Transmission model of endemic human malaria in a partially immune population

C. Chiyaka\textsuperscript{a,}\textsuperscript{*}, W. Garira\textsuperscript{a}, S. Dube\textsuperscript{b}

\textsuperscript{a} Department of Applied Mathematics, National University of Science and Technology, Box AC 939, Ascot, Bulawayo, Zimbabwe
\textsuperscript{b} Department of Applied Biology/Biochemistry, National University of Science and Technology, Box AC 939, Bulawayo, Zimbabwe

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Abstract

A new transmission model of human malaria in a partially immune population with three discrete delays is formulated for variable host and vector populations. These are latent period in the host population, latent period in the vector population and duration of partial immunity. The results of our mathematical analysis indicate that a threshold parameter $R_0$ exists. For $R_0 > 1$, the expected number of mosquitoes infected from humans $R_{hm}$ should be greater than a certain critical value $R_{hm}^*$ or should be less than $R_{hm}^*$ when $R_{hm}^* > 1$, for a stable endemic equilibrium to exist. We deduce from model analysis that an increase in the period within which partial immunity is lost increases the spread of the disease. Numerically we deduce that treatment of the partially immune humans assists in reducing the severity of the disease and that transmission blocking vaccines would be effective in a partially immune population. Numerical simulations support our analytical conclusions and illustrate possible behaviour scenarios of the model.

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1. Introduction

Human malaria is caused by one of the four species of the genus Plasmodium — a protozoan parasite transmitted by the bite of an infected female Anopheles mosquito. The following Plasmodium species are causative agents for malaria in humans: Plasmodium falciparum, the most deadly of the human parasites\textsuperscript{1}, is the most widespread in the tropics. Plasmodium vivax is a major cause of clinical malaria, but rarely fatal. Plasmodium malariae infrequently causes clinical malaria, especially in Africa. It can persist as low-grade parasitaemia for several decades. Plasmodium ovale causes clinically significant but non-fatal disease, but might be found in mixed infections with other species. Zoonosis is absent in malaria.

The infection takes place when an infected mosquito injects sporozoites into a human host, which are carried through the blood to the liver within 30 min\textsuperscript{2}. They invade hepatocytes and undergo a process of asexual replication (exoerythrocytic schizogony) to give rise to 10–40 thousand merozoites per sporozoite. Up to this point, the infection...
is non-pathogenic and clinically silent. After about 7–9 days, the liver schizonts rupture to release the merozoites into the blood. Each merozoite invades an erythrocyte and divides to form an erythrocytic schizont containing about 16 daughter merozoites [3]. These merozoites either reinfect fresh erythrocytes, giving rise to cyclical blood-stage infection with a periodicity of 48–72 h, depending on the Plasmodium species, or differentiate into sexual transmission stages called gametocytes. The factors that induce gametocyte production are unknown [4,5] but it has been suggested that merozoites convert into gametocytes when micro-environmental conditions become unfavourable to parasite multiplication [6,7].

The gametocytes are taken up by a feeding mosquito, giving rise to extracellular gametes. In the mosquito mid-gut, the gametes fuse to form a motile zygote (ookinete), which penetrates the mid-gut wall and forms an oocyst, within which meiosis takes place and haploid sporozoites develop. These sporozoites migrate to the salivary glands. The incubation period within the mosquito may last 8–22 days [4]. The variation in the length of time is due to the environmental temperature. For P. falciparum the average time is 12 days [8,9]. Malaria can also be transmitted through blood transfusion, organ transplantation and transplacental malaria (i.e. congenital malaria) can also be significant in populations which are partially immune to malaria [10].

Falciparum malaria is far more severe than other types of malaria because the parasite attacks all red blood cells, not just the young or old cells as do other types [11]. A person infected with this type of malaria can die within a short time from the onset of symptoms. If the fever is prolonged many red blood cells are destroyed. It causes the red blood cells to clump together thereby blocking vessels in vital organs (especially the kidneys) and causing the spleen to become enlarged [12]. The brain may be damaged leading to coma and convulsions. There might also be kidney and liver failure.

The major vectors in Africa are A. gambiae sensu lato [13–15], which is considered the most important in most regions, and the most common parasite in sub-Saharan Africa is P. falciparum [16]. Our paper will mainly be centred on this vector and parasite. An adult female mosquito disperses from the water body where she was born and begins a life cycle which is maintained throughout the rest of life, alternating between obtaining a blood meal and ovipositing in a water body. Transmission of the malaria parasite to human hosts involves only adult mosquitoes since the larval stages are aquatic and do not feed on humans.

Tropical nations, the majority of which are underdeveloped, are the epicentres of malaria which is one of the main global causes of death from infectious diseases [17] and an ancient scourge of humanity. Even in those countries where malaria was thought to have been eliminated, there is evidence of rapid re-establishment due to mosquitoes and parasites that are resistant to chemicals to which they were previously susceptible [4,18–20]. Malaria epidemics display the full explosive power of vector-borne infections, erupting with a suddenness and intensity that can overwhelm vulnerable communities (for example, in Burundi 2000–2001, [21] and the 1998 epidemic in Rwanda [1]).

Partial immunity to malaria confers protection against severe illness without eliminating chronic, mild infections [12]. In endemic areas, children younger than five years have repeated and often serious attacks of malaria. The survivors develop and maintain partial immunity that reduces the severity of the disease but does not prevent subsequent infections. Thus in these areas older children and adults often have asymptomatic parasitaemia, that is, presence of Plasmodia in the blood stream without clinical manifestation. In endemic areas people obtain acquired immunity due to frequent exposure [22]. Epidemiological evidence for immunity to P. falciparum malaria comes from areas with intense transmission [23]. In areas of low malaria transmission, immunity develops slowly and malaria affects all age groups [24,25]. Incomplete immunity to malaria complicates disease control strategies [26] as the partially immune individuals suffer only mild infections and therefore might not seek medical attention but continue to transmit the parasite in the community. While a single case of measles grants the sufferer lifelong immunity from the disease, even multiple bouts of malaria do not imply fully protective immunity against reinfection. Parasite population growth may be slower, and clearance of parasites from the blood more rapid, in second or subsequent infections but individuals may still be infectious to mosquitoes [9]. Malaria parasites have different epitopes hence partial immunity to one species does not confer immunity to the other species. Even with the same species the various stages exhibit different epitopes such that immunity could be partially conferred against one stage only.

It is important to establish the transmission dynamics of an epidemic in order to understand and predict it. Mathematical models are particularly helpful as experimental tools with which to evaluate and compare control procedures and preventive strategies, and to investigate the relative effects of various sociological, biological and environmental factors on the spread of diseases. These models have played a very important role in the history
and development of vector-host epidemiology. Several authors have used mathematical models to analyse the transmission and spread of malaria. Mathematical models of malaria transmission that include both mosquito and human populations have been reviewed and discussed in detail [2,4,9,26,27]. Nedelman [28], did some further work on malaria model of Dietz et al. [29] and showed that the inoculation rate depends on a pseudo-equilibrium approximation to the differential equation describing the mosquito dynamics in the malaria model.

