Analysis of continuous and discrete mathematical models of malaria propagation

by

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DECLARATION

I, Parna Mandal, do hereby declare that this thesis titled "Analysis of continuous and discrete mathematical models of malaria propagation" and the work presented in it is a record of bonafied work carried out by me in partial fulfilment of the requirements for Master of Science in Mathematics and its Applications at Central European University, Budapest, Hungary.

I also declare that except where due acknowledgement is made, this work has never been presented wholly or in part for the award of any degree at Central European University or any other university .

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Abstract

The present dissertation dealing with a compartmental epidemiological model to study the propagation of malaria between two interacting population–human (host) and mosquito (vector), is investigated. The total human population is compartmentalised into four classes, namely, the susceptible, the exposed, the infected and the recovered class. The total mosquito population is classified into three subclasses, e.g., the susceptible, the exposed and the infected class. A region is found out where the model is epidemiologically feasible and mathematically well-posed. The existence of equilibrium along with its stability is derived. The stability criteria do depend on the reproduction number which is calculated by the next-generation matrix technique. For a quantitative insight of the model, a thorough large-scale numerical simulation has been performed and the predicted results are presented graphically. The sequential and Strang-Marchuk splitting schemes together with RK4 numerical method have been leveraged to get the splitting solution of the matrix differential equation. However, the reference solution of the unsplit system is obtained by solving the system of ODEs by the RK4 method. Since the exact solution of the unsplit system considered is not known, this numerical solution is compared with the numerical solution obtained by using the explicit Euler method. The order and accuracy of the methods have been derived both analytically and numerically, and we have also calculated the numerical error (local/global practical error) associated with the methods. Our results agree well with several existing results available in the literature.

Contents

1 Introduction

1.1 Background

A model is a caricature of reality as represented by empirical data. It helps us to understand reality because it simplifies it. The model which more closely captures essential features of reality-we usually refer to it as a 'better fit'. The word exact fit does not arise in model studies as no model can wholly resembles reality. There is a temptation to assume that only models that are incredibly detailed can be useful–but this is not the case always. A model should be as complex as needed, depending upon the questions of interest. The choice of an optimal level of complexity obeys good bargaining. Mathematical models help to describe physical systems using mathematical concepts and language. For example, epidemiology is essentially a population biology discipline concerned with public health and is thus heavily influenced by mathematical theory. In epidemiological modelling, mathematical models are being enriched with several biological, clinical and epidemiological phenomena to explain the dynamics of the disease. In this context, the use of mathematical models aims to unearth processes from a large scale perspective. The apparently unpredictable nature of an infectious disease has been a source of fear and superstition as well since the beginning of human civilization. One of the primary aims of epidemic modelling is helping to understand the spatio-temporal spread of disease in host populations. The process of systematically clarifying inherent model assumptions, interpreting its variables, and estimating parameters are invaluable in uncovering precisely the mechanism giving rise to the observed patterns. Deterministic models are those in which there is no element of chance or uncertainty. When the population size is large enough so that demographic stochasticity may be ignored, a deterministic model may be appropriate.

Infectious diseases, also known as transmissible diseases or communicable diseases consist of clinically evident illness resulting from the infection, presence and growth of pathogenic biological agents in an individual host organism. Infectious diseases are caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi. The diseases can spread, directly or indirectly, from one person to another through droplet contact, fecal-oral transmission, sexual transmission, vertical transmission, iatrogenic transmission and vector-borne transmission. Malaria, an infectious disease which remains one of the most prevalent and lethal human infection worldwide, is caused by infection with single-celled (protozoan) parasites of genus Plasmodium. The parasites are transmitted to humans through the bites of infected female Anopheles mosquitoes (vectors). Of the five parasite species (*Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae and Plasmodium knowlesi*) that cause malaria in humans, plasmodium falciparum is the most deadly form and it predominates in Africa. The parasite is responsible for the greatest number of deaths and clinical cases in the tropics. In the human body, the parasites multiply in the liver, and then infect red blood cells. The infected red blood cells burst after 2 to 3 days to release merozoites and gametocytes into the blood stream. Anopheles mosquitoes become infected when they feed and ingest human blood that contains mature gametocytes. The gameto-

cytes develop into male and female gametes that fertilize to become zygotes in the mid-gut wall of the mosquito. The zygote elongates to become ookinete and penetrates the mid-gut epitheliums that later develops and ultimately produce sporozoites which become infective when they migrate to the salivary glands. Its infection can lead to serious complications affecting the brain, lungs, kidneys, and other organs. Symptoms of malaria are generally non-specific and most commonly consist of fever, malaise, weakness, gastrointestinal complaints (nausea, vomiting, and diarrhea), neurologic complaints(dizziness, confusion, disorientation, and coma), headache, back pain, malign, chills, and/or cough [1].

According to a survey in 2015 [1], it affected 99 countries and territories throughout the world, mostly afflicted sub-Saharan Africa, approximately 3000 lives were lost each day. Annual infection reports were almost 300 to 500 million among which $700,000$ to $881,000$ resulted in death. It affected mostly the age group of $0-5$ and pregnant women. If malaria is not treated well, it can cause cerebral malaria which affects approximately 57500 children per year in Africa, kills $10-40\%$ of patients whereas $5-20\%$ of those who survive experience neurological problems. Many measures have been taken to lower the threats of malaria and ultimately to eliminate and to eradicate it, but there come many problems such as development and spread of drug-resistant malaria parasites, mosquito resistant to insecticides, climatic change, and many more. Malaria is very sensitive to climatic conditions. It is most prevalent in tropical climates, where the breeding sites are enough and favourable temperature for mosquito. The protozoan itself survives in certain favourable temperature. Hence, a slight change in temperature can drastically affect the lifespan and population of mosquitoes. Water is another factor that significantly contributes to the spread of the disease owing to the fact that mosquitoes breed in pools of water. More rainfall leads to the increase of possible breeding sites for mosquito, which results in increase of more vectors to spread malaria. Little rainfall leads to few breeding sites for mosquitoes.

Malaria has for many years been considered a global issue, and many epidemiologists and other scientists invest their effort in learning the dynamics of malaria and to control its transmission. There exist an impressive variety of epidemiological models and exhaustive reviews to study the dynamics of malaria transmission and growth, giving an insight into the interaction between the host and vector population. These literature also predicted how to control malaria transmission, and eventually how to eradicate it. The use of mathematical models increases to influence the theory and practice of disease management and control.

Finally, to tackle such problems, an appropriate mathematical model is developed and successfully solved numerically to get a quantitative insight of the model. The propagation of this disease is generally modelled by a system of linear and non-linear ordinary differential equations (ODEs) and partial differential equations (PDEs). Due to the highly nonlinearity of these equations, it may not be solved analytically, in general, instead, an appropriate numerical method may be leveraged to solve the system of equations considered.

1.2 Objective of the Study

The main objective of the study is two-folded, namely, i) On Mathematical Modelling and ii) On Numerical Experiments

i) On Mathematical Modelling

- to formulate appropriate mathematical model that captures the dynamics of the propagation of malaria using a system of nonlinear differential equations.
- to study the feasiblity of the solution and the stability of the equilibria of the system.
- to analyse the simulated results of the model considered.

ii) On Numerical Experiments

- to solve numerically the system of equations by Runge-Kutta method of order 4 (RK4) and we treat the solutions as the reference solutions or the numerical solution.
- to convert the system of nonlinear differential equations into a non-homogeneous matrix differential equations.
- to solve numerically the non-homogeneous matrix differential equation by sequential splitting and Strang-Marchuk splitting methods and we term it as numerical split solutions.
- to deduce the order of the splitting method analytically and order of the local practical error numerically.
- to calculate the error associated with the numerical methods used.
- to compare our results with regard to the numerical methods applied with some established results of [2].

1.3 Significance of the Study

Despite malaria being preventable and treatable, it remains one of the deadliest infectious disease for developing world specially in Africa. This reseach will shed light on some important points

- to predict the propagation of the disease at long run.
- to find the parametric structures so that the disease can be controlled and eradicated.

- to use the operator splitting methods for non-homogeneous matrix differential equations.
- to use the results as an input for the future research.

1.4 Statement of the Problem

Malaria is the fifth leading killer among infectious diseases worldwide, and the second leading cause of death in Africa behind HIV/AIDS [3]. It continues to raise major public health and socio-economic burdens in developing countries especially in African countries. Malaria is the largest single component of the disease burden in Africa, causing an annual loss of 35 million future life-years from disability and premature mortality. Each year many international travelers fall ill with malaria while visiting countries/territories where malaria is endemic, and well over 10000 are reported to become ill with malaria after returning home. The rapid adaptability of the species to changing environmental conditions makes it resistant to many forms of interventions developed to combat mosquito populations, and eventually, it continues to play a major role in residual malaria transmission. Insecticide-treated nets are among the control interventions which have been promoted for use in malaria-endemic regions. The impacts of temperature and rainfall play a pivotal role in the transmission of malaria. The burden of malaria has been increasing due to a combination of large population movements, increasing large scale epidemics, mixed infections of *Plasmodium vivax* and *P. falciparum*, increasing parasite resistance to malaria drugs, vector resistance to insecticides, low coverage of malaria prevention services, and general poverty. In this research work, we are going to address the following basic questions.

1. How can we formulate a temporal mathematical model describing the disease dynamics?
2. What are the basic assumptions to formulate such problem?
3. What are the parametric structures so that the disease can be controlled and eradicated?
4. What are the biological significances of the results simulated?
5. How can we split the operator for non-homogeneous matrix differential equation?
6. What are the numerical errors?
7. What are the order of the methods used?

1.5 Scope of the Study

The present dissertation is dealt with a unique compartmental model where some characteristics of the dynamical system like positiveness and boundedness of the solutions obtained are checked. A region is found out where the model is epidemiologically feasible and mathematically well-posed. The existence of equilibria along with their stability is derived. The stability criteria do depend on the reproduction number which is calculated by the next-generation matrix technique, and there are some conditions for stable and unstable equilibrium points as well as saddle points.

For a quantitative insight of the model, a thorough large-scale numerical simulation has been performed to get the solution of the matrix differential equation which is generated from the given system of ODEs. The sequential and Strang-Marchuk splitting schemes together with RK4 numerical method have been leveraged to get the splitting solution of the matrix differential equation. However, the reference (numerical) solution of the system is obtained by solving the system of ODEs by the RK4 method only. Since the exact solution of the system considered is not known, this numerical solution is compared with the numerical solution obtained by using the explicit Euler method. The order and accuracy of the methods have been derived both analytically and numerically, and we have also calculated the numerical error (local/global practical error) associated with the methods. The in-house developed codes in Matlab have been used for this purpose. A section containing limitations and the scope of future study has been included to study forward.

1.6 Literature Review

Mathematical models play an important role in the transmission of disease and elimination in the future. The very first epidemiological model was formulated by Daniel Bernoulli with the aim of evaluating the impact of variolation on human life expectancy [4]. Sir Ronald Ross discussed malaria with Manson while in the United Kingdom, but conducted his research while serving in a military post in India, and in 1897, he demonstrated that mosquitoes transmit malaria parasites [5]. Almost immediately thereafter, Ross argued that mosquito population densities could be reduced through larval control and combined with other measures to prevent mosquito-transmitted diseases [6]. Sir Ronald Ross was the first person to develop a deterministic mathematical model to study malaria transmission [7]. This model has an important role in understanding the dynamics of disease and controlling it. There are two types of the mathematical model of malaria so far– deterministic and stochastic. The past century has witnessed the rapid emergence and development of a substantial theory of epidemics. Kermack and McKendrick [8] derived the celebrated threshold theorem in 1927, which is one of the key results in epidemiology. The pattern of malaria in West Africa is holoendemic and stable as defined by Macdonald in 1957 [9] which implies that the transmission of the disease is throughout the year and the inten-

sity of the disease is almost uniform. He considered the latency period in mosquito and later extended Ross's work which is known as the Ross-Macdonald model. Ross-Macdonald models are best defined by a consensus set of assumptions. The mathematical model is just one part of a theory for the dynamics and control of mosquito-transmitted pathogens that also includes epidemiological and entomological concepts and metrics for measuring transmission. The Ross-Macdonald theory has since played a central role in the development of research on mosquito-borne pathogen transmission and the development of strategies for mosquito-borne disease prevention.

Later, Anderson and May considered the latency period in humans [10]. They included age structure in the simple Ross model by considering the density of infected humans as the function of age and time. Separate immune classes have been introduced in some models [11, 12, 13, 14, 15, 16, 17, 18] whereas some others such as Filipe et al. [19] have used complex immunity functions in their models. Aron and May [20] proposed an age-specific immunity model with a new compartment Immune in humans. In another study, Chitins [16] included constant immigration of susceptible human population.

