_1 & -z_4 & 0 & 0 & pr_2\delta_2 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & -z_5 & -\mu_r & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & z_5 & 0 & -z_6 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & \alpha_2 & -z_7 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & z_8 & -z_9 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & \rho q\omega & -z_{10} & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \alpha_3 & -z_{11} & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & r_3\delta_3 & -z_{12} & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -z_{13}
\end{bmatrix}$$

where

$$\begin{aligned}
z_1 =& \beta_1\frac{\Lambda_h}{\mu_h}, \quad z_2 = \alpha_1 + \mu_{ih}, \quad z_3 = \delta_1 + \mu_{th}, \quad z_4 = \beta_2\frac{\Lambda_r}{\mu_r} + \mu_m, \quad z_5 = \beta_2\frac{\Lambda_r}{\mu_r}, \\
z_6 =& \alpha_2 + \mu_{ir}, \quad z_7 = \delta_2 + \mu_{tr}, \quad z_8 = (1-p)r_2\delta_2, \quad z_9 = q\omega + \mu_{gb}, \quad z_{10} = \alpha_3 + \mu_{gm}, \\
z_{11} =& \delta_3 + \mu_c, \quad z_{12} = a\nu + \mu_{sm}, \quad z_{13} = \beta_1\frac{\Lambda_h}{\mu_h} + \mu_{sh}
\end{aligned} \tag{2}$$

The MFE is locally assympotically stable if and only if trace of $J(E^0)$ is strictly negative and determinat of $J(E_0)$ is strictly positive. We obtain the following results,

$$trace(J(E^0)) = -\left[(\mu_h+\mu_r)+(\mu_{th}+\mu_{tr})+(\mu_{ih}+\mu_{ir})+(\alpha_1+\alpha_2+\alpha_3)+(\delta_1+\delta_2+\delta_3)\right.$$
$$\left.+(\mu_m+\mu_{gb}+\mu_c+\mu_{sm}+mu_{sh})+\frac{\beta_1\Lambda_h}{\mu_h}+\frac{\beta_2\Lambda_r}{\mu_r}+(q\omega+\mu_{gm}++a\nu)\right]<0 \tag{3}$$

and

$$det(J(E^0)) =(\beta_1\Lambda_h+\mu_{sh}\mu_h)(\delta_1+\mu_{th})(\alpha_1+\mu_{ih})(q\omega+\mu_{gb})(\alpha_3+\mu_{gm})(\delta_3+\mu_c)(a\nu+\mu_{sm})$$
$$(\mu_{tr}+\delta_2)(\alpha_2+\mu_{ir})(\beta_2\Lambda_r+\mu_m\mu_r)\left[1-\mathcal{R}_0\right]>0 \tag{4}$$

where

$$\mathcal{R}_0=\frac{\beta_2\Lambda_r}{\beta_2\Lambda_r+\mu_m\mu_r}.\frac{\alpha_2}{(\alpha_2+\mu_{ir})}.\frac{pr_2\delta_2}{(\delta_2+\mu_{tr})}$$

Equation (4) holds only if $\mathcal{R}_0<1$ ; and because of this requirement $\mathcal{R}_0$ is interpreted as the basic reproduction number. This leads us to the following theorem.

**Theorem 1.** *The malaria-free equilibrium, $E^0$ is locally asymptotically stable when $\mathcal{R}_0<1$ and unstable otherwise.*

### 3.1.2. Global Stability of MFE

We establish the global stability of $E^0$ using the Metzler matrix theory technique used in Castillo-Chávez *et al.* (2002); Kamgang and Sallet (2008); Mpeshe *et al.* (2014). In this approach, we re-write the model system in the form:

$$\begin{cases}\frac{dX_n}{dt}=A_1(x)(X_n-X_{E^0,n})+A_{12}(x)X_e\\ \\ \frac{dX_e}{dt}=A_2(x)X_e\end{cases}$$

where $X_n$ is the vector of uninfected classes and $X_e$ is the vector of infected classes. For our case, we have

$$X_n=(H,\ R)\text{ and }X_e=(I_h,T_h,M,I_r,T_r,G_b,G_m,C,S_m,S_h) \tag{5}$$

$$X_{E^0,n}=\left(\frac{\Lambda_h}{\mu_h},\ \frac{\Lambda_r}{\mu_r}\right) \tag{6}$$

and

$$A_1(x)=\begin{pmatrix}-\mu_h & 0\\ 0 & -\mu_r\end{pmatrix}, \tag{7}$$

$$A_{12}(x) = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\beta_1 H \\ 0 & 0 & -\beta_2 R & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{8}$$

and

$$A_2(x) = \begin{pmatrix} -w_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \beta_1 H \\ \alpha_1 & -w_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & r_1\delta_1 & -w_3 & 0 & pr_2\delta_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_2 R & -w_4 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \alpha_2 & -w_5 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & w_6 & -w_7 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \rho q\omega & -w_8 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \alpha_3 & -w_9 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & r_3\delta_3 & -w_{10} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & w_{11} & -w_{12} \end{pmatrix} \tag{9}$$

where

$$\begin{aligned} w_1 =& \alpha_1 + \mu_{ih},\ w_2 = \delta_1 + \mu_{th},\ w_3 = \frac{\beta_2 \Lambda_r}{\mu_r} + \mu_m, w_4 = \alpha_2 + \mu_{ir}, \\ w_5 =& \delta_1 + \mu_{tr},\ w_6 = (1-p) r_2 \delta_2,\ \ w_7 = q\omega + \mu_{gb}, w_8 = \alpha_3 + \mu_{gm}, \\ w_9 =& \delta_3 + \mu_c,\ w_{10} = a\nu + \mu_{sm},\ w_{11} = \frac{ab\nu}{S_m} \text{ and } w_{12} = \beta_1 H + \mu_{sh} \end{aligned} \tag{10}$$

It can easily be seen from (7) that, all eigenvalues of $A_1$ are real and negative.
So, the system

$$\frac{\mathrm{d}X_n}{\mathrm{d}t} = A_1(x)(X_n - X_{E^0,n}) + A_{12}(x) X_e$$

is globally assymptotically stable at $X_{E^0}$. From (9) and (10) it can be observed that all off diagonal elements of $A_2$ are non-negative. Therefore, $A_2$ is a Metzler stable matrix. Thus, the MFE is GAS. To investigate under which conditions MFE is GAS, we need to prove the following proposition .