Several authors have put forward models in an attempt to explain the dynamics of malaria infection in humans, for example [2,4,9,12,25–27]. Some of these models were developed under the assumption that the total population size is constant [2,4,12]. The aspect of growing population size and malaria induced death rate are often neglected for the sake of mathematical tractability. Of the authors who considered exposed and infectious classes [4,9,26], one of them [26] considered that transition from one class to another is instantaneous. Of the two authors who considered a constant latent period [4,9], none of them captured the effect of the duration of partial immunity. The effect of partial host immunity on the transmission of malaria parasites is crucial to malaria epidemiology [7]. In modelling immunity to malaria [12] continuing exposure appears to sustain immunity. It has been shown that the rate of development of clinical immunity to malaria correlates with the length of infection, asymptomatic status is reached sooner when the infections are longer [30]. Time to develop this immunity was found to be proportional to parasite diversity and inversely proportional to transmission intensity [31]. Partial immunity can further reduce Plasmodium transmission success by reducing gametocyte infectivity through inactivation of gametocytes and/or of the resultant gametes in the mosquito (transmission blocking immunity) [32,33].

To the best of our knowledge none of the previous work considered delay in both disease latency and immunity. These aspects differentiate our model from other malaria models and make it more realistic by allowing it to describe the effects of disease latency and partial immunity. In an effort to describe and create a model based on reasonable biological findings on partial immunity of P. falciparum malaria transmission, we formulate our model as an integro-differential equation system [34] with delay in latency for the human and mosquito populations and delay due to partial immunity for the human population. We introduce in the model a partially immune class for the human population who may also be infectious, and for the mosquito population, induced death rate and input rate that is temperature dependent are included. The rest of the paper is organized as follows: In Section 2 we briefly describe the formulation of the model. Model analysis is performed in Section 3 where we show that the solutions of the model are always positive provided the initial conditions are positive. The basic reproductive number is derived and discussed in Section 4. Analysis of local and global stability of the disease free equilibrium is performed in Section 5 and in Section 6, we show the existence of the stable endemic equilibrium when certain conditions are met. Numerical simulations follow in Section 7 and finally a discussion rounds up the paper.

2. Model formulation

A malaria transmission model is developed based on the discussed biological aspects. The model considers human hosts as SEIRS model and vector mosquitoes as SEI model. The flow between several compartments is shown in Fig. 1 where Z is the egg class not considered in the model. For humans, the four compartments represent the total population of humans at a given time \( t \), who are susceptible \( S_h \), exposed \( E_h \), infectious \( I_h \) and partially immune \( R_h \). At the infectious stage a host may die from the disease, recover into the susceptible class or may recover with acquired partial immunity. Exposed humans are those without infectious gametocytes but with asexual stages of the parasite. Infectious human hosts are those with infectious gametocytes in the blood stream. Partially immune hosts still have protective antibodies and other immune effectors at low levels. If inoculated with sporozoites, an effective immune response will be elicited before asexual parasitaemia develops. For mosquitoes the three compartments represent susceptible mosquitoes \( S_m \), exposed \( E_m \) and infectious \( I_m \) populations at a given time \( t \). Exposed mosquitoes are those that have ingested gametocytes but without infectious sporozoites in their salivary glands. Infectious mosquitoes are those that have sporozoites in their salivary glands [35]. Because mosquitoes are poikilothermal, temperature is a critical variable in malaria epidemiology. In the range of 18–26 °C, for instance, a change of only 1 °C in mean temperature can change a mosquito’s life span by more than a week [36]. \( T \) is temperature in the model. The egg-to-adult development time is shortened with higher temperature, thus producing more mosquitoes within a short period of time [13].

The assumptions made for the model are:

- Longevity of the vector is unaffected by the infection.
• The probability of feeding on hosts is unaffected by the number of previous feeds or by differences in host type.
• Parasite presence does not affect preference by vectors.
• There is no superinfection.
• Latent period for both populations and duration of partial immunity are constant.
• The infectious period of a mosquito ends with its death.
• Mosquitoes do not die from the malaria infection.
• The infectiousness of partially immune and infectious humans are different.

For the human population: \( \Lambda_h > 0 \) is the human input (birth) rate, \( \mu_h > 0 \) and \( \alpha_h > 0 \) are the natural and disease induced death rates respectively, \( r_h > 0 \) is the rate of recovery into the susceptible class from being infectious and \( \tau_h > 0 \) is the period of time from being infected until the appearance of gametocytes in the blood. The duration of partial immunity is represented by \( \omega > 0 \). After the period \( \omega \) has elapsed, the partially immune human becomes susceptible. \( \beta_h c > 0 \) is the inoculation rate, where \( \beta_h \) is the probability that a bite by an infectious mosquito results in transmission of the disease to the susceptible human and \( c \) is the contact rate between the two. \( q_h^{-1} > 0 \) is the average time to build up an effective immune response.

For the mosquito population: \( \rho > 0 \) is the rate of oviposition. The parameters that are dependent on temperature \( T \) are the rate at which eggs become non-viable \( \mu_e(T) > 0 \), the cycle duration, from the egg to the mature adult \( \epsilon^{-1}(T) > 0 \) and the duration of sporogony (development from the gametocytes to the appearance of infectious sporozoites in the salivary glands) in the mosquito \( \tau_m > 0 \). \( \mu_m > 0 \) and \( \alpha_m > 0 \) are the natural and induced (for example, by insecticides) mortality rates of mosquitoes respectively. \( \beta_m c > 0 \) is the rate of transmission where \( \beta_m \) is the probability that a bite results in transmission of the parasite to a susceptible mosquito. The transmission of the parasite to a mosquito from a partially immune human is reduced by a factor \( 1 - (1 - \sigma_m) \), where \( \sigma_m \) is the effectiveness of the immune system in reducing infectiousness from a partially immune individual to a susceptible mosquito. If \( \sigma_m = 0 \), then rate of infection is the same for infectious and partially immune humans. If \( \sigma_m = 1 \), then there is no transmission of parasites from a partially immune human to a susceptible mosquito. The probability of egg transformation during the time period of \( \epsilon^{-1}(T) \) into an adult mosquito is the ratio \( \frac{\epsilon(T)}{\epsilon(T) + \mu_e(T)} \) [4].