Modern application of molecular typing methods has shown that there exists diversity among hosts and parasites in responding to infection. Models developed in these studies are called Resistance-Strain models. The model proposed by Koella and Antia [21], divides the infected population into two compartments, infected by drug-sensitive strain and drug-resistant strain of the parasite, and further divides the first class into two classes-treated and untreated. They concluded that the resistance does not spread if the fraction of infected individuals treated is less than a threshold value; if drug treatment exceeds this threshold, the resistance will eventually become fixed in the population. The impact of climate change on human health has attracted considerable attention in recent years. Its effects on malaria have been of particular interest because of its disease burden and its transmission sensitivity to environmental conditions. Malaria is considered as one of the major vector-borne diseases that is most sensitive to changing environmental conditions. A large volume of work as well as report on the modelling of malaria transmission, its control and the environmental impact on the disease dynamics has been carried out [22, 23, 24, 59, 26, 27, 28, 29, 30, 31, 32, 33, 35, 36, 34, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48]. In [34], a compartmental model with a system of coupled ordinary differential equations describing the transmission of *Plasmodium falciparum* malaria between humans and mosquitoes with nonlinear forces of infection in form of saturated incidence rates has been considered. The incidence rate is an important factor in the transmission dynamics of the disease. The incidence of malaria infection is referred to as the number of newly infected individuals (humans or mosquitoes) yielding in unit time [49].

In this dissertation, we revisited the model developed in [34]. The model presented consists of four compartments in humans (host) and three compartments in mosquitoes (vector), with the inclusion of nonlinear forces of infection in the form of saturated incidence rates in both the host and vector populations. The disease-induced death rates for humans and mosquitoes are also incorporated into the model. The governing system of ODEs is solved by using the operator splitting method [50, 51] and we term the solution as 'Split Solution'.

We have used two types of splitting scheme,v.i.z, the sequential splitting and Strang-Marchuk splitting to get the split solution [52, 53, 54, 55, 56, 57]. We have also solved the system of ODEs by numerical methods like the RK4 method and the explicit Euler method to get a numerical solution (reference solution) of the system considered. Following [2, 58], we have calculated the errors (both local and global) and are represented graphically in the dissertation. We have also derived the order of the methods both analytically and numerically. A thorough sensitivity analysis has been carried out in order to find out the momentous parameters involved in the system.

2 Mathematical Model and Background Material

2.1 Equilibrium and Stability Criteria

2.1.1 Equilibrium Point

The points at which the differential equation of the system equal to zero are referred to as equilibrium points or steady state solution. Let $x^* \in \mathbb{R}$ is an equilibrium point of the differential equation $\frac{dx}{dt} = f(x)$. Then $f(x^*) = 0 \; \forall x \in \mathbb{R}^n$

2.1.2 Routh-Hurwitz Stability Criteria

In dynamical system, Routh-Hurwitz stability criteria is a mathematical test that is a necessary and sufficient condition for the stability of the equilibrium point of the system that examine the location of the roots of the characteristic polynomial of the system.

Let $P(\lambda)$ be the polynomial of the form $P(\lambda) = \lambda^n + b_1\lambda^{n-1} + b_2\lambda^{n-2} + ... + b_{n-1}\lambda + b_n$, where b_i; $(i = 1, 2, ..., n)$ are real constant coefficients. Using the coefficient b_i of the polynomial, we get the sequence of n principal submatrices as follows:

$H_1 = [b_1]$,

$$H_2 = \begin{bmatrix} b_1 & 1 \\ b_3 & b_2 \end{bmatrix}, \; H_3 = \begin{bmatrix} b_1 & 1 & 0 \\ b_3 & b_2 & b_1 \\ b_5 & b_4 & b_3 \end{bmatrix}, ..., \; H_n = \begin{bmatrix} b_1 & 1 & 0 & 0 & \cdots & 0 \\ b_3 & b_2 & b_1 & 1 & \cdots & 0 \\ b_5 & b_4 & b_3 & b_2 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots & & \\ 0 & 0 & 0 & 0 & \cdots & 0 \end{bmatrix}, \text{ where } b_j = 0 \text{ for}$$

$j > n$.
The roots of $P(\lambda) = 0$ will be negative or have negative real part if and only if the determinants of the principal submatrices H_i, $\forall i = 1(1)n$ (also called principal determinants)

are positive. Therefore,

$$det(H_j) > 0,\ j = 1(1)n.$$

For polynominals of degree n=2,3,4 and 5, the explicit Routh-Hurwitz stability conditions are summarised in Table 1 [59].

n	Stability conditions
n=2	$b_1 > 0$ and $b_2 > 0$
n=3	$b_1 > 0$ and $b_3 > 0$ and $b_1 b_2 > b_3$
n=4	$b_1 > 0,\ b_3 > 0$ and $b_4 > 0$ and $b_1 b_2 b_3 > b_3^2 + b_1^2 b_4$
n=5	$b_i > 0, i = 1, 2, ..., 5,\ b_1 b_2 b_3 > b_3^2 + b_1^2 b_4$ and $(b_1 b_4 - b_5)(b_1 b_2 b_3 - b_3^2 - b_1^2 b_4) > b_5(b_1 b_2 - b_3)^2 + b_1 b_5^2$

Table 1: Explicit Routh-Hurwitz stability conditions for n=2,3,4 and 5.

2.2 Basic Reproduction Number

In epidemiological models, one of the most important factors that govern the disease dynamics is the basic reproduction number which is usually denoted by R_0. The basic reproduction number of an infection can be thought of as the expected number of cases directly generated by one case in a population where all individuals are susceptible to infection. This quantity determines whether the infection will spread exponentially, die out or remain constant.

We use the next generation matrix technique as described in [60, 61]. To apply this method the whole population is divided into n compartments in which $m(< n)$ compartments are infected. Let $x_i, i = 1, 2, 3, ..., m$ be the number of individuals in i^{th} infected compartment at time t. Now the epidemiological model can be described as

$$\frac{dx_i}{dt} = F_i(x) - V_i(x), \tag{2.1}$$

where $V_i(x) = V_i^-(x) - V_i^+(x)$.

In the above equation, $F_i(x)$ reprsents the rate of appearance of new infected people in the i^{th} compartment, $V_i^+(x)$ represents the rate of transfer of individuals into compartment i, and $V_i^-(x)$ represents the rate of transfer of individuals out of the compartment i. The above model can also be written as

$$\frac{d\mathbf{x}}{dt} = F(\mathbf{x}) - V(\mathbf{x}), \tag{2.2}$$

where $F(\mathbf{x}) = (F_1(x), F_2(x), ..., F_m(x))^T$ and $V(\mathbf{x}) = (V_1(x), V_2(x), ..., V_m(x)$. Here F and V are $m \times m$ matrices. On differentiating F and V at the disease-free equilibrium point

gives

$$f = \frac{\partial F_i}{\partial x_j},\ v = \frac{\partial V_i}{\partial x_j}. \tag{2.3}$$

Now, the matrix fv^{-1} is known as the next generation matrix. The spectral radius of fv^{-1} is the basic reproduction number (R_0).

3 Formulation of the Problem

A compartmental epidemiological model to study the propagation of malaria between two interacting population–human (host) and mosquito (vector), is investigated in the present dissertation. We assume the total human population $N_h(t)$ at any instant of time t which is compartmentalised into four classes, namely, the susceptible ($S_h(t)$), the exposed ($E_h(t)$), the infected ($I_h(t)$) and the recovered ($R_h(t)$). Hence, we may write

$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t). \tag{3.4}$$

Likewise, the total mosquito population $N_m(t)$ at time t is classified into three subclasses, e.g., the susceptible ($S_m(t)$), the exposed ($E_m(t)$) and the infected ($I_m(t)$). It may be reasonable to assume that there is no recovered class of mosquitoes due to their short lifespan. Therefore, we have

$$N_m(t) = S_m(t) + E_m(t) + I_m(t). \tag{3.5}$$

When an infectious female anopheles bites a susceptible human, the parasite (in the form of sporozoites) is injected into the blood and the susceptible human moves to the infected class. However, the exposed humans having the parasite in asexual stages are not capable of transmitting the disease. Eventually, the parasite travels to the liver for cell division and they (in the form of merozoites) enters the bloodstream, and then the human moves to the infectious class. After an expiry of some certain time, the infectious humans recover and move to the recovered class. The recovered humans have some immunity to the disease, but they still harbour low levels of parasite in their blood and later loses the immunity to become susceptible again. Every class of human population is decreased by natural death or through emigration, though infected class has a disease induced death rate as an addition.

In a similar fashion, the susceptible mosquito grows through a certain birth rate. The parasite (in the form of gametocytes) enters into the mosquito population with some probability β_m, when a susceptible mosquito bites an infectious human. Then, the mosquito moves from the susceptible to the exposed class. Depending upon the temperature and humidity, the parasite develops into sporozoites and enters into the mosquito's salivary glands, and as a result, it moves to the infectious class. Mosquitoes leave the population through natural as well as disease-induced death rates.

The model is formulated based on the following assumptions:

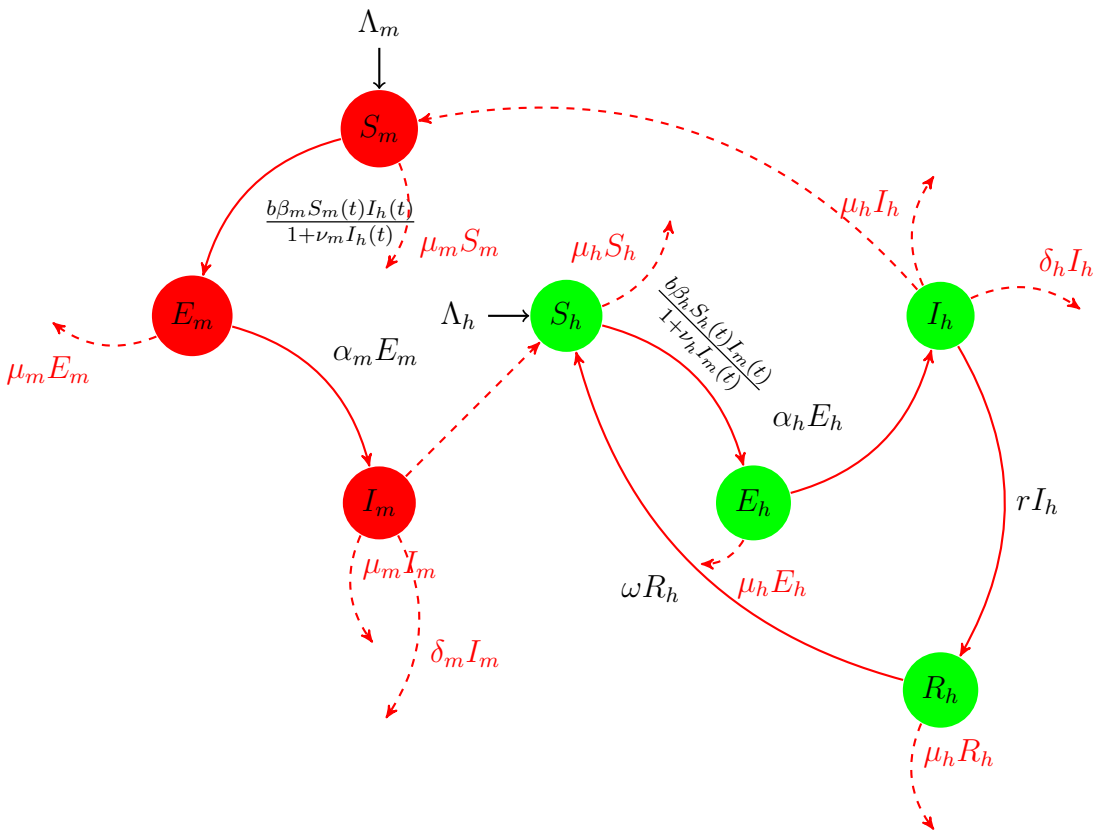


Figure 1: Flow chart for the transmission of malaria disease. The small dashed arrows indicate the natural and the disease-induced death rate in each compartment of human and mosquito. The long dashed arrows indicate the interaction of mosquito with human. The bold arrows indicate the rate of flow among mosquito and human populations classes. The small bold arrows show recruitment of human and mosquito population

.

- The population of both humans and mosquitoes in every compartment are positive and so are all the parameters involved.
- All newborns are susceptible to infection.
- The recovered humans do not develop permanent immunity.
- The propagation of malaria does start when the female mosquito bites the human host.
- Individuals move from one class to another as the disease evolves.
- Both humans and mosquitoes have natural death rate and disease-induced death rate.

