USING MATHEMATICAL MODEL TO ILLUSTRATE THE SPREAD OF MALARIA

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Abstract

We present an ordinary differential equation mathematical model for the spread of malaria in human and Mosquito populations.Susceptible humans can be infected when the are bitten by an infectious Mosquito.They then progress through the infectious and asymptomatic classes, before re-entering the susceptible class.Susceptible Mosquitoes can become infected when they bite infectious and asymptomatic humans, and once infected they move through infectious class. The basic reproduction number R_0 is established and used to determine whether the disease dies out or persists in the population. We show that given $R_0 \leq 1$, the disease-free equilibrium is globally asymptotically stable and the disease always dies out and if $R_0 > 1$, there exists a unique endemic equilibrium which is globally stable and the disease persists.

Contents

1 INTRODUCTION

1.1 Malaria

Malaria is an ancient disease having huge social, economic and health burden. It is predominantly present in the tropical countries. Even though the disease has been investigated for hundreds of years, it still remains a major public health problem. The WHO estimates that in 2010 there were 219 million cases of malaria resulting in 660,000 deaths [1,2]. Others have estimated the number of cases at between 350 and 550 million for *falciparum malaria* [3] and deaths in 2010 at 1.24 million [4] up from 1.0 million deaths in 1990 [5]. The majority of cases (65 percent) occur in children under 15 years old [4]. About 125 million pregnant women are at risk of infection each year; in Sub-Saharan Africa, maternal malaria is associated with up to 200,000 estimated infant deaths yearly [6]. There are about 10,000 malaria cases per year in Western Europe, and 1300-1500 in the United States [7]. About 900 people died from the disease in Europe between 1993 and 2003 [8]. Both the global incidence of disease and resulting mortality have declined in recent years. According to WHO, deaths attributable to malaria in 2010 were reduced by over a third from a 2000 estimate of 985,000, largely due to the widespread use of insecticide-treated nets and artemisinin-based combination(ACT) therapies [9].

Malaria is presently endemic in a broad band around the equator, in areas

of the Americas, many parts of Asia, and much of Africa; 85-90 percent of malaria fatalities occur in Sub-Saharan Africa [10]. An estimate for 2009 reported that countries with the highest death rate per 100,000 of population were Ivory Coast (86.15), Angola (56.93) and Burkina Faso (50.66) [11]. A 2010 estimate indicated the deadliest countries per population were Burkina Faso, Mozambique and Mali [4]. The Malaria Atlas Project aims to map global endemic levels of malaria, providing a means with which to determine the global spatial limits of the disease and to assess disease burden [12,13]. This effort led to the publication of a map of *P. falciparum* endemicity in 2010 [20]. As of 2010, about 100 countries have endemic malaria [2,14]. Every year, 125 million international travellers visit these countries, and more than 30,000 contract the disease [8].

The geographic distribution of malaria within large regions is complex, and malaria-afflicted and malaria-free areas are often found close to each other [15]. Malaria is prevalent in tropical and subtropical regions because of rainfall, consistent high temperatures and high humidity, along with stagnant waters in which mosquito larvae readily mature, providing them with the environment they need for continuous breeding [16]. In drier areas, outbreaks of malaria have been predicted with reasonable accuracy by mapping rainfall [17]. Malaria is more common in rural areas than in cities. For example, several cities in the Greater Mekong Subregion of Southeast Asia are essentially malaria-free, but the disease is prevalent in many rural regions, including along international borders and forest fringes [18]. In contrast, malaria in

Africa is present in both rural and urban areas, though the risk is lower in the larger cities [19].

1.2 Causes of malaria

Malaria is caused by *Plasmodium* parasite which can be spread to humans through the bites of an infected Mosquitoes. There are many different types of *Plasmodium* parasite, but only five types cause malaria in humans [21,22]. These are:

- *Plasmodium falciparum*- mainly found in Africa and responsible for most malaria deaths worldwide.
- *Plasmodium vivax*- mainly found in Asia and Latin America. This parasite produces less severe symptoms than Plasmodium falciparum, but it can stay in the liver for up to three years, which can result in relapses.
- *Plasmodium Ovale*-fairly uncommon and usually found in west Africa. It can remain in human liver for several years without producing symptoms.
- *Plasmodium Malariae*- this is quite rare and usually found in Africa.
- *Plasmodium Knowlesi*- this is very rare and found in parts of Southeast Asia.

Of these *Plasmodium falciparum* is the most common cause of infection in Africa and Southeast Asia, and is responsible for approximately 80 percent of all malaria cases and approximately 90 percent of deaths [1].

1.3 Life cycle of Plasmodium and how malaria spreads

In the life cycle of *Plasmodium*, a female Anopheles mosquito (the definitive host) transmits a motile infective form (called the *sporozoite*) to a vertebrate host such as a human (the secondary host), thus acting as a transmission vector. A *sporozoite* travels through the blood vessels to liver cells (hepatocytes), where it reproduces asexually (tissue *schizogony*), producing thousands of *merozoites*. These infect new red blood cells and initiate a series of asexual multiplication cycles (blood *schizogony*) that produce 8 to 24 new infective *merozoites*, at which point the cells burst and the infective cycle begins a new [23].

Other *merozoites* develop into immature gametocytes, which are the precursors of male and female gametes. When a fertilised mosquito bites an infected person, gametocytes are taken up with the blood and mature in the mosquito gut. The male and female gametocytes fuse and form a *ookinetea* fertilized, motile zygote. *Ookinetes* develop into new *sporozoites* that migrate to the insect's salivary glands, ready to infect a new vertebrate host. The sporozoites are injected into the skin, in the saliva, when the mosquito takes a subsequent blood meal [24].

Only female mosquitoes feed on blood; male mosquitoes feed on plant nectar, and thus do not transmit the disease. The females of the Anopheles genus of mosquito prefer to feed at night. They usually start searching for a meal at dusk, and will continue throughout the night until taking a meal [25]. Malaria parasites can also be transmitted by blood transfusions, although this is rare [26]

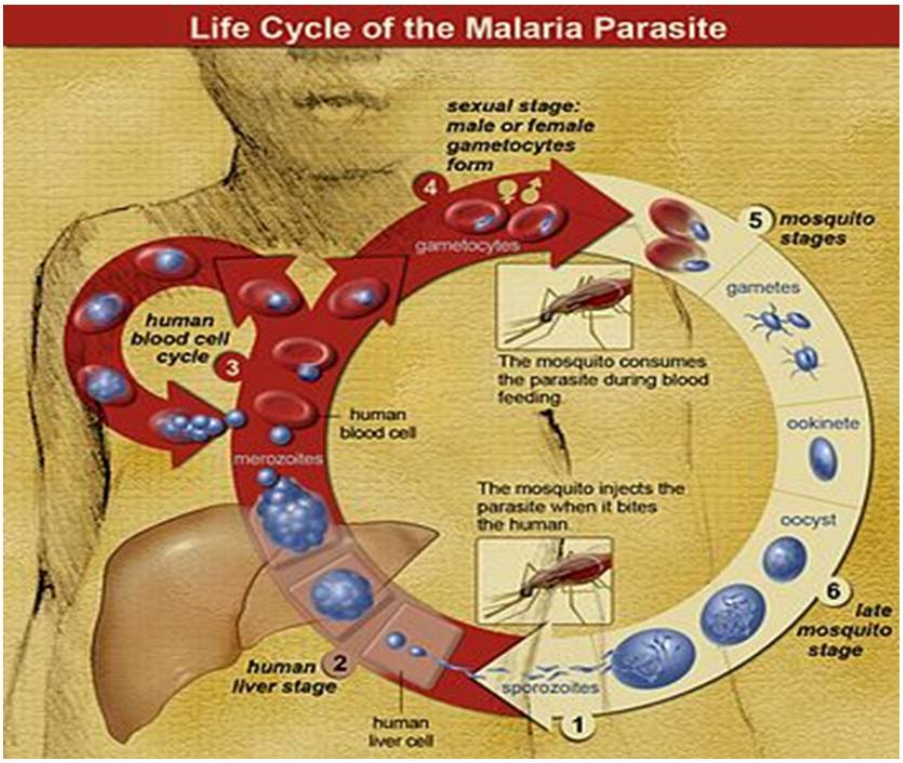


Figure 1: Life cycle of Plasmodium parasite

1.4 Signs and Symptoms of Malaria

The signs and symptoms of malaria typically begin 8-25 days following infection [27]; however, symptoms may occur later in those who have taken antimalarial medications as prevention [1]. Initial manifestations of the disease-common to all malaria species-are similar to flu-like symptoms [28], and can resemble other conditions such as septicemia, gastroenteritis, and viral diseases [1]. The presentation may include headache, fever, shivering, joint

pain, vomiting, hemolytic anemia, jaundice, hemoglobin in the urine, retinal damage, and convulsions [29].

The classic symptom of malaria is paroxysm-a cyclical occurrence of sudden coldness followed by shivering and then fever and sweating, occurring every two days (tertian fever) in P. vivax and *P. ovale* infections, and every three days (quartan fever) for P. malariae. P. falciparum infection can cause recurrent fever every 36-48 hours or a less pronounced and almost continuous fever [30].

Severe malaria is usually caused by *P. falciparum* (often referred to as *falciparum* malaria). Symptoms of *falciparum* malaria arise 9-30 days after infection [28]Individuals with cerebral malaria frequently exhibit neurological symptoms, including abnormal posturing, nystagmus, conjugate gaze palsy (failure of the eyes to turn together in the same direction), opisthotonus, seizures, or coma [28].

1.5 Asymptomatic malaria

Human host is considered asymptomatic when it is a carrier for malaria or infection but experiences no symptoms.In malaria-endemic countries, a large proportion of *P. falciparum* infections are asymptomatic or sub-clinical. Microscopy-detected levels of asymptomatic carriage as high as 39 percent have been reported [88-92]. Invariably, this hidden pool of parasites is es-

sential for maintaining the cycle of infection.In high transmission areas, continuous exposures to Plasmodium parasites lead to partial immunity and consequently, create asymptomatic carriers in a given population [93]. In addition, asymptomatic cases provide a fundamental reservoir of parasites and they might become gametocyte carriers, contributing in the persistence of malaria transmission [94]. Therefore, the presence of asymptomatic cases is a big challenge for the management of the elimination programme in any malaria endemic area. In order to achieve a successful elimination, detection of all parasite carriers by active case detection and then treatment of all cases must be considered to interrupt the malaria transmission in endemic areas.