Taking into account the assumptions made above, the interaction between human hosts and the mosquito vector population, is described by the following system of equations:

\[
\begin{align*}
S'_h(t) &= \Lambda_h + r_h I_h(t) - \beta_h c I_m(t) S_h(t) \frac{S_h(t)}{N_h(t)} - \mu_h S_h(t) + q_h I_h(t) - \omega) e^{-\mu_h \omega}; \\
E_h(t) &= \int_{t-\tau_h}^t \beta_h c I_m(u) S_h(u) \frac{S_h(u)}{N_h(u)} e^{-\mu_h (t-u)} du; \\
I'_h(t) &= \beta_h c I_m(t - \tau_h) S_h(t - \tau_h) \frac{S_h(t - \tau_h)}{N_h(t - \tau_h)} e^{-\mu_h \tau_h} - (r_h + \mu_h + q_h + \alpha_h) I_h(t); \\
R_h(t) &= \int_{t-\omega}^t q_h I_h(u) e^{-\mu_h (t-u)} du; \\
S'_m(t) &= \rho \frac{\epsilon(T)}{\epsilon(T) + \mu_e(T)} I_h(t) + (1 - \sigma_m) R_h(t) \frac{I_h(t) + (1 - \sigma_m) R_h(t)}{N_h(t)} - (\mu_m + \alpha_m) S_m(t); \\
E_m(t) &= \int_{t-\tau_m}^t \beta_m c S_m(u) \frac{I_h(u) + (1 - \sigma_m) R_h(u)}{N_h(u)} e^{-(\mu_m + \alpha_m)(t-u)} du; \\
I'_m(t) &= \beta_m c S_m(t - \tau_m) \frac{I_h(t - \tau_m) + (1 - \sigma_m) R_h(t - \tau_m)}{N_h(t - \tau_m)} e^{-(\mu_m + \alpha_m)(t)} - (\mu_m + \alpha_m) I_m(t). \\
\end{align*}
\]

The second and sixth integrals in (1) represent the summation over the interval \([t - \tau_h, t]\) and \([t - \tau_m, t]\) of those individual humans and mosquitoes who become exposed at time \( u \geq 0 \) and have neither become infectious nor died.

Differentiating the integral equations in system (1), we get the ordinary differential equations of \( E_h \) and \( E_m \) as

\[
\begin{align*}
E'_h(t) &= \beta_h c I_m(t) \frac{S_h(t)}{N_h(t)} - \beta_h c I_m(t - \tau_h) \frac{S_h(t - \tau_h)}{N_h(t - \tau_h)} e^{-\mu_h \tau_h} - \mu_h E_h(t), \\
\end{align*}
\]
with positive initial data will describes host and vector populations and therefore the susceptible, infectious and partially immune equivalent system of differential equations by letting $\rho$

Using the fact that $E(t) = N(t) - S(t) - I(t) - R(t)$ and $E(t) = N(t) - S(t) - I(t)$ we analyze the following equivalent system of differential equations by letting $\rho = \Lambda$, $\beta m = \xi h$, $\beta I c = \zeta m$ and $(1 - \sigma m) = \eta m$,

$$
\begin{align*}
E_m'(t) &= \beta m c S_m(t) I_h(t) + (1 - \sigma m) R_h(t) - \beta m c S_m(t - \tau_m) \\
&\quad \times \frac{I_h(t - \tau_m) + (1 - \sigma m) R_h(t - \tau_m)}{N_h(t - \tau_m)} e^{-(\mu m + \alpha m)\tau_m} - (\mu m + \alpha m) E_m(t).
\end{align*}
$$

Using the fact that $E_h(t) = N_h(t) - S_h(t) - I_h(t) - R_h(t)$ and $E_m(t) = N_m(t) - S_m(t) - I_m(t)$ we analyze the following equivalent system of differential equations by letting $\rho = \Lambda$, $\beta_h c = \xi_h$, $\beta m c = \zeta m$ and $(1 - \sigma m) = \eta m$,

3. Analysis of the model

First, we note that the region of biological interest

$$
\Omega = \{(S_h, I_h, R_h, N_h, S_m, I_m, N_m) \in \mathbb{R}^7_+ | S_h + I_h + R_h \leq N_h, S_m + I_m \leq N_m, N_h, N_m > 0\}
$$

is positively invariant for system (2).

3.1. Positivity of solutions

The model (2) describes host and vector populations and therefore the susceptible, infectious and partially immune populations should be positive for all times. We prove that all solutions of system (2) with positive initial data will remain positive for all time $t > 0$. 

Fig. 1. Schematic diagram of malaria transmission: Human host (A) and mosquito vector (B).
Theorem 3.1. Let \( S_h(0) = S_{h0} > 0, I_h(u) = I_{h0}(u) ≥ 0 \) for all \( u \in [-\omega, 0] \) with \( I_{h0}(0) > 0, R_h(0) = R_{h0} > 0 \) for the human population and \( S_m(0) = S_{m0} > 0, I_m(0) = I_{m0} > 0 \) for the mosquito population, be the initial data. Then \( S_h(t), I_h(t), R_h(t), S_m(t) \) and \( I_m(t) \) are positive for all \( t > 0 \).

Proof 3.1. Assume that there exists some time \( t_1 \) such that \( I_h(t_1) = 0 \). Define:

\[
B = \min_{0 ≤ t ≤ t_1} \left\{ \frac{I_h(t) - \tau_h}{I_h(t)} - (r_h + \mu_h + \alpha_h + q_h) \right\}.
\]

Then, for \( t ∈ [0; t_1] \), \( I_h(t) ≥ B I_h(t) \). Solving, we get \( I_h(t) ≥ I_h(0)e^{Bt} \). For \( t = t_1 \), we get \( I_h(t_1) ≥ I_h(0)e^{Bt_1} > 0 \), which is a contradiction. Thus, \( I_h(t) > 0 \) for all \( t > 0 \).

Equation for \( R_h(t) \) is as shown in Eq. (1). Since it was established that \( I_h(t) \) is positive for all \( t > 0 \), then it follows that \( R_h(t) \) is also positive for all \( t > 0 \).

Assume that there exist the first time \( t_1 \) such that \( S_m(t_1)(I_h(t_1) + \eta_m R_h(t_1)) = 0 \). We have already proved that \( I_h(t), R_h(t) > 0 \) for all \( t > 0 \). This implies that \( S_m(t) = 0 \) for all \( t ∈ [0; t_1] \). From the equation of \( S_m'(t) \) in system (2), we have:

\[
S_m'(t)|_{t=t_1} = A_m - \zeta_m S_m(t_1) - \frac{I_h(t_1) + \eta_m R_h(t_1)}{N_h(t_1)} \left( \frac{\mu_m + \alpha_m}{N_m} \right) S_m(t_1).
\]

Since \( S_m(0) > 0, S_m(t_1) = 0 \) we must have \( S_m'(t)|_{t=t_1} ≤ 0 \) which is a contradiction.

By the same argument it can be proved that \( S_h \) is positive. Suppose not. Let \( t_1 \) be the first time when: \( I_m(t)S_h(t) = 0 \). Assume that \( S_h(t_1) = 0 \). Then \( I_m ≥ 0 \) for all \( t ∈ [0, t_1] \). From the first equation, we have:

\[
S_h'(t)|_{t=t_1} = \frac{A_h + r_h I_h(t_1) - \zeta_h I_m(t_1) - \mu_h S_h(t_1)}{N_h(t_1)} - \frac{(\mu_m + \alpha_m)I_m(t_1)}{N_m}.
\]

Since \( S_h(0) > 0, S_h(t_1) = 0 \) we must have \( S_h'(t)|_{t=t_1} ≤ 0 \) which is a contradiction.

Suppose that for some time \( t_1, I_m(t_1) = 0 \). We have already shown that \( S_m(t), R_h(t), I_h(t) > 0 \) for all \( t > 0 \). Then:

\[
I_m'(t)|_{t=t_1} = \frac{\zeta_m S_m(t_1 - \tau_m) - I_h(t_1 - \tau_m) + \eta_m R_h(t_1 - \tau_m)e^{-\mu_m \tau_m (\mu_m + \alpha_m)}}{N_h(t_1 - \tau_m)} - \frac{(\mu_m + \alpha_m)I_m(t_1)}{N_m}.
\]

But \( I_m(0) > 0, I_m(t_1) = 0 \) to hold \( I_m'(t)|_{t=t_1} ≤ 0 \) which is a contradiction.