Based on the above assumptions, the propagation of the disease in the human and mosquito population may be represented by a system of seven ODEs whose mathematical forms are as follows:

$$\frac{dS_h}{dt} = \Lambda_h - \frac{b\beta_h S_h(t) I_m(t)}{1 + \nu_h I_m(t)} - \mu_h S_h(t) + \omega R_h(t), \tag{3.6a}$$

$$\frac{dE_h}{dt} = \frac{b\beta_h S_h(t) I_m(t)}{1 + \nu_h I_m(t)} - (\alpha_h + \mu_h) E_h(t), \tag{3.6b}$$

$$\frac{dI_h}{dt} = \alpha_h E_h(t) - (r + \mu_h + \delta_h) I_h(t), \tag{3.6c}$$

$$\frac{dR_h}{dt} = r I_h(t) - (\mu_h + \omega) R_h(t), \tag{3.6d}$$

$$\frac{dS_m}{dt} = \Lambda_m - \frac{b\beta_m S_m(t) I_h(t)}{1 + \nu_m I_h(t)} - \mu_m S_m(t), \tag{3.6e}$$

$$\frac{dE_m}{dt} = \frac{b\beta_m S_m(t) I_h(t)}{1 + \nu_m I_h(t)} - (\alpha_m + \mu_m) E_m(t), \tag{3.6f}$$

$$\frac{dI_m}{dt} = \alpha_m E_m(t) - (\mu_m + \delta_m) I_m(t), \tag{3.6g}$$

together with the initial conditions
$Y_0 = \{S_{0h}, E_{0h}, I_{0h}, R_{0h}, S_{0m}, E_{0m}, I_{0m}\}$ where the description of the state variables and the parameters involved are appended in Tables 2 & 3 respectively.

$S_h(t)$	Number of the host humans susceptible to malaria infection at time t
$E_h(t)$	Number of the host humans exposed to malaria infection at time t
$I_h(t)$	Number of the infectious host humans at time t
$R_h(t)$	Number of the recovered host humans at time t
$S_m(t)$	Number of the susceptible mosquitoes at time t
$E_m(t)$	Number of the exposed mosquitoes at time t
$I_m(t)$	Number of the infected mosquitoes at time t

Table 2: Description of state variables involved.

Λ_h	Recruitment term of the susceptible humans
Λ_m	Recruitment term of the susceptible mosquitoes
b	Biting rate of the mosquito
β_h	Probability that a bite by an infectious mosquito results in transmission of disease to human
β_m	Probability that a bite results in transmission of parasite to a susceptible mosquito
μ_h	Per capita death rate of human
μ_m	Per capita death rate of mosquito
δ_h	Disease-induced death rate of human
δ_m	Disease-induced death rate of mosquito
α_h	Per capita rate of progression for humans from the exposed state to the infectious state
α_m	Per capita rate of progression for mosquitoes from the exposed state to the infectious state
r	Per capita recovery rate for humans from the infectious state to the recovered state
ω	Per capita rate of loss of immunity
ν_h	Proportion of antibody produced by human in response to the incidence of infection caused by mosquito
ν_m	Proportion of antibody produced by mosquito in response to the incidence of infection caused by mosquito

Table 3: Description of the parameters involved in the model equations (3.6).

4 Boundedness and Positivity of the Solutions

In this section, we provide some results which conclude the epidemiological and mathematical well-posedness of the model in a feasible region D given by,
$D = D_h \times D_m \subset \mathbb{R}^4_+ \times \mathbb{R}^3_+$ where

$$\begin{aligned} D_h &= \left\{ (S_h, E_h, I_h, R_h) \in \mathbb{R}^4_+ : N_h \leq \frac{\Lambda_h}{\mu_h} \right\}, \\ D_m &= \left\{ (S_m, E_m, I_m) \in \mathbb{R}^3_+ : N_m \leq \frac{\Lambda_m}{\mu_m} \right\}. \end{aligned}$$

We will carry out the following proofs by using ideas in [34, 36, 37].

Theorem 1. *There exists a domain D in which the solution set $\{S_h, E_h, I_h, R_h, S_m, E_m, I_m\}$ with non-negative initial conditions in D is bounded above.*

Proof. We have the given solution set with positive initial conditions. The total population sizes of host (human) and vector (mosquito) are respectively given by

$$V_1(S_h, E_h, I_h, R_h) = S_h + E_h + I_h + R_h, \quad V_2(S_m, E_m, I_m) = S_m + E_m + I_m.$$

The total dynamics of the human population is obtained by adding the first four equations

of the model (3.6a-3.6d) and is given by

$$\begin{aligned}\frac{dV_1}{dt} &= \frac{dS_h}{dt}+\frac{dE_h}{dt}+\frac{dI_h}{dt}+\frac{dR_h}{dt}\\ &= \Lambda_h-\mu_h\left(S_h+E_h+I_h+R_h\right)-\delta_h I_h\\ &\leq \Lambda_h-\mu_h\left(S_h+E_h+I_h+R_h\right)\\ &= \Lambda_h-\mu_h V_1. \end{aligned} \tag{4.7}$$

Likewise, the total dynamics of the mosquito population is obtained by adding the last three equations of the model (3.6e-3.6g) and we have

$$\begin{aligned}\frac{dV_2}{dt} &= \frac{dS_m}{dt}+\frac{dE_m}{dt}+\frac{dI_m}{dt}\\ &\leq \Lambda_m-\mu_m V_2. \end{aligned} \tag{4.8}$$

For biological considerations, we study the behavior of the system (3.6) in the closed set

$$\begin{aligned}\Psi &= \Big\{(S_h,E_h,I_h,R_h,S_m,E_m,I_m)\in \mathbb{R}^7_+ \mid 0\leq S_h+E_h+I_h+R_h\leq \frac{\Lambda_h}{\mu_h},\\ &\quad 0\leq S_m+E_m+I_m\leq \frac{\Lambda_m}{\mu_m}\Big\}. \end{aligned} \tag{4.9}$$

From (4.7), we have

$$\frac{dV_1}{dt}\leq \Lambda_h-\mu_h\left(S_h+E_h+I_h+R_h\right),$$

then by comparison theorem presented in [38], there exists $t_1>0$, such that

$$S_h+E_h+I_h+R_h\leq \frac{\Lambda_h}{\mu_h}=N_h \quad \text{for} \quad t>t_1.$$

From (4.8), we also have

$$\frac{dV_2}{dt}\leq \Lambda_m-\mu_m\left(S_m+E_m+I_m\right),$$

by using comparison theorem once again, for $t_2>t_1$, one should have

$$S_m+E_m+I_m\leq \frac{\Lambda_m}{\mu_m}=N_m \quad \text{for} \quad t>t_2.$$

Let $N=\max\left(N_h,N_m\right)$, then $(S_h,E_h,I_h,R_h,S_m,E_m,I_m)\leq N$. Hence, the solutions of the system (3.6) are bounded above. □

Theorem 2. *The solutions* $(S_h, E_h, I_h, R_h, S_m, E_m, I_m)$ *of the model (3.6) remain non-negative for all* $t > 0$ *provided that the initial conditions are non-negative in the feasible domain* D.

Proof. If possible, let $\exists\, t^*$ such that $S_h(t^*) > 0$ and $S_h'(t^*) \leq 0$ and $S_h, E_h, I_h, R_h, S_m, E_m, I_m > 0$ for $0 < t < t^*$, then we get from (3.6a)

$$\begin{aligned} \frac{dS_h(t^*)}{dt} &= \Lambda_h - \frac{b\beta_h S_h(t^*) I_m(t^*)}{1+\nu_h I_m(t^*)} - \mu_h S_h(t^*) + \omega R_h(t^*) \\ &= \Lambda_h - \omega R_h(t^*) \\ &> 0, \end{aligned} \tag{4.10}$$

which is a contradiction. Hence $S_h(t) > 0$.
Assume that, $\exists\, t^* = \sup\{t > 0 : S_h, ..., I_m > 0\}$, then we get from (3.6b)

$$\frac{d\left(E_h e^{(\alpha_h+\mu_h)t}\right)}{dt} = \frac{b\beta_h S_h(t) I_m(t)}{1+\nu_h I_m(t)} e^{(\alpha_h+\mu_h)t}. \tag{4.11}$$

Integrating from 0 to t^*, we get

$$E_h(t^*)e^{(\alpha_h+\mu_h)t^*} - E_h(0) = \int_0^{t^*} \frac{b\beta_h S_h(\theta) I_m(\theta)}{1+\nu_h I_m(\theta)} e^{(\alpha_h+\mu_h)\theta} d\theta.$$

Therefore,

$$\begin{aligned} E_h(t^*) &= E_h(0)e^{-(\alpha_h+\mu_h)t^*} + e^{-(\alpha_h+\mu_h)t^*} \int_0^{t^*} \frac{b\beta_h S_h(\theta) I_m(\theta)}{1+\nu_h I_m(\theta)} e^{(\alpha_h+\mu_h)\theta} d\theta \\ &> 0. \end{aligned} \tag{4.12}$$

Hence, $E_h(t) > 0$.

For $I_h(t)$, suppose for $t^* > 0, I_h(t^*) = 0$ and $I_h'(t^*) > 0$ where $0 < t < t^*$. Then we get from (3.6c)

$$\frac{d\left(I_h e^{(r+\mu_h+\delta_h)t}\right)}{dt} = \alpha_h E_h(t) e^{(r+\mu_h+\delta_h)t}. \tag{4.13}$$

Integrating from 0 to t^*, we get

$$\begin{aligned} I_h(t^*) &= I_h(0)e^{-(r+\mu_h+\delta_h)t^*} + e^{-(r+\mu_h+\delta_h)t^*} \int_0^{t^*} \alpha_h E_h(\theta) e^{(r+\mu_h+\delta_h)\theta} d\theta \\ &> 0, \end{aligned} \tag{4.14}$$

which is a contradiction. Hence $I_h(t) > 0$.

Similarly, for $R_h(t)$, we assume $\exists\ t^* > 0$ such that $R_h(t^*) = 0$ and $R_h'(t^*) > 0$ where $0 < t < t^*$. Therefore, from (3.6d)

$$\begin{aligned} R_h(t^*) &= R_h(0)e^{-(\mu_h+\omega)t^*} + e^{-(\mu_h+\omega)t^*}\int_0^{t^*} rI_h(\theta)d\theta \\ &> 0, \end{aligned} \tag{4.15}$$

which is again a contradiction. Hence $R_h(t) > 0$.

Further, we assume that $S_m(t^*)$ is non-increasing and other variables are positive with $S_m(t) > 0$ for $0 \le t < t^*$. Now we get from (3.6e),

$$\begin{aligned} \frac{dS_m(t^*)}{dt} &= \Lambda_m - \frac{b\beta_m S_m(t^*)I_m(t^*)}{1+\nu_m I_h(t^*)} - \mu_m S_m(t^*) \\ &> 0, \end{aligned} \tag{4.16}$$

which is a contradiction. Hence $\nexists\ t^*$ for which $S_m(t^*) = 0$.
Similarly, for $E_m(t)$, we get from (3.6f)

$$\frac{d\left(E_m e^{(\alpha_m+\mu_m)t}\right)}{dt} = \frac{b\beta_m S_m(t)I_h(t)}{1+\nu_m I_h(t)}e^{(\alpha_m+\mu_m)t}. \tag{4.17}$$

Integrating from 0 to t^* for some $t^* > 0$ where $0 \le t < t^*$ such that $E_m(t^*) = 0$, we get

$$\begin{aligned} E_m(t^*) &= E_m(0)e^{-(\alpha_m+\mu_m)t^*} + e^{-(\alpha_m+\mu_m)t^*}\int_0^{t^*} \frac{b\beta_m S_m(\theta)I_h(\theta)}{1+\nu_m I_h(\theta)}e^{(\alpha_m+\mu_m)\theta}d\theta \\ &> 0, \end{aligned} \tag{4.18}$$

which shows that $E_m(t) > 0$.
Finally, for $I_m(t)$, it is easy to see from (3.6g) that

$$\frac{dI_m(t)}{dt} \ge -\mu_m I_m(t). \tag{4.19}$$

Therefore,

$$I_m(t) \ge I_m(0)e^{-\mu_m t} \ge 0. \tag{4.20}$$

This completes the proof. □

It is to be concluded from Theorems 1 and 2 that for all $Y_0 \in D$, the solution set $Y(t) \in D$ for all $t > 0$, i.e., the domain D is invariant and the solution set is bounded.

5 Existence and Stability of Equilibrium Points

5.1 Existence of Equilibria

In our model, we have two types of equilibrium points, namely, the disease-free and the endemic. The disease free equilibrium points are the steady state solutions where there is no infected individual in the population.

Therefore, for the disease-free equilibrium point, E_0, in our model, $E_h^* = 0, I_h^* = 0, R_h^* = 0, E_m^* = 0, I_m^* = 0$. Solving the equations (3.6a, 3.6e), we get

$$S_h^* = \frac{\Lambda_h}{\mu_h} \text{ and } S_m^* = \frac{\Lambda_m}{\mu_m}.$$

So, the disease-free equilibrium point is $E_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, \frac{\Lambda_m}{\mu_m}, 0, 0\right)$.