Asymptomatic malaria infections were frequently described in high and intermediate transmission areas including Ghana [95,96], Kenya [94], Senegal [97,98], Gabon [97,100], Nigeria [101,102], Uganda [103], Thailand [104], Burma [105] and Yemen [110]. However, in recent years, such cases have also been reported from low endemic areas such as Amazon region of Brazil and Peru [107,89], Colombia [90], Solomon Island [91] and Principe [75]. Notably, John and colleagues [76] reported that administration of different malaria control interventions reduced the asymptomatic malaria cases in an unstable malaria transmission area of Kenya and also in high transmission endemic area of Sri Lanka [77]. Since symptomless malaria consequences in the persistence of the parasite reservoirs and increases malaria transmission in human population, it can interfere with malaria elimination strategies. Therefore, to achieve successful elimination and finally eradication of malaria from the

world, survey on the presences and the prevalence of asymptomatic cases in diverse malaria settings is recommended.

1.6 Mathematical models and epidemiology

Among all areas in biology, researchers in infectious diseases were one of the foremost to realize the important role of mathematics and mathematical models. That is, it providing an explicit framework for understanding the disease transmission dynamics within and between hosts and parasites. In a mathematical expression or a model, several known clinical and biological information are included in a simplified form by selecting features that seem to be important to the question being investigated in the disease progression and dynamics. Therefore, a model is an "approximation" of the complex reality, and its structure depends upon the processes being studied and aimed for extrapolation. Based on the question being investigated, these studies can help fit empirical observations, and can be applied to make theoretical predictions on lesser known or unknown situations. For example, mathematical models have been widely used by epidemiologists as tools to predict the occurrence of epidemics of infectious diseases, and also as a tool for guiding research for eradication of malaria at the present time [31,32].

Malaria is one of the oldest diseases studied for a long time from all angles, and vast literature exists describing a host of modeling approaches. Different approaches are helpful in guiding different stages of the disease through

synthesizing available information and extrapolating it. It is felt that combination of different approaches, rather than a single type of modeling, may have long term usefulness in eradication and control [31].

Mathematical models that study transmission of malaria are based on the "reproduction number", which defines the most important aspects of transmission for any infectious disease. Specifically, it is defined as the expected number of infected organisms that can trace their infection directly back to a single organism after one disease generation. The solution to controlling the disease is to arrive at a reproduction number at which the disease-free state can be established and maintained [33,34].

Previous studies used ordinary differential equations to model the transmission of malaria, in which human populations are classified as susceptible, exposed, infectious and recovered. Likewise, mosquito populations are divided into susceptible, exposed and infectious groups.

1.7 Problem Statement

To consider the asymptomatic class of humans as it is a major problem which is the *Plasmodium* parasite reservoir.

1.8 Objectives of the study

The overall objective of this study is to come up with a mathematical model on how malaria spreads.

1.8.1 Specific objectives

The specific objectives of this study are:

- Formulate a deterministic dynamic model to represent the transmission of the disease in different compartments.
- Compute the basic reproduction number, R_0 for the model.
- Establish the disease free equilibrium, DFE and endemic equilibrium, EE.
- Stability analysis of equilibrium states.
- Numerical simulation to show the variation of the population with time.

2 LITERATURE REVIEW

2.1 History of Malaria

Although the parasite responsible for *P. falciparum* malaria has been in existence for 50,000-100,000 years, the population size of the parasite did not increase until about 10,000 years ago, concurrently with advances in agriculture [35] and the development of human settlements. Close relatives of the human malaria parasites remain common in chimpanzees. Some evidence suggests that the *P. falciparum* malaria may have originated in gorillas [36].

References to the unique periodic fevers of malaria are found throughout recorded history, beginning in 2700 BC in China [37]. Malaria may have contributed to the decline of the Roman Empire, [38] and was so pervasive in Rome that it was known as the "Roman fever" [39]. Several regions in ancient Rome were considered at-risk for the disease because of the favorable conditions present for malaria vectors. This included areas such as southern Italy, the island of Sardinia, the Pontine Marshes, the lower regions of coastal Etruria and the city of Rome along the Tiber River. The presence of stagnant water in these places was preferred by mosquitoes for breeding grounds. Irrigated gardens, swamp-like grounds, runoff from agriculture, and drainage problems from road construction led to the increase of standing water [40].

The term malaria originates from Medieval Italian: "mala aria" - "bad air"; the disease was formerly called ague or marsh fever due to its association with

swamps and marshland [41]. Malaria was once common in most of Europe and North America, [42] where it is no longer endemic,[43] though imported cases do occur [44].

Malaria was the most important health hazard encountered by U.S. troops in the South Pacific during World War II, where about 500,000 men were infected [45]. According to Joseph Patrick Byrne, "Sixty thousand American soldiers died of malaria during the African and South Pacific campaigns." [46] Scientific studies on malaria made their first significant advance in 1880, when Charles Louis Alphonse Laveran a French army doctor working in the military hospital of Constantine in Algeria observed parasites inside the red blood cells of infected people for the first time. He therefore proposed that malaria is caused by this organism, the first time a protist was identified as causing disease [47]. For this and later discoveries, he was awarded the 1907 Nobel Prize for Physiology or Medicine. A year later, Carlos Finlay, a Cuban doctor treating people with yellow fever in Havana, provided strong evidence that mosquitoes were transmitting disease to and from humans [48]. This work followed earlier suggestions by Josiah C. Nott, [49] and work by Sir Patrick Manson, the "father of tropical medicine", on the transmission of filariasis [50].

In April 1894, a Scottish physician Sir Ronald Ross visited Sir Patrick Manson at his house on Queen Anne Street, London. This visit was the start of four years of collaboration and fervent research that culminated in 1898

when Ross, who was working in the Presidency General Hospital in Calcutta, proved the complete life-cycle of the malaria parasite in mosquitoes. He thus proved that the mosquito was the vector for malaria in humans by showing that certain mosquito species transmit malaria to birds. He isolated malaria parasites from the salivary glands of mosquitoes that had fed on infected birds [51]. For this work, Ross received the 1902 Nobel Prize in Medicine. After resigning from the Indian Medical Service, Ross worked at the newly established Liverpool School of Tropical Medicine and directed malaria-control efforts in Egypt, Panama, Greece and Mauritius [52]. The findings of Finlay and Ross were later confirmed by a medical board headed by Walter Reed in 1900. Its recommendations were implemented by William C. Gorgas in the health measures undertaken during construction of the Panama Canal. This public-health work saved the lives of thousands of workers and helped develop the methods used in future public-health campaigns against the disease [53].

The first effective treatment for malaria came from the bark of *cinchona* tree, which contains quinine. This tree grows on the slopes of the Andes, mainly in Peru. The indigenous peoples of Peru made a tincture of cinchona to control fever. Its effectiveness against malaria was found and the Jesuits introduced the treatment to Europe around 1640; by 1677, it was included in the London *Pharmacopoeia* as an antimalarial treatment.[54] It was not until 1820 that the active ingredient, quinine, was extracted from the bark, isolated and named by the French chemists Pierre Joseph Pelletier and Joseph Bienaim

Caventou [55,56].

Quinine become the predominant malarial medication until the 1920s, when other medications began to be developed. In the 1940s, chloroquine replaced quinine as the treatment of both uncomplicated and severe malaria until resistance supervened, first in Southeast Asia and South America in the 1950s and then globally in the 1980s [57]. Artemisinins, discovered by Chinese scientist Tu Youyou and colleagues in the 1970s from the plant *Artemisia annua*, became the recommended treatment for *P. falciparum* malaria, administered in combination with other antimalarials as well as in severe disease [58].

Plasmodium vivax was used between 1917 and the 1940s for malariotherapy-deliberate injection of malaria parasites to induce fever to combat certain diseases such as tertiary syphilis. In 1917, the inventor of this technique, Julius Wagner-Jauregg, received the Nobel Prize in Physiology or Medicine for his discoveries. The technique was dangerous, killing about 15 percent of patients, so it is no longer in use [59].

The first pesticide used for indoor residual spraying was DDT [60]. Although it was initially used exclusively to combat malaria, its use quickly spread to agriculture. In time, pest control, rather than disease control, came to dominate DDT use, and this large-scale agricultural use led to the evolution of resistant mosquitoes in many regions. The DDT resistance shown by Anopheles mosquitoes can be compared to antibiotic resistance shown by bacteria. During the 1960s, awareness of the negative consequences of its indiscrim-

inate use increased, ultimately leading to bans on agricultural applications of DDT in many countries in the 1970s [61]. Before DDT, malaria was successfully eliminated or controlled in tropical areas like Brazil and Egypt by removing or poisoning the breeding grounds of the mosquitoes or the aquatic habitats of the larva stages, for example by applying the highly toxic arsenic compound Paris Green to places with standing water [62]

Malaria vaccines have been an elusive goal of research. The first promising studies demonstrating the potential for a malaria vaccine were performed in 1967 by immunizing mice with live, radiation-attenuated *sporozoites*, which provided significant protection to the mice upon subsequent injection with normal, viable *sporozoites*. Since the 1970s, there has been a considerable effort to develop similar vaccination strategies within humans [63].

2.2 Mathematical modeling of malaria

More than a century has passed since Ross [64,65,74] introduced the first deterministic differential equation model of malaria by dividing the human population into susceptible S_h and infected I_h compartments, with the infected class returning to susceptible class again leading to the SIS structure. The mosquito population also has only two compartments (S_m, I_m), but they do not recover from infection due to their short life span, and thereby follow the SI structure. Time evolution of the fraction of individuals in the infected classes (I_h, I_m) is studied using two differential equations, one each

for the human and mosquito as given below. It is clear that the parameters, m, a, b,and c, that contribute to the increase of R_0 in this model, are related to mosquitoes and humans, and any change in them can significantly affect malaria transmission. Increasing mosquito mortality and reducing mosquito biting rate can reduce R_0. The Ross model outlines the basic features of malaria transmission, and puts the main burden of transmission on mosquito-specific features, thereby paving the way for mosquito-based malaria control programmes.

