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A mathematical model for the dynamics of malaria in a human host and mosquito vector with temporary immunity

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Abstract

In the paper, we propose a model that tracks the dynamics of malaria in the human host and mosquito vector. Our model incorporates some infected humans that recover from infection and immune humans after loss of immunity to the disease to join the susceptible class again. All the new borne are susceptible to the infection and there is no vertical transmission. The stability of the system is analyzed for the existence of the disease-free and endemic equilibria points. We established that the disease-free equilibrium point is globally asymptotically stable when the reproduction number, $R_0 \leqslant 1$ and the disease always dies out. For $R_0 > 1$ the disease-free equilibrium becomes unstable and the endemic equilibrium is globally asymptotically stable. Thus, due to new births and immunity loss to malaria, the susceptible class will always be refilled and the disease becomes more endemic.

Keywords: Reproduction number; Immunity; Stability; Compound matrices

1. Introduction

Malaria remains one of the most prevalent and lethal human infection worldwide. It is caused by the protozoan *Plasmodium*, transmitted to vertebrates by female genus *Anopheles* mosquitoes when they feed on blood. Four species of the parasite, namely: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale* and *Plasmodium malariae* infect humans. Of the four species, *P. falciparum* is the most virulent and potentially lethal to humans. It is responsible for the greatest number of deaths and clinical cases and is the most widespread in the tropics. Its infection can lead to serious complications affecting the brain, lungs, kidneys and other organs.

The malaria parasites are transmitted to the human host through a bite by an infected female anopheles mosquito. Clinical symptoms such as fever, pain, chills and sweats may develop a few days after an infected mosquito bite. The gametocytes are produced after some two weeks independent of the ambient temperature.

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When a second mosquito bites the infected human, the gametocytes are ingested. These after fertilization pass the gut wall, develop and ultimately produce sporozoites which become infective when they migrate to the salivary glands. This process is ambient-temperature dependent.

Immunity to a disease can be acquired at birth through maternal antibodies (for children borne to immune mothers) or by vaccination or infection. However, it wanes overtime and needs to be boosted through exposure to infection or vaccination. Incidence of malaria disease tends to decline uniformly with age such that children in the 5–9 year age class experience significantly fewer episodes than those in the 1–4 year age class [17].

An important aspect of malaria is that where the disease has long been highly endemic, as in many parts of Africa, people are infected so frequently that they develop a degree of acquired immunity, and may become asymptomatic carriers of infection [5]. As a result of heavy exposure to malaria, they may show enlargement of spleen and liver because of chronic infection. This process is slow and may take years or decades to develop [12] and probably never results in sterile immunity. However, low level exposure to infection is important and acts as vaccination and develops immunity against the disease [6]. For example, people who use mosquito nets in the night are not generally infected by the disease since the small number of bites they receive when they are outside the nets are not sufficient to cause the disease, but rather, the small exposure to infection gives them immunity. Thus humans are susceptible to reinfections because the immune protection may wane over time (temporary immunity) or may not be fully protective (partial immunity).

It is estimated that clinical episodes vary from 350 to 650 million annually [28,26]. This especially occurs in Africa where more than one million children mostly under 5 years die each year and at least one child dies every 30 s [29]. Another group who are particularly at risk from malaria are pregnant women. Pregnancy lowers the mothers immunity to malaria, making them more susceptible to infection.

Eradication programmes based upon vector control and antimalarial drugs have successfully eliminated malaria from many parts of Europe, Asia and North America, although it remains prevalent throughout tropical and subtropical areas. Many control strategies have been advocated for in an effort to fight the pandemic. For example, the global campaign to eradicate malaria launched in 1955 and phased out by the end of 1960s has been dubbed a misguided failure [23]. The disease reappeared in the late 1970s and today is considered as an emergent or resurgent disease [13,30]. Resurgence of the disease can be associated with ecological changes that have favored increased mosquito densities. There has been also abandonment of control efforts and generalized collapse of public health services and the existing tools may not be optimal, and are liable to fail with time, just like the previous ones did [21]. Among the major epidemic diseases, malaria is not directly transmitted. Thus its control is uniquely site specific, dependent on climate patterns, vector ecology and biology, and human activity.

The use of mathematical modelling increasing influence the theory and practice of disease management and control. This is because they can help in figuring out decisions that are of significant importance on the outcomes and provide comprehensive examinations that enter into decisions in a way that human reasoning and debate cannot. Their use in the study of malaria originates from the early work of Ross [22]. He used a mathematical model to show that bringing a mosquito population below a certain threshold was sufficient to eliminate malaria. This threshold naturally depended on biological factors such as the biting rate and vectorial capacity. For the purpose of estimating infection and recovery rates, Macdonald [16] used a model in which he assumed the amount of infective material to which a population is exposed remains unchanged. Macdonald's model shows that reducing the number of mosquitoes is an inefficient control strategy that would have little effect on the epidemiology of malaria in areas of intense transmission. The Ross–Macdonald mathematical model involves an interaction between infected human hosts and infected mosquito vectors. Some epidemic models as in Aron and May [2], and Anderson and May [1] use the assumption that acquired immunity is independent of duration of exposure. Bailey [5] and Aron [3,4] models take into account that acquired immunity to malaria depends on exposure (i.e. that immunity is boosted by additional infections). Tumwiine et al. [27] used an SIS and SI model in the human hosts and mosquito vectors respectively, for the study of malaria epidemic that lasts for a short period in which birth and immunity to the disease were ignored. They observed that the system was in equilibrium only at the point of extinction, that was neither stable nor unstable. However, some important results were revealed numerically.