If the initial conditions are positive, then the solutions of the system (2) stay positive for all \( t > 0 \).

The proof is complete. \( \square \)

3.2. Steady state solutions

By calculating the zeros of the model (2), two equilibrium points are obtained. These are disease-free and endemic states which will be denoted by \( E_0 \) and \( E_e \) respectively.

\[
E_0 = (S_h^*, I_h^*, R_h^*, N_h^*, S_m^*, I_m^*, N_m^*) = \left( \frac{A_h}{\mu_h}, 0, \frac{A_m}{\mu_h}, \frac{A_m}{(\mu_m + \alpha_m)}, 0, \frac{A_m}{(\mu_m + \alpha_m)} \right).
\]

The determination of the endemic equilibrium \( E_e \) will be discussed in Section 6. The two steady states have a strong influence on the behaviour of disease transmission in a community. Even though there could be infinitely many different initial distributions of malaria in a community these equilibrium points are the final reachable situations.

4. The basic reproductive number

The basic reproductive number is defined as the expected number of secondary cases produced, in a susceptible population, by a typical infective individual during his/her entire period of infectiousness [34] and mathematically as the dominant eigenvalue of a positive linear operator [37].
Consider a single newly infectious mosquito entering the disease free population at equilibrium. This mosquito is still present in the population at time \( t = 0 \) with a probability \( \frac{s_0}{N_h} e^{- \mu_h t} \), of surviving its infectious period, infects humans at a rate \( \zeta_h \frac{s_0}{N_h} N_h e^{- \mu_h t} \). These humans become infectious at time \( t \geq \tau_h \) with probability \( e^{- \mu_h \tau_h} \). Hence the total number of humans who become infectious due to this mosquito during its entire infectious period is approximately:

\[
\int_0^\infty \zeta_h \frac{s_0}{N_h} e^{- \mu_h t} e^{- (\mu_m + \alpha_m) t} \, dt = \frac{\zeta_h e^{- \mu_h \tau_h}}{\mu_m + \alpha_m} = R_{mh}. \tag{4}
\]

Consider again a single infectious human entering the disease free population at equilibrium. This human, still present in the population, remains infectious for time \( t \geq \tau_m \) with a probability \( e^{- (\mu_m + \alpha_m) \tau_m} \). The total number of mosquitoes infected from infectious and partially immune humans is:

\[
\int_0^\infty \frac{\zeta_m s_0}{N_h} e^{- (\mu_m + \alpha_m) t_m} e^{- (r_h + \mu_h + q_h + \alpha_h) t_m} \, dt = \frac{\zeta_m A_m \mu_h e^{- (\mu_m + \alpha_m) \tau_m}}{A_h (\mu_m + \alpha_m) (r_h + \mu_h + q_h + \alpha_h)}. \tag{5}
\]

Suppose now, that the human is partially immune, then following the same argument, this human still present in the population, remains infectious for time \( t \leq \omega \) and infects mosquitoes at a rate \( \zeta_m \eta_m \frac{s_0}{N_h} \int_0^\omega q_h e^{- \mu_h u} \, du \). The expected number of mosquitoes which become infectious due to this partially immune individual is approximately:

\[
\zeta_m \eta_m \frac{s_0}{N_h} e^{- (\mu_m + \alpha_m) t_m} q_h \int_0^\infty \int_0^\omega e^{- (r_h + \mu_h + q_h + \alpha_h) u} e^{- \mu_h u} \, du \, dt = \frac{\zeta_m A_m e^{- (\mu_m + \alpha_m) \tau_m}}{A_h (\mu_m + \alpha_m) (r_h + \mu_h + q_h + \alpha_h)} (1 - e^{- \mu_h \omega}) q_h \eta_m. \tag{6}
\]

The total number of mosquitoes infected from infectious and partially immune humans is:

\[
\frac{\zeta_m A_m e^{- (\mu_m + \alpha_m) \tau_m}}{A_h (\mu_m + \alpha_m) (r_h + \mu_h + q_h + \alpha_h)} ((1 - e^{- \mu_h \omega}) q_h \eta_m + \mu_h) = R_{hm}. \tag{7}
\]

Therefore \( R_{mh} \) and \( R_{hm} \) are the disease reproductive numbers from mosquitoes to humans and from humans to mosquitoes. The product \( R_{hm} R_{mh} = R_0 \) gives the disease reproductive number from host to host or from vector to vector. Therefore, the long-term expected number of secondary cases produced per generation by an infectious human is:

\[
R_0 = \frac{\zeta_h \frac{s_0}{N_h} A_m e^{- (\mu_m + \alpha_m) \tau_m} e^{- \mu_h \tau_h}}{A_h (\mu_m + \alpha_m)^2 (r_h + \mu_h + q_h + \alpha_h)} (1 - e^{- \mu_h \omega}) q_h \eta_m + \mu_h). \tag{8}
\]

The most critical insights into the entomological aspects of malaria transmission relevant to malaria control come directly from the parameters in the formula for \( R_0 \). The parameters that are easy to control are those of the vector population. The gametocytes taken up by mosquitoes and the injection of sporozoites in the human host occur when female \( Anopheles \) mosquitoes bite humans. Hence \( R_0 \) is proportional to both the inoculation rate \( \zeta_h = \beta_h c \) and the transmission rate \( \zeta_m = \beta_m c \). The contact rate \( c \), therefore is a squared term. If contact rate between mosquitoes and humans is made almost impossible, then the disease transmission is greatly reduced. From the formula of \( R_0 \), an increase in mosquito mortality \( (\mu_m + \alpha_m) \) has three effects. First, the probability of surviving the latent period \( e^{- (\mu_m + \alpha_m) \tau_m} \) is reduced. Second, initially susceptible mosquito density, \( \frac{A_m}{\mu_m + \alpha_m} \), is reduced and third, the infectious period of mosquitoes \( \frac{1}{\mu_m + \alpha_m} \) is also reduced. Reduction in mosquito emergence or in the duration of the human infectious period has linearly proportional effects on transmission.

If \( q_h = 0 \), which is the same as saying that there is no acquired partial immunity in the population and is also equivalent to saying that \( \omega = 0 \) then the model becomes an SEIS model for the human population and \( R_0 \) becomes

\[
R_0 = \frac{\zeta_m e^{- (\mu_m + \alpha_m) \tau_m}}{r_h + \mu_h + \alpha_h} \times \frac{\zeta_h e^{- \mu_h \tau_h}}{\mu_m + \alpha_m} \times \frac{A_m \mu_h}{(\mu_m + \alpha_m) A_h}. \nonumber
\]
The first factor is the number of susceptible mosquitoes infected with gametocytes (and survive to become infectious) by an infectious human, during his/her entire infectious period. The second factor is the number of humans infected with sporozoites (and become infectious) by an infectious mosquito, during its entire period of infectiousness. Finally, the last factor is the initial mosquito density per human.