Endemic equilibrium point is a positive steady state solution where the disease persists in the population. Let $E_e = (S_h^{**}, E_h^{**}, I_h^{**}, R_h^{**}, S_m^{**}, E_m^{**}, I_m^{**})$ be the non-trivial equilibrium point of the model. If we set all the differential equations (3.6) to zero we get

$$\begin{cases} \Lambda_h - \frac{b\beta_h S_h(t) I_m(t)}{1+\nu_h I_m(t)} - \mu_h S_h(t) + \omega R_h(t) = 0, \\ \frac{b\beta_h S_h(t) I_m(t)}{1+\nu_h I_m(t)} - (\alpha_h + \mu_h) E_h(t) = 0, \\ \alpha_h E_h(t) - (r + \mu_h + \delta_h) I_h(t) = 0, \\ r I_h(t) - (\mu_h + \omega) R_h(t) = 0, \\ \Lambda_m - \frac{b\beta_m S_m(t) I_h(t)}{1+\nu_m I_h(t)} - \mu_m S_m(t) = 0, \\ \frac{b\beta_m S_m(t) I_h(t)}{1+\nu_m I_h(t)} - (\alpha_m + \mu_m) E_m(t) = 0, \\ \alpha_m E_m(t) - (\mu_m + \delta_m) I_m(t) = 0. \end{cases} \tag{5.21}$$

Solving the above equations (5.21), we get

$$\begin{aligned} S_h^{**} &= \frac{\{(\alpha_m + \mu_m)(\mu_m + \delta_m) b\beta_m + \nu_h R_m\} \Lambda_h I_h^{**} + \Lambda_h}{\mu_h R_0^2}, \\ E_h^{**} &= \frac{(r + \delta_h + \mu_h) I_h^{**}}{\alpha_h}, \\ R_h^{**} &= \frac{r I_h^{**}}{\mu_h + \omega}, \\ S_m^{**} &= \frac{\Lambda_m}{\frac{b\beta_m I_h^{**}}{1+\nu_m I_h^{**}} + \mu_m}, \\ E_m^{**} &= \frac{b\beta_m S_m^{**} I_h^{**}}{(1 + \nu_m I_h^{**})(\alpha_m + \mu_m)}, \\ I_m^{**} &= \frac{R_m I_h^{**}}{1 + \{(\alpha_m + \mu_m)(\mu_m + \delta_m) b\beta_m + \nu_m\} I_h^{**}}, \end{aligned}$$

where I_h^{**} is a positive solution of an equation given by

$$C_1 \left(I_h^{**}\right)^2 + C_2 I_h^{**} + C_3 = 0, \tag{5.22}$$

with

$$\begin{cases} C_1 &= \Lambda_h \phi \times (\mu_h + \omega) \left(b\beta_h K_m + \mu_h \phi - \omega r \mu_h R_0^2 \phi\right), \\ C_2 &= \Lambda_h \left(\mu_h + \omega\right) \left(b\beta_h K_m + 2\mu_h \phi - \mu_h R_0^2 \phi\right) - \omega r \mu_h R_0^2 \phi, \\ C_3 &= \Lambda_h \mu_h \left(\mu_h + \omega\right) \left(1 - R_0^2\right), \end{cases} \tag{5.23}$$

where $K_m = \frac{b\alpha_m \beta_m \Lambda_m}{\mu_m(\alpha_m+\mu_m)(\delta_m+\mu_m)}$ and $\phi = \left(\alpha_m + \mu_m\right)\left(\mu_m + \delta_m\right) b\beta_m + \nu_m + \nu_h K_m$.

It is clear that for $C_1 > 0$, $C_2 > 0$ and $R_0 < 1$, we get $C_3 > 0$ and eventually, the model has no positive solution. On the contrary, for $R_0 > 1$, we have $C_3 < 0$ implying that the endemic equilibrium point exists.

5.2 Basic Reproduction Number

We use the next generation matrix as described in Sec. 2. The only disease states are I_h and I_m. Let $\mathbf{x} = (E_h, I_h, E_m, I_m, S_h, R_h, S_m)^{\mathrm{T}}$, then the model can be written as

$$\frac{d\mathbf{x}}{dt} = F(\mathbf{x}) - V(\mathbf{x}), \tag{5.24}$$

where the disease states F and the transfer state V are given by

$$F(\mathbf{x}) = \begin{bmatrix} \frac{b\beta_h S_h I_m}{1+\nu_h I_m} \\ 0 \\ \frac{b\beta_m S_m I_h}{1+\nu_m I_h} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \; V(\mathbf{x}) = \begin{bmatrix} \left(\alpha_h + \mu_h\right) E_h \\ \left(r + \delta_h + \mu_h\right) I_h - \alpha_h E_h \\ \left(\alpha_m + \mu_m\right) E_m \\ \left(\mu_m + \delta_m\right) I_m - \alpha_m E_m \\ \mu_h \delta_h - \Lambda_h - \omega R_h \\ \left(\mu_h + \omega\right) R_h - r I_h \\ \mu_m \delta_m - \Lambda_m \end{bmatrix}.$$

The partial derivatives of F and V at the disease-free equilibrium point E_0 are as follows:

$$f = \begin{bmatrix} 0 & 0 & 0 & \frac{b\beta_h \Lambda_h}{\mu_h} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{b\beta_m \Lambda_m}{\mu_m} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \; v = \begin{bmatrix} \alpha_h + \mu_h & 0 & 0 & 0 \\ -\alpha_h & r + \mu_h + \delta_h & 0 & 0 \\ 0 & 0 & \alpha_m + \mu_m & 0 \\ 0 & 0 & -\alpha_m & \delta_m + \mu_m \end{bmatrix} \text{ so that}$$

$$v^{-1} = \begin{bmatrix} 0 & 0 & \frac{b\alpha_m \beta_h \Lambda_h}{\mu_h(\delta_m+\mu_m)(\alpha_m+\mu_m)} & \frac{b\beta_h \Lambda_h}{\mu_h(\delta_m+\mu_m)} \\ 0 & 0 & 0 & 0 \\ \frac{b\alpha_m \beta_m \Lambda_m}{\mu_m(r+\delta_h+\mu_h)} & \frac{b\beta_m \Lambda_m}{\mu_m(r+\delta_h+\mu_h)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\text{Now } fv^{-1} = \begin{bmatrix} 0 & 0 & \frac{b\alpha_m\beta_h\Lambda_h}{\mu_h(\delta_m+\mu_m)(\alpha_m+\mu_m)} & \frac{b\beta_h\Lambda_h}{\mu_h(\delta_m+\mu_m)} \\ 0 & 0 & 0 & 0 \\ \frac{b\alpha_m\beta_m\Lambda_m}{\mu_m(r+\delta_h+\mu_h)(\alpha_h+\mu_h)} & \frac{b\beta_m\Lambda_m}{\mu_m(r+\delta_h+\mu_h)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

The matrix fv^{-1} is called the next generation matrix. Now to find the reproduction number R_0, we find the largest eigenvalue of fv^{-1}. Taking the spectral radius (dominant eigenvalue) of the matrix fv^{-1}, we can calculate the eigenvalues to determine the basic reproduction number R_0 by setting $\det(fv^{-1} - \lambda I) = 0$. For the model considered, we have the basic reproduction number R_0 as

$$R_0 = \sqrt{\frac{b^2\alpha_h\beta_h\Lambda_h\alpha_m\beta_m\Lambda_m}{\mu_h\mu_m\left(\alpha_h+\mu_h\right)\left(\alpha_m+\mu_m\right)\left(r+\delta_h+\mu_h\right)\left(\delta_m+\mu_m\right)}}. \tag{5.25}$$

In (5.25), the factor $\frac{\alpha_h}{\alpha_h+\mu_h}$ is the probability that a human will survive the exposed state to become infectious, while the factor $\frac{\alpha_m}{\alpha_m+\mu_m}$ is the probability that a mosquito will survive the exposed state to become infectious. The average duration of the infectious period of human is $\frac{1}{r+\delta_h+\mu_h}$ and that of mosquito is $\frac{1}{\delta_m+\mu_m}$. Let the basic reproduction number R_0 be written as

$$R_0 = \sqrt{K_h K_m}$$

where $K_h = \frac{b\alpha_h\beta_h\Lambda_h}{\mu_h(\alpha_h+\mu_h)(r+\delta_h+\mu_h)}$. Here, K_h describes the number of humans that one infectious mosquito infects over its expected infection period in a completely susceptible human population, while K_m, the number of mosquitoes that one infectious human infects over its expected infection period in a completely susceptible mosquitoe population. From (5.25), we can make inferences that the higher value of b can result into epidemic and, for the smaller values of b, the disease dies out.

5.3 Stability of the Disease-free Equilibrium Point

We analyze the stability of the disease-free equilibrium point with the help of the basic reproduction number obtained from the previous section.

Theorem 3. *The disease-free equilibrium point E_0 is asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof. The stability of the disease-free equilibrium point E_0 is determined from the signs of the eigenvalues of the Jacobian matrix of the system. The Jacobian matrix at E_0 is given by

$J(E_0) =$

$$\begin{bmatrix} -\mu_h & 0 & 0 & 0 & 0 & 0 & \frac{-b\beta_h\Lambda_h}{\mu_h} \\ 0 & -(\alpha_h+\mu_h) & 0 & 0 & 0 & 0 & \frac{b\beta_h\Lambda_h}{\mu_h} \\ 0 & \alpha_h & -(r+\delta_h+\mu_h) & 0 & 0 & 0 & 0 \\ 0 & 0 & r & -(\mu_h+\omega) & 0 & 0 & 0 \\ 0 & 0 & \frac{-b\beta_m\Lambda_m}{\mu_m} & 0 & -\mu_m & 0 & 0 \\ 0 & 0 & \frac{b\beta_m\Lambda_m}{\mu_m} & 0 & 0 & -(\alpha_m+\mu_m) & 0 \\ 0 & 0 & 0 & 0 & 0 & \alpha_m & -(\delta_m+\mu_m) \end{bmatrix}$$

We need to show that the eigenvalues of $J(E_0)$ are negative. The first and fifth contains the only diagonal terms giving two negative eigenvalues $-\mu_h$ and $-\mu_m$. The other five eigenvalues can be obtained by eliminating first and fifth rows and columns of $J(E_0)$. Thus, we get, $J_1(E_0) =$

$$\begin{bmatrix} -(\alpha_h+\mu_h) & 0 & 0 & 0 & \frac{b\beta_h\Lambda_h}{\mu_h} \\ \alpha_h & -(r+\delta_h+\mu_h) & 0 & 0 & 0 \\ 0 & r & -(\mu_h+\omega) & 0 & 0 \\ 0 & \frac{b\beta_m\Lambda_m}{\mu_m} & 0 & -(\alpha_m+\mu_m) & 0 \\ 0 & 0 & 0 & \alpha_m & -(\delta_m+\mu_m) \end{bmatrix}$$

The third column of the matrix $J_1(E_0)$ gives a negative eigenvalue $-(\mu_h+\omega)$. Rest of the eigenvalues are obtained from the matrix $J_2(E_0)$ by eliminating third row and column. Thus, $J_2(E_0) =$

$$\begin{bmatrix} -(\alpha_h+\mu_h) & 0 & 0 & \frac{b\beta_h\Lambda_h}{\mu_h} \\ \alpha_h & -(r+\delta_h+\mu_h) & 0 & 0 \\ 0 & \frac{b\beta_m\Lambda_m}{\mu_m} & -(\alpha_m+\mu_m) & 0 \\ 0 & 0 & \alpha_m & -(\delta_m+\mu_m) \end{bmatrix}$$

The eigenvalues of $J_2(E_0)$ are obtained from the characteristics equations of $J_2(E_0)$, that is, from

$$\begin{aligned} &(\lambda+\alpha_h+\mu_h)(\lambda+r+\delta_h+\mu_h)(\lambda+\alpha_m+\mu_m)(\lambda+\delta_m+\mu_m) \\ &-\frac{b^2\alpha_h\beta_h\Lambda_h\alpha_m\beta_m\Lambda_m}{\mu_h\mu_m} = 0. \end{aligned} \tag{5.26}$$