In this paper, we introduce vital (birth and death) dynamics both in the human and mosquito populations. The infected humans either acquire some immunity or are susceptible again since immunity to malaria needs

continuous exposure to reinfection. They may also die from the disease. Thus our model is based on the susceptible-infective-immune SIRS in human population and SI for the mosquito vector population. The recovery rate corresponds to how quickly parasites are cleared from the human host due to treatment. Thus we have an endemic model [8] to study the dynamics of malaria over long periods as there is a renewal of susceptible humans due to births and immunity loss.

2. Model formulation

We formulate a model for the spread of malaria in the human and mosquito population with the total population size at time t given is by $N_H(t)$ and $N_V(t)$, respectively. These are further compartmentalized into epidemiological classes shown below. The vector component of the model does not include immune class [5,9] as mosquitoes never recover from infection, that is, their infective period ends with their death due to their relatively short life-cycle. Thus the immune class in the mosquito population is negligible and death occurs equally in all groups. Our model also excludes the immature mosquitoes since they do not participate in the infection cycle and are, thus, in the waiting period, which limits the vector population growth.

Our model has the following variables and parameters:

$S_H(t)$	the number of susceptible human hosts at time t
$I_H(t)$	the number of infected human hosts at time t
$R_H(t)$	the number of partially immune human hosts at time t
$S_V(t)$	the number of susceptible mosquito vectors at time t
$I_V(t)$	the number of infected mosquito vectors at time t
$m = \frac{N_V}{N_H}$	number of female mosquitoes per human host
a	the average daily biting rate on man by a single mosquito (infection rate)
b	the proportion of bites on man that produce an infection
c	the probability that a mosquito becomes infectious
γ	the per capita rate of loss of immunity in human hosts
r	the rate at which human hosts acquire immunity
δ	the per capita death rate of infected human hosts due to the disease
v	the rate of recovery of human hosts from the disease
λ_h	the per capita natural birth rate of humans
λ_v	the per capita natural birth rate of the mosquitoes
μ_h	the per capita natural death rate of the humans
μ_v	the per capita natural death rate of the mosquitoes

The following assumptions are made in order to formulate the equations of the model:

(i) The development of malaria starts when the infectious female mosquito bites the human host.
(ii) We ignore bites of an infected female mosquito onto an infected human host.
(iii) Mosquitoes bite human hosts randomly (independent of their infective status).
(iv) Recovered human hosts have temporary immunity that can be lost and are again susceptible to reinfection.
(v) All newborns are susceptible to infection and there is no vertical transmission.
(vi) Mosquitoes never recover from infection, as it is regulated by mortality of its individuals.
(vii) Total human and mosquito populations are not constant.

2.1. Equations of the model

2.1.1. Human host–vector host equations

Applying the assumptions, definitions of variables and parameters and description of terms above, the differential equations which describe the dynamics of malaria in the human and mosquito populations are formulated as shown below:

$$\frac{dS_H}{dt} = \lambda_h N_H - \frac{abS_H I_V}{N_H} + vI_H + \gamma R_H - \mu_h S_H, \tag{1}$$

$$\frac{dI_H}{dt} = \frac{abS_H I_V}{N_H} - vI_H - rI_H - \delta I_H - \mu_h I_H, \tag{2}$$

$$\frac{dR_H}{dt} = rI_H - \gamma R_H - \mu_h R_H, \tag{3}$$

$$\frac{dS_V}{dt} = \lambda_v N_V - \frac{acS_V I_H}{N_H} - \mu_v S_V, \tag{4}$$

$$\frac{dI_V}{dt} = \frac{acS_V I_H}{N_H} - \mu_v I_V. \tag{5}$$

The total population sizes N_H and N_V can be determined by $S_H + I_H + R_H = N_H$ and $S_V + I_V = N_V$ or from the differential equations

$$\frac{dN_H}{dt} = (\lambda_h - \mu_h)N_H - \delta I_H \tag{6}$$

$$\text{and} \quad \frac{dN_V}{dt} = (\lambda_v - \mu_v)N_V \tag{7}$$

which are derived by adding Eqs. (1)–(3) for the human population and (4) and (5) for mosquito vector population.

In the model, the term $\frac{abS_H I_V}{N_H}$ denotes the rate at which the human hosts S_H get infected by infected mosquitoes I_V and $\frac{acS_V I_H}{N_H}$ refers to the rate at which the susceptible mosquitoes S_V are infected by the infected human hosts I_H. It is important to note that the rate of infection of human host S_H by infected vector I_V is dependent on the total number of humans N_H available per infected vector (see [20]).

We consider the equations for the normalized quantities. Moreover, it is easier to analyze our model in terms of proportions of quantities instead of actual populations. This can be done by scaling the population of each class by the total species populations. We make the transformation $s_h = \frac{S_H}{N_H}$, $i_h = \frac{I_H}{N_H}$, $r_h = \frac{R_H}{N_H}$, $s_v = \frac{S_V}{N_V}$ and $i_v = \frac{I_V}{N_V}$ in the classes S_H, I_H, R_H, S_V and I_V in the population respectively and $m = \frac{N_V}{N_H}$. This is done by differentiating the fractions with respect to time t and simplifying as follows:

$$\begin{aligned}\frac{ds_h}{dt} &= \frac{1}{N_H}\left[\frac{dS_H}{dt} - s_h\frac{dN_H}{dt}\right]\\ &= \lambda_h - abms_h i_v + vi_h + \gamma r_h - \mu_h s_h - s_h[(\lambda_h - \mu_h) - \delta i_h]\\ &= \lambda_h(1 - s_h) - abms_h i_v + vi_h + \gamma r_h + \delta s_h i_h,\end{aligned} \tag{8}$$

$$\begin{aligned}\frac{di_h}{dt} &= \frac{1}{N_H}\left[\frac{dI_H}{dt} - i_h\frac{dN_H}{dt}\right]\\ &= abms_h i_v - vi_h - ri_h - \delta_h i_h - \mu_h i_h - i_h[(\lambda_h - \mu_h) - \delta i_h]\\ &= abms_h i_v - (v + r + \lambda_h + \delta)i_h + \delta i_h^2,\end{aligned} \tag{9}$$