From (8), we deduce that an increase in the duration of partial immunity, \( \omega \), increases the reproductive number. Partial immunity is therefore good for an individual who has it but for the population at large it increases chances of infection because it increases the reservoir of infection.

The stricter way of bringing a disease under control in a population of varying size is to demand that the total number of infectives, that is the reservoir of infection, \( I_h, I_m \) (and possibly \( R_h \)) \( \to 0 \) with increasing time. Another way is to seek conditions on the parameters of the disease transmission process that will guarantee the existence of a stable disease-free state. The required conditions are provided by the stability analysis results of both the disease-free and the endemic equilibrium states in the following sections, where we will show that stability of these states depend critically on the parameter \( R_0 \).

5. Stability of the disease-free equilibrium

5.1. Local stability of the disease-free equilibrium

The stability of the disease-free equilibrium state can be obtained from studying the eigenvalues of the Jacobian matrix evaluated at the equilibrium point. If all the eigenvalues have negative real parts, then the equilibrium point is stable. At the disease-free equilibrium \( E_0, I_h = R_h = I_m = 0 \) and the populations \( S_h, N_h, S_m, N_m \) are non zero. From the equations of system (2), we deduce that four of the eigenvalues of the model are

\[-\mu_h \text{ (of multiplicity two)} \quad \text{and} \quad -(\mu_m + \alpha_m) \text{ (of multiplicity two)}.\]

Since the four eigenvalues are negative the stability of \( E_0 \) is determined by eigenvalues from the infectious classes \( I_h(t), R_h(t) \) and \( I_m(t) \). From the system of equations (2) these classes can be written as integral equations

\[
I_h(t) = \int_{-\infty}^{t+\tau_h} \zeta_h S_h(s - \tau_h) I_m(s - \tau_h) e^{-\mu_h \tau_h} e^{-(\mu_h + \mu_m + q_h + \alpha_h)(t-(s-\tau_h))} ds;
\]

\[
R_h(t) = \int_{t-\omega_h}^{t} q_h I_h(u) e^{-\mu_h(u-t)} du;
\]

\[
I_m(t) = \int_{-\infty}^{t+\tau_m} \zeta_m S_m(s - \tau_m) I_h(s - \tau_m) + \eta_m R_h(s - \tau_m) e^{-(\mu_m + \alpha_m) \tau_m} e^{-(\mu_m + \alpha_m)(t-(s-\tau_m))} ds.
\]

To get the characteristic equation for the integral equations (9), we follow closely the method of Kribs-Zaleta [38].

Consider the equation for \( I_h(t) \) with \( M = r_h + \mu_h + q_h + \alpha_h \).

We let \( I_m(t) = I_m^* + i_m(t), S_h(t) = S_h^* + s_h(t), N_h(t) = N_h^* + n_h(t) \) and allowing quadratic and constant terms to drop out, we have:

\[
i_h(t) = \int_{-\infty}^{t+\tau_h} \zeta_h S_h^* i_m(s - \tau_h) + I_m^* S_h(s - \tau_h) + I_h^* S_m(s - \tau_m) + \eta_m R_h(s - \tau_m) e^{-(\mu_m + \alpha_m) \tau_m} e^{-(\mu_m + \alpha_m)(t-(s-\tau_m))} ds.
\]

Using the substitution \( x = t - (s - \tau_h) \) and noting that at \( E_0, I_m^* = 0 \) and \( S_h^* = N_h^* \), this can be written as

\[
i_h(t) - \zeta_h e^{-\mu_h \tau_h} \int_{0}^{\infty} i_m(t-x)e^{-Mx} dx = 0.
\]

Since we are looking for the roots of the characteristic equation, which describes the rate of exponential growth of the linearized system, we assume temporarily that \( i_m(t) \) has the form of an exponential function: \( k_{mi} e^{\lambda t} \), so that \( \lambda \) is our root. Substituting in the integral we get

\[
i_h(t) - \zeta_h e^{-\mu_h \tau_h} \int_{0}^{\infty} k_{mi} e^{\lambda t} e^{-\lambda x} e^{-Mx} dx = 0.
\]

If \( k_{mi} e^{\lambda t} \) is pulled outside the bracket, and the substitution undone, this finally yields
\[(M + \lambda)i_h(t) - \xi_h e^{-\mu_h t} i_m(t) = 0.\]

Repeating the process on the remaining equations of system (9) gives us a set of equations whose characteristic equation simplifies to

\[A_3(\lambda) = \det(\mathcal{J}_3 - \lambda I_{3\times3}) = 0,\]

where \(\mathcal{J}_3\) is the matrix:

\[
\mathcal{J}_3 = \begin{pmatrix}
-M & q_h (1 - e^{-\mu_h t}) & 0 \\
q_h (1 - e^{-\mu_h t}) & -\mu_h & \xi_h e^{-\mu_h t} \\
2 - \frac{q_i h (1 - e^{-\mu_h t})}{(\mu_m + \alpha_m) \bar{A}_h} & \xi_m A_m \mu_h e^{-\mu_m \alpha_m t} & 0 \\
-\frac{q_i h (1 - e^{-\mu_h t})}{(\mu_m + \alpha_m) \bar{A}_h} & \xi_m A_m \mu_h e^{-\mu_m \alpha_m t} & -(\mu_m + \alpha_m) \bar{A}_h \\
\end{pmatrix}.
\]

The diagonal elements of \(-\mathcal{J}_3\) are positive and the off diagonal elements are non positive. Hence \(-\mathcal{J}_3\) is an \(M\)-matrix (see [39], proof of theorem 2), and therefore the expression:

\[\lambda^3 + x_2 \lambda^2 + x_1 \lambda + x_0 = 0\]

where

\[x_2 = M + \mu_h + \mu_m + \alpha_m;\]

\[x_1 = M(\mu_m + \alpha_m) \left( \frac{\mu_h (M + \mu_m + \alpha_m)}{M(\mu_m + \alpha_m)} + 1 - G_0 \right);\]

\[x_0 = M \mu_h (\mu_m + \alpha_m)(1 - R_0);\]

\[G_0 = \frac{\xi_m \xi_h A_m \mu_h e^{-\mu_m \alpha_m t} e^{-\mu_h t}}{A_h (\mu_m + \alpha_m)^2}.
\]

Using the Routh-Hurwitz stability criterion, the necessary condition for \(A_3(\lambda)\) to have negative roots is that all coefficients must have the same sign and must be nonzero. This is satisfied if \(R_0 < 1\) since both \(x_2\) and \(x_0\) are both positive when \(R_0 < 1\). It can be shown that the condition \(x_1 x_2 - x_0 > 0\) is satisfied for values of \(R_0 < 1\), since \(G_0 < 1\) whenever \(R_0 < 1\). We therefore deduce that \(E_0\) is locally stable if \(R_0 < 1\).