**Proposition 1.** *(Kamgang and Sallet, 2008; Dumont* et al.*, 2008)*
*Let $M$ be a square block decomposed Metzler matrix: $M = \begin{pmatrix} A & B \\ C & D \end{pmatrix}$ with $A$ and $D$ square matrices. Then $M$ is Metzler stable if and only if matrices $A$ and $D - CA^{-1}A$ are Metzler stable.*

For this case we have $M = A_2$, and $A = \begin{pmatrix} -w_1 & 0 & 0 & 0 & 0 \\ \alpha_1 & -w_2 & 0 & 0 & 0 \\ 0 & r_1\delta_1 & -w_3 & 0 & pr_2\delta_2 \\ 0 & 0 & \beta_2 R & -w_4 & 0 \\ 0 & 0 & 0 & \alpha_2 & -w_5 \end{pmatrix}$

$$B = \begin{pmatrix} 0 & 0 & 0 & 0 & \beta_1 H \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \quad C = \begin{pmatrix} 0 & 0 & 0 & 0 & w_6 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and $D = \begin{pmatrix} -w_7 & 0 & 0 & 0 & 0 \\ \rho q \omega & -w_8 & 0 & 0 & 0 \\ 0 & \alpha_3 & -w_9 & 0 & 0 \\ 0 & 0 & r_3\alpha_3 & -w_{10} & 0 \\ 0 & 0 & 0 & w_{11} & -w_{12} \end{pmatrix}$

immediately we have

$$D - CA^{-1}B = \begin{pmatrix} -w_{11} & 0 & 0 & 0 & \frac{r_1\delta_1\alpha_1\alpha_2 w_6 \Lambda_h \Lambda_r \beta_1 \beta_2}{w_1 w_2 \mu_h (w_3 w_4 w_5 \mu_r - \beta_2 \Lambda_r p r_2 \delta_2 \alpha_2)} \\ w_{12} & -w_{13} & 0 & 0 & 0 \\ 0 & \alpha_3 & -w_{14} & 0 & 0 \\ 0 & 0 & w_{15} & -w_{16} & 0 \\ 0 & 0 & 0 & w_{17} & -w_{18} \end{pmatrix}$$

**Definition:**
A Metzler matrix $M$ is said to be stable if all of its diagonal elements are negative.

By that definition, $A$ is Metzler stable matrix, and $D - CA^{-1}B$ is Metzler stable matrix if and only if

$$\frac{r_1\delta_1\alpha_1\alpha_2 w_6 \Lambda_h \Lambda_r \beta_1 \beta_2}{w_1 w_2 \mu_h (w_3 w_4 w_5 \mu_r - \beta_2 \Lambda_r p r_2 \delta_2 \alpha_2)} > 0 \tag{11}$$

which holds only when

$$\frac{\beta_2 \Lambda_r p r_2 \delta_2 \alpha_2}{w_3 w_4 w_5 \mu_r} < 1 \tag{12}$$

Using $w_3$, $w_4$, and $w_5$ as given in equation (10), we get

$$\frac{\frac{\beta_2\Lambda_r}{\mu_r}\alpha_2 p r_2 \delta_2}{\left(\frac{\beta_2\Lambda_r}{\mu_r} + \mu_m\right)(\alpha_2 + \mu_{ir})(\delta_2 + \mu_{tr})} < 1 \tag{13}$$

equivalently,

$\mathcal{R}_0 < 1$.

This leads us to the following theorem.

**Theorem 2.** *The MFE of the model system* (1a)-(1l) *is globally assymptotically stable in* $\Omega$ *if* $\mathcal{R}_0 < 1$ *and unstable if* $\mathcal{R}_0 > 1$.

### 3.2. Existence of MIE

The model has one positive malaria infection equilibrium $E^*$ which is given by

$$E^* = (H^*, I_h^*, T_h^*, M^*, R^*, I_r^*, T_r^*, G_b^*, G_m^*, C^*, S_m^*, S_h^*)$$

where

$$H^* = \frac{\Lambda_h}{\beta_1 S_h^* + \mu_h}, \quad I_h^* = \frac{\beta_1 \Lambda_h S_h^*}{(\alpha_1 + \mu_{ih})(\beta_1 S_h^* + \mu_h)}, \quad T_h^* = \frac{\beta_1 \Lambda_h \alpha_1 S_h^*}{(\delta_1 + \mu_{th})(\alpha_1 + \mu_{ih})(\beta_1 S_h^* + \mu_h)},$$

$$R^* = \frac{\Lambda_r}{\beta_2 M^* + \mu_r}, \quad I_r^* = \frac{\beta_2 \Lambda_2 M^*}{(\alpha_2 + \mu_{ir})(\beta_2 M^* + \mu_r)}, \quad T_r^* = \frac{\mathcal{R}_0(\beta_2 \Lambda_r + \mu_r \mu_m) M^*}{p r_2 \delta_2 (\beta_2 M^* + \mu_r)}$$

$$G_b^* = \frac{(1-p)\mathcal{R}_0}{p(q\omega + \mu_{gb})} \frac{(\beta_2 \Lambda_r + \mu_r \mu_m) M^*}{(\beta_2 M^* + \mu_r)}, \quad G_m = \left[\frac{\rho q \omega}{\alpha_3 + \mu_{gm}}\right] \left[\frac{(1-p)\mathcal{R}_0}{p(q\omega + \mu_{gb})} \frac{(\beta_2 \Lambda_r + \mu_r \mu_m) M^*}{(\beta_2 M^* + \mu_r)}\right],$$

$$C = \frac{\alpha_3}{\delta_3 + \mu_c} \left[\frac{\rho q \omega}{\alpha_3 + \mu_{gm}}\right] \left[\frac{(1-p)\mathcal{R}_0}{p(q\omega + \mu_{gb})} \frac{(\beta_2 \Lambda_r + \mu_r \mu_m) M^*}{(\beta_2 M^* + \mu_r)}\right],$$

$$S_m^* = \frac{r_3 \delta_3}{a\nu + \mu_{sm}} \frac{\alpha_3}{\delta_3 + \mu_c} \left[\frac{\rho q \omega}{\alpha_3 + \mu_{gm}}\right] \left[\frac{(1-p)\mathcal{R}_0}{p(q\omega + \mu_{gb})} \frac{(\beta_2 \Lambda_r + \mu_r \mu_m) M^*}{(\beta_2 M^* + \mu_r)}\right],$$