$$\begin{aligned}\frac{dr_h}{dt} &= \frac{1}{N_H}\left[\frac{dR_H}{dt} - r_h\frac{dN_H}{dt}\right]\\ &= ri_h - \gamma r_h - \mu_h r_h - r_h[(\lambda_h - \mu_h) - \delta i_h]\\ &= ri_h - (\gamma + \lambda_h)r_h + \delta i_h r_h,\end{aligned} \tag{10}$$

$$\begin{aligned}\frac{ds_v}{dt} &= \frac{1}{N_v}\left[\frac{dS_v}{dt} - s_v\frac{dN_v}{dt}\right]\\ &= \lambda_v - aci_h s_v - \mu_v s_v - s_v(\lambda_v - \mu_v)\\ &= \lambda_v(1 - s_v) - aci_h s_v\end{aligned} \tag{11}$$

$$\begin{aligned}\frac{di_v}{dt} &= \frac{1}{N_v}\left[\frac{dI_v}{dt} - i_v\frac{dN_v}{dt}\right]\\ &= acs_v i_h - \mu_v i_v - i_v(\lambda_v - \mu_v)\\ &= acs_v i_h - \lambda_v i_v\end{aligned} \tag{12}$$

subject to the restrictions $s_h + i_h + r_h = 1$ and $s_v + i_v = 1$ We note that the total population sizes $N_H(t)$ and $N_V(t)$ do not appear in the system. Using the relations $r_h = 1 - s_h - i_h$ and $s_v = 1 - i_v$ lead to studying the system of differential equations

$$\frac{ds_h}{dt} = \lambda_h(1 - s_h) - abms_h i_v + vi_h + \gamma(1 - s_h - i_h) + \delta s_h i_h, \tag{13}$$

$$\frac{di_h}{dt} = abms_h i_v - (v + r + \lambda_h + \delta)i_h + \delta i_h^2, \tag{14}$$

$$\frac{di_v}{dt} = aci_h(1 - i_v) - \lambda_v i_v \tag{15}$$

in the feasible region (i.e. where the model makes biological sense)

$$T = \{(s_h, i_h, i_v) \in \mathbf{R}^3_+ : 0 \leqslant s_h, 0 \leqslant i_h, s_h + i_h \leqslant 1, 0 \leqslant i_v \leqslant 1\}$$

that can be shown to be positively invariant with respect to the system (13)–(15), where $\mathbf{R}^3_+$ denotes the non-negative cone of $\mathbf{R}^3$ including its lower dimensional faces. We denote the boundary and the interior of T by ∂T and $\dot{T}$ respectively.

3. Model analysis

In this section, the model is qualitatively analyzed to investigate the existence and stability of its associated equilibria. We assume that all the parameters are non-negative. We solve for the equilibrium points by setting the right-hand sides of (13)–(15) to zero and the system takes the form

$$\lambda_h(1 - s_h^*) - abms_h^* i_v^* + vi_h^* + \gamma(1 - s_h^* - i_h^*) + \delta s_h^* i_h^* = 0, \tag{16}$$

$$abms_h^* i_v^* - (v + r + \lambda_h + \delta)i_h^* + \delta i_h^{*2} = 0, \tag{17}$$

$$aci_h^*(1 - i_v^*) - \lambda_v i_v^* = 0. \tag{18}$$

3.1. Existence and stability of equilibrium points

3.1.1. Local stability of disease-free equilibrium E_0

In the absence of infection, the model has a steady state, E_0 called the disease-free equilibrium, where $E_0 = (1, 0, 0)$. To establish the stability of this equilibrium, the Jacobian of (16)–(18) is computed and evaluated at E_0. The local stability of E_0 is then determined based on the signs of the eigenvalues of this Jacobian. The equilibrium E_0 is locally stable if the real parts of these eigenvalues are all negative.

At the steady states of the model, the Jacobian matrix is given by

$$J_E = \begin{bmatrix} -(\lambda_h + \gamma + abmi_v^* - \delta i_h^*) & v - \gamma + \delta s_h^* & -abms_h^* \\ abmi_v^* & -H_T + 2\delta i_h^* & abms_h^* \\ 0 & ac(1 - i_v^*) & -\lambda_v - aci_h^* \end{bmatrix}. \tag{19}$$

Evaluating the Jacobian in Eq. (19) at E_0 gives

$$J_{E_0} = \begin{bmatrix} -(\lambda_h + \gamma) & v + \delta - \gamma & -abm \\ 0 & -H_T & abm \\ 0 & ac & -\lambda_v \end{bmatrix}, \tag{20}$$

where $H_T = v + r + \lambda_h + \delta$.

The eigenvalues of the Jacobian are given by

$$-(\lambda_h + \gamma), \ \frac{-(H_T + \lambda_v) \pm \sqrt{(H_T + \lambda_v)^2 - 4H_T\lambda_v(1 - R_0)}}{2}.$$

Defining

$$R_0 = \frac{a^2 bmc}{\lambda_v H_T},$$

it is easy to see that the two eigenvalues have negative real parts if $R_0 < 1$ and we have thus established the following lemma.

Lemma 1. *The disease-free equilibrium E_0 is locally stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

R_0 is called the basic reproduction number [1], defined as the number of secondary infectious cases produced by one primary case introduced into an entirely susceptible population at the disease-free equilibrium. It is a useful quantity in the study of a disease as it sets the threshold for its establishment. If $R_0 < 1$, then the disease-free equilibrium is locally stable.