Ross model

$$\frac{dI_h}{dt} = abmI_m(1 - I_h) - \gamma I_h$$

$$\frac{dI_m}{dt} = acI_h(1 - I_h) - \mu_2 I_m$$

with

$$R_0 = \frac{ma^2bc}{r\mu_2}$$

with parameters and their values as;

a : Man biting rate [0.01-0.5 day per day].

b : Proportion of bites that produce infection in human [0.2-0.5].

c : Proportion of bites by which one susceptible mosquito becomes infected [0.5].

m : Ratio of number of female mosquitoes to that of humans [0.5-40].

γ : Average recovery rate of human [0.005-0.05 per day].

μ_1: Per capita rate of human mortality [0.017 year per year].

μ_2: Per capita rate of mosquito mortality [0.05-0.5 per day].

τ_m: Latent period of mosquito [5-15 days].

τ_h: Latent period of human [10-100 day].

The malaria parasite spends approximately 10 days inside a mosquito during its life cycle. The simple Ross model did not consider this latency period of the parasite in mosquitoes and their survival during that period. This resulted in the model predicting a rapid progress of the epidemic in human, and a higher equilibrium prevalence of infectious mosquitoes. MacDonald (1955-1969) considered this latency period t_m, and introduced the Exposed E_m class in the mosquitoes [66-69,73]. Therefore, in the model below, the mosquito population is divided into three compartments (SEI), and the model studies the time evolution of the exposed E_m and infected I_m classes in mosquito. The R_0 for this model is consequently scaled down with increasing latency period.

MacDonald model

$$\frac{dI_h}{dt} = abmI_m(1 - I_h) - \gamma I_h$$

$$\frac{dE_m}{dt} = acI_h(1 - E_m - I_m)$$

$$-acI_h(t - \tau_m)[1 - E_m(t - \tau_m - I_m(t - \tau_m)]e^{-\mu_2\tau_m} - \mu_2 E_m$$

$$\frac{dI_m}{dt} = acI_h(t - \tau_m)[1 - E_m(t - \tau_m - I_m(t - \tau_m)]e^{-\mu_2\tau_m} - \mu_2 I_m$$

with

$$R_0 = \frac{ma^2bc}{r\mu_2}e^{-\mu_2\tau_m}$$

In a natural extension to the Ross and McDonald's models, Anderson and May(1991) considered the 21 days latency period of the parasite in humans, and introduced the Exposed E_h class in human population in their model [85,64,65]. This divided the host population into three compartments (S_h, E_h, I_h), along with that in the mosquito population (S_m, E_m, I_m). This, therefore, is a SEIS model for the human population, and the model consists of four differential equations as shown below, describing the time evolution of both the exposed and infected classes for humans and mosquitoes (E_h, I_h, E_m, I_m). The R_0 for this model is further reduced due to inclusion of human latency period.

Anderson and May model

$$\frac{dE_h(t)}{dt} = abmI_m(t)(1 - E_h(t) - I_h(t)) - abmI_m(t - \tau_h)[1 - E_h(t - \tau_h) - I_h(t - \tau_h)]e^{-(r+\mu_1)\tau_h}$$

$$-rE_h(t) - \mu_1 E_h(t)$$

$$\frac{dI_h(t)}{dt} = abmI_m(t-\tau_h)[1-E_h(t-\tau_h)-I_h(t-\tau_h)]e^{-(r+\mu_1)\tau_h}$$
$$-rI_h(t)-\mu_1 I_h(t)$$

$$\frac{dE_m}{dt} = acI_h(1-E_m-I_m)$$
$$-acI_h(t-\tau_m)[1-E_m(t-\tau_m-I_m(t-\tau_m)]e^{-\mu_2\tau_m}-\mu_2 E_m$$

$$\frac{dI_m}{dt} = acI_h(t-\tau_m)[1-E_m(t-\tau_m-I_m(t-\tau_m)]e^{-\mu_2\tau_m}$$
$$-\mu_2 I_m$$

with

$$R_0 = \frac{ma^2bc}{r\mu_2}e^{-\mu_2\tau_m}e^{-\mu_1\tau_h}$$

As a result of continuous exposure and the ability to develop a degree of immunity to the disease. Immunity, therefore, are known to be important inter-related factors for transmission of malaria in a population. The importance of incorporation of immunity in malaria models is aptly described by Koella (1991) [71] - "Incorporating immunity into malaria models is important for two reasons. First, the neglect of immunity leads to unrealistic predictions. Incorporating immunity can help to make models more realistic."

Ngwa and Shu proposed an immunity model in which disease related death rate is considered to be significantly high, and the total population is not constant. The Ngwa-Shu model (2000) [84] consists of four compartments in humans - Susceptible S_h, Exposed E_h, Infected I_h and Immune R_h - and three compartments in mosquitoes - Susceptible S_m, Exposed E_m, and Infected I_m . Mathematical analysis of the model shows that the Basic Reproductive Number, R_0, can describe the malaria transmission dynamics of the disease, where a globally stable disease-free state exists if $R_0 < 1$, while for $R_0 > 1$, the endemic equilibrium becomes globally stable. This model explicitly shows the role of inclusion of demographic effects (net population growth) in predicting the number of fatalities that may arise as a result of the disease. In a similar theme, Chitins et al (2005) [85] included constant immigration of susceptible human population. Considering immigration of people and excluding direct human recovery from the infectious to susceptible class, they showed that the population approaches the locally asymptotically stable endemic equilibrium point, or stable disease-free equilibrium point, depending on the initial size of the susceptible class.

Immunity can be described as a continuum of different levels of protection rather than a single class, as anti-malarial immunity develops slowly among people exposed to continuous and intense malaria transmission. Yang (2000) [72] divided the immune class R_h in human population into immune R_{h1}, partially immune R_{h2} and non-immune but with immunologic memory R_{h3}, with each class having differential immunity. The mathematical analysis of

Yang model shows that the effects of these three types of immune responses lead to delay in the reappearance of the individuals, who already had experienced malaria, to the susceptible population. Hence the community under high threat of malaria (high R_0) shows low prevalence of individuals with asexual blood-stage infection and without infectious gametocytes, whereas, the same community is relatively free of severe infection due to the increase in immunity by re-infection.

The models discussed in the earlier section consider the immune individuals as a separate class, with no consideration of the types of processes that drive acquisition of immunity and its role in disease progression. In an insightful approach, Filipe et al (2007) [82,83] introduced three age-specific "immunity-functions" in their SEI model for the human host, in which the infected humans are divided into three classes - infected with severe disease I_{h1}, asymptomatic patent infection I_{h2}, and infected with undetectable parasite density R_{h3}. The effect of mosquito density is incorporated through the force of infection h.

3 MODEL DESCRIPTION AND ANALYSIS

3.1 Model formulation

The compartmental model below was considered;

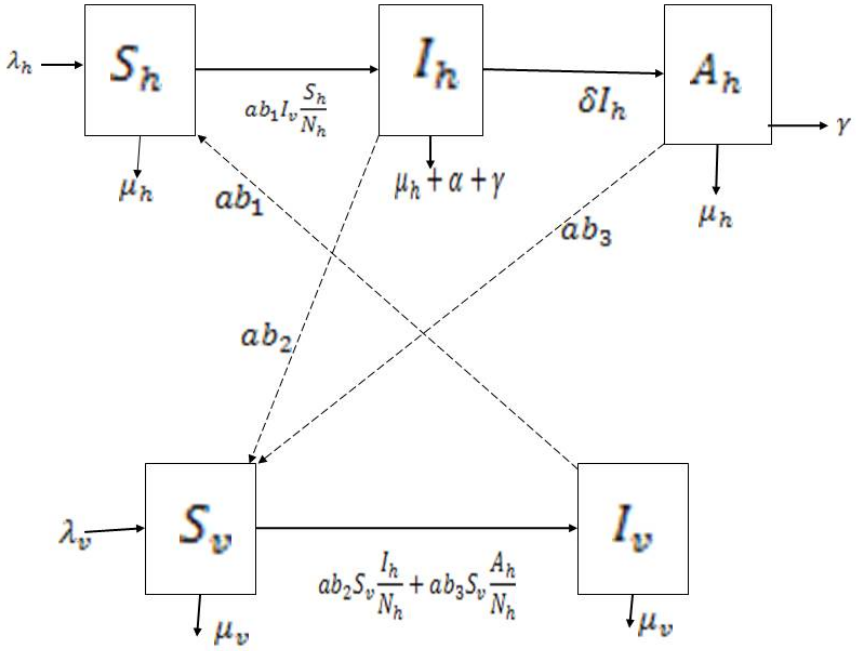


Figure 2: Compartmental Model

where in the dotted line indicates the human-mosquito interaction, while the solid line indicates movement from one compartment to the other within the same population, i.e. either human or mosquito population.

The mathematical model helps to understand better the transmission and spread of malaria. We model the spread of the disease using ordinary differential equations (ODEs) where humans and mosquitoes interact and infect each other. In the model N_h and N_v are respective notations of total population sizes for the human hosts and the female anopheles mosquitoes respectively. In the model the human population is divided into three classes: the Susceptible (S_h) , the Infectious (I_h) and the Asymptomatic (A_h). The mosquito population is divided into two classes: the Susceptible (S_v) and the Infectious (I_v). A human host or mosquito vector is said to be susceptible if they are not infected and are capable of being infected and the susceptible compartment is the collection of such individuals. A human host or mosquito vector is infectious if they have been infected and can infect others while infectious compartment is a collection of such individuals.Human host is considered asymptomatic when it is a carrier for malaria or infection but experiences no symptoms while asymptomatic compartment is its collection.

state variables and parameters	**Definitions**
S_h	Number of susceptible humans at time t
I_h	Number of infectious humans at time t
A_h	Number of asymptomatic humans at time t
S_v	Number of susceptible vectors(mosquitoes) at time t
I_v	Number of infectious vectors (mosquitoes) at time t
λ_h	constant human recruitment by birth
λ_v	constant vector recruitment
μ_h	human death rate
μ_v	mosquito death rate
α	disease dependent death rate
γ	recovery rate of humans
δ	rate which infectious humans become asymptomatic
a	man biting rate of vectors
b_1	proportion of infectious bites to a human at time t
b_2	probability that a susceptible vector gets infected when it bites an infectious human at time t
b_3	probability that a susceptible vector gets infected when it bites an asymptomatic human at time t

Assumptions in the model

- The total human population varies with time.
- The total mosquito population is constant.
- There is homogenous interaction in the population.
- No recovery for infected mosquito.
- Mosquitoes die naturally and not due to disease infection.
- All parameters in the model are non-negative.