$S_h^*$ and $M^*$ are positive solutions of $F(S_h^*) = 0$ and $G(M^*) = 0$ respectively, where $F(S_h^*) = A_3 S_h^{*2} + A_2 S_h^* + A_1$, $G(M^*) = B_3 M^{*2} + B_2 M^* + B_1$ and

$A_3 = \beta_1 \mu_{sh}$, $A_2 = \beta_1(\Lambda_h - ab\nu) + \mu_{sh}\mu_h$, $A_1 = -ab\nu\mu_h$,
$B_3 = \beta_2 \mu_m$, $B_2 = -\left[(\beta_2 \Lambda_r + \mu_m \mu_r)(\mathcal{R}_0 - 1) + \beta_2 \lambda^*\right]$, $B_1 = -\mu_r \lambda^*$ and
$\lambda(S_h^*) = \dfrac{\theta S_h^*}{\beta_1 S_h^* + \mu_h}$

Now we need to determine necessary and sufficient conditions for existence of malaria-infection equilibrium $E^*$ by proving the following theorem

**Theorem 3.** *The model system* (1a)*-1l has a unique malaria infection equilibrium*

$$E^* = (H^*, I_h^*, T_h^*, M^*, R^*, I_r^*, T_r^*, G_b^*, G_m^*, C^*, S_m^*, S_h^*)$$

*if* $\mathcal{R}_0 > 1$, $\Lambda_h > ab\nu$, $A_3 S_h^{*2} + A_2 S_h^* + A_1 = 0$ *and* $B_3 M^{*2} + B_2 M^* + B_1 = 0$ *have roots* $S_h^* > 0$ *and* $M^* > 0$ *respectively.*

**Proof:**
Let $E^* = (H^*, I_h^*, T_h^*, M^*, R^*, I_r^*, T_r^*, G_b^*, G_m^*, C^*, S_m^*, S_h^*)$ be malaria infection equilibrium of the system (1a)-(1l). Substituting the expression for $H^*$ into equation (1l), we have

$$ab\nu - \frac{\beta_1 S_h^* \Lambda_h}{\beta_1 S_h^* + \mu_h} - \mu_{sh} S_h^* = 0$$

which yields to

$$\beta_1 \mu_{sh} S_h^{*2} + \left[\beta_1(\Lambda_h - ab\nu) + \mu_{sh}\mu_h\right] S_h^* - ab\nu\mu_h = 0 \tag{14}$$

Since $A_1 < 0$ and $A_3 > 0$, then the quadratic equation (14) has unique positive root $S_h^*$ given by

$$S_h^* = \frac{-\left[\beta_1(\Lambda_h - ab\nu) + \mu_{sh}\mu_h\right] + \sqrt{\triangle_1}}{2\beta_1\mu_{sh}} \tag{15}$$

where

$$\triangle_1 = (\beta_1(\Lambda_h - ab\nu) + \mu_{sh}\mu_h)^2 + 4\beta_1 ab\nu\mu_{sh}\mu_h \tag{16}$$

only if $A_2 > 0$.

Hence, $A_2 = \beta_1(\Lambda_h - ab\nu) + \mu_{sh}\mu_h > 0$ only if $\Lambda_h > ab\nu$ (recruitment rate of uninfected HLCs is greater than recruitment of sporozoites into human liver).

Substituting expressions for $T_h^*$, $T_r^*$ and $R^*$ into equation (1d) gives

$$\frac{\beta_1\Lambda_h\alpha_1 r_1\delta_1 S_h^*}{(\delta_1+\mu_{th})(\alpha_1+\mu_h+d_h)(\beta_1 S_h^*+\mu_h)} + \frac{\mathcal{R}_0(\beta_2\Lambda_r+\mu_m\mu_r)M^*}{(\beta_2 M^*+\mu_r)} - \frac{\beta_2\Lambda_r M^*}{\beta_2 M^*+\mu_r} - \mu_m M^* = 0 \tag{17}$$

Letting $\theta = \dfrac{\beta_1\Lambda_h\alpha_1 r_1\delta_1}{(\delta_1+\mu_{th})(\alpha_1+\mu_h+d_h)}$ equation (17) becomes

$$\frac{\theta S_h^*}{(\beta_1 S_h^*+\mu_h)} + \frac{\left[\mathcal{R}_0(\beta_2\Lambda_r+\mu_m\mu_r) - \beta_2\Lambda_r - \mu_m(\beta_2 M^*+\mu_r)\right] M^*}{(\beta_2 M^*+\mu_r)} = 0 \tag{18}$$

which can be further simplified to

$$\beta_2\mu_m M^{*2} - \left[(\beta_2\Lambda_r+\mu_m\mu_r)(\mathcal{R}_0-1) + \beta_2\lambda^*\right] M^* - \mu_r\lambda^* = 0 \tag{19}$$

where

$$\lambda^* = \frac{\theta S_h^*}{(\beta_1 S_h^*+\mu_h)}$$

Equation (19) has a unique positive real root $M^*$ given by

$$M^* = \frac{\left[(\beta_2\Lambda_r+\mu_m\mu_r)(\mathcal{R}_0-1) + \beta_2\lambda^*\right] + \sqrt{\triangle_2}}{2\beta_2\mu_m\mu_r\lambda^*} \tag{20}$$

where

$$\triangle_2 = (\mathcal{R}_0 - 1)^2(\beta_2\Lambda_r + \mu_m\mu_r)^2 + 2\beta_2\lambda^* \left[\beta_2\Lambda_r + \mu_m\mu_r(\mathcal{R}_0 - 1)\right] + \beta_2^2\lambda^{*2} + 4\beta_2\mu_m\mu_r\lambda^*$$

only if $\mathcal{R}_0 > 1$.