3.1.2. Global stability of disease-free equilibrium E_0

Theorem 1. *The disease-free equilibrium $E_0 = (1, 0, 0)$ of (13)–(15) is globally asymptotically stable in T if $R_0 \leqslant 1$ and unstable if $R_0 > 1$.*

Proof. Consider the Lyapunov function $L = aci_h + H_T i_v$, where $H_T = v + r + \lambda_h + \delta$. Its derivative along the solutions of (13)–(15) is

$$\begin{aligned} L' &= a^2 bmcs_h i_v - aci_h[H_T - \delta i_h] + H_T[aci_h(1 - i_v) - \lambda_v i_v] = a^2 bmcs_h i_v - H_T \lambda_v i_v + aci_h(\delta i_h - H_T i_v) \\ &= H_T \lambda_v i_v \left[\frac{a^2 bmcs_h}{H_T \lambda_v} - 1\right] + aci_h(\delta i_h - H_T i_v) = H_T \lambda_v i_v[R_0 s_h - 1] - aci_h(H_T i_v - \delta i_h) \leqslant H_T \lambda_v i_v[R_0 s_h - 1] \\ &\leqslant 0 \quad \text{if } R_0 \leqslant 1. \end{aligned}$$

It is shown that $L' \leqslant 0$, if $R_0 \leqslant 1$ and the equality, $L' = 0$ holds when $R_0 = 1$ and $i_h = i_v = 0$. If $R_0 > 1$, then $L' > 0$ when s_h is sufficiently close to 1 except when $i_h = i_v = 0$. From Lyapunov–Lasalle's Theorem (see [7]), this implies that all paths in T approach the largest positive invariant subset of the set where $L' = 0$ is $\{(s_h, i_h, i_v) \in T | L' = 0\}$. On the boundary of T where $i_h = i_v = 0$ (s_h-axis), $s_h' = (\lambda_h + \gamma)(1 - s_h)$ so that $s_h = \left(1 + e^{-(\lambda_h + \gamma)t}\right) \to 1$ as $t \to +\infty$. Thus all solutions paths in T will approach the disease-free equilibrium point E_0. Hence, the disease-free equilibrium point is globally asymptotically stable and this completes the proof of Theorem 1. □

It is noted that the reproduction number depends on the product of the transmission coefficients *abm* and *ac*, the average residence time $1/(v + r + \lambda_h + \delta)$ in the infective class and the average life span $1/\lambda_v$ of the mosquito. It is important to note that the reproduction number, R_0 is independent of the immunity loss rate. However, we can quantify that higher values of m and a can allow the establishment of the disease. This implies that even when malaria does not confer disease-induced immunity and there is no vaccine yet, the existing tools can be used for its control if properly used.

We have established that the disease-free equilibrium point E_0 is globally asymptotically stable if $R_0 \leqslant 1$. This indicates that the infected mosquito vectors and humans eventually vanish and the disease dies out.

3.1.3. Local stability of endemic equilibrium E_1

For the existence and uniqueness of endemic equilibrium $E_1 = (s_h^*,\ i_h^*,\ i_v^*)$, its coordinates should satisfy the conditions $s_h^* > 0,\ i_h^* > 0,\ i_v^* > 0$.

Adding Eqs. (16)–(18), we have

$\lambda_h(1 - s_h^* - i_h^*) + \gamma(1 - s_h^* - i_h^*) - \delta i_h^*(1 - s_h^* - i_h^*) - ri_h^* + aci_h^*(1 - i_v^*) - \lambda_v i_v^* = 0.$

From Eq. (18), $aci_h^*(1 - i_v^*) - \lambda_v i_v^* = 0.$

This gives $(\lambda_h + \gamma - \delta i_h^*)(1 - s_h^* - i_h^*) = ri_h^*$ since $(1 - s_h^* - i_h^*) > 0$ and from $\delta i_h^* < \lambda_h + \gamma \Rightarrow i_h^* < \frac{\lambda_h + \gamma}{\delta}$.

Thus, an endemic equilibrium point exists, where i_h^* lies in the interval $\left(0, \min\left\{1, \frac{\lambda_h + \gamma}{\delta}\right\}\right)$.

The assumption that $\delta < \lambda_h + \gamma$ is of significant importance and plays a great role when malaria persists. It shows that mortality rate due to malaria should be less than that at which the susceptible human population is refilled due to birth and loss of immunity to malaria.

In order to analyze the stability of the endemic equilibrium, the additive compound matrices approach as in [19,15] (see Appendix A) is used. From the Jacobian matrix J_E, the second additive compound matrix is given by

$$J_E^{[2]} = \begin{bmatrix} -(K - 3\delta i_h^*) & abms_h^* & abms_h^* \\ ac(1 - i_v^*) & -(M - \delta i_h^*) & v - \gamma + \delta s_h^* \\ 0 & abmi_v^* & -(N - 2\delta i_h^*) \end{bmatrix}, \tag{21}$$

where

$$K = (H_T + \lambda_h + abmi_v^* + \gamma),$$
$$M = \lambda_h + \lambda_v + aci_h^* + \gamma + abmi_v^*$$

and

$$N = H_T + \lambda_v + aci_h^*.$$

The following lemma stated and proved in McCluskey and van den Driessche [18] is used to demonstrate the local stability of endemic equilibrium point E_1.