The model equations are:

$$\dot{S}_h = \frac{dS_h}{dt} = \lambda_h - ab_1 I_v \frac{S_h}{N_h} - \mu_h S_h + \gamma(I_h + A_h),$$

$$\dot{I}_h = \frac{dI_h}{dt} = ab_1 I_v \frac{S_h}{N_h} - (\mu_h + \alpha + \delta + \gamma) I_h,$$

$$\dot{A}_h = \frac{dA_h}{dt} = \delta I_h - (\mu_h + \gamma) A_h,$$

$$\dot{S}_v = \frac{dS_v}{dt} = \lambda_v - ab_2 S_v \frac{I_h}{N_h} - ab_3 S_v \frac{A_h}{N_h} - \mu_v S_v,$$

$$\dot{I}_v = \frac{dI_v}{dt} = ab_2 S_v \frac{I_h}{N_h} + ab_3 S_v \frac{A_h}{N_h} - \mu_v I_v.$$

The term λ_h in the susceptible hosts compartment corresponds to a constant recruitment of susceptible hosts by birth. The transmission term $ab_1 I_v \frac{S_h}{N_h}$ corresponds to frequency dependent infection of of susceptible hosts by infectious mosquitoes, on infection they move to infectious compartment. The infected and asymptomatic hosts γI_h and γA_h respectively who recover become susceptible again as malaria has no permanent immunity. The respective terms $\mu_h S_h$, $\mu_h I_h$ and $\mu_h A_h$ represents the per capita deaths of the susceptible, infectious and asymptomatic hosts respectively. The term $-\alpha I_h$ in the infectious compartment represents deaths due to infection while δI_h represents the number of infectious humans which gain immunity and move to the asymptomatic compartment. In the susceptible mosquito vectors, λ_v

represent the recruitment of susceptible mosquitoes by birth. The respective terms $ab_2S_v\frac{I_h}{N_h}$ and $ab_3S_v\frac{A_h}{N_h}$ corresponds to transmission of malaria to a susceptible mosquito by the infected and asymptomatic host respectively. Both susceptible and infectious mosquitoes are subject to natural deaths as defined in the terms $\mu_v S_v$ and $\mu_v I_v$ respectively. Infective period of mosquitoes ends with their death due to their relatively short life-cycle, so we do not have recovery or immune term in the vector equations [86,87].

3.2 Model analysis

To analyze the system we know that the total human population varies with time due to disease induced death, i.e. for the human population we have;

$\dot{N}_h = \dot{S}_h + \dot{I}_h + \dot{A}_h$

From the model equations above we have;

$\dot{N}_h = \dot{S}_h + \dot{I}_h + \dot{A}_h$

$=\lambda_h - ab_1 I_v\frac{S_h}{N_h} - \mu_h S_h + \gamma(I_h + A_h) + ab_1 I_v\frac{S_h}{N_h} - (\mu_h + \alpha + \delta + \gamma)I_h + \delta I_h - (\mu_h + \gamma)A_h$

$=\lambda_h - \mu_h(S_h + I_h + A_h) - \alpha I_h$

$=\lambda_h - \mu_h N_h - \alpha I_h$,since $N_h = S_h + I_h + A_h$ Hence,

$$\dot{N}_h(t) = \lambda_h - \mu_h N_h - \alpha I_h$$

which is a clear indication that the human population varies with time.

If we consider the model at disease free state i.e $I_h = 0$, we have from above equation;

$$\dot{N}_h = \lambda_h - \mu_h N_h$$

$$\frac{dN_h}{dt} = \lambda_h - \mu_h N_h$$

or

$$\frac{dN_h}{dt} + \mu_h N_h = \lambda_h$$

and using the integrating factor

$$e^{\int \mu_h dt} = e^{\mu_h t}$$

we have;

$$e^{\mu_h t}\frac{dN_h}{dt} + e^{\mu_h t}\mu_h N_h = \lambda_h e^{\mu_h t}$$

or

$$\frac{d}{dt}(N_h e^{\mu_h t}) = \lambda_h e^{\mu_h t}$$

or

$$d(N_h e^{\mu_h t}) = \lambda_h e^{\mu_h t} dt$$

or

$$\int d(N_h e^{\mu_h t}) = \int \lambda_h e^{\mu_h t} dt$$

or

$$\int d(N_h e^{\mu_h t}) = \lambda_h \int e^{\mu_h t} dt$$

or

$$N_h e^{\mu_h t} = \frac{\lambda_h}{\mu_h} e^{\mu_h t} + C_1$$

or

$$N_h(t) = \frac{\lambda_h}{\mu_h} + C_1 e^{-\mu_h t}$$

giving human population at disease free state as t approaches 0 as $N_h(0) =$

$N_h^0 = \frac{\lambda_h}{\mu_h} + C_1$, where C_1 is a constant of integration. The limit of $N_h(t) = \frac{\lambda_h}{\mu_h} + C_1 e^{-\mu_h t}$ as t approaches infinity is $N_h^\infty = \frac{\lambda_h}{\mu_h}$, which is the carrying capacity of the human population. From this it implies that the human population is constant in the absence of the disease.

For the vector population we have at disease free state;

$$\dot{N}_v = \dot{S}_v + \dot{I}_v$$

$$= \lambda_v - ab_2 S_v \frac{I_h}{N_h} - ab_3 S_v \frac{A_h}{N_h} - \mu_v S_v + ab_2 S_v \frac{I_h}{N_h} + ab_3 S_v \frac{A_h}{N_h} - \mu_v I_v$$

$$= \lambda_v - \mu_v (S_v + I_v) = 0$$

or

using $N_v = S_v + I_v$, we have;

$$\frac{dN_v}{dt} = \lambda_v - \mu_v N_v$$

or

$$\frac{dN_v}{dt} + \mu_v N_v = \lambda_v$$

and using the integrating factor

$$e^{\int \mu_v dt} = e^{\mu_v t}$$

we have;

$$e^{\mu_v t}\frac{dN_v}{dt} + e^{\mu_v t}\mu_v N_v = \lambda_v e^{\mu_v t}$$

or

$$\frac{d}{dt}(N_v e^{\mu_v t}) = \lambda_v e^{\mu_v t}$$

or

$$d(N_v e^{\mu_v t}) = \lambda_v e^{\mu_v t} dt$$

or

$$\int d(N_v e^{\mu_v t}) = \int \lambda_h e^{\mu_v t} dt$$

or

$$\int d(N_v e^{\mu_v t}) = \lambda_v \int e^{\mu_v t} dt$$

or

$$N_v e^{\mu_v t} = \frac{\lambda_v}{\mu_v} e^{\mu_v t} + C_2$$

or

$$N_v(t) = \frac{\lambda_v}{\mu_v} + C_2 e^{-\mu_h t}$$

giving mosquito population at disease free state as t approaches 0 as $N_v(0) = N_v^0 = \frac{\lambda_v}{\mu_v} + C_2$, where C_2 is a constant of integration. The limit of $N_v(t) = \frac{\lambda_v}{\mu_v} + C_2 e^{-\mu_v t}$ as t approaches infinity is $N_v^\infty = \frac{\lambda_v}{\mu_v}$, which is the carrying capacity of the mosquito population. Which implies that the mosquito population is a constant.

3.3 A compact positively invariant set

Using Barrier theorems [79,80] we prove that the set
$T = \left\{(I_h, A_h, I_v, N_h, N_v) | 0 \leq A_h \leq I_h \leq N_h \leq \frac{\lambda_h}{\mu_h}, 0 \leq I_v \leq N_v \leq \frac{\lambda_v}{\mu_v}\right\}$ is a positively invariant compact set for the system. Moreover T is a global attractor on the non-negative orthant R_+^5.

Since the ODE is Lipschitz we check that the vector field induced by the system is either tangent or entering T on the boundary T. We have the following clear implications:

- $N_v = 0 \Rightarrow \dot{N}_v > 0$ and $N_v \geq \frac{\lambda_v}{\mu_v} \Rightarrow \dot{N}_v \leq 0$;
- $I_h = 0 \Rightarrow \dot{I}_h \geq 0$;
- $A_h = 0 \Rightarrow \dot{A}_h \geq 0$;

- Since $I_v \leq N_v$ we have $I_V = 0 \Rightarrow \dot{I}_v \geq 0$
- $N_h = 0 \Rightarrow \dot{N}_h > 0$ and $N_h \geq \frac{\lambda_h}{\mu_h} \Rightarrow \dot{N}_h \leq 0$;
- When $N_v = I_v$ and $N_v \geq \frac{\lambda_v}{\mu_v}$ we have $\dot{N}_v - \dot{I}_v = \lambda_v - 2\mu_v N_v \leq 0$;
- When $N_h = (I_h + A_h)$ and $N_h \geq \frac{\lambda_h}{\mu_h}$ we have $\dot{N}_h - (\dot{I}_h + \dot{A}_h) = \lambda_h - (2\mu_h + 2\alpha + \gamma)N_h \leq 0$.

The above relations prove that all trajectories tends to T, which ends the proof of the above claim.This also implies that all trajectories are forward bounded.We denote the demographic equilibria by $N_h^* = \frac{\lambda_h}{\mu_h}$ and $N_v^* = \frac{\lambda_v}{\mu_v}$.

3.4 Reduction of the model

We see that in the equation $\dot{N}_v = \lambda_v - \mu_v N_v$ that only N_v is appearing. Hence our system can be reduced to a four equations. Using Vidyasagar theorem on T [80] we can reduce the stability study to the stability of the equivalent system.

$$\dot{I}_h = \frac{dI_h}{dt} = ab_1 I_v \frac{S_h}{N_h} - (\mu_h + \alpha + \delta + \gamma)I_h,$$

$$\dot{A}_h = \frac{dA_h}{dt} = \delta I_h - (\mu_h + \gamma)A_h,$$

$$\dot{I}_v = \frac{dI_v}{dt} = ab_2 S_v \frac{I_h}{N_h} + ab_3 S_v \frac{A_h}{N_h} - \mu_v I_v.$$

$$\dot{N}_h = \frac{dN_h}{dt} = \lambda_h - \mu_h N_h - \alpha I_h$$

which is considered on

$$\Omega = \{(I_h, A_h, I_v, N_h) | 0 \leq I_h \leq A_h \leq N_h \leq N_h^*, 0 \leq I_v \leq N_v \leq N_v^*\}$$

A similar argument, as in the preceding section shows that Ω is a global attractor on the non-negative orthant R_+^4 for the above system.