### 5.2. Global stability of the disease-free equilibrium

**Lemma 5.1.** For the system (2), the disease free equilibrium is globally asymptotically stable if \(R_0 < 1\).

**Proof 5.1.** From the equation of \(I_h(t)\) from system (9), we use the substitution \(x = t - (s - \tau_h)\), take the lim sup of both sides of the equation and apply the fact that \(\lim \sup f \leq \int \lim \sup f\) (see [38], Lemma 2) to get

\[
\lim \sup_{t \to \infty} I_h(t) = \lim \sup_{t \to \infty} \int_0^\infty \frac{S_h(t - x) I_m(t - x)}{N_h(t - x)} e^{-\mu_h t} e^{-M x} dx,
\]

\[
\leq \int_0^\infty \lim \sup_{t \to \infty} \frac{S_h(t - x)}{N_h(t - x)} \xi_h e^{-\mu_h t} \lim \sup_{t \to \infty} I_m(t - x) e^{-M x} dx,
\]

\[
\leq \lim \sup_{t \to \infty} \frac{S_h(t)}{N_h(t)} \xi_h e^{-\mu_h t} \lim \sup_{t \to \infty} I_m(t) \int_0^\infty e^{-M x} dx,
\]

\[
\leq \xi_h e^{-\mu_h t} \frac{1}{M} \lim \sup_{t \to \infty} I_m(t). \tag{14}
\]
Similarly for the second equation of (9), using the substitution \( x = t - u \) and taking \( \lim \sup \) of both sides of \( R_h(t) \) we get:

\[
\lim_{t \to \infty} \sup R_h(t) \leq \frac{q_h}{\mu_h} (1 - e^{-\mu_h \omega}) \lim_{t \to \infty} I_h(t).
\]

Using the substitution \( x = t - (s - \tau_m) \) in the equation of \( I_m(t) \) and taking \( \lim \sup \) of both sides we get:

\[
\lim_{t \to \infty} I_m(t) \leq \frac{\xi_m A_m \mu_h e^{-(\mu_m + \alpha_m) \tau_m}}{(\mu_m + \alpha_m)^2 \Lambda_h} \left[ \lim_{t \to \infty} I_h(t) + \eta_m \lim_{t \to \infty} R_h \right].
\]

Substituting (15) into (16) and the result into (14), we obtain:

\[
\lim_{t \to \infty} I_h(t) \leq \frac{\xi_m \alpha_h \Lambda_m e^{-(\mu_m + \alpha_m) \tau_m}}{(r_h + \mu_h + q_h + \alpha_h) \Lambda_h} \left[ (1 - e^{-\mu_h \omega}) \eta_m + \mu_h \right] \lim_{t \to \infty} I_h(t) = R_0 \lim_{t \to \infty} I_h(t).
\]

If \( R_0 < 1 \), we have a strict inequality (and contradiction) \( \lim_{t \to \infty} I_h(t) < \lim_{t \to \infty} I_h(t) \) unless \( \lim_{t \to \infty} I_h(t) = 0 \). If \( \lim_{t \to \infty} I_h(t) = 0 \) it follows that \( \lim_{t \to \infty} R_h(t) = \lim_{t \to \infty} I_m(t) = 0 \). Thus the disease free equilibrium is globally asymptotically stable if \( R_0 < 1 \). \( \square \)

6. Existence and stability of the endemic equilibrium

We have shown in the previous section that when \( R_0 < 1 \), then the disease free state is globally asymptotically stable and an endemic equilibrium is not feasible. When this condition is violated then system (2) has an endemic equilibrium \( E_e = (S_{h*}, I_{h*}, R_{h*}, N_{h*}, S_{m*}, I_{m*}, N_{m*}) \). The expression for the endemic equilibrium is very long if expressed explicitly. We shall therefore show the existence of endemic equilibria and analyse their stability using numerical simulations.

**Proposition 6.1.** Let

\[
R_{hm}^* = \frac{\alpha_h \Lambda_m e^{-(\mu_m + \alpha_m) \tau_m}}{(r_h + \mu_h + q_h + \alpha_h) \Lambda_h} \quad \text{and} \quad R_{mh}^* = \frac{\alpha_h \Lambda_m e^{-(\mu_m + \alpha_m) \tau_m}}{\xi_m \phi}.
\]

For \( R_0 > 1 \), the model system (2) has a unique stable endemic equilibrium if either of the following conditions hold:

(i) \( R_{hm} > R_{hm}^* \) or \( R_{mh} > R_{mh}^* \),
(ii) \( R_{hm} < R_{hm}^* \) or \( R_{mh} < R_{mh}^* \) for \( R_{hm}^* > 1 \) or \( R_{mh}^* > 1 \).

**Proof 6.1.** Expressing the endemic equilibrium in terms of \( I_{h*} \), from the equations in (2), we get:

\[
E_e = \left\{ \begin{array}{l}
S_{h*}(I_{h*}) = \frac{\Lambda_h + (r_h + q_h e^{-\mu_h \omega}) I_{h*}}{\xi_h I_{h*} + \mu_h + \mu_h} \\
R_{h*}(I_{h*}) = \frac{q_h}{\mu_h} (1 - e^{-\mu_h \omega}) I_{h*} \\
N_{h*}(I_{h*}) = \frac{\mu_h}{\Lambda_h} I_{h*} \\
S_{m*}(I_{h*}) = \frac{\zeta_m \Phi + (\mu_m + \alpha_m)}{\zeta_m \Phi + (\mu_m + \alpha_m) \Lambda_m} \\
I_{m*}(I_{h*}) = \frac{\zeta_m \Phi + (\mu_m + \alpha_m)}{\zeta_m \Phi + (\mu_m + \alpha_m) \Lambda_m} \\
N_{m*}(I_{h*}) = \frac{\mu_m}{\mu_m + \alpha_m}
\end{array} \right.
\]

where \( \Phi = \frac{q_h I_{h*}}{\Lambda_h + \alpha_h I_{h*}} \) and \( \varphi = \mu_h + (1 - e^{-\mu_h \omega}) q_h \eta_m \). Let \( \phi_1 = \xi_h A_m e^{-(\mu_m + \alpha_m) \tau_m} + \Lambda_h (\mu_m + \alpha_m) \). After substituting the expressions for \( S_{h*}, R_{h*}, N_{h*}, S_{m*}, I_{m*}, N_{m*} \) in the second equation of (2) and equating to zero we get:

\[
I_{h*} (I_{h*}^2 + A_1 I_{h*} + A_0) = 0
\]
where
\[
A_1 = \frac{A_h (\mu_m + \alpha_m)^2 (2\alpha_h + (r_h + q_h e^{-\mu_h \alpha}) R_0) - \zeta_m \varphi \varphi_1}{\alpha_h (\mu_m + \alpha_m)(\zeta_m \varphi - \alpha_h (\mu_m + \alpha_m))},
\]
\[
A_0 = \frac{(\mu_m + \alpha_m) A_h^2 (R_0 - 1)}{\alpha_h (\zeta_m \varphi - \alpha_h (\mu_m + \alpha_m))}.
\]

By solving the equation in (18), we get the solutions of \( I_{h^*} \). \( I_{h^*} = 0 \) gives the disease-free equilibrium while the remaining quadratic equation can be analysed for the possible existence of endemic equilibria. By inspection of coefficients \( A_0 \) and \( A_1 \) of the quadratic equation in (18) the following cases (a), (b) and (c) give scenarios where existence of endemic equilibria for the model is possible.