This is condition for the existence of malaria infection equilibrium.
Therefore, if $\mathcal{R}_0 > 1$, $\Lambda_h > ab\nu$ and quadratic equations $A_3S_h^{*2} + A_2S_h^* + A_1 = 0$ and $B_3M^{*2} + B_2M^* + B_1 = 0$ have respectively positive roots $S_h^*$ and $M^*$, with

$$S_h^* = \frac{-\left[\beta_1(\Lambda_h - ab\nu) + \mu_{sh}\mu_h\right] + \sqrt{\triangle_1}}{2\beta_1\mu_{sh}} \text{ and } M^* = \frac{\left[(\beta_2\Lambda_r + \mu_m\mu_r)(\mathcal{R}_0 - 1) + \beta_2\lambda^*\right] + \sqrt{\triangle_2}}{2\beta_2\mu_m\mu_r\lambda^*}$$

### 3.3. Global Stability of MIE

When $\mathcal{R}_0 < 1$, MFE is locally asymptotically stable. This suggests local stability of the MIE when $\mathcal{R}_0 > 1$ (Van den Driessche and Watmough, 2002).

So we only investigate the global stability of the MIE. We adopted the techiniques used by Pedro *et al.* (2014).

**Theorem 4.** *if $\mathcal{R}_0 > 1$, the model described by equations (1a)-(1l) has unique positive MIE, $E^*$, such that*

$$\begin{aligned}
\frac{S_h^*H^*}{S_hH} \geq \frac{H^*}{H} \geq 1, \quad &for\ 0 < S_h < S_h^*\ and\ 0 < H < H^* \\
\frac{S_h^*H^*}{S_hH} \geq \frac{S_h^*}{S_h} \geq 1 \quad &for\ 0 < S_h < S_h^*\ and\ 0 < H < H^* \\
\frac{R^*M^*}{RM} \geq \frac{M^*}{M} \geq 1 \quad &for\ 0 < M < M^*\ and\ 0 < R < R^* \\
\frac{R^*M^*}{RM} \geq \frac{R^*}{R} \geq 1 \quad &for\ 0 < M < M^*\ and\ 0 < R < R^*
\end{aligned}$$

*Then, $E^*$ is globally asymptotic stable in $\mathring{\Omega} \subset \Omega$.*

**Proof:** To estabilish the global stability of MIE, $E^*$, we define the Lyapunov function of the form

$$L(x) = \sum z_i(x_i - x_i^* \ln \frac{x}{x^*}), \text{ for } i = 1,\ 2, \ldots 12$$

as proposed by Castillo-Chávez *et al.* (2002) where $x_i$ is a number of cells in the i$^{\text{th}}$ class, $x_i^*$ are equilibrium values and $z_i$ are constants. This approach has been found useful for more complex compartmental models of *in vivo* dynamics (Korobeinikov, 2004).

Now, we constructed the following lyapunov function

$$\begin{aligned} L =& z_1\left(H - H^* \ln\frac{H}{H^*}\right) + z_2\left(I_h - I_h^* \ln\frac{I_h}{I_h^*}\right) + z_3\left(T_h - T_h^* \ln\frac{T_h}{T_h^*}\right) \\ &+ z_4\left(M - M^* \ln\frac{M}{M^*}\right) + z_5\left(R - R^* \ln\frac{R}{R^*}\right) + z_6\left(I_r - I_r^* \ln\frac{I_r}{I_r^*}\right) \\ &+ z_7\left(T_r - T_r^* \ln\frac{T_r}{T_r^*}\right) + z_8\left(G_b - G_b^* \ln\frac{G_b}{G_b^*}\right) + z_9\left(G_m - G_m^* \ln\frac{G_m}{G_m^*}\right) \\ &+ z_{10}\left(C - C^* \ln\frac{C}{C^*}\right) + z_{11}\left(S_m - S_m^* \ln\frac{S_m}{S_m^*}\right) + z_{12}\left(S_h - S_h^* \ln\frac{S_h}{S_h^*}\right) \end{aligned} \tag{21}$$

Using equations (1a)-(1l) evaluated at MIE into time derivative of (21) gives

$$\begin{aligned} \frac{dL}{dt} =& - z_1\mu_h H\left[1 - \frac{H^*}{H}\right]^2 - z_2(\alpha_1 + \mu_{ih})I_h\left[1 - \frac{I_h^*}{I_h}\right]^2 - z_3(\delta_1 + \mu_{th})T_h\left[1 - \frac{T_h^*}{T_h}\right]^2 \\ &- z_4\mu_m M\left[1 - \frac{M^*}{M}\right]^2 - z_5\mu_r R\left[1 - \frac{R^*}{R}\right]^2 - z_6(\alpha_2 + \mu_{ir})I_r\left[1 - \frac{I_r^*}{I_r}\right]^2 \\ &- z_7(\delta_2 + \mu_{tr})T_r\left[1 - \frac{T_r^*}{T_r}\right]^2 - z_8(q\omega + \mu_{gb})G_b\left[1 - \frac{G_b^*}{G_b}\right]^2 - z_9(\alpha_3 + \mu_{gm})G_m\left[1 - \frac{G_m^*}{G_m}\right]^2 \\ &- z_{10}(\delta_3 + \mu_c)C\left[1 - \frac{C^*}{C}\right]^2 - z_{11}(a\nu + \mu_{sm})S_m\left[1 - \frac{S_m^*}{S_m}\right]^2 - z_{12}\mu_{sh}S_h\left[1 - \frac{S_h^*}{S_h}\right]^2 + f(\Omega) \end{aligned}$$

where

$$\begin{aligned} f(\Omega) =& z_1\beta_1 S_h H\left[1 - \frac{H^*}{H}\right]\left[\frac{S_h^* H^*}{S_h H} - 1\right] + z_4\beta_2 RM\left[1 - \frac{M^*}{M}\right]\left[\frac{R^* M^*}{RM} - 1\right] \\ &+ z_5\beta_2 RM\left[1 - \frac{R^*}{R}\right]\left[\frac{R^* M^*}{RM} - 1\right] + z_{12}\beta_1 S_h H\left[1 - \frac{S_h^*}{S_h}\right]\left[\frac{S_h^* H^*}{S_h H} - 1\right] \end{aligned}$$