Disease Free Equilibrium

Equating the right hand side of the model odes to zero and using the fact that at Disease Free Equilibrium; $I_h^* = A_h^* = I_v^* = 0$, $S_v = N_v$ and $S_v = N_v$, We have;

$$\dot{N}_h = \lambda_h - \mu_h N_h = 0$$

$$\dot{I}_h = 0$$

$$\dot{A}_h = 0$$

$$\dot{N}_v = \lambda_v - \mu_v N_v = 0$$

$$\dot{I}_v = 0$$

From the first and the third equations above we have $N_h^* = \frac{\lambda_h}{\mu_h}$ and $N_v^* = \frac{\lambda_v}{\mu_v}$ as the other equilibrium points. From this we see that $N_h^* = S_h^* = \frac{\lambda_h}{\mu_h}$ and $N_v^* = S_v^* = \frac{\lambda_v}{\mu_v}$, which are the equilibrium populations for both human and vector respectively. Which implies that the ODEs at disease free state are always greater than or equal to zero hence the well-posedness of the

compartmental model differential equations at disease free state.

3.5 The Basic Reproduction Number

We use the next generation matrix K to obtain the basic reproduction number and we let F denote the matrix for new infection term and V denote the matrix for transition term [78]. Using the fact that $S_h = N_h - (A_h + I_h)$ and $S_v = N_v - I_v$. Since the human population is not constant due to disease induced death, we study the four equations below, that is;

$$\dot{I}_h = \frac{dI_h}{dt} = ab_1 I_v \frac{S_h}{N_h} - (\mu_h + \alpha + \delta + \gamma) I_h,$$

$$\dot{A}_h = \frac{dA_h}{dt} = \delta I_h - (\mu_h + \gamma) A_h,$$

$$\dot{I}_v = \frac{dI_v}{dt} = ab_2 S_v \frac{I_h}{N_h} + ab_3 S_v \frac{A_h}{N_h} - \mu_v I_v.$$

$$\dot{N}_h = \frac{dN_h}{dt} = \lambda_h - \mu_h N_h - \alpha I_h$$

which can be written in matrix form as,

$$\begin{bmatrix} \\ \dot{I}_h \\ \dot{A}_h \\ \dot{I}_v \\ \dot{N}_h \end{bmatrix} = \begin{bmatrix} -(\mu_h + \alpha + \delta + \gamma) & 0 & \frac{ab_1 S_h}{N_h} & 0 \\ \delta & -(\mu_h + \gamma) & 0 & 0 \\ \frac{ab_2 S_v}{N_h} & \frac{ab_3 S_v}{N_h} & -\mu_v & 0 \\ -\alpha & 0 & 0 & -\mu_h \end{bmatrix} \begin{bmatrix} I_h \\ A_h \\ I_v \\ N_h \end{bmatrix}$$

or

$$\begin{bmatrix} \\ \dot{I}_h \\ \dot{A}_h \\ \dot{I}_v \\ \dot{N}_h \end{bmatrix} = \left\{ \begin{bmatrix} 0 & 0 & \frac{ab_1 S_h}{N_h} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{ab_2 S_v}{N_h} & \frac{ab_3 S_v}{N_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} - \begin{bmatrix} (\mu_h + \alpha + \delta + \gamma) & 0 & 0 & 0 \\ -\delta & (\mu_h + \gamma) & 0 & 0 \\ 0 & 0 & \mu_v & 0 \\ \alpha & 0 & 0 & \mu_h \end{bmatrix} \right\} \begin{bmatrix} I_h \\ A_h \\ I_v \\ N_h \end{bmatrix}$$

or

$$\begin{bmatrix} \\ \dot{I}_h \\ \dot{A}_h \\ \dot{I}_v \\ \dot{N}_h \end{bmatrix} = \left\{ \begin{bmatrix} 0 & 0 & \frac{ab_1 S_h}{N_h} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{ab_2 S_v}{N_h} & \frac{ab_3 S_v}{N_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} I_h \\ A_h \\ I_v \\ N_h \end{bmatrix} - \begin{bmatrix} (\mu_h + \alpha + \delta + \gamma) & 0 & 0 & 0 \\ -\delta & (\mu_h + \gamma) & 0 & 0 \\ 0 & 0 & \mu_v & 0 \\ \alpha & 0 & 0 & \mu_h \end{bmatrix} \begin{bmatrix} I_h \\ A_h \\ I_v \\ N_h \end{bmatrix} \right\}$$

or

$$\begin{bmatrix} \\ \dot{I}_h \\ \dot{A}_h \\ \dot{I}_v \\ \dot{N}_h \end{bmatrix} = [F - V] \begin{bmatrix} I_h \\ A_h \\ I_v \\ N_h \end{bmatrix}$$

where, $[F - V] = J$, the Jacobian matrix of the system of differential equa-

tions on linearizing, with;

$$F = \begin{bmatrix} 0 & 0 & \frac{ab_1 S_h}{N_h} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{ab_2 S_v}{N_h} & \frac{ab_3 S_v}{N_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

and

$$V = \begin{bmatrix} (\mu_h + \alpha + \delta + \gamma) & 0 & 0 & 0 \\ -\delta & (\mu_h + \gamma) & 0 & 0 \\ 0 & 0 & \mu_v & 0 \\ \alpha & 0 & 0 & \mu_h \end{bmatrix}$$

Now linearizing at disease free equilibrium $E_0 = (0, 0, 0, N_h^*)$ we have $N_h^* = S_h^* = \frac{\lambda_h}{\mu_h}, N_v^* = S_v^* = \frac{\lambda_v}{\mu_v}$ and $A_h^* = I_h^* = I_v^* = 0$ we have F and V matrices as;

$$F = \begin{bmatrix} 0 & 0 & \frac{ab_1 S_h^*}{N_h^*} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{ab_2 S_v^*}{N_h^*} & \frac{ab_3 S_v^*}{N_h^*} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & 0 & \frac{ab_1 N_h^*}{N_h^*} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{ab_2 N_v^*}{N_h^*} & \frac{ab_3 N_v^*}{N_h^*} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & 0 & ab_1 & 0 \\ 0 & 0 & 0 & 0 \\ \frac{ab_2 \lambda_v \mu_h}{\mu_v \lambda_h} & \frac{ab_3 \lambda_v \mu_h}{\mu_v \lambda_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V = \begin{bmatrix} (\mu_h + \alpha + \delta + \gamma) & 0 & 0 & 0 \\ -\delta & (\mu_h + \gamma) & 0 & 0 \\ 0 & 0 & \mu_v & 0 \\ \alpha & 0 & 0 & \mu_h \end{bmatrix}$$

It follows that the basic reproduction number, R_0 is given by; $R_0 = \rho(FV^{-1})$. From Diekmann and Heesterbeek, the matrix $K = FV^{-1}$ is referred to as the next generation matrix for the system of differential equations at the disease free equilibrium. We use the theorem below in calculating, R_0 i.e,

Theorem 1:$s(F - V) < 0 \Leftrightarrow \rho(FV^{-1}) < 1$. *The matrix* $K = FV^{-1}$ *is the next generation matrix and its spectral radius,* $R_0 = \rho(FV^{-1})$*, is the basic reproduction number.*

We now use the Gauss-Jordan method of matrix inversion to find the inverse matrix, V^{-1} of matrix, V by setting the system as,

$$[V \quad | \quad I_3] = \left[\begin{array}{cccc|cccc} (\mu_h + \alpha + \delta + \gamma) & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ -\delta & (\mu_h + \gamma) & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & \mu_v & 0 & 0 & 0 & 1 & 0 \\ \alpha & 0 & 0 & \mu_h & 0 & 0 & 0 & 1 \end{array}\right]$$

In which after row reduction becomes,

$$[I_3 \quad | \quad V^{-1}] = \left[\begin{array}{cccc|cccc} 1 & 0 & 0 & 0 & \frac{1}{\mu_h+\alpha+\delta+\gamma} & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & \frac{\delta}{(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{1}{(\mu_h+\gamma)} & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & \frac{1}{\mu_v} & 0 \\ 0 & 0 & 0 & 1 & -\frac{\alpha}{\mu_h(\mu_h+\alpha+\delta+\gamma)} & 0 & 0 & \frac{1}{\mu_h} \end{array}\right]$$

where,

$$V^{-1} = \begin{bmatrix} \frac{1}{\mu_h+\alpha+\delta+\gamma} & 0 & 0 & 0 \\ \frac{\delta}{(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{1}{(\mu_h+\gamma)} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_v} & 0 \\ -\frac{\alpha}{\mu_h(\mu_h+\alpha+\delta+\gamma)} & 0 & 0 & \frac{1}{\mu_h} \end{bmatrix}$$

or

$$V^{-1} = \frac{1}{(\mu_h+\alpha+\delta+\gamma)} \begin{bmatrix} 1 & 0 & 0 & 0 \\ \frac{\delta}{(\mu_h+\gamma)} & \frac{(\mu_h+\alpha+\delta+\gamma)}{(\mu_h+\gamma)} & 0 & 0 \\ 0 & 0 & \frac{(\mu_h+\alpha+\delta+\gamma)}{\mu_v} & 0 \\ -\frac{\alpha}{\mu_h} & 0 & 0 & \frac{(\mu_h+\alpha+\delta+\gamma)}{\mu_h} \end{bmatrix}$$

$$K = FV^{-1} = \begin{bmatrix} 0 & 0 & ab_1 & 0 \\ 0 & 0 & 0 & 0 \\ \frac{ab_2\lambda_v\mu_h}{\mu_v\lambda_h} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\mu_h+\alpha+\delta+\gamma} & 0 & 0 & 0 \\ \frac{\delta}{(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{1}{(\mu_h+\gamma)} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_v} & 0 \\ -\frac{\alpha}{\mu_h(\mu_h+\alpha+\delta+\gamma)} & 0 & 0 & \frac{1}{\mu_h} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{ab_1}{\mu_v} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{a\lambda_v\mu_h[(\mu_h+\gamma)b_2+\delta b_3]}{\mu_v\lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h(\mu_h+\gamma)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