The roots of (5.26) are the eigenvalues of $J_2(E_0)$. Let $C_4 = \alpha_h+\mu_h, C_5 = r+\delta_h+\mu_h, C_6 = \alpha_m+\mu_m, C_7 = \mu_m+\delta_m$, then the characteristics equation becomes

$$A_4\lambda^4 + A_3\lambda^3 + A_2\lambda^2 + A_1\lambda + A_0 = 0, \tag{5.27}$$

where

$$\begin{aligned} A_4 &= 1 \\ A_3 &= C_4 + C_5 + C_6 + C_7 \\ A_2 &= (C_4+C_5)(C_6+C_7) + C_4C_5 + C_6C_7 \end{aligned}$$

$$A_1 = (C_4 + C_5)C_6C_7 + (C_6 + C_7)C_4C_5$$

$$A_0 = C_4C_5C_6C_7 - \frac{b^2\alpha_h\beta_h\Lambda_h\alpha_m\beta_m\Lambda_m}{\mu_h\mu_m}.$$

From the expression of R_0, we get,

$$A_0 = C_4C_5C_6C_7\left(1 - R_0^2\right).$$

From Routh-Hurwitz criterion, we know that all roots of (5.27) have negative real parts iff the coefficients A_i as well as $\det(H_i)$ are positive $\forall i = 0, 1, 2, 3, 4$; H_i being the Hurwitz matrices. We can easily see that $A_1 > 0, A_2 > 0, A_3 > 0, A_4 > 0$ since all C_i's are positive. Furthermore, $A_0 > 0$ if $R_0 < 1$. Also the determinants of Hurwitz matrices are positive for (5.27), since $\left|H_1\right| = A_3 > 0$, $\left|H_2\right| = \begin{vmatrix} A_3 & A_4 \\ A_1 & A_2 \end{vmatrix} > 0$, $\left|H_3\right| = \begin{vmatrix} A_3 & A_4 & 0 \\ A_1 & A_2 & A_3 \\ 0 & A_0 & A_1 \end{vmatrix} > 0$,

$$\left|H_4\right| = \begin{vmatrix} A_3 & A_4 & 0 & 0 \\ A_1 & A_2 & A_3 & A_4 \\ 0 & A_0 & A_1 & A_2 \\ 0 & 0 & 0 & A_0 \end{vmatrix} > 0.$$

Therefore all the eigenvalues of the Jacobian matrix $J(E_0)$ have negative real parts when $R_0 < 1$ and the disease-free equilibrium point E_0 is locally asymptotically stable.

However, when $R_0 > 1$, we get $A_0 < 0$ and by Descartes' Rule of Sign, there is one eigenvalue with positive real part and hence E_0 is unstable. □

6 Operator Splitting Method

Complex physical processes are frequently modelled by systems of linear or nonlinear differential equations. Due to the complexity, these equations can not be solved analytically, in general. In order to get solution of the system, we have to choose a proper numerical method so that the error of the numerical solution is minimum. Operator splitting is a numerical method based on 'Divide-and-Conquer' strategy. The main idea behind this method is to separate the original equations into a number of parts. At first, we transform the system of differential equations into a matrix differential equation, then we split the

operator appeared in the matrix differential equation into a number of sub-operators of simpler structure. Mathematically, we may write the scheme as

$$\frac{\partial u}{\partial t} = AX + E,$$

where $A = \sum_{i=1}^{S} A_i$. It may be noted that the decomposition of A is not unique. We now treat them individually using specialised numerical algorithms of computing the solution. The subproblems are connected by the initial conditions. The numerical methods used to solve the subproblems can also cause a certain amount of error. If the numerical method is not chosen properly, this can lead to order reduction and loss of accuracy. Moreover, the numerical step sizes chosen for the method play an important role too. There exist a plethora of literatures describing the operator splitting schemes by taking S=2, however, there do exist some limited results for bigger S. The novelty of this dissertation is the consideration of bigger S together with the non-homogeneity of the model equations.

6.1 Sequential and Strang-Marchuk Splitting

To simplify the understanding, the splitting procedures are described here only for a system of ODEs. Also two types of splitting method are discussed here which are applied to the original model of malaria for simulation purpose.
Let $A : \mathbb{R}^N \to \mathbb{R}^N$ is a bounded linear operator (i.e., it can be represented as a matrix $A \in \mathbb{R}^{N\times N}$) which can be considered as a sum of three bounded linear operators. Consider the non-homogeneous matrix differential equation of the form

$$\frac{du(t)}{dt} = Au(t) + E(t) = (A_1 + A_2 + A_3)u(t) + E(t), \;\; u(0) = u_0, \;\; t \in (0, \tau], \tag{6.28}$$

where $u : (0, T] \to \mathbb{R}^N$ is the state variables, $u_0 \in \mathbb{R}^N$ is a given element and A, A_1, A_2, A_3 are operators of type $\mathbb{R}^N \to \mathbb{R}^N$ and $E \in \mathbb{R}^{N\times 1}$. We assume that the equation (6.28) has a unique solution. Let us divide the time interval $[0, T]$ into $m \in N$ equal subintervals with length τ so that $\tau = \frac{T}{m}$. Here, τ is called the splitting time step.

6.1.1 Sequential Splitting

The sequential splitting method is described by the following subproblems:

$$\begin{cases} \frac{du_1^{(k)}}{dt} = A_1 u_1^{(k)}(t) + E^{(k)}, \;\; t \in [(k-1)\tau, k\tau] \\ u_1^{(k)}\left((k-1)\tau\right) = u_{spl}\left[(k-1)\tau\right] \end{cases} \tag{6.29}$$

$$\begin{cases} \frac{du_2^{(k)}}{dt} = A_2 u_2^{(k)}(t), \;\; t \in [(k-1)\tau, k\tau] \\ u_2^{(k)}\left((k-1)\tau\right) = u_1^{(k)}(k\tau) \end{cases} \tag{6.30}$$

$$\begin{cases} \frac{du_3^{(k)}}{dt} = A_3 u_3^{(k)}(t), \;\; t \in [(k-1)\tau, k\tau] \\ u_3^{(k)}\left((k-1)\tau\right) = u_2^{(k)}(k\tau). \end{cases} \tag{6.31}$$

Then the split solution of (6.28) defined at the mesh-points $k\tau$, $(k = 1, \ldots, m)$ is given by

$$u_{spl}(k\tau) = u_3^{(k)}(k\tau), \tag{6.32}$$

where $u_{spl}(0) = u_0$. The above systems (6.29-6.31) are solved by a suitable numerical method to get the numerical split solution $y_{spl}(k\tau)$.

6.1.2 Strang-Marchuk Splitting

Another splitting technique is the Strang-Marchuk Splitting, defined by the following algorithm to get the splitting solution of (6.28):

$$\begin{cases} \frac{du_1^{(k)}}{dt} = A_1 u_1^{(k)}(t) + E_1^{(k)}, \;\; t \in \left[(k-1)\tau, (k-\frac{1}{2})\tau\right] \\ u_1^{(k)}\left((k-1)\tau\right) = u_{spl}\left((k-1)\tau\right) \end{cases} \tag{6.33}$$

$$\begin{cases} \frac{du_2^{(k)}}{dt} = A_2 u_2^{(k)}(t) + E_2, \;\; t \in \left[(k-1)\tau, (k-\frac{1}{2})\tau\right] \\ u_2^{(k)}\left((k-1)\tau\right) = u_1^{(k)}\left((k-\frac{1}{2})\tau\right) \end{cases} \tag{6.34}$$

$$\begin{cases} \frac{du_3^{(k)}}{dt} = A_3 u_3^{(k)}(t) + E_3, \;\; t \in [(k-1)\tau, k\tau] \\ u_3^{(k)}\left((k-1)\tau\right) = u_2^{(k)}\left((k-\frac{1}{2})\tau\right) \end{cases} \tag{6.35}$$

$$\begin{cases} \frac{du_4^{(k)}}{dt} = A_2 u_2^{(k)}(t) = E_2, \;\; t \in \left[(k-\frac{1}{2})\tau, k\tau\right] \\ u_4^{(k)}\left((k-\frac{1}{2})\tau)\right) = u_3^{(k)}(k\tau). \end{cases} \tag{6.36}$$

$$\begin{cases} \frac{du_5^{(k)}}{dt} = A_1 u_1^{(k)}(t) + E_1, \;\; t \in \left[(k-\frac{1}{2})\tau, k\tau\right] \\ u_5^{(k)}\left((k-\frac{1}{2})\tau)\right) = u_4^{(k)}(k\tau), \end{cases} \tag{6.37}$$

where $E = E_1 + E_2 + E_3$. Therefore, the split solution of (6.28) defined at the mesh-points $k\tau$, $(k = 1, \ldots, m)$ is given by

$$u_{spl}(k\tau) = u_4^{(k)}(k\tau), \tag{6.38}$$

where $u_{spl}(0) = u_0$. The above systems (6.33-6.36) are solved by a suitable numerical method to get the numerical split solution $y_{spl}(k\tau)$.

(6.39)

6.2 Error and Order Analysis of the Splitting Methods

Since, the exact (analytical) solution of the system of equations describing the transmission of malaria is not known, a direct comparison with the numerical solution can never be made, however, the numerical solution of the original system of ODEs (unsplit) by RK4 method can be treated as the "Reference Solution or Numerical Solution" for the matrix differential solution. Two types of splitting scheme have been used here, namely, sequential splitting and Strang-Marchuk splitting. In a bid to validate our numerical solution, we compare this solution of the system of ODEs with that of obtained from the explicit Euler method. Let

- $y_{spl}^{(k)}$ denotes the numerical split solution of the matrix differential equation at $t = k\tau$; τ is the splitting time step and $k = 1, ..., m$.
- $y_{num}^{(kn)}$ denotes the numerical solution (reference solution) of the system of equations at $t = k\tau$. where the numerical time-step (h) is given by $h = \frac{\tau}{n}$.

Using the above notation, the practical error $(E_{prac}(k\tau))$ at $t = k\tau$ is defined as $E_{prac}(k\tau) := \|y_{num}^{kn} - y_{spl}^{(k)}\|$, where $k = 1, 2, ...m$. Now, the errors $E_{prac}(\tau)$ and $E_{prac}(m\tau)(= E_{prac}(T))$ are termed as the 'local practical error' and 'global practical error' respectively. In the sequel, $E(\tau)$ denotes the local practical error $E_{prac}(\tau)$, wherever it appears.

Definition 1:
The local error $E(\tau)$ has an order of p if

$$p := \sup\{q \in \mathbb{N} : \lim_{\tau \to 0} \frac{E(\tau)}{\tau^{q+1}} = c < +\infty\}. \tag{6.40}$$

Therefore, $E(\tau) = \mathcal{O}(\tau^{p+1})$, or, alternatively, we can say that $E(\tau) = C \times \mathcal{O}(\tau^{p+1})$ for sufficiantly small values of τ, c being a constant. When the sub-operators are non-stiff, then the global error $E(T)$ can be written as

$$E(T) = m\mathcal{O}(\tau^{p+1}) = \frac{T}{\tau}\mathcal{O}(\tau^{p+1}) = \mathcal{O}(\tau^p).$$

Hence, it may be concluded that the local error dictates the order of the global error.

We will now calculate the numerical order of the local (practical) error. It can be determined in two ways.

First Method:
Let us now introduce a notation

$$H_q(\tau) := \frac{E(\tau)}{\tau^{q+1}},$$

where $q \in \mathbb{R}$. Now we will apply Definition 1 to calculate

$$\lim_{\tau \to 0} H_q(\tau), \tag{6.41}$$

for different fixed values of q. The numerical order of $E_{prac}(\tau)$ is determined as the supremum of those values of q for which the limit in (6.41) is finite and let it be denoted by $\mathcal{Q}_{num}$.

Second Method:
From Definition 1, we can write

$$\frac{E(\tau)}{\tau^{q+1}} \approx c < +\infty, \tag{6.42}$$

where τ is small enough. Taking the logarithm of both sides in (6.42), we have

$$\log E(\tau) \approx (q+1)\log\tau + \log c. \tag{6.43}$$

Here, the slope $q+1$ of the line corresponds to the numerical order of the local (practical) error, that is, the required order is q.

Splitting of operator:
The system of ODEs (3.6) representing the dynamics of the transmission of malaria disease can the written in the matrix differential form as

$$Y' = AY + E = (S + V + D)Y + E, \tag{6.44}$$

where $A = S + V + D, S, V$ and D, are 7×7 matrices and E is a 7×1 matrix. Here, Y and Y' are the column vectors of seven dependent variables and their first derivatives respectively. The matrices S, V, D and E consisting of interacting terms, interclass movement of host and vector, death rates and birth rates respectively may be defined as

$$S = \begin{bmatrix} -\frac{b\beta_h I_m}{1+\nu_h I_m} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{b\beta_h S_h}{1+\nu_h I_m} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\frac{b\beta_m I_h}{1+\nu_m I_h} & 0 & 0 \\ 0 & 0 & \frac{b\beta_m I_m}{1+\nu_m I_h} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}, V = \begin{bmatrix} 0 & 0 & 0 & \omega & 0 & 0 & 0 \\ 0 & -\alpha_h & 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha_h & -r & 0 & 0 & 0 & 0 \\ 0 & 0 & r & -\omega & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\alpha_m & 0 \\ 0 & 0 & 0 & 0 & 0 & \alpha_m & 0 \end{bmatrix},$$

$$D = \begin{bmatrix} -\mu_h & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\mu_h & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -(\mu_h+\delta_h) & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_m & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\mu_m & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -(\mu_m+\delta_m) \end{bmatrix}, E = \begin{bmatrix} \Lambda_h \\ 0 \\ 0 \\ 0 \\ \Lambda_m \\ 0 \\ 0 \end{bmatrix}.$$

It may be noted that E is a constant matrix (independent of time t).