and $\Omega = \{(H, I_h, T_h, M, R, I_r, T_r, G_b, G_m, C, S_m,\ S_h) > 0\}$

By hypothesis of Theorem 4, we have

$$z_1\beta_1 S_h H\left[1 - \frac{H^*}{H}\right]\left[\frac{S_h^* H^*}{S_h H} - 1\right] \le 0, \quad z_4\beta_2 RM\left[1 - \frac{M^*}{M}\right]\left[\frac{R^* M^*}{RM} - 1\right] \le 0$$

$$z_5\beta_2 RM\left[1 - \frac{R^*}{R}\right]\left[\frac{R^* M^*}{RM} - 1\right] \le 0, \quad z_{12}\beta_1 S_h H\left[1 - \frac{S_h^*}{S_h}\right]\left[\frac{S_h^* H^*}{S_h H} - 1\right] \le 0$$

where equality applies only when $H = H^*,\ S_h = S_h^*,\ M = M^*,\ R = R^*$ Therefore $f(\Omega) \le 0$ for all $H = H^*,\ S_h = S_h^*,\ M = M^*,\ R = R^*$.

Hence, $\frac{dL}{dt} \le 0$ for all $(H, I_h, T_h, M, R, I_r, T_r, G_b, G_m, C, S_m,\ S_h) > 0$ and $\frac{dL}{dt} = 0$ only when $H = H^*, I_h = I_h^*, T_h = T_h^*, M = M^*, R = R^*, I_r = I_r^*, T_r = T_r^*, G_b = G_b^*, G_m = G_m^*$, $C = C^*, S_m = S_m^*,\ S_h = S_h^*$, and $E^*$ is the only equilibrium state of the system on this plane. Therefore, the largest compact invariant set in $\Omega$ such that $\frac{dL}{dt} = 0$ is the singleton $\{E^*\}$ which is the MIE. LaSalles invariant principle (LaSalle, 1976) guarantees that $E^*$ is globally asymptotically stable (GAS) in the interior $\mathring{\Omega}$ of $\Omega$.

## 4. Numerical simulations

In this section, we perform some numerical simulations of the model (1a)-(1l), to illustrate the dynamics of model using MATLAB symbolic package run in intel (R) Pentium (R) CPU B980 2.40GHz, 2.40GHz, 4.00GB machine. The initial values used in simulation of this model are largely assummed to allow computer executions, and their values are listed in Table 3.

**Table 3.** Initial values of variables of the model (1a)-(1l)

| **Variable** | $H$ | $I_h$ | $T_h$ | $M$ | $R$ | $I_r$ | $T_r$ | $G_b$ | $G_m$ | $C$ | $S_m$ | $S_h$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Initial values** | 3000 | 0 | 0 | 2000 | 500000 | 0 | 1000 | 3000 | 1500 | 1000 | 2000 | 2000 |

Although the decision on values of parameters for the in vivo dynamincs is challenging (Chiyaka *et al.*, 2008), the numerical values of parameters used in the numerical simulation of this model are presented in Table 2. These values are either estimated or taken from various articles among existing literature. The reason why some parameters values have been estimated is that modelling of liver and mosquito stages dynamics of malaria parasite have not been done or the parameter values found in existing literature are not suitable in our model. Even those that have been taken from other related studies may not be as accurate as we need for our mathematical forecasts. However, the main issue here is the effect of these parameters on the basic reproduction number, which gives the clues on how to eradicate or control the disease (Chiyaka *et al.*, 2008).

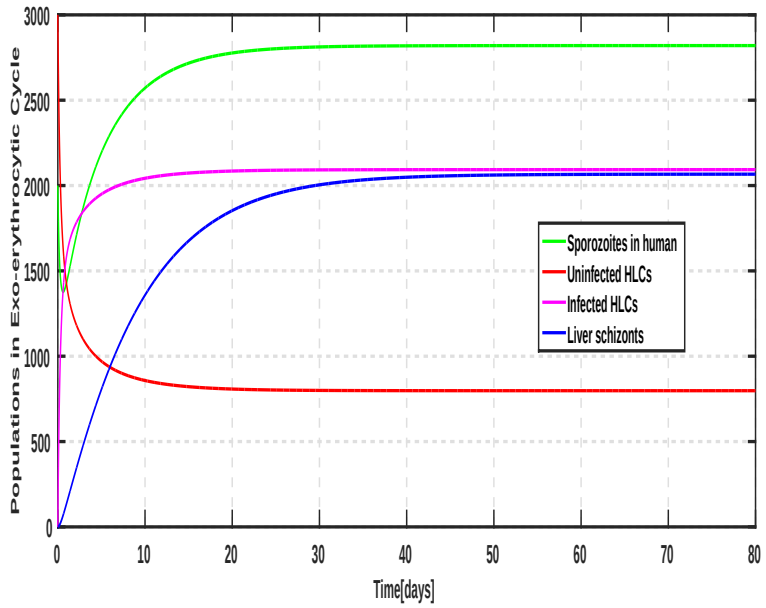
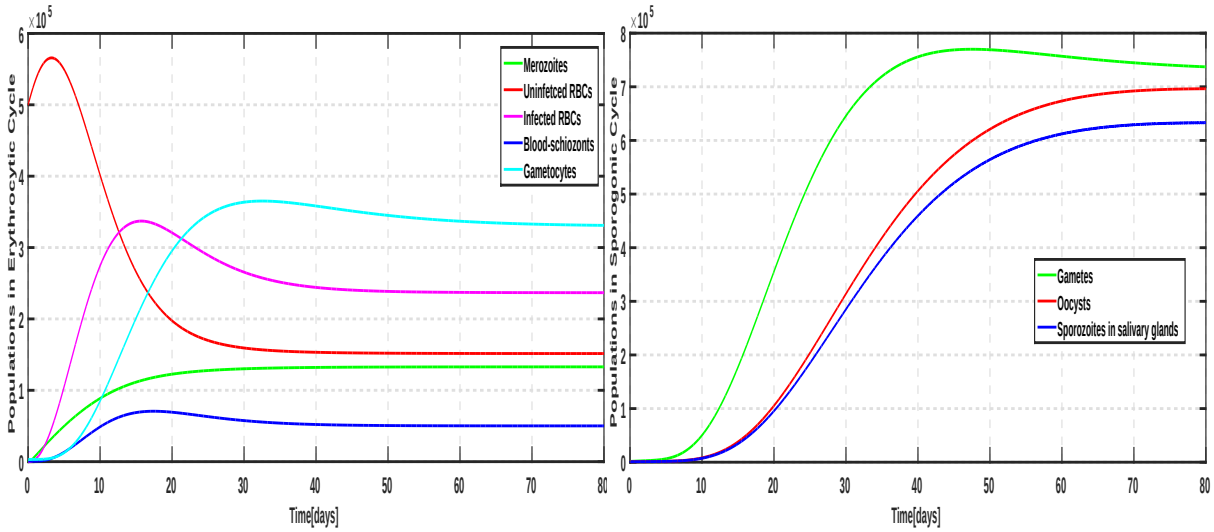