The characteristic polynomial of the matrix K is given by,

$P(\lambda) = |K - \lambda I| = 0$

or

$$P(\lambda) = |K - \lambda I| = \begin{vmatrix} -\lambda & 0 & \frac{ab_1}{\mu_v} & 0 \\ 0 & -\lambda & 0 & 0 \\ \frac{a\lambda_v\mu_h[(\mu_h+\gamma)b_2+\delta b_3]}{\mu_v\lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h(\mu_h+\gamma)} & -\lambda & 0 \\ 0 & 0 & 0 & -\lambda \end{vmatrix}$$

$$= -\lambda \left[\begin{vmatrix} -\lambda & 0 & \frac{ab_1}{\mu_v} \\ 0 & -\lambda & 0 \\ \frac{a\lambda_v\mu_h[(\mu_h+\gamma)b_2+\delta b_3]}{\mu_v\lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h(\mu_h+\gamma)} & -\lambda \end{vmatrix} \right] = 0$$

On expanding along the fourth row then along the second row of the 3 by 3 matrix, we have;

$$P(\lambda) = |K - \lambda I| = -\lambda \left[-\lambda \begin{vmatrix} -\lambda & \frac{ab_1}{\mu_v} \\ \frac{a\lambda_v\mu_h[(\mu_h+\gamma)b_2+\delta b_3]}{\mu_v\lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} & -\lambda \end{vmatrix} \right] = 0$$

$$P(\lambda) = \lambda^2 \left\{ \lambda^2 - \frac{a^2 b_1 \lambda_v \mu_h[(\mu_h+\gamma)b_2 + \delta b_3]}{\mu_v^2 \lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} \right\} = 0$$

with the eigenvalues of K as ;

$$\lambda_1 = \lambda_2 = 0$$

$$\lambda_3 = -\left\{ \frac{a^2 b_1 \lambda_v \mu_h[(\mu_h+\gamma)b_2 + \delta b_3]}{\mu_v^2 \lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} \right\}^{\frac{1}{2}}$$

and

$$\lambda_4 = \left\{ \frac{a^2 b_1 \lambda_v \mu_h[(\mu_h+\gamma)b_2 + \delta b_3]}{\mu_v^2 \lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} \right\}^{\frac{1}{2}}$$

Since all parameters are positive we have;

$$\lambda_4 = \left\{ \frac{a^2 b_1 \lambda_v \mu_h[(\mu_h+\gamma)b_2 + \delta b_3]}{\mu_v^2 \lambda_h(\mu_h+\gamma)(\mu_h+\alpha+\delta+\gamma)} \right\}^{\frac{1}{2}} > 0$$

Since ρ is the spectral radius of $K = FV^{-1}$ and using the fact that we are

considering two populations for both human and mosquito, we have;

$$\rho = R_0 = \lambda_4^2 = \frac{a^2 b_1 \lambda_v \mu_h[(\mu_h + \gamma)b_2 + \delta b_3]}{\mu_v^2 \lambda_h(\mu_h + \gamma)(\mu_h + \alpha + \delta + \gamma)}$$

or using the expressions for $N_h^* = \frac{\lambda_h}{\mu_h}$ and $N_v^* = \frac{\lambda_v}{\mu_v}$

$$\rho = R_0 = \lambda_4^2 = \frac{a^2 b_1 N_v^*[(\mu_h + \gamma)b_2 + \delta b_3]}{\mu_v N_h^*(\mu_h + \gamma)(\mu_h + \alpha + \delta + \gamma)}$$

which is the basic reproduction number.

3.6 Stability analysis

In this section we establish the local and global stability of the disease free equilibrium (D.F.E) and local stability of endemic equilibrium (EE).

3.6.1 Disease Free Equilibrium (DFE), E_0

In the absence of the disease in the population we have $I_h^* = 0, A_h^* = 0$ and $I_v^* = 0$ which gives $N_h^* = \frac{\lambda_h}{\mu_h}$ and $N_v^* = \frac{\lambda_v}{\mu_v}$. This implies that the disease free equilibrium is the set $E_0 = (0, 0, 0, \frac{\lambda_h}{\mu_h})$

3.6.2 Local stability analysis of the DFE, E_0

We let $\bar{\gamma} = (\mu_h + \alpha + \delta + \gamma)$ and consider the reduced system;

$$\dot{I}_h = \frac{dI_h}{dt} = ab_1 I_v \frac{S_h}{N_h} - \bar{\gamma} I_h,$$

$$\dot{A}_h = \frac{dA_h}{dt} = \delta I_h - (\mu_h + \gamma) A_h,$$

$$\dot{I}_v = \frac{dI_v}{dt} = ab_2 S_v \frac{I_h}{N_h} + ab_3 S_v \frac{A_h}{N_h} - \mu_v I_v,$$

$$\dot{N}_h = \frac{dN_h}{dt} = \lambda_h - \mu_h N_h - \alpha I_h$$

we analyse the stability of the disease free equilibrium by linearizing the above system of differential equations to give the Jacobian matrix as,

$$J = \begin{bmatrix} -\bar{\gamma} & 0 & \frac{ab_1 S_h}{N_h} & 0 \\ \delta & -(\mu_h + \gamma) & 0 & 0 \\ \frac{ab_2 S_v}{N_h} & \frac{ab_3 S_v}{N_h} & -\mu_v & 0 \\ -\alpha & 0 & 0 & -\mu_h \end{bmatrix}$$

the Jacobian at the disease free equilibrium is given by,

$$J_{DFE} = \begin{bmatrix} -\bar{\gamma} & 0 & ab_1 & 0 \\ \delta & -(\mu_h + \gamma) & 0 & 0 \\ \frac{ab_2\lambda_v\mu_h}{\mu_v\lambda_h} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} & -\mu_v & 0 \\ -\alpha & 0 & 0 & -\mu_h \end{bmatrix}$$

with the characteristic polynomial $P(\lambda)$ at disease free equilibrium given by,

$$P(\lambda) = |J_{DFE} - \lambda I| = 0$$

or

$$P(\lambda) = |J_{DFE} - \lambda I| = \begin{vmatrix} -\bar{\gamma} & 0 & ab_1 & 0 \\ \delta & -(\mu_h + \gamma + \lambda) & 0 & 0 \\ \frac{ab_2\lambda_v\mu_h}{\mu_v\lambda_h} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} & -(\mu_v + \lambda) & 0 \\ -\alpha & 0 & 0 & -(\mu_h + \lambda) \end{vmatrix} = 0$$

Expanding along the fourth row we have;

$$P(\lambda) = \alpha \begin{vmatrix} 0 & ab_1 & 0 \\ -\bar{\gamma} & 0 & 0 \\ \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} & -(\mu_v+\lambda) & 0 \end{vmatrix}$$

$$-(\mu_h+\lambda) \begin{vmatrix} -(\bar{\gamma}+\lambda) & 0 & ab_1 \\ \delta & -(\mu_h+\gamma+\lambda) & 0 \\ \frac{ab_2\lambda_v\mu_h}{\mu_v\lambda_h} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} & -(\mu_v+\lambda) \end{vmatrix}$$

$$= \alpha[0] - (\mu_h+\lambda) \begin{vmatrix} -(\bar{\gamma}+\lambda) & 0 & ab_1 \\ \delta & -(\mu_h+\gamma+\lambda) & 0 \\ \frac{ab_2\lambda_v\mu_h}{\mu_v\lambda_h} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} & -(\mu_v+\lambda) \end{vmatrix}$$

$$= -(\mu_h+\lambda) \begin{vmatrix} -(\bar{\gamma}+\lambda) & 0 & ab_1 \\ \delta & -(\mu_h+\gamma+\lambda) & 0 \\ \frac{ab_2\lambda_v\mu_h}{\mu_v\lambda_h} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} & -(\mu_v+\lambda) \end{vmatrix} = 0$$

which gives $-(\mu_v+\lambda) = 0$, that is $\lambda_1 = -\mu_v$ or;

$$P(\lambda) = \begin{vmatrix} -(\bar{\gamma}+\lambda) & 0 & ab_1 \\ \delta & -(\mu_h+\gamma+\lambda) & 0 \\ \frac{ab_2\lambda_v\mu_h}{\mu_v\lambda_h} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} & -(\mu_v+\lambda) \end{vmatrix} = 0,$$

Expanding this along the first row we have

$$P(\lambda) = -(\bar{\gamma}+\lambda)\begin{vmatrix} -(\mu_h+\gamma+\lambda) & 0 \\ \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} & -(\mu_v+\lambda) \end{vmatrix} + ab_1 \begin{vmatrix} \delta & -(\mu_h+\gamma+\lambda) \\ \frac{ab_2\lambda_v\mu_h}{\mu_v\lambda_h} & \frac{ab_3\lambda_v\mu_h}{\mu_v\lambda_h} \end{vmatrix} = 0$$

or

$$\begin{aligned} P(\lambda) &= \lambda^3 + \lambda^2[2(\mu_h+\gamma)+\alpha+\delta+\mu_v] \\ &+\lambda\left\{\bar{\gamma}(\mu_h+\gamma+\mu_v)+(\mu_h+\gamma)\mu_v - \frac{a^2b_1b_2\lambda_v\mu_h}{\mu_v\lambda_h}\right\} \\ &+\left\{(\mu_h+\gamma)\mu_v\bar{\gamma} - \frac{a^2b_1\lambda_v\mu_h[b_2(\mu_h+\gamma)+b_3\delta]}{\mu_v\mu_h}\right\} = 0 \end{aligned}$$

which is equivalent to the polynomial

$$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

where

$$a_0 = 1 > 0$$

$$a_1 = 2(\mu_h + \gamma) + \alpha + \delta + \mu_v > 0$$

$$a_2 = \bar{\gamma}(\mu_h + \gamma + \mu_v) + (\mu_h + \gamma)\mu_v - \frac{a^2 b_1 b_2 \lambda_v \mu_h}{\mu_v \lambda_h}$$