6.2.1 Order of Sequential Splitting Method

For one splitting time step τ, we write the solution of (6.44) as

$$Y_{exact} = e^{\tau A} Y_0 + E \int_0^\tau e^{(\tau - s)A}\, ds, \tag{6.45}$$

where the initial values of seven state variables are given by $Y_0 = \{S_{0h}, E_{0h}, I_{0h}, R_{0h}, S_{0m}, E_{0m}, I_{0m}\}$.

We now split the given problem (6.44) into the following subproblems by making use of (6.29-6.31):

$$\begin{cases} Y_1' = SY_1 + E; \;\; t \in [0, \tau] \\ Y_1(0) = Y_0 \end{cases} \tag{6.46}$$

$$\begin{cases} Y_2' = VY_2; \;\; t \in [0, \tau] \\ Y_2(0) = Y_1(\tau) \end{cases} \tag{6.47}$$

$$\begin{cases} Y_3' = DY_3; \;\; t \in [0, \tau] \\ Y_3(0) = Y_2(\tau). \end{cases} \tag{6.48}$$

Therefore, the solution of the split subproblems (6.46-6.48) is given by

$$Y_{seq} = e^{\tau D} e^{\tau V} e^{\tau S} Y_0 + E e^{\tau D} e^{\tau V} \int_0^\tau e^{(\tau - s)S} ds \tag{6.49}$$

The splitting error $E_{seq}(Y; \tau)$ defined as the difference between Y_{exact} and Y_{seq} is given by

$$E_{seq}(Y; \tau) = Y_{exact} - Y_{seq} \tag{6.50}$$

We now calculate the difference of the terms (see 6.45,6.49) by using Taylor-series expansion as (in all terms in the Taylor-series for $e^X e^Y$, X always comes before Y.)

$$\begin{aligned} e^{\tau A} - e^{\tau D} e^{\tau V} e^{\tau S} &= \left(1 + \tau A + \frac{\tau^2 A^2}{2}\right) - \left(1 + \tau D + \frac{\tau^2 D^2}{2}\right)\left(1 + \tau V + \frac{\tau^2 V^2}{2}\right) \times \\ &\quad \left(1 + \tau S + \frac{\tau^2 S^2}{2}\right) + \mathcal{O}(\tau^3) \\ &= \frac{\tau^2}{2}\left[A^2 - \left(S^2 + V^2 + D^2 + 2SV + 2VD + 2DS\right)\right] + \mathcal{O}(\tau^3) \\ &= \frac{\tau^2}{2}\{[S, D] + [D, V] + [V, S]\} + \mathcal{O}(\tau^3), \end{aligned} \tag{6.51}$$

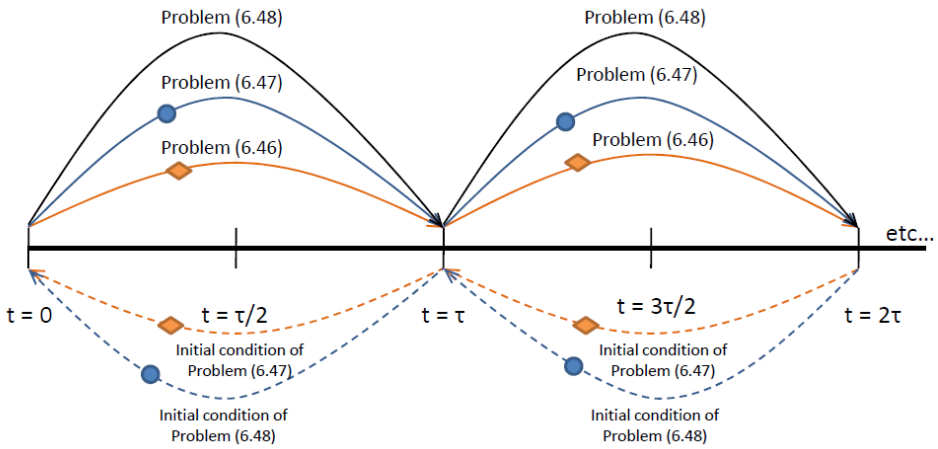


Figure 2: Flow chart for the sequential splitting technique.

where $[,]$ denotes the commutator. Again, we calculate the difference of the terms (see 6.45,6.49) as

$$\begin{aligned}\int_0^\tau e^{(\tau-s)A}\,ds - e^{\tau D}e^{\tau V}\int_0^\tau e^{(\tau-s)S}ds &= \int_0^\tau e^{(\tau-s)A}\,ds - \int_0^\tau e^{\tau D}e^{\tau V}e^{(\tau-s)S}ds \\ &= -\frac{\tau^2}{2}(D+V)+\mathcal{O}(\tau^3). \qquad (6.52)\end{aligned}$$

Using (6.51,6.52), we have the local error of the sequential splitting method method from (6.50) as

$$E_{seq}(Y;\tau) = \frac{\tau^2}{2}\Big[Y_0\{[S,D]+[D,V]+[V,S]\} - E\,(D+V)\Big]+\mathcal{O}(\tau^3), \qquad (6.53)$$

Hence, the sequential splitting scheme (6.46-6.48) applied to the non-homogeneous system of ODEs (6.44) has second order local error, i.e., the scheme has first order accuracy.

6.2.2 Order of Strang-Marchuk Splitting Method

Following [58], we have split the non-homogeneour operator E in the form $E = E_1+E_2+E_3$. Now, for one splitting time step τ, we split the given problem (6.44) into the following subproblems:

$$\begin{cases} Y_1' = SY_1 + E_1; \quad t \in \left[0, \frac{\tau}{2}\right] \\ Y_1(0) = Y_0 \end{cases} \qquad (6.54)$$

$$\begin{cases} Y_2' = VY_2 + E_2; \;\; t \in [0, \frac{\tau}{2}] \\ Y_2(0) = Y_1(\frac{\tau}{2}) \end{cases} \tag{6.55}$$

$$\begin{cases} Y_3' = DY_3 + E_3; \;\; t \in [0, \tau] \\ Y_3(0) = Y_2(\frac{\tau}{2}) \end{cases} \tag{6.56}$$

$$\begin{cases} Y_4' = VY_4 + E_2; \; t \in [\frac{\tau}{2}, \tau] \\ Y_4(0) = Y_3(\tau) \end{cases} \tag{6.57}$$

$$\begin{cases} Y_5' = SY_5 + E_1; \;\; t \in [\frac{\tau}{2}, \tau] \\ Y_5(0) = Y_4(\tau) \end{cases} \tag{6.58}$$

Therefore, the solution of the split subproblems (6.54-6.58) is given by

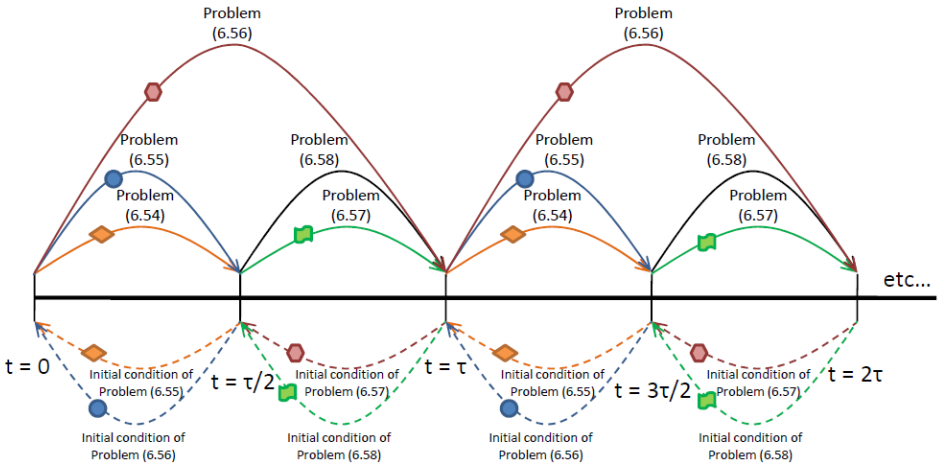


Figure 3: Flow chart for the Strang-Marchuk splitting technique.

$$\begin{aligned} Y_{SM} = e^{\frac{\tau}{2}S}e^{\frac{\tau}{2}V}e^{\tau D}e^{\frac{\tau}{2}V}e^{\frac{\tau}{2}S}Y_0 + E_1e^{\frac{\tau}{2}S}e^{\frac{\tau}{2}V}e^{\tau D}e^{\frac{\tau}{2}V}\int_0^{\frac{\tau}{2}} e^{(\frac{\tau}{2}-s)S}ds \\ +E_2e^{\frac{\tau}{2}S}e^{\frac{\tau}{2}V}e^{\tau D}\int_0^{\frac{\tau}{2}} e^{(\frac{\tau}{2}-s)V}ds + E_3e^{\frac{\tau}{2}S}e^{\frac{\tau}{2}V}\int_0^{\tau} e^{(\tau-s)D}ds \\ +E_2e^{\frac{\tau}{2}S}\int_{\frac{\tau}{2}}^{\tau} e^{(\tau-s)V}ds + E_1\int_{\frac{\tau}{2}}^{\tau} e^{(\tau-s)S}ds \end{aligned} \tag{6.59}$$

We have from (6.45),

$$Y_{exact} = e^{\tau A}Y_0 + E\left(\tau + \frac{\tau^2}{2}A + \frac{\tau^3}{6}A^2\right) \tag{6.60}$$

The splitting error $E_{SM}(Y;\tau)$ defined as the difference between Y_{exact} and Y_{SM} is given by

$$E_{SM}(Y;\tau) = Y_{exact} - Y_{SM}. \tag{6.61}$$

Now,

$$e^{\tau A} - e^{\frac{\tau}{2}S}e^{\frac{\tau}{2}V}e^{\tau D}e^{\frac{\tau}{2}V}e^{\frac{\tau}{2}S} = \Big[1 + \tau A + \frac{\tau^2}{2}A^2 + \frac{\tau^3}{6}A^3\Big]$$

$$-\Big[1 + \tau(S+V+D) + \frac{\tau^2}{2}\left(S^2+V^2+D^2+SV+VS+VD+DV+SD+DS\right)$$

$$+\frac{\tau^3}{24}(4S^3+4V^3+4D^3+3S^2V+6SV^2+3V^2D+6VD^2+3S^2D+6SD^2$$

$$+3VS^2+6V^2S+3DV^2+6D^2V+3DS^2+6D^2S$$

$$+6\{SVD+SDV+VDV+SVS+SDS+VDS+DVS\})\Big] + \mathcal{O}(\tau^4)$$

$$= \frac{\tau^3}{24}\Big[S^2V - 2SV^2 + V^2D - 2VD^2 + S^2D - 2SD^2 + VS^2 - 2V^2S + DV^2 - 2D^2V$$

$$+DS^2 - 2D^2S - 2SVD - 2SDV - 2VDV - 2SVS - 2SDS - 2VDS - 2DVS + 4VSV$$

$$+4DSD + 4DSV + 4DVD + 4VSD\Big] + \mathcal{O}(\tau^4) \tag{6.62}$$

Simplifying terms with E_1 in (6.59),

$$E_1 e^{\frac{\tau}{2}S}e^{\frac{\tau}{2}V}e^{\tau D}e^{\frac{\tau}{2}V}\int_0^{\frac{\tau}{2}} e^{(\frac{\tau}{2}-s)S}ds + E_1\int_{\frac{\tau}{2}}^{\tau} e^{(\tau-s)S}ds$$

$$= E_1\int_0^{\frac{\tau}{2}}\Big[e^{S\frac{\tau}{2}}e^{V\frac{\tau}{2}}e^{D\tau}e^{V\frac{\tau}{2}}e^{S(\frac{\tau}{2}-s)} - e^{S(\tau-s)}\Big]ds + E_1\int_0^{\tau} e^{S(\tau-s)}ds$$

$$= E_1\Big[\frac{\tau^2}{2}(V+D) - \frac{\tau^3}{8}(V+D)S + \frac{\tau^3}{4}(S^2+V^2+D^2+SV+SD+VD+DV+VS+DS)\Big]$$

$$+E_1\Big[\tau + \frac{\tau^2}{2}S + \frac{\tau^3}{6}S^2\Big] + \mathcal{O}(\tau^4. \tag{6.63}$$