Lemma 2. *Let M be a 3×3 real matrix. If $\mathrm{tr}(M)$, $\det(M)$, and $\det(M^{[2]})$ are all negative, then all eigenvalues of M have negative real part.*

Proof. From the Jacobian matrix J_E in Eq. (19), we have

$$\begin{aligned} \mathrm{tr}(J_{E_1}) &= \delta i_h^* - (\lambda_h + \gamma) - abmi_v^* + 2\delta i_h^* - H_T - (\lambda_v + aci_h^*) \\ &= 3\delta i_h^* - (\lambda_h + \gamma + abmi_v^* + H_T + \lambda_v + aci_h^*) < 0. \end{aligned} \tag{22}$$

In order to determine $\det(J_{E_1})$, the following simplified form of equations of system (16)–(18) is used:

$$\frac{\lambda_h + vi_h^* + \gamma(1 - i_h^*)}{s_h^*} = \lambda_h + \gamma + abmi_v^* - \delta i_h^*, \tag{23}$$

$$\frac{-abms_h^* i_v^*}{i_h^*} = -H_T + \delta i_h^*, \tag{24}$$

$$\frac{aci_h^*(1 - i_v^*)}{i_v^*} = \lambda_v. \tag{25}$$

Then from the Jacobian $J(E_1)$ and the simplified expressions (23)–(25), we have

$$\det(J(E_1)) = \begin{vmatrix} -(\lambda_h + abmi_v^* + \gamma - \delta i_h^*) & v + \delta s_h^* - \gamma & -abms_h^* \\ abmi_v^* & -H_T + 2\delta i_h^* & abms_h^* \\ 0 & ac(1 - i_v^*) & -\lambda_v - aci_h^* \end{vmatrix} \tag{26}$$

$$= \begin{vmatrix} -\frac{\lambda_h + vi_h^* + \gamma(1 - i_h^*)}{s_h^*} & v + \delta s_h^* - \gamma & -abms_h^* \\ abmi_v^* & -\frac{abms_h^* i_v^*}{i_h^*} + \delta i_h^* & abms_h^* \\ 0 & \frac{\lambda_v i_v^*}{i_h^*} & \frac{-aci_h^*}{i_v^*} \end{vmatrix}$$

$$= -[\lambda_h + vi_h^* + \gamma(1 - i_h^*)]\left[a^2 bmc - \frac{ac\delta i_h^{*2}}{s_h^* i_v^*} - \frac{abm\lambda_v i_v^*}{i_h^*}\right] + a^2 bms_h^*\left[\frac{c(v - \gamma + \delta s_h^*)}{s_h^*} - \frac{bm\lambda_v i_v^{*2}}{i_h^*}\right]$$

$$= -\Phi\left[a^2 bmc - \frac{ac\delta i_h^{*2}}{s_h^* i_v^*} - \frac{abm\lambda_v i_v^*}{i_h^*}\right] + a^2 bms_h^*\left[\frac{c(v - \gamma + \delta s_h^*) i_h^*}{s_h^*} - abmc(1 - i_v^*) i_v^*\right]$$

$$
\begin{aligned}
&= -\Phi\left[a^2bmc - \frac{ac\delta i_h^{*2}}{s_h^* i_v^*} - \frac{abm\lambda_v i_v^*}{i_h^*}\right] + a^2bmcs_h^*\left[\frac{(v-\gamma+\delta s_h^*)i_h^*}{s_h^*} - abm(1-i_v^*)i_v^*\right]\\
&= -\Phi\left[a^2bmci_v^* - \frac{ac\delta i_h^{*2}}{s_h^* i_v^*}\right] + a^2bmcs_h^*\left[\frac{(\lambda_h+\gamma)(s_h^*-1)}{s_h^*} + abmi_v^{*2}\right]\\
&= \frac{\Phi ac}{s_h^* i_v^*}[abms_h^* i_v^{*2} - \delta i_h^{*2}] - a^2bmc[(\lambda_h+\gamma)(1-s_h^*) - abms_h^* i_v^{*2}]\\
&= [a^2bmci_v^*(abms_h^* i_v^* - \Phi)] + \frac{ac[\Phi\delta i_h^{*2} - abms_h^* i_v^*(\lambda_h+\gamma)(1-s_h^*)]}{s_h^* i_v^*}\\
&= -[a^2bmcs_h^* i_v^*(\lambda_h+\gamma-\delta i_h^*] + \frac{ac[\Phi\delta i_h^{*2} - abms_h^* i_v^*(\lambda_h+\gamma)(1-s_h^*)]}{s_h^* i_v^*},
\end{aligned}
\tag{27}
$$

where $\Phi = \lambda_h + vi_h^* + \gamma(1-i_h^*)$ and since $\delta < \lambda_h + \gamma$, then $\det(J(E_1))$ is negative.

From the second additive compound matrix $J^{[2]}(E_1)$ in Eq. (21), $\det(J^{[2]}(E_1)) < 0$ is demonstrated (see [14]) as follows:

For the endemic equilibrium point $E_1 = (s_h^*, i_h^*, i_v^*)$, let $P = \mathrm{diag}(i_v^*, i_h^*, s_h^*)$ be the diagonal matrix. Then the matrix $J^{[2]}(E_1)$ is similar to the matrix given by

$$
PJ^{[2]}(E_1)P^{-1} = \begin{bmatrix}
-(K-3\delta i_h^*) & \frac{abms_h^* i_v^*}{i_h^*} & abmi_v^* \\
\frac{ac(1-i_v^*)i_h^*}{i_v^*} & -(M-\delta i_h^*) & \frac{(v-\gamma+\delta s_h^*)i_h^*}{s_h^*} \\
0 & \frac{abms_h^* i_v^*}{i_h^*} & -(N-2\delta i_h^*)
\end{bmatrix}.
\tag{28}
$$