$$= \bar{\gamma}(\mu_h + \gamma) + (\mu_h + \gamma)\mu_v + \bar{\gamma}\mu_v$$

$$- \frac{a^2 b_1 b_2 \lambda_v \mu_h (\mu_h + \gamma)}{\mu_v \lambda_h (\mu_h + \gamma)} - \frac{a^2 b_1 b_3 \lambda_v \mu_h \delta}{\mu_v \lambda_h (\mu_h + \gamma)} + \frac{a^2 b_1 b_3 \lambda_v \mu_h \delta}{\mu_v \lambda_h (\mu_h + \gamma)}$$

$$= (\mu_h + \gamma)(\mu_v + \bar{\gamma}) + \frac{a^2 b_1 b_3 \lambda_v \mu_h \delta}{\mu_v \lambda_h (\mu_h + \gamma)}$$

$$+ \bar{\gamma}\mu_v \left[1 - \frac{a^2 b_1 \lambda_v \mu_h [(\mu_h + \gamma) b_2 + \delta b_3]}{\mu_v^2 \lambda_h (\mu_h + \gamma)\bar{\gamma}}\right]$$

$$= (\mu_h + \gamma)(\mu_v + \bar{\gamma}) + \frac{a^2 b_1 b_3 \lambda_v \mu_h \delta}{\mu_v \lambda_h (\mu_h + \gamma)} + (\mu_h + \alpha + \delta + \gamma)\mu_v [1 - R_0],$$

which is always greater than zero when$(\mu_h + \alpha + \delta + \gamma)\mu_v[1 - R_0] > 0$ that is, if and only if $R_0 \leq 1$

$$a_3 = (\mu_h + \gamma)\mu_v \bar{\gamma} - \frac{a^2 b_1 \lambda_v \mu_h [b_2(\mu_h + \gamma) + b_3 \delta]}{\mu_v \mu_h}$$

$$= (\mu_h + \gamma)\mu_v \bar{\gamma} \left[1 - \frac{a^2 b_1 \lambda_v \mu_h [(\mu_h + \gamma) b_2 + \delta b_3]}{\mu_v^2 \lambda_h (\mu_h + \gamma)\bar{\gamma}}\right]$$

$$= (\mu_h + \gamma)\mu_v \bar{\gamma}[1 - R_0]$$

which is greater than zero if and only if $R_0 \leq 1$

Since solving the above characteristic polynomial for eigenvalues is tedious we will use the Routh-Hurwitz criterion to determine whether all roots have negative real parts and establish the stability of the system without solving the characteristic equation itself. We use the following lemma.

Lemma 1 (**Routh-Hurwitz criterion**): *The roots of the characteristic equation have negative real parts if and only if all the principal diagonal minors of the Hurwitz matrix are positive provided that* $a_0 > 0$.

For our case of a third order system, the stability criterion is defined by the inequalities $a_0 > 0, a_1 > 0, a_2 > 0$ and $a_1 a_2 - a_0 a_3 > 0$. Now,

$$
\begin{aligned}
&a_1 a_2 - a_0 a_3 = [2(\mu_h + \gamma) + \alpha + \delta + \mu_v] \times \\
&\left[(\mu_h + \gamma)(\mu_v + \bar{\gamma}) + \frac{a^2 b_1 b_3 \lambda_v \mu_h \delta}{\mu_v \lambda_h (\mu_h + \gamma)} + \bar{\gamma}\mu_v[1 - R_0]\right] \\
&- [(\mu_h + \gamma)\mu_v \bar{\gamma}[1 - R_0]] \\
&= [2(\mu_h + \gamma) + \alpha + \delta + \mu_v] \times \\
&\left[(\mu_h + \gamma)(\mu_v + \bar{\gamma}) + \frac{a^2 b_1 b_3 \lambda_v \mu_h \delta}{\mu_v \lambda_h (\mu_h + \gamma)}\right] \\
&+ [2(\mu_h + \gamma) + \alpha + \delta + \mu_v]\bar{\gamma}\mu_v[1 - R_0] \\
&- [(\mu_h + \gamma)\mu_v \bar{\gamma}[1 - R_0]] \\
&= [2(\mu_h + \gamma) + \alpha + \delta + \mu_v] \times \\
&\qquad \left[(\mu_h + \gamma)(\mu_v + \bar{\gamma}) + \frac{a^2 b_1 b_3 \lambda_v \mu_h \delta}{\mu_v \lambda_h (\mu_h + \gamma)}\right] + \bar{\gamma}\mu_v[1 - R_0][\mu_v + \bar{\gamma}]
\end{aligned}
$$

which is always greater than zero if and only if $R_0 \leq 1$

It is clear from the above that all coefficients and $a_1a_2 - a_0a_3$ are greater than zero when $R_0 \leq 1$. Hence from Routh-Hurwitz criterion we have all the real parts of eigenvalues of the Hurwitz matrix being negative, hence the stability. From the above criterion we can state the following lemma.

Lemma 2: *The Disease Free Equilibrium, E_0 is locally asymptotically stable if $R_0 \leq 1$, and unstable if $R_0 > 1$.*

The quantity, R_0 is a measure of the number of secondary infections infected by a single infected vector or individual [82]. It is an important threshold parameter that plays a big role in the control of malaria infection. The reduction of the infection targets the parameters that will bring its value to less than unity. When the reproduction number, is less than unity, the disease free equilibrium is locally asymptotically stable, and therefore, the disease dies out after some period of time.

3.6.3 Global stability analysis of the DFE, E_0

The global stability of the disease free equilibrium, E_0 is established from the following theorem.

Theorem 2: *The disease free equilibrium $E_0 = (0, 0, 0, \frac{\lambda_h}{\mu_h})$ of the system of differential equations is globally asymptotically stable if $R_0 \leq 1$, and unstable if $R_0 > 1$*

proof: Consider the Lyapunov function

$$L = \mu_v(\mu_h + \gamma)I_h + \frac{a^2 b_1 b_3 \lambda_v \mu_h A_h}{\mu_v \lambda_h} + a b_1(\mu_h + \gamma)I_v$$

Its derivative along the solutions of the system of differential equations is;

$$\begin{aligned}
\dot{L} &= \mu_v(\mu_h+\gamma)\dot{I}_h + \frac{a^2b_1b_3\lambda_v\mu_h\dot{A}_h}{\mu_v\lambda_h} + ab_1(\mu_h+\gamma)\dot{I}_v \\
&= \mu_v(\mu_h+\gamma)[\frac{ab_1S_hI_v}{N_h} - \bar{\gamma}I_h] \\
&\quad + \frac{a^2b_1b_3\lambda_v\mu_h}{\mu_v\lambda_h}[\delta I_h - (\mu_h+\gamma)A_h] \\
&\quad + ab_1(\mu_h+\gamma)\left[\frac{ab_2I_hS_v}{N_h} + \frac{ab_3A_hS_v}{N_h} - \mu_vI_v\right] \\
&\leq \mu_v(\mu_h+\gamma)[ab_1I_v - \bar{\gamma}I_h] \\
&\quad + \frac{a^2b_1b_3\lambda_v\mu_h}{\mu_v\lambda_h}[\delta I_h - (\mu_h+\gamma)A_h] \\
&\quad + ab_1(\mu_h+\gamma)\left[\frac{ab_2\lambda_v\mu_hI_h}{\mu_v\lambda_h} + \frac{ab_3\lambda_v\mu_hA_h}{\mu_v\lambda_h} - \mu_vI_v\right] \\
&= \left[\frac{a^2b_1\lambda_v\mu_hb_2(\mu_h+\gamma)}{\mu_v\lambda_h} + \frac{a^2b_1\lambda_v\mu_h\delta b_3}{\mu_v\lambda_h} - \mu_v(\mu_h+\gamma)\bar{\gamma}\right]I_h \\
&\quad + \left[\frac{a^2b_1b_3\lambda_v\mu_h(\mu_h+\gamma)}{\mu_v\lambda_h} - \frac{a^2b_1b_3\lambda_v\mu_h(\mu_h+\gamma)}{\mu_v\lambda_h}\right]A_h \\
&\quad + [a(\mu_h+\gamma)\mu_vb_1 - a(\mu_h+\gamma)\mu_vb_1]I_v \\
&= \left[\frac{a^2b_1\lambda_v\mu_h[(\mu_h+\gamma)b_2+\delta b_3]}{\mu_v\lambda_h} - \mu_v(\mu_h+\gamma)\bar{\gamma}\right]I_h + 0A_h + 0I_v \\
&= \left[\frac{a^2b_1\lambda_v\mu_h[(\mu_h+\gamma)b_2+\delta b_3]}{\mu_v\lambda_h} - \mu_v(\mu_h+\gamma)\bar{\gamma}\right]I_h \\
&= \mu_v(\mu_h+\gamma)\bar{\gamma}\left[\frac{a^2b_1\lambda_v\mu_h[(\mu_h+\gamma)b_2+\delta b_3]}{\mu_v^2\lambda_h(\mu_h+\gamma)\bar{\gamma}} - 1\right]I_h \\
&= \mu_v(\mu_h+\gamma)\bar{\gamma}[R_0-1]I_h \leq 0 \quad iff \quad R_0 \leq 1.
\end{aligned}$$

Thus we have established that $\dot{L} \leq 0$ if $R_0 \leq 1$ and the equality $\dot{L} = 0$ holds if and only if $R_0 = 1$ and $I_h = A_h = I_v = 0$. If $R_0 > 1$, then

$\dot{L} > 0$ when $S_h(t)$ and $S_v(t)$ is sufficiently close to $\frac{\lambda_h}{\mu_h}$ and $\frac{\lambda_v}{\mu_v}$ respectively except when $A_h = I_h = I_v = 0$. Therefore the largest compact invariant set $D = \left\{(I_h^*, A_h^*, I_v^*, N_v^*, N_h^*) \in D : \dot{L} = 0\right\}$, when $R_0 \leq 1$, is the singleton $\{E_0\}$. On the boundary when $I_h = A_h = I_v = 0$, $\dot{N}_h(t) = \lambda_h - \mu_h N_h$ and $\dot{N}_v(t) = \lambda_v - \mu_v N_v$ and $N_h(t) \longrightarrow \frac{\lambda_h}{\mu_h}$, $N_v(t) \longrightarrow \frac{\lambda_v}{\mu_v}$ as $t \longrightarrow \infty$. From Lasalle-Lyapunov theorem, every solution that starts in the region D approaches E_0 as $t \longrightarrow \infty$. When $R_0 \leq 1$ this proves the theorem and thus the disease free equilibrium is globally asymptotically stable.