**Figure 2.** Variation of populations at Exo-erythrocytic cycle with time

It is observed from Figure 2 that population density for sporozoites, uninfected HLCs, and infected HLCs vary with time and attain constant values (malaria infection point). However, sporozoites injected into human starts by falling within very short time before

starting to rise. This fall is probably due the fact that when sporozoites injected into the human, they travel to the liver through bloodstream where they ingested by phagocytes (Smyth and Wakelin, 1994) or they probably die due to change of environment from mosquito's salivary gland to human bloodstream. Then its population increases after they succefully reach the liver and start the asexual replication (exo-erythrocytic schizogony) within HLCs. In contrary to population of sporozoites, population of uninfected HLCs decreases with time until it reaches its equilibrium value. This population decreases because of infection of HLCs by sporozoites, which on other hand cause rise in population of infected HLCs and liver schizonts.

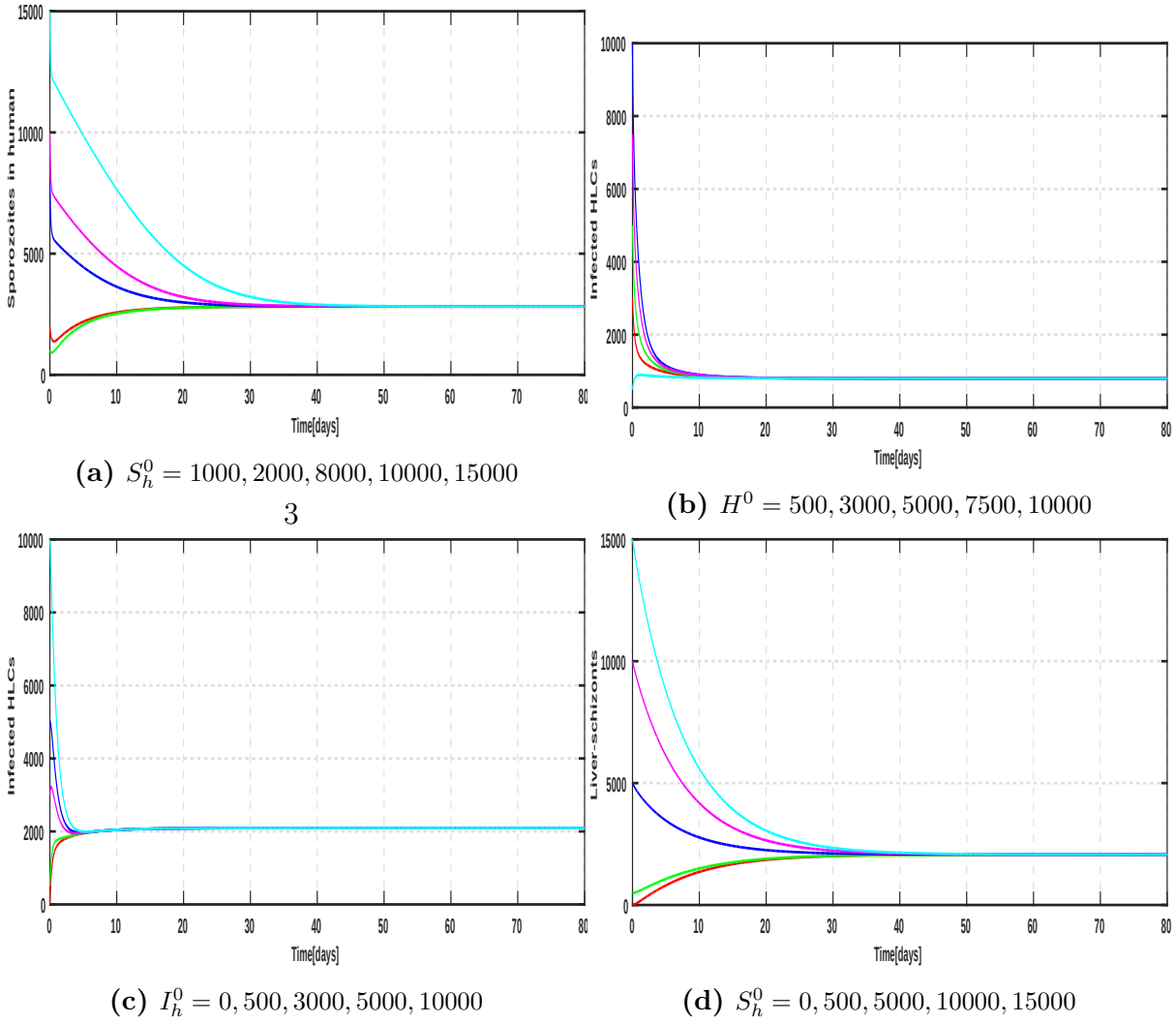



**(a)** Erythrocytic cycle **(b)** Sporogonic cycle

**Figure 3.** Variation of populations at Erythrocytic and Sporogonic cycles with time

Figure 3b shows that the density of Gametes rises to its maximum value before falling to its equilibrium value, while those of oocysts and in-mosquito sporozoites increase with time until they attain constant values (values at malaria infection equilibrium). The decrease of gametes may be it is due to the formation of ookinetes. Therefore from the Figure 3, we conclude that the malaria-infection equilibrium, $E^*$ for this model exists. Now let us assess for stability of $E^*$.