Since similarity preserves the eigenvalues, then matrix $J^{[2]}(E_1)$ is stable if and only if the matrix $PJ^{[2]}(E_1)P^{-1}$ is stable. This can be done by examining if the matrix $PJ^{[2]}(E_1)P^{-1}$ is diagonally dominant in rows, since its diagonal elements are negative

$$
\begin{aligned}
h_1 &= -(K-3\delta i_h^*) + abmi_v^* + \frac{abms_h^* i_v^*}{i_h^*}\\
&= -(H_T + \lambda_h + \gamma - 3\delta i_h^*) + \frac{abms_h^* i_v^*}{i_h^*},
\end{aligned}
\tag{29}
$$

$$
\begin{aligned}
h_2 &= -(M-\delta i_h^*) + \frac{(v-\gamma+\delta s_h^*)i_h^*}{s_h^*} + \frac{ac(1-i_v^*)i_h^*}{i_v^*}\\
&= -(\lambda_h + \lambda_v + \gamma + aci_h^* + abmi_v^* - \delta i_h^*) + \frac{(v-\gamma+\delta s_h^*)i_h^*}{s_h^*} + \frac{ac(1-i_v^*)i_h^*}{i_v^*}\\
&= -(\lambda_h + \gamma + aci_h^* + abmi_v^* - \delta i_h^*) + \frac{(v-\gamma+\delta s_h^*)i_h^*}{s_h^*},
\end{aligned}
\tag{30}
$$

$$
\begin{aligned}
h_3 &= -(N-2\delta i_h^*) + \frac{abms_h^* i_v^*}{i_h^*}\\
&= -(H_T + \lambda_v + aci_h^* - 2\delta i_h^*) + \frac{abms_h^* i_v^*}{i_h^*}.
\end{aligned}
\tag{31}
$$

Substituting (23)–(25) into (29)–(31) simplifies to the following:

$$
\begin{aligned}
h_1 &= -(\lambda_h + \gamma - 2\delta i_h^*),\\
h_2 &= \frac{-[\lambda_h + \gamma - \delta s_h^* i_h^* + acs_h^* i_h^*]}{s_h^*},\\
h_3 &= -(\lambda_v + (ac-\delta)i_h^*).
\end{aligned}
$$

We have all values $h_1, h_2, h_3 < 0$ for $\delta < \lambda_h + \gamma$, $\delta < ac$ and so all the diagonals are negative. Thus, from Lemma 2, the system has a local stability at the endemic equilibrium point. □

3.1.4. Global stability of endemic equilibrium E_1

We need to establish the global stability of the unique endemic equilibrium point of the disease when it persists. Since (13)–(15) is a 3-dimensional asymptotical autonomous differential system, we use the property of competitive systems [24,25,10] and additive compound matrices and differential equations [19] for the analysis of our system.

We begin by giving the definition of a competitive system. Let $x \mapsto f(x)$ be a smooth vector field defined for x in an open set $D \subset \mathbf{R}^n$. The differential equation

$$x' = f(x), \quad x \in D$$

is said to be competitive in D if, for some diagonal matrix $H = \mathrm{diag}(\epsilon_1, \epsilon_2, \ldots, \epsilon_n)$, where each ϵ_i is either 1 or -1, $H(\partial f/\partial x)H$ has non positive off-diagonal elements for all $x \in D$. If D is convex, the flow of a competitive system (13)–(15) preserves, for $t < 0$, the partial ordering in $\mathbf{R}^n$ defined by the orthant $K = \{(x_1, \ldots, x_n) \in \mathbf{R}^n : \epsilon_i x_i \geqslant 0\}$.

We choose the matrix H as

$$H = \begin{bmatrix} 1 & 0 & 0 \\ 0 & -1 & 0 \\ 0 & 0 & 1 \end{bmatrix}. \tag{32}$$

Then from the matrix H and the Jacobian given in Eq. (19), we get

$$H(J_E)H = \begin{bmatrix} -(\lambda_h + abmi_v^* + \gamma - \delta i_h^*) & -v - \delta s_h^* + \gamma & -abms_h^* \\ -abmi_v^* & -H_T + 2\delta i_h^* & -abms_h^* \\ 0 & -ac(1 - i_v^*) & -(\lambda_v + aci_h^*) \end{bmatrix}. \tag{33}$$

It is observed that the system is competitive in $\dot{T}$ with respect to the partial ordering defined by the orthant

$$K = \{(s_h^*, i_h^*, i_v^*) \in \mathbf{R}^3 : s_h^* \geqslant 0, i_h^* \leqslant 0, i_v^* \geqslant 0\}.$$

This property is satisfied if the conditions $\delta < \lambda_h + \gamma$, $\gamma < v + \delta$ hold.

It is also proved in Hirsch [11] and Smith [25] that three-dimensional competitive systems that live in convex sets have the Poincare–Bendixson property. That is, any non-empty compact omega limit set that contains no equilibria must be a closed orbit.

Let $p(t)$ with minimal period ω and orbit $\Gamma = \{p(t) : 0 \leqslant t \leqslant \omega\}$ be the periodic solution of competitive system. The following definitions (see [7]) are used to establish the stability of the orbit.

Definition 1. The orbit Γ is orbitally stable if and only if for each $\epsilon > 0$, there exists a δ such that any solution $\tilde{x}(t)$, for which the distance of $\tilde{x}(0)$ from Γ is less than δ, remains a distance less than ϵ from Γ, for all $t \geqslant 0$.

Definition 2. The orbit Γ is asymptotically orbitally stable, if it is orbitally stable and the distance of $\tilde{x}(t)$ from Γ also tends zero as t goes to infinity.

Since (13)–(15) is a 3-dimensional competitive system that is convex in D, the following theorem stated and proved in Li and Mouldowney [15] for a system of an SEIR model is used to generalize results of systems that are competitive, persistent and have the property of stability of periodic orbits.

Theorem 2. *For $n = 3$, and D convex and bounded and suppose that (13)–(15) is competitive, permanent and have the property of stability of periodic orbits. If $\tilde{x}_0$ is the only equilibrium point in* $\mathrm{int}\, D$, *and if it is locally asymptotically stable, then it is globally asymptotically stable in* $\mathrm{int}\, D$.

Proof. According to Muldowney [19], the asymptotic orbital stability of a periodic orbit of a general autonomous system, it is sufficient to prove that the linear non-autonomous system

$$w'(t) = (J_E^{[2]}(p(t)))w(t) \tag{34}$$

is asymptotically stable, where $J_E^{[2]}$ is the second additive compound matrix of the Jacobian matrix J_E.