(a) If \( \zeta_m \varphi - \alpha_h (\mu_m + \alpha_m) > 0 \), then the model has
   (i) an endemic equilibrium if \( R_0 < 1 \iff A_0 < 0 \);
   (ii) two endemic equilibria if \( R_0 > 1 \), \( A_1 < 0 \) and \( A_1^2 - 4 A_0 > 0 \);
   (iii) no endemic equilibria otherwise.

(b) If \( \zeta_m \varphi - \alpha_h (\mu_m + \alpha_m) < 0 \), then the model has
   (i) an endemic equilibrium if \( R_0 > 1 \iff A_0 < 0 \);
   (ii) two endemic equilibria if \( R_0 < 1 \), \( A_1 < 0 \) and \( A_1^2 - 4 A_0 > 0 \);
   (iii) no endemic equilibria otherwise.

(c) If \( A_0 = 0 \), or \( A_1^2 - 4 A_0 = 0 \), then an endemic equilibrium exists if \( A_1 < 0 \).

For case (a), the condition \( \zeta_m \varphi - \alpha_h (\mu_m + \alpha_m) > 0 \) reduces to
\[
R_{hm} > R_{hm}^* \quad \text{or} \quad R_{mh} > R_{mh}^*.
\]
(19)

For case (b), the condition \( \zeta_m \varphi - \alpha_h (\mu_m + \alpha_m) < 0 \) reduces to
\[
R_{hm} < R_{hm}^* \quad \text{or} \quad R_{mh} < R_{mh}^*.
\]
(20)

The pairs of inequalities in (19) and (20) are (mathematically) equivalent.

For cases (a) and (b), the endemic equilibria exist for \( R_0 < 1 \). When \( R_0 < 1 \), the global stability of the disease-free equilibrium ensures that any endemic equilibrium that exists will be unstable. Therefore the endemic equilibria for cases (a) and (b) are unstable. When \( R_0 > 1 \), the endemic equilibria exist for both \( R_{hm} > R_{hm}^* \) and \( R_{hm} < R_{hm}^* \) in cases (a) and (b). It can be shown that case (b) is feasible only when \( R_{hm}^* > 1 \).

Cases (a) and (b) are clearly illustrated in Fig. 2. Cases (a), (a), (b) and (b) are explained in regions C, B, A and D respectively. \( \square \)

We conclude therefore that for the existence of a stable endemic equilibrium the condition \( R_{hm} > R_{hm}^* \) should be satisfied or \( R_{mh} < R_{mh}^* \) for \( R_{hm}^* > 1 \) should be satisfied.

Since we have not obtained the explicit form of the endemic equilibrium, analysing the roots of the quasi polynomial obtained from the linearized Jacobian matrix near the endemic equilibrium is too cumbersome to be produced here. We however use numerical simulations to show the stability and existence of endemic equilibrium. The bifurcation diagram from numerical methods to illustrate this is shown in Fig. 3. This bifurcation diagram shows that when \( R_0 < 1 \), there is a stable disease-free equilibrium. If any endemic equilibrium exists, it is unstable, and therefore cannot be shown numerically. When \( R_0 > 1 \), there exists a stable endemic equilibrium. The other endemic equilibrium that exists is unstable since it could not be obtained by numerical methods used. This diagram also supports the scenarios in cases (a) and (b).

The bifurcation diagram in Fig. 3 was obtained through numerical simulations and it shows an exchange of stability between the disease free and endemic equilibria. The graph was obtained by varying the contact rate \( c \) while the other parameters were fixed. If \( R_0 < 1 \), the disease free state is always the stable final reachable situation. The disease establishes itself in a community at endemic levels when \( R_0 > 1 \). This bifurcation diagram confirms our analytic results which show that a stable endemic equilibrium exists when \( R_0 > 1 \), and that the disease free becomes unstable when the same condition holds.
Fig. 2. Diagram that explains cases (a) and (b) where endemic equilibria exist in regions A, B, C, D. A—unique endemic equilibrium, stable. B—two endemic equilibria, one unstable. C—unique endemic equilibrium, unstable. D—two endemic equilibrium, both unstable.

Fig. 3. Bifurcation diagram for the model which shows an exchange of stability between disease-free and endemic equilibria at $R_0 = 1$. $R_0$ was obtained by varying the contact rate from 0 to 1.4 and the other parameters were fixed at $\alpha_h = 0.3$, $\alpha_m = 0.09$, $q_h = 0.35$, $r_h = 0.02$, $\Lambda_h = 0.55$, $\Lambda_m = 3.2$, $\beta_h = 0.8$, $\beta_m = 0.8$, $\mu_h = 0.02$, $\mu_m = 0.06$, $\tau_h = 14$, $\tau_m = 12$, $\omega = 100$, $\eta_m = 0.7$. Bold lines show stability and dashed lines show instability.

7. Simulations

To explore the behaviour of the system and to demonstrate stability of the steady state solutions, programs were written in C++ to integrate the equations in system (2), using the fourth order Runge Kutta method. All the numerical values of parameters used for the model were estimated. The units for all parameters are day$^{-1}$ except $\tau_h$, $\tau_m$ and $\omega$ which are in days.

Fig. 4 shows the initial and long term behaviour of the populations in the following classes: susceptible humans $S_h$, infectious humans $I_h$, partially immune humans $R_h$, susceptible mosquitoes $S_m$ and infectious mosquitoes $I_m$. 
Fig. 4. Graphs showing initial and long-term behaviour of (a) susceptible humans, (b) infectious humans, (c) partially immune humans, (d) susceptible mosquitoes and (e) infectious mosquitoes. The initial conditions at time $t = 0$, are $S_h = 155$, $I_h = 3$, $R_h = 0$, $S_m = 36$ and $I_m = 2$. The parameters used are $\alpha_h = 0.03$, $\alpha_m = 0.2$, $q_h = 0.35$, $r_h = 0.38$, $\Lambda_h = 0.5$, $\Lambda_m = 3.2$, $\zeta_h = 10.0$, $\zeta_m = 0.7$, $\mu_h = 0.0031$, $\mu_m = 0.055$, $\tau_h = 14$, $\tau_m = 12$, $\omega = 100$, $\eta_m = 0.7$, $R_0 \approx 2.8$ and $R_{hm} \approx 1.5$. 
Fig. 5. Graphs showing the effect of $\eta_m$ on the long-term behaviour of (a) susceptible humans, (b) infectious humans, (c) partially immune humans and (d) infectious mosquitoes. The initial conditions at time (days) $t = 0$, are $S_h = 150$, $I_h = 30$, $S_m = 50$, $I_m = 30$. The parameters used are $\alpha_h = 0.014$, $\alpha_m = 0.2$, $q_h = 0.05$, $r_h = 0.48$, $A_h = 0.005$, $A_m = 2.2$, $\zeta_h = 0.77$, $\zeta_m = 0.7$, $\mu_h = 0.0031$, $\mu_m = 0.06$, $\omega = 100$, $\tau_h = 14$, $\tau_m = 12$. The values for $\eta$ are 0, 0.5, 1 and corresponding values of $R_0$ are 0.8, 2.6, 4.5 and corresponding values of $R_{hm}$ are 6.4, 20.2, 34.1.