Using the parameters values given in Table 2, we obtained $\mathcal{R}_0 = 1.59025 > 1$. Thus, by Theorem 4 implies that the malaria infection equilibrium $E^*$ is globally assymptotically stable as depicted in Figures 4, 5 and 6. It has observed that with different initial values, solutions trajectories for all state variables converge to malaria infection equilibrium.




**(a)** $S_h^0 = 1000, 2000, 8000, 10000, 15000$

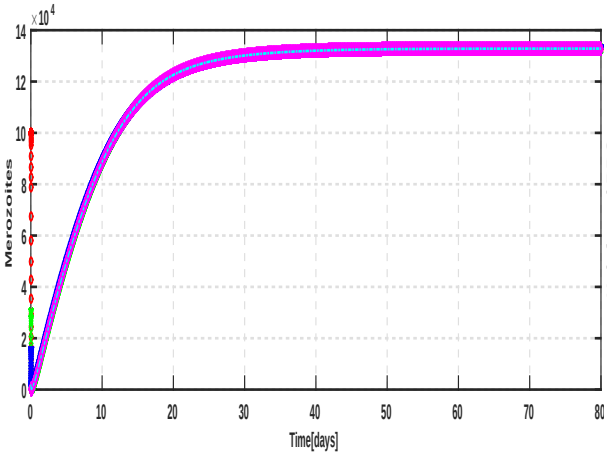
**(b)** $H^0 = 500, 3000, 5000, 7500, 10000$

3

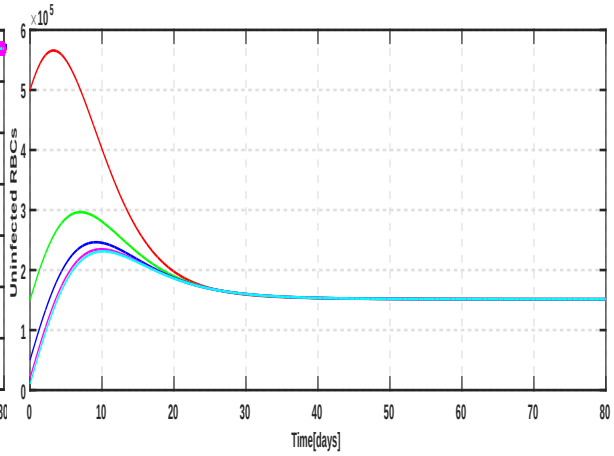
**(c)** $I_h^0 = 0, 500, 3000, 5000, 10000$

**(d)** $S_h^0 = 0, 500, 5000, 10000, 15000$

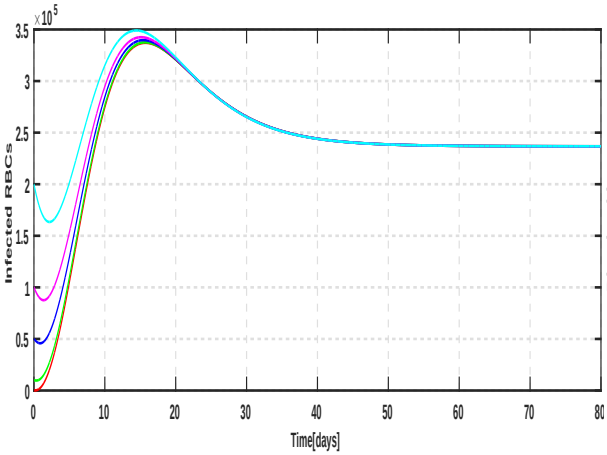
**Figure 4.** Numerical simulation to show global stability of MIE for variables in exo-erythrocytic cycle