From the second additive compound matrix in Eq. (21) given by

$$J_E^{[2]} = \begin{bmatrix} -(K-3\delta i_h) & abms_h & abms_h \\ ac(1-i_v) & -(M-\delta i_h) & v-\gamma+\delta s_h \\ 0 & abmi_v & -(N-2\delta i_h) \end{bmatrix} \tag{35}$$

we have a linear system with respect to the solutions $(s_h(t), i_h(t), i_v(t))$ written as

$$\begin{aligned} w_1'(t) &= -(K-3\delta i_h(t))w_1(t) + abms_h(t)w_2(t) + abms_h(t)w_3(t), \\ w_2'(t) &= ac(1-i_v(t))w_1(t) - (M-\delta i_h(t))w_2(t) + (v-\gamma+\delta s_h(t))w_3(t), \\ w_3'(t) &= (abmi_v(t))w_2(t) - (N-2\delta i_h(t))w_3(t). \end{aligned}$$

In order to prove that the system (25) is asymptotically stable, we shall use the following Lyapunov function that is positive but not differentiable everywhere:

$$V(w_1(t), w_2(t), w_3(t); s_h(t), i_h(t), i_v(t)) = \sup\left\{|w_1|, \frac{i_h(t)}{i_v(t)}(|w_2| + |w_3|)\right\}.$$

Denoting the left-hand derivative of $V(t)$ by $D_+V(t)$, we get the following inequalities:

$$\begin{aligned} D_+(|w_1(t)|) &\leqslant (K-3\delta i_h(t))|w_1(t)| + abms_h(|w_2(t)| + |w_3(t)|), \\ &\leqslant -(K-3\delta i_h(t))|w_1(t)| + \frac{abms_h(t)i_v(t)}{i_h(t)}\left(\frac{i_h(t)}{i_v(t)}|w_2(t)| + |w_3(t)|\right) \end{aligned} \tag{36}$$

$$D_+(|w_2(t)|) \leqslant ac(1-i_v)|w_1(t)| - (M-\delta i_h(t))|w_2(t)| + (v-\gamma+\delta s_h(t))|w_3(t)|, \tag{37}$$

$$D_+(|w_3(t)|) \leqslant abmi_v)|w_2(t)| - (N-2\delta i_h(t))|w_3(t)|. \tag{38}$$

We also have

$$D_+\frac{i_h(t)}{i_v(t)}(|w_2(t)| + |w_3(t)|) = \left[\frac{i_h'(t)}{i_h(t)} - \frac{i_v'(t)}{i_v(t)}\right]\frac{i_h(t)}{i_v(t)}(|w_2(t)| + |w_3(t)|) + \frac{i_h(t)}{i_v(t)}D_+(|w_2(t)| + |w_3(t)|). \tag{39}$$

Adding Eqs. (37) and (38) we have

$$\begin{aligned} &D_+(|w_2(t)| + |w_3(t)|) \\ &\quad = ac(1-i_v(t))|w_1(t)| - (M - abmi_v - \delta i_h)|w_2(t)|[v-\gamma+\delta s_h(t) + 2\delta i_h(t) - N]|w_3(t)| \\ &\quad = ac(1-i_v(t))|w_1(t)| - (\lambda_h + \lambda_v + aci_h + \gamma - \delta i_h(t))|w_2(t)| - [\lambda_h + \lambda_v + aci_h + \gamma - \delta i_h(t) \\ &\qquad + r - \delta(1 - s_h(t) - i_h(t))]|w_3(t)| \\ &\quad \leqslant ac(1-i_v(t))|w_1(t)| - (\lambda_h + \lambda_v + aci_h + \gamma - \delta i_h(t))(|w_2(t)| + |w_3(t)|). \end{aligned} \tag{40}$$

Substituting Eq. (40) into Eq. (39) yields

$$\begin{aligned} D_+\frac{i_h(t)}{i_v(t)}(|w_2(t)| + |w_3(t)|) &\leqslant \frac{i_h(t)}{i_v(t)}\left[\frac{i_h'(t)}{i_h(t)} - \frac{i_v'(t)}{i_v(t)}\right](|w_2(t)| + |w_3(t)|) + \frac{i_h(t)}{i_v(t)}[ac(1-i_v(t))|w_1(t)| \\ &\quad - (\lambda_h + \lambda_v + aci_h + \gamma - \delta i_h(t))(|w_2(t)| + |w_3(t)|) \\ &\leqslant ac(1-i_v(t))\frac{i_h(t)}{i_v(t)}|w_1(t)| \\ &\quad + \left[\frac{i_h'(t)}{i_h(t)} - \frac{i_v'(t)}{i_v(t)} - \lambda_h - \lambda_v - aci_h - \gamma + \delta i_h(t)\right]\frac{i_h(t)}{i_v(t)}(|w_2(t)| + |w_3(t)|). \end{aligned} \tag{41}$$

From Eqs. (36) and (41) we have

$$D_+V(t) \leqslant \sup(g_1(t), g_2(t))V(t)$$

in which

$$g_1(t) = -(K - 3\delta i_h(t)) + \frac{abms_h(t)i_v(t)}{i_h(t)}, \tag{42}$$

$$g_2(t) = ac(1 - i_v(t))\frac{i_h(t)}{i_v(t)} + \left(\frac{i_h'(t)}{i_h(t)} - \frac{i_v'(t)}{i_v(t)} - \lambda_h - \lambda_v - aci_h(t) - \gamma + \delta i_h(t)\right). \tag{43}$$