Simplifying terms with E_2 (6.59),

$$E_2 e^{\frac{\tau}{2}S}e^{\frac{\tau}{2}V}e^{\tau D}\int_0^{\frac{\tau}{2}} e^{(\frac{\tau}{2}-s)V}ds + E_2 e^{\frac{\tau}{2}S}\int_{\frac{\tau}{2}}^{\tau} e^{(\tau-s)V}ds = E_2\int_0^{\frac{\tau}{2}}\left[e^{\frac{\tau}{2}S}e^{\frac{\tau}{2}V}e^{\tau D}e^{(\frac{\tau}{2}-s)V} - e^{\frac{\tau}{2}S}e^{(\tau-s)V}\right]ds$$

$$+E_2\int_0^{\tau} e^{\frac{\tau}{2}S}e^{(\tau-s)V}ds = E_2\Big[\frac{\tau^2}{2}D - \frac{\tau^3}{8}DV + \frac{\tau^3}{4}\left(D^2+SV-VS+SD+VD+DV\right)\Big]$$

$$+E_2\Big[\tau+\frac{\tau^2}{2}(V+S)+\frac{\tau^3}{2}\left(\frac{V^2}{3}+\frac{SV}{2}-V^2\right)\Big]+\mathcal{O}(\tau^4). \tag{6.64}$$

Simplifying the term with E_3 (6.59),

$$E_3\int_0^\tau e^{S\frac{\tau}{2}}e^{V\frac{\tau}{2}}e^{D(\tau-s)}ds = E_3\Big[\tau+\frac{\tau^2}{2}(D+S+V)+\frac{\tau^3}{2}(\frac{D^2}{3}+\frac{S^2}{4}+\frac{V^2}{4}$$

$$+\frac{SV}{2}+SD+VD)\Big]+\mathcal{O}(\tau^4). \tag{6.65}$$

Using (6.63-6.65), we have from (6.59),

$$Y_{SM} = e^{\frac{\tau}{2}S}e^{\frac{\tau}{2}V}e^{\tau D}e^{\frac{\tau}{2}V}e^{\frac{\tau}{2}S}Y_0+E\tau+E\frac{\tau^2}{2}A+\frac{\tau^3}{2}\Bigg[E_1\left(\frac{A^2}{2}+\frac{VS}{4}+\frac{DS}{4}+\frac{S^2}{3}\right)$$

$$+E_2\left(\frac{D^2}{2}-\frac{2V^2}{3}+SV+\frac{VS}{2}+\frac{SD}{2}+\frac{VD}{2}-\frac{DV}{2}\right)$$

$$+E_3\left(\frac{S^2}{8}+\frac{V^2}{8}+\frac{D^2}{6}+\frac{SV}{4}+\frac{SD}{2}+\frac{VD}{2}\right)\Bigg]+\mathcal{O}(\tau^4). \tag{6.66}$$

From (6.60, 6.61, 6.62, 6.66), we have

$$E_{SM}(Y;\tau) = \frac{\tau^3}{24}Y_0\Big[S^2V-2SV^2+V^2D-2VD^2+S^2D-2SD^2+VS^2-2V^2S+DV^2-2D^2V$$

$$+DS^2-2D^2S-2SVD-2SDV-2VDV-2SVS-2SDS-2VDS-2DVS$$

$$+4VSV+4DSD+4DSV+4DVD+4VSD\Big]$$

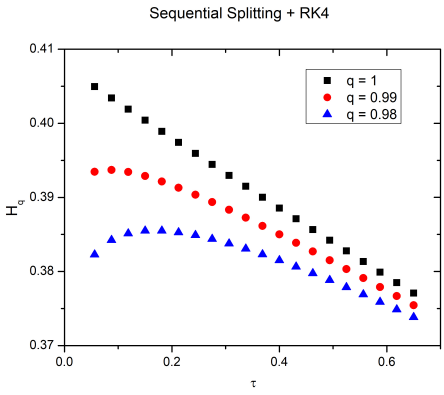
$$+\frac{\tau^3}{2}\Bigg[E\frac{A^2}{3}-\Bigg\{E_1\left(\frac{A^2}{2}+\frac{VS}{4}+\frac{DS}{4}+\frac{S^2}{3}\right)$$

$$+E_2\left(\frac{D^2}{2}-\frac{2V^2}{3}+SV+\frac{VS}{2}+\frac{SD}{2}+\frac{VD}{2}-\frac{DV}{2}\right)$$

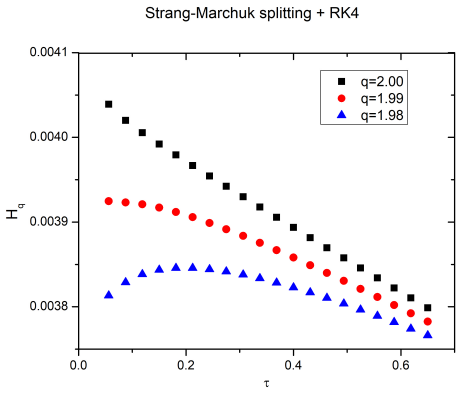
$$+E_3\left(\frac{S^2}{8}+\frac{V^2}{8}+\frac{D^2}{6}+\frac{SV}{4}+\frac{SD}{2}+\frac{VD}{2}\right)\Bigg\}\Bigg]+\mathcal{O}(\tau^4) \tag{6.67}$$

Hence, the Strang-Marchuk splitting scheme (6.54-6.58) applied to the non-homogeneous system of ODEs (6.44) has third order local error, i.e., the scheme is of second order accuracy.

Figures 4 show as to how to determine the approximate value of the threshold q_0. In Fig. 4a, the sequential splitting scheme is used together with the RK4 method, while in Fig.



(a)



(b)

Figure 4: a) Values of the term $H_q(\tau)$ defined in Sec. 6.2 (First Method) as a function of τ applying the sequential splitting procedure with the RK4 method for different values of q. b) Values of the term $H_q(\tau)$ defined in Sec. 6.2 (First Method) as a function of τ applying Strang-Marchuk splitting procedure with the RK4 method for different values of q

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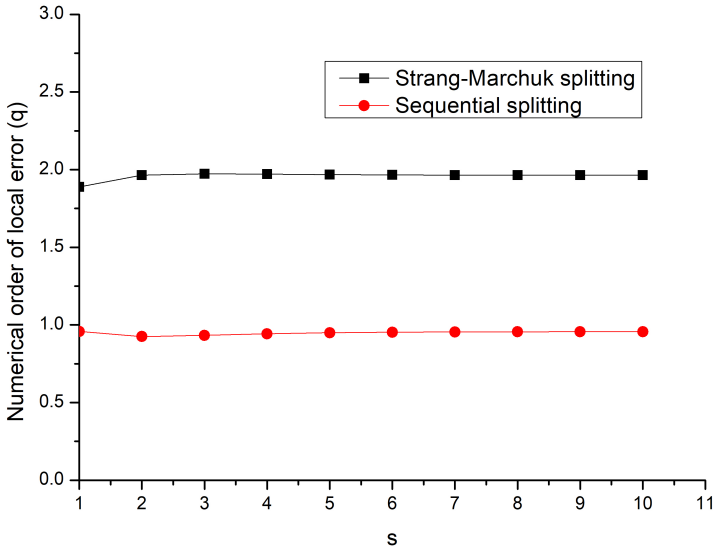


Figure 5: Numerical order (q) in the case of the local practical error as function of s for the sequential splitting scheme and the Strang-Marchuk splitting scheme (Note that for the sequential splitting scheme $h = \tau^s$ and for the Starng-Marchuk splitting scheme $h = \frac{1}{r^4}\tau^s$, r being the order of the numerical method applied).

4b, the Strang-Marchuk splitting scheme is used with RK4 method. The numerical time step h is taken as $h = 10^{-6}$ in both cases. The values of q are chosen for the sequential

splitting scheme around the order of the scheme, i.e., 1 and that for the Strang-Marchuk scheme around 2. The last value of q for which the limit is still finite is considered to be an approximate order of the corresponding splitting scheme.

Using the "Second Method" in Sec. 6.2, we calculate the numerical error for different splitting schemes as a function of s, and is depicted in Fig. 5. To reduce the effect of the interaction error, the numerical time step has to be chosen small enough. Hence, for a fixed splitting timestep (τ), we choose smaller h for the Strang-Marchuk splitting scheme (close to the computer zero). However, to reduce computational cost, we can choose h as appeared in [2], but in that case, a threshold of s will come into play to retain the numerical order of Strang-Marchuk scheme, whose graphical representation is not presented here for the sake of brevity.

7 Numerical Experiments and Discussion

For a quantitative insight, the plausible baseline values of the parameters involved in the model are taken as [34] $S_{0h} = 100, E_{0h} = 20, I_{0h} = 10, R_{0h} = 0, S_{0m} = 1000, E_{0m} = 20, I_{0m} = 30, \lambda_h = 0.000215, \Lambda_m = 0.07, b = 0.12, \beta_h = 0.1, \beta_m = 0.09, \mu_h = 0.0000548, \mu_m = 1/15, \delta_h = 0.001, \delta_m = 0.01, \alpha_h = \frac{1}{17}, \alpha_m = \frac{1}{18}, r = 0.05, \omega = \frac{1}{730}, v_h = 1, v_m = 0.5$.

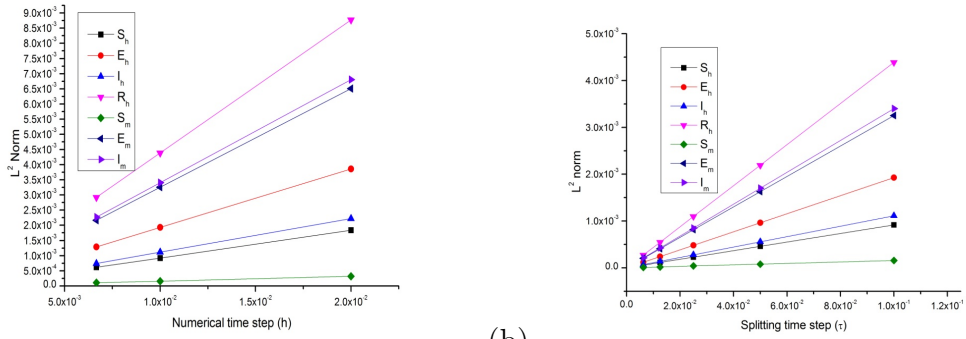
It may be recalled that we have solved the system of ODEs by RK4 method to get the 'Numerical Solution' or the 'Reference Solution' of the unsplit problem (3.6). We have used the explicit Euler method to solve again the unsplit problem (3.6) and calculated the error associated with the methods in a bid to validate the 'Reference Solution' obtained. The Table 4 exhibiting the errors associated with the solutions for Euler-RK4 at $h = 10^{-3}$ and Euler-RK4 at $h = 10^6$ for seven classes clearly justifies the validity of the 'Reference Solution' in the present model.

Description	L^2 Norm (Euler-RK4) $h = 10^{-3}$	L^2Norm (Euler-RK4) $h = 10^{-6}$
Susceptible human (S_h)	4.4109E-6	4.4E-9
Exposed human (E_h)	3.7375E-6	3.7E-9
Infected human (I_h)	9.8879E-6	9.9E-9
Recovered human (R_h)	9.0295E-6	9.0E-9
Susceptible mosquitoes (S_m)	1.5806215E-3	1.5794E-6
Exposed mosquitoes (E_m)	4.106788E-4	4.104E-7
Infected mosquitoes ((I_m)	1.19275E-4	1.192E-7

Table 4: Comparison of errors in Euler and RK4 Methods in at t=1.0 for $h = 10^{-3}, 10^{-6}$.

Figure 6 depicts the global practical errors for several cases, v.i.z., i) τ is constant with varying h (cf. Fig. 6a), and ii) both τ and h, at T=140 (cf. Fig. 6b). It is evident that the global practical error decreases with decreasing numerical step length (h) when the

splitting step length (τ) is fixed (cf. Fig. 6a). However, the error drastically decreases when both the splitting time step (τ) and the numerical time step (h) do decrease (cf. Fig. 6b).



(a) (b)

Figure 6: a) Estimation of global practical error using the sequential splitting technique a) for different h, $\tau = 0.1, T = 140$, b) for different τ and $h = \frac{\tau}{10}$ at $T = 140$.
.