The initial conditions were chosen by giving a small perturbation to the disease free point. As time increases, the susceptible humans decrease while the infectious humans and mosquitoes increase. Those humans who recover enter the susceptible class or may recover with acquired partial immunity, which explains the increase in the partially immune class. As the infectives and partially immune individuals increase, susceptible mosquitoes decrease due to the increase in the reservoir of infection. As time increases further the populations in the respective classes seem not to change. They would have reached an endemic equilibrium. This is a typical situation when an epidemic occurs in a community.

The probability of reducing transmission from a partially immune human $\eta_m = (1 - \sigma_m)$ is varied in Fig. 5 to determine its effect on the behaviour of the different subpopulations as time increases. The graphs in Fig. 5(a) show that, for the susceptible humans, as $\eta_m$ increases then the number of susceptible humans decreases. This is
Fig. 6. Phase plane portrait of infective humans against susceptible humans. The graph shows the existence of the disease free state. The graph was obtained by varying the initial conditions of $S_h$ and $I_h$. (a) $S_h = 0.1$ and $I_h = 0.5$ (b) $S_h = 0.2$ and $I_h = 1.0$. (c) $S_h = 0.3$ and $I_h = 1.5$. (d) $S_h = 0.4$ and $I_h = 2.0$ The parameters are fixed as follows: $\alpha_h = 0.3$, $\alpha_m = 0.2$, $q_h = 0.35$, $r_h = 0.38$, $\Lambda_h = 0.5$, $\Lambda_m = 3.2$, $\zeta_h = 10.0$, $\zeta_m = 0.7$, $\mu_h = 0.0031$, $\mu_m = 0.06$, $\tau_h = 14$, $\tau_m = 12$, $\omega = 100$, $\eta_m = 0$, $R_0 \approx 0.08$ and $R_{hm} \approx 0.05$.

because from the other graphs, Fig. 5(b)–(d), it is clear that increasing $\eta_m$ increases the infectious and partially immune populations resulting in more numbers of susceptible being infected. The graphs show that when infectivity of mosquitoes is blocked from partially immune humans then the population can reach a state with $I_h = I_m = 0$ but $R_h \neq 0$. This will be a disease free state since the partially immune class will be completely immune and will cease to be a reservoir of infection.

The existence of the disease-free equilibrium point is confirmed by the phase plane portrait in Fig. 6. Using different initial conditions for the populations in the different classes the final reachable condition is the non-endemic state using the parameters shown in the figure. The parameters used give a reproductive number that is less than one so the only equilibrium that exists is the disease-free state. Thus if $R_0 < 1$ the stable endemic equilibrium does not exist.

8. Discussion

A model for transmission of malaria was developed taking into account partial immunity in the human host, latent period in both populations, induced death rate and input rate for the mosquito population that is temperature dependent since temperature is a critical regulator of growth and development within each stage of the mosquito life cycle. It determines the end of one stage and the beginning of the next and in regulating the sporogonic cycle. The model was analysed and the equilibrium points were determined. The equilibrium points play an important role depending on the value of $R_0$. Unlike other models with partial immunity, for example [4], our model shows that the presence of a partially immune population and the duration of partial immunity has some effects on the endemicity of the disease. We have mentioned that some parameters are temperature dependent and therefore vary seasonally, but we have treated them as constants in the model. This makes our model applicable over time scales during which temperature does not vary significantly.

Analysis yielded a generalization of the formula for the basic reproductive number for malaria. From the formula we have shown that if more and more humans become asymptomatic immune carriers with enough parasite loads to transmit the infection to mosquitoes, then the value of $R_0$ gets larger and it becomes more difficult to control the infection in a population with partially immune individuals. The number of mosquitoes per human and
number/infectivity of those partially immune humans favour the establishment and endemicity of malaria in the community. If this class is eliminated (by treating them with anti-malarial drugs), then it is possible to eradicate malaria in a population by reducing the number of mosquitoes per human (i.e. by increasing the induced death rate). We deduce that as the duration of partial immunity $\omega$ decreases, the term $\left(1 - e^{-\mu h \omega}\right)$ describing the probability of being in the partially immune class, decreases and thus results in a decrease in $R_0$. In the analysis of $R_0$, we have shown that benefits of killing adult mosquitoes are disproportionately high.

Development of partial immunity, an important feature of $P. falciparum$ malaria, reduces the frequency of symptomatic episodes and therefore decreases disease-associated morbidity and mortality. Since the development of protective vaccines against malaria are being pursued, it will be effective in a partially immune population to introduce transmission blocking vaccines. It has been shown numerically that by blocking transmission from partially immune humans, that is making the immune response 100% effective, $\sigma_m = 1$, greatly reduces the reservoir of infection and increases the number of susceptible humans. This will make an effective intervention. Transmission blocking vaccines will also reduce the probability of parasites evolving resistance to multiple anti-malaria drugs.

Factors affecting transmission by appropriate vector stages are (1) density of vectors in relation to human hosts, (2) effectiveness of the vector in acquiring and maturing the infection after feeding on an infective subject, (3) frequency with which the vector takes a blood meal and the fraction of these blood meals that is taken on man, (4) duration of sporogony and (5) longevity of the vector [40]. Most of these factors are included in our expression for $R_0$ and some of them, for example (4) and (5), are temperature dependent. Adult mosquitoes fly long distances and can reach far places by taking shelter in motor vehicles, ships and aircraft. Larvae of most mosquitoes can live for several days on a wet surface but do not succeed in pupating except in water. In relative terms larva control might be more effective. From the formula for $R_0$, these are indirectly dealt with by increasing the rate at which eggs become non viable $\mu_e$, thus doing away with the stagnant waters near homes. Where displaced people are resettled in forested areas insecticide treated mosquito nets should be issued thus reducing $c^2$ and increasing $\alpha_m$, and retreatment ensured in areas of local transmission to reduce $R_0$.

Better systems for collecting relevant information to make appropriate decisions on vector control and personal protection should be developed, so that limited resources are targeted at those in need. Malaria is an environmental disease since it is limited largely by environmental factors such as rainfall, minimum and maximum temperature, vegetation index (amount of vegetation) and vegetation classification (types of vegetation). Temperature limits the development cycle of the malaria parasite inside the mosquito (the sporogonic/sexual cycle) as well as mosquito development and population turnover.

While stable and unstable malaria-endemic areas would benefit from general strengthening of health infrastructure, epidemic-specific interventions make sense wherever extended periods of low-level transmission are punctuated by bursts of infection triggered by climatic conditions and social and environmental changes. Such areas benefit from specific strategies which emphasize strong surveillance systems, intensive anti-vector interventions, and reserve capacity in anti-malarial drugs and services to handle the more precipitous outbreaks. The intervention methods should be focused on diminishing the exposure of the population to new infections and providing early and adequate treatment of malaria cases as they appear thus increasing the recovery rate $r_h$. Before and during epidemics antivector interventions should focus on indoor residual spraying because this method can most rapidly reduce the clear and present danger of infectious mosquitoes, as well as reducing the longevity of those that might otherwise become infectious.

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