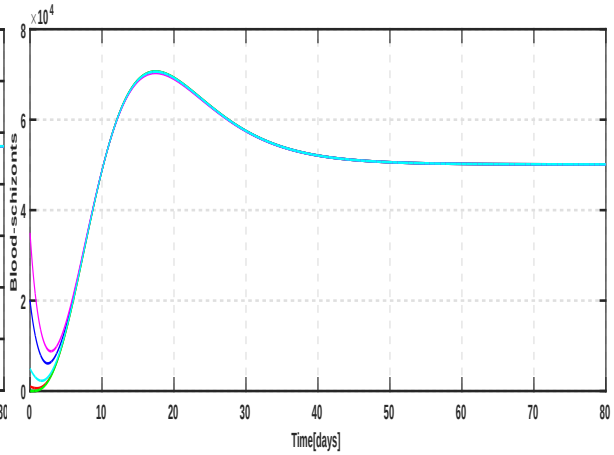

**(a)** $M^0 = 0, 2000, 15000, 30000, 100000$



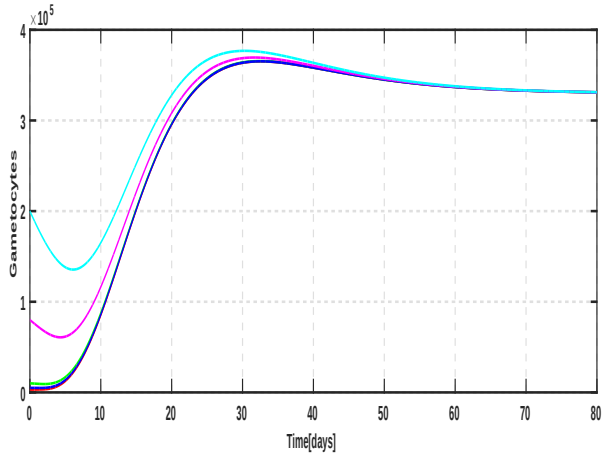

**(b)** $R^0 = 10000, 20000, 50000, 150000, 500000$




**(c)** $I_r^0 = 0, 10000, 50000, 100000, 200000$

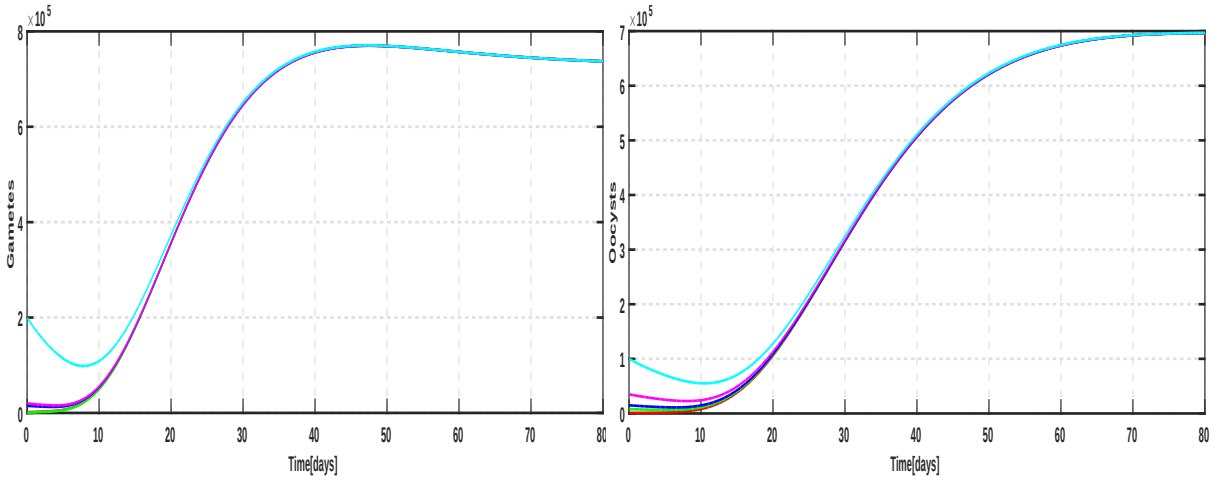



**(d)** $T_r^0 = 0, 1000, 5000, 20000, 35000$

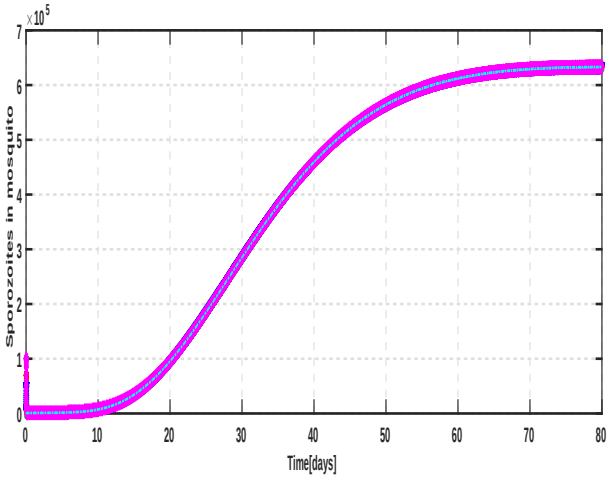



**(e)** $G_b^0 = 3000, 5000, 10000, 80000, 200000$

**Figure 5.** Numerical simulation to show global stability of MIE for variables in erythrocytic cycle




**(a)** $G_m^0 = 500, 1500, 3000, 15000, 20000$ **(b)** $C^0 = 1000, 8000, 15000, 35000, 100, 000$




**(c)** $S_m^0 = 2000, 15000, 50000, 7000, 100, 000$

**Figure 6.** Numerical simulation to show global stability of MIE for variables in Sporogonic cycle

## 5. Discussion and Conclusion

The mathematical model for in-human host and in-mosquito dynamics of malaria parasites was developed and analyzed. The model involved three main phases in life cycle of malaria parasites. We considered four, five and three compartments in the liver, blood and mosquito stages respectively.

In analysis of the model, two steady states, malaria-free equilibrium (MFE) and malaria-infection equilibrium (MIE) were determined. The threshold, $\mathcal{R}_0$, was obtained and found to a function that depends only on parameters in erythrocytic phase. This implies that the erythrocytic invasion may propagate without new infection from the liver (implying that even when an individual is not bitten by the mosquitoes, s/he may maintain some level of malaria in the blood).

Stability (in terms of $\mathcal{R}_0$) of equilibrium points was established. The necessary condition for stability of MFE was established using trace-determinant of jacobian matrix of the model evaluated at this point showed that, MFE is locally assymptotically stable provided $\mathcal{R}_0 < 1$ and unstable otherwise. The global stability of this equilibrium was investigated using Metlzer matrix technique, and proven that MFE is globally asymptotically stable when $\mathcal{R}_0 < 1$. MIE exists only if the recruitnent rate of sporozoites into human host less than recruitment hepatocytes liver cells and $\mathcal{R}_0 > 1$. Global stability of this was investigated using Lyaponuv function.

An insight of dynamics of malaria parasites within human host and within mosquito is significant in development and assessment of transmission blocking intervetions (TBIs). Merozoites play an important role in propagation of malaria infection in human, and they initially procuded in the HLCs after invasion of sporozoites. This may suggest that blocking this invasion to be one of the best targets for TBIs as it will significantly inhibits the infection of HLCs, and eventually the production of merozoites from the liver schizonts. Therefore, it reduces the possibility for infection of RBCs by merozites from the liver. However, as it has been stated earlier that infection of RBCs by merozoites may propagate without a new infection from the liver, but this would occur only when initial invasion of RBCs by merozoites from the liver was successful. Therefore, implementing the TBIs at liver stage will probably reduce possibility of having erythrocyte invasion of merozoites and finally the human-mosquito transmission may be stopped.

This work provides a basic model for studying the in-human host and in-mosquito vector dynamics of malaria parasite. At this time where malaria eradication is on world agenda, this work may be used as starting point to examine how and which are new control strategies of malaria can be established to overcome the disease. It will be useful to study the effect of immune response and/or treatment in the extension of this model.

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