Figure 7 shows the effects of the proportion of antibody (ν_h) when the reproduction number (R_0) is less than unity. Fig. 7a shows that the susceptible human population drops as a result of infection by infectious mosquitoes (ν_h =0) and thereafter stabilizes when the human develops an antibody against the parasite-causing malaria ($\nu_h = 0.5, 1.0$). It may be noted that an increase in the proportion of the antibody reduces the sharp decrease in the susceptible human population. The magnitudes of the exposed human population in Fig. 7b does decrease with an increased presence of antibody. Figs. 7(c-d) display the time-dependent behavior of the infected and recovered human population for different ν_h. Comparing all the Figs. 7(a-d), we may conclude that the decreased number of infectious human population contributes much in the number of recovered human which eventually influences the reduction in the sharp decrease experienced by the susceptible human population.

Figure 8 exhibits the time-dependent behaviour of the susceptible, exposed and infected mosquitoes for different values of the proportion of antibody (ν_m), produced against parasite, on mosquito populations. It is observed that the number of susceptible mosquito decreases with time as there is no recovered class for mosquito population. However, increasing the proportion of antibody (ν_m) inhibits the reduction in the number of susceptible mosquito. Also, the number of the exposed and infectious mosquito population decreases due to the increase in resistance to the malaria parasite.

The impact of antibody (ν_h) produced by the susceptible human in response to the presence of the parasite on susceptible as well as exposed human population for R_0 >1 is depicted in Figures 9(a,b)respectively. It may be noted that the basic reproduction number R_0 can be made greater than unity by increasing the mosquito's biting rate (b). We notice

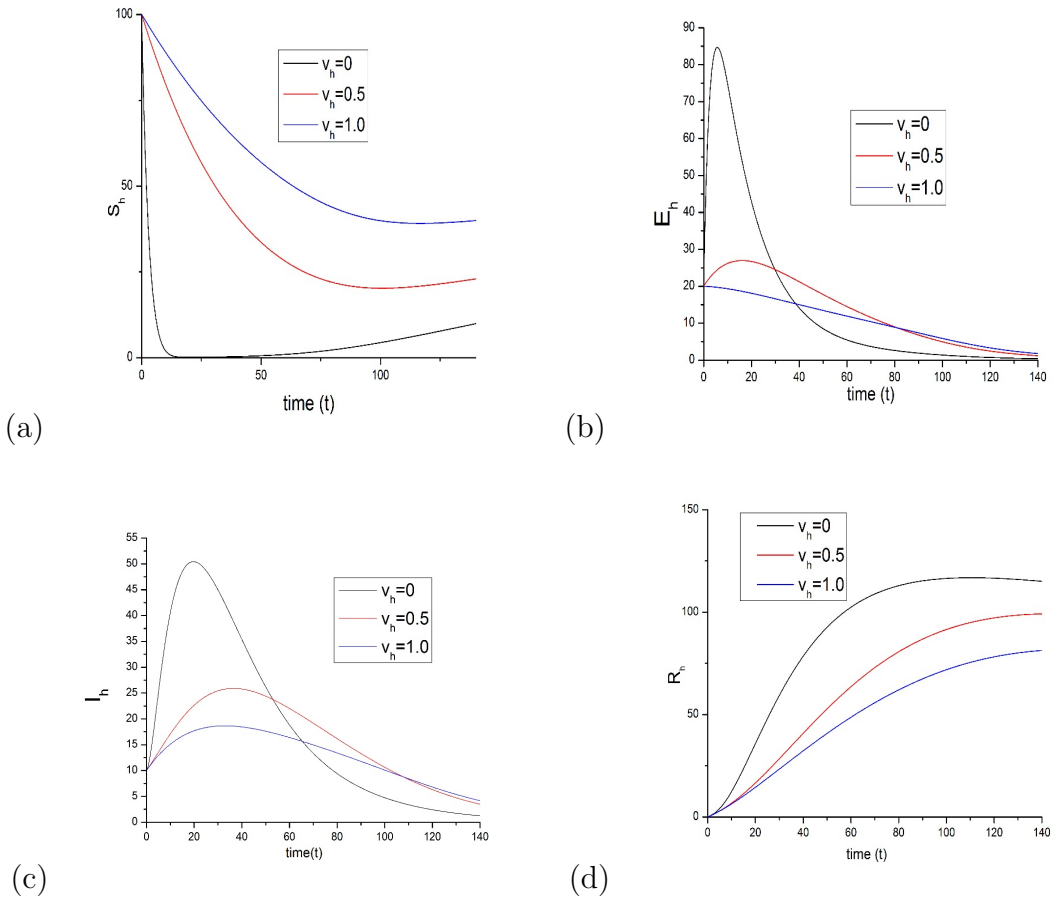
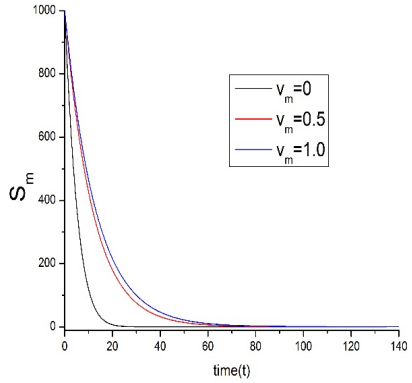
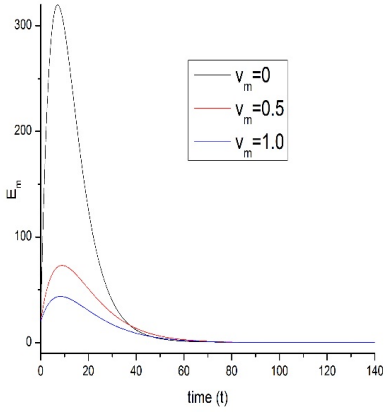


Figure 7: The temporal behaviour for different proportion of antibody (ν_h) produced by human when $R_0 < 1$, a) susceptible human, b) exposed human, c) infected human, d) recovered human.

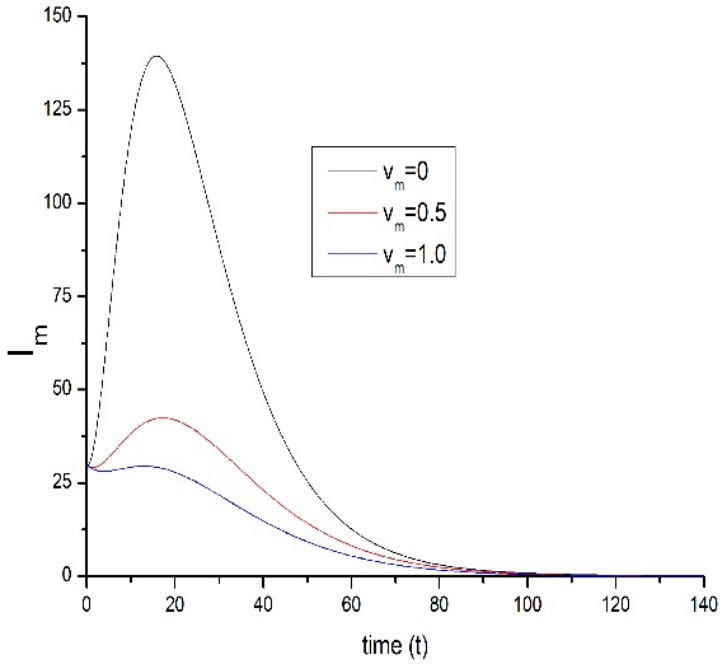
that increasing the proportion of the antibody with the biting rate, has a lower effect in reducing the burden of the endemic malaria infection when compared the case for $R_0 < 1$. Figures 9(c,d) display the variations of the results for infected and recovered human with varying ν_h. It is observed that when $R_0 > 1$, there are meagre effects of ν_h on the infected and susceptible human population as compared with the case for $R_0 < 1$. The above phenomena may be justified in the sense that the increased proportions of antibodies together with the increasing biting rate (b) has a lower effect in reducing the burden of malaria.



(a)



(b)



(c)

Figure 8: The temporal behaviour for different proportion of antibody (ν_m) produced against parasite when $R_0 < 1$, a) susceptible mosquitoes, b) exposed mosquitoes, c) infected mosquitoes.

8 Conclusion

We have formulated a temporal model to describe the dynamics of disease transmission of malaria parasites in a well-mixed human and mosquito environment. We have investigated

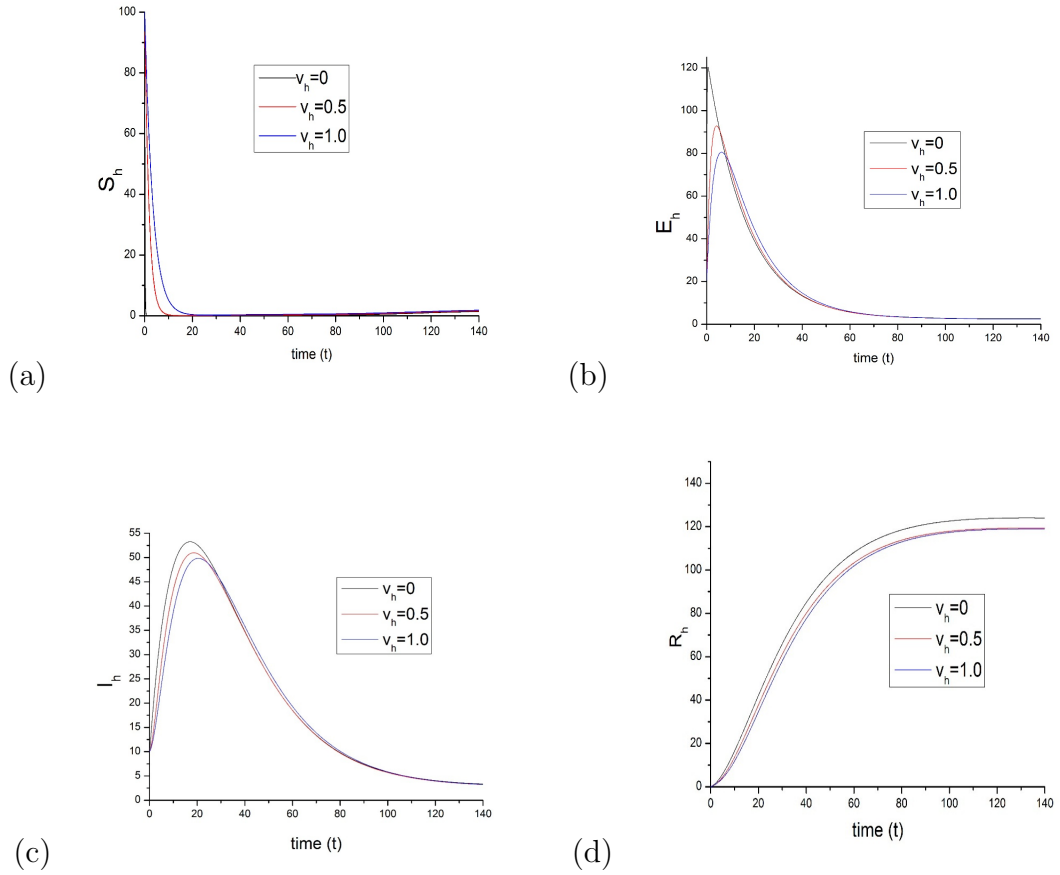


Figure 9: The temporal behaviour for different proportion of antibody (ν_h) produced by human when $R_0 > 1$, b=3, a) susceptible human, b) exposed human, c) infected human, d) recovered human.

the dynamics of the system both analytically and numerically. More specifically, we have solved the system of ODEs describing the temporal model by the RK4 method and we term it as 'Reference Solution'. To validate the reference solution, we have again solved the temporal model by the explicit Euler method and calculated the error associated with it. We have converted the system of ODEs into a non-homogeneous matrix differential equation, then we have split the operators involved in the matrix differential equation to get various splitting scheme. We have used the sequential splitting scheme and the Strang-Marchuk splitting scheme to get the numerical split solution. We have also calculated the order and error for both the schemes. Results predicted show that the susceptible human population drops as a result of infection by infectious mosquitoes and thereafter stabilizes when the human develops an antibody against parasite-causing malaria. It may be noted that an increase in the proportion of the antibody reduces the sharp decrease in the susceptible human population. Moreover, the decreased number of infectious human population contributes much in the number of recovered human which eventually influences the reduction in the sharp decrease experienced by susceptible human population.

Furthermore, the number of the susceptible mosquito decreases with time as there is no recovered class for mosquito population and increasing the proportion of antibody inhibits the reduction in the number of susceptible mosquitoes.

9 Study Limitations and Scope of Future Work

Due to the huge complexity of epidemiological modelling, a lot of assumptions (simplifications) may be made while studying it mathematically and/ numerically. It is worthy to mention that our model does not contain the age-structure and the environmental effects (namely, the temperature and humidity). Our model also did not consider the spatial impact on the transmission of malaria, even though, the spatio-temporal dynamics of disease transmission is a much-researched topic in the case of epidemiological modelling. We intend to investigate the topics mentioned in this section as part of our future research.

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