Using the following expressions from Eqs. (17) and (18) given by

$$\frac{abms_h(t)i_h(t)}{i_v(t)} = \frac{i_h'(t)}{i_h(t)} + v + r + \lambda_h + \delta - \delta i_h(t),$$

$$ac(1 - i_v(t))\frac{i_h(t)}{i_v(t)} = \frac{i_v'(t)}{i_v(t)} + \lambda_v,$$

Eqs. (42) and (43) simplify to

$$\begin{aligned} g_1(t) &= -(H_T + \lambda_h + abmi_v(t) + \gamma - 3\delta i_h(t)) + \frac{abms_h(t)i_v(t)}{i_h(t)} \\ &= -(H_T + \lambda_h + abmi_v + \gamma - 3\delta i_h) + \frac{i_h'(t)}{i_h(t)} + H_T - \delta i_h(t) \\ &= \frac{i_h'(t)}{i_h(t)} + (2\delta i_h - (\lambda_h + abmi_v + \gamma)), \end{aligned} \tag{44}$$

$$\begin{aligned} g_2(t) &= ac(1 - i_v(t))\frac{i_h(t)}{i_v(t)} + \left(\frac{i_h'(t)}{i_h(t)} - \frac{i_v'(t)}{i_v(t)} - \lambda_h - \lambda_v - aci_h(t) - \gamma + \delta i_h(t)\right) \\ &= \frac{i_h'(t)}{i_h(t)} + (\delta i_h - (\lambda_h + aci_h(t) + \gamma)) \end{aligned} \tag{45}$$

so that

$$\sup\{g_1(t), g_2(t)\} \leqslant \frac{i_h'(t)}{i_h(t)} - \delta. \tag{46}$$

From Eq. (46), we have

$$\int_0^\omega \sup\{g_1(t), g_2(t)\}\,dt \leqslant [\ln i_h(t)]_0^\omega - \delta\omega = -\delta\omega < 0. \tag{47}$$

This shows that the periodic solution $(s_h(t), i_h(t), i_v(t))$ is asymptotically stable. This establishes the fact the endemic equilibrium point of the disease is globally stable. □

4. Discussion

We proposed a model with standard incidence for the dynamics of malaria within human hosts and mosquito vectors in which the reservoir of the susceptible human hosts is refilled by immunity loss to the disease and newborns. The model was then reformulated in terms of the proportions of the classes of the respective populations. Two equilibria points were obtained and their stabilities analyzed. We identified the basic reproduction number, R_0 in terms of the model parameters.

It was noted that R_0 is independent of the rate of loss of immunity, γ. It was also established that for the basic reproduction number, $R_0 \leqslant 1$, the disease-free equilibrium point is globally stable so that the disease always dies out, and if $R_0 > 1$, the disease-free equilibrium point is unstable while the endemic equilibrium emerges as a unique equilibrium point and re invasion is always possible and the disease never dies out.

Since malaria induced immunity wanes over time and there are no effective vaccines against it at the moment, the available tools can be used for its control. These may be based on the parameters of the threshold quantity, R_0. We notice that in order to reduce the basic reproduction number below 1, intervention strategies

need to be focused on treatment and reduction on the contact between mosquito vector and human host. Thus, there is need for effective drugs, treated bed nets and insecticides that would reduce the mosquito population. Since malaria induced immunity is non everlasting, it remains a major obstacle to eradicate the disease even if individuals are protected.

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Appendix A. Compound matrices

In this section, we give the definition of an additive compound matrix. The details of compound matrices and ordinary differential equations are given in [17].

Definition A.1. Let A be any $n \times m$ matrix of real and complex numbers, and let $a_{i_1,\ldots,j_k}$ be the minor of A determined by the rows $(i_1,\ldots,i_k)$ and the columns $(j_1,\ldots,j_k)$, $1 \leqslant i_1 < i_2 < \cdots < j_k \leqslant n$, $1 \leqslant j_1 < j_2 < \ldots j_k \leqslant m$. The kth multiplicative compound matrix of A^k of A is the $\binom{n}{k} \times \binom{m}{k}$ matrix whose entries , written in a lexicographic order are $a_{i_1\ldots,j_k}$. When A is a $n \times m$ matrix with columns $a_1, a_2, \ldots, a_k$, A^k is the exterior product $a_1 \wedge a_2 \wedge \cdots \wedge a_k$.

For the case $m = n$, the additive compound matrices are defined in the following way.

Definition A.2. If $A = a_{ij}$ be an $n \times n$ matrix, its kth additive compound $A^{[k]}$ of A is the $\binom{n}{k} \times \binom{n}{k}$ matrix given by

$$A^{[k]} = D(I + hA)^{(k)}| = 0,$$

where D is the differentiation with respect to h. For any integer $i = 1, \ldots, \binom{n}{k}$, let $(i) = (i_1, \ldots, i_k)$ be the ith member in the lexicographic ordering of all $k-$tuples of integers such that $1 \leqslant i_1 < i_2 < \cdots < i_k \leqslant i_n$. Then

$$b_{ij} = \begin{cases} a_{i_1 i_1} + \cdots + a_{i_k i_k} & \text{if } (i) = (j), \\ (-)^{r+s} a_{i_s i_r} & \text{if exactly one entry of } i_s \text{ of } (i) \text{ does not occur in } (j) \text{ and } j_s \text{ does not occur in } (i), \\ 0 & \text{if } (i) \text{ differs from } (j) \text{ in two or more entries.} \end{cases}$$

In the special cases $k = 1$, $k = n$, we find $A^{[1]} = A, A^{[n]} = \mathrm{Tr}A$. For $n = 3$, the matrices $A^{[k]}$ are as follows:

$$A^{[1]} = A, \quad A^{[2]} = \begin{bmatrix} a_{11} + a_{22} & a_{23} & -a_{13} \\ a_{32} & a_{11} + a_{33} & a_{12} \\ -a_{31} & a_{21} & a_{22} + a_{33} \end{bmatrix}, \quad A^{[3]} = a_{11} + a_{22} + a_{33}.$$

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