3.6.4 Endemic equilibrium

Endemic equilibrium points $E_1 = (\bar{I}_h, \bar{A}_h, \bar{I}_v, \bar{N}_h)$

To establish the endemic equilibrium we equate to zero the right hand side of the below and using the fact that at endemic equilibrium $\bar{S}_h = \bar{N}_h - \bar{I}_h - \bar{A}_h$, $\bar{S}_v = N_v^* - \bar{I}_v$ and $\bar{\gamma} = (\mu_h + \alpha + \delta + \gamma)$;

$$\dot{I}_h = \frac{dI_h}{dt} = ab_1 I_v \frac{S_h}{N_h} - (\mu_h + \alpha + \delta + \gamma) I_h,$$

$$\dot{A}_h = \frac{dA_h}{dt} = \delta I_h - (\mu_h + \gamma) A_h,$$

$$\dot{I}_v = \frac{dI_v}{dt} = ab_2 S_v \frac{I_h}{N_h} + ab_3 S_v \frac{A_h}{N_h} - \mu_v I_v.$$

$$\dot{N}_h = \frac{dN_h}{dt} = \lambda_h - \mu_h N_h - \alpha I_h$$

that is,

$$ab_1\bar{I}_v\frac{(\bar{N}_h-\bar{I}_h-\bar{A}_h)}{\bar{N}_h}-\bar{\gamma}\bar{I}_h=0,$$

$$\delta\bar{I}_h-(\mu_h+\gamma)\bar{A}_h=0,$$

$$ab_2(N_v^*-\bar{I}_v)\frac{\bar{I}_h}{\bar{N}_h}+ab_3(N_v^*-\bar{I}_v)\frac{\bar{A}_h}{\bar{N}_h}-\mu_v\bar{I}_v=0$$

$$\lambda_h-\mu_h\bar{N}_h-\alpha\bar{I}_h=0$$

or

$$ab_1\bar{I}_v(\bar{N}_h-\bar{I}_h-\bar{A}_h)-\bar{\gamma}\bar{I}_h\bar{N}_h=0, \tag{1}$$

$$\delta\bar{I}_h-(\mu_h+\gamma)\bar{A}_h=0, \tag{2}$$

$$ab_2(N_v^*-\bar{I}_v)\bar{I}_h+ab_3(N_v^*-\bar{I}_v)\bar{A}_h-\mu_v\bar{I}_v\bar{N}_h=0, \tag{3}$$

and

$$\lambda_h-\mu_h\bar{N}_h-\alpha\bar{I}_h=0 \tag{4}$$

From equations 2 and 4 we can solve for $\bar{A}_h$ and $\bar{N}_h$ in terms of $\bar{I}_h$, that is;

$$\bar{A}_h=\frac{\delta}{(\mu_h+\gamma)}\bar{I}_h \tag{5}$$

and

$$\bar{N}_h = \frac{\lambda_h}{\mu_h} - \frac{\alpha}{\mu_h}\bar{I}_h \tag{6}$$

using equations 5 and 6 we simplify equation 1 and hence solve for $\bar{I}_v$ in terms of $\bar{I}_h$, that is;

$$ab_1\bar{I}_v(\bar{N}_h - \bar{I}_h - \bar{A}_h) = \bar{\gamma}\bar{I}_h\bar{N}_h$$

or

$$ab_1\bar{I}_v\left[\frac{\lambda_h}{\mu_h} - \frac{\alpha}{\mu_h}\bar{I}_h - \bar{I}_h - \frac{\delta}{(\mu_h+\gamma)}\bar{I}_h\right] = \bar{\gamma}\bar{I}_h\left[\frac{\lambda_h}{\mu_h} - \frac{\alpha}{\mu_h}\bar{I}_h\right]$$

or

$$ab_1\bar{I}_v\left[\frac{(\mu_h+\gamma)(\lambda_h - \alpha\bar{I}_h) - \mu_h(\mu_h+\gamma)\bar{I}_h - \mu_h\delta\bar{I}_h}{\mu_h(\mu_h+\gamma)}\right] = \bar{\gamma}\bar{I}_h\left[\frac{\lambda_h}{\mu_h} - \frac{\alpha}{\mu_h}\bar{I}_h\right]$$

or

$$ab_1\bar{I}_v\left[(\mu_h+\gamma)(\lambda_h - \alpha\bar{I}_h) - \mu_h(\mu_h+\gamma)\bar{I}_h - \mu_h\delta\bar{I}_h\right] = \bar{\gamma}(\mu_h+\gamma)(\lambda_h - \alpha\bar{I}_h)\bar{I}_h$$

or

$$ab_1\bar{I}_v\left[(\mu_h+\gamma)\lambda_h - [(\mu_h+\gamma)(\alpha+\mu_h) + \mu_h\delta]\bar{I}_h\right] = \bar{\gamma}(\mu_h+\gamma)[\lambda_h - \alpha\bar{I}_h]\bar{I}_h$$

or

$$\bar{I}_v = \frac{\bar{\gamma}(\mu_h + \gamma)[\lambda_h - \alpha\bar{I}_h]\bar{I}_h}{ab_1[(\mu_h + \gamma)\lambda_h - [(\mu_h + \gamma)(\alpha + \mu_h) + \mu_h\delta]\bar{I}_h]} \tag{7}$$

With the same argument we use equations 5 and 6 in equation 3 to determine the value of $\bar{I}_v$ in terms of $\bar{I}_h$ with $N_v^* = \frac{\lambda_v}{\mu_v}$, that is;

$$ab_2(N_v^* - \bar{I}_v)\bar{I}_h + ab_3(N_v^* - \bar{I}_v)\bar{A}_h = \mu_v\bar{I}_v\bar{N}_h$$

or

$$ab_2\left[\frac{\lambda_v}{\mu_v} - \bar{I}_v\right]\bar{I}_h + ab_3\left[\frac{\lambda_v}{\mu_v} - \bar{I}_v\right]\left[\frac{\delta}{(\mu_h + \gamma)}\bar{I}_h\right] = \mu_v\bar{I}_v\left[\frac{\lambda_h}{\mu_h} - \frac{\alpha}{\mu_h}\bar{I}_h\right]$$

or

$$ab_2\lambda_v\mu_h(\mu_h + \gamma)\bar{I}_h + ab_3\lambda_v\mu_h\delta\bar{I}_h$$
$$= \left\{\mu_v^2(\mu_h + \gamma)[\lambda_h - \alpha\bar{I}_h] + ab_2\mu_h\mu_v(\mu_h + \gamma)\bar{I}_h + ab_3\mu_h\mu_v\delta\bar{I}_h\right\}\bar{I}_v$$

or

$$a\mu_h\lambda_v[b_2(\mu_h + \gamma) + b_3\delta]\bar{I}_h$$
$$= \left\{\mu_v^2(\mu_h + \gamma)\lambda_h - \mu_v^2(\mu_h + \gamma)\alpha\bar{I}_h + a\mu_h\mu_v[b_2(\mu_h + \gamma) + b_3\delta]\bar{I}_h\right\}\bar{I}_v$$

or

$$a\mu_h\lambda_v[b_2(\mu_h+\gamma)+b_3\delta]\bar{I}_h$$

$$=\left\{\mu_v^2(\mu_h+\gamma)\lambda_h+[a\mu_h\mu_v[b_2(\mu_h+\gamma)+b_3\delta]-\mu_v^2(\mu_h+\gamma)\alpha]\bar{I}_h\right\}\bar{I}_v$$

or

$$\bar{I}_v=\frac{a\mu_h\lambda_v[b_2(\mu_h+\gamma)+b_3\delta]\bar{I}_h}{\mu_v^2(\mu_h+\gamma)\lambda_h+[a\mu_h\mu_v[b_2(\mu_h+\gamma)+b_3\delta]-\mu_v^2(\mu_h+\gamma)\alpha]\bar{I}_h}$$

or

$$\bar{I}_v=\frac{a\mu_h\lambda_v K\bar{I}_h}{\mu_v^2(\mu_h+\gamma)\lambda_h+[a\mu_h\mu_v K-\mu_v^2(\mu_h+\gamma)\alpha]\bar{I}_h} \tag{8}$$

where $K=[b_2(\mu_h+\gamma)+b_3\delta]$.

Equating the values of $\bar{I}_v$ in equations 7 and 8 we obtain the value of $\bar{I}_h$ as an expression of parameters only, that is;

$$\frac{\bar{\gamma}(\mu_h+\gamma)[\lambda_h-\alpha\bar{I}_h]\bar{I}_h}{ab_1[(\mu_h+\gamma)\lambda_h-[(\mu_h+\gamma)(\alpha+\mu_h)+\mu_h\delta]\bar{I}_h]}$$
$$=\frac{a\mu_h\lambda_v K\bar{I}_h}{\mu_v^2(\mu_h+\gamma)\lambda_h+[a\mu_h\mu_v K-\mu_v^2(\mu_h+\gamma)\alpha]\bar{I}_h}$$

or

$$\left\{\bar{\gamma}(\mu_h+\gamma)[\lambda_h-\alpha\bar{I}_h]\bar{I}_h\right\}\left\{\mu_v^2(\mu_h+\gamma)\lambda_h+[a\mu_h\mu_vK-\mu_v^2(\mu_h+\gamma)\alpha]\bar{I}_h\right\}$$
$$=\left\{a\mu_h\lambda_vK\bar{I}_h\right\}\left\{ab_1[(\mu_h+\gamma)\lambda_h-[(\mu_h+\gamma)(\alpha+\mu_h)+\mu_h\delta]\bar{I}_h]\right\}$$

or

$$A\bar{I}_h^2+B\bar{I}_h+C=0 \tag{9}$$

where;

$$A=\bar{\gamma}(\mu_h+\gamma)\alpha\left[a\mu_h\mu_vK-\mu_v^2(\mu_h+\gamma)\alpha\right]$$
$$=\bar{\gamma}(\mu_h+\gamma)\mu_v\alpha\left\{a\mu_hK-\mu_v(\mu_h+\gamma)\alpha\right\}$$
$$=\bar{\gamma}(\mu_h+\gamma)\mu_v\alpha\left\{\frac{\bar{\gamma}(\mu_h+\gamma)\lambda_h\mu_v^2}{ab_1\lambda_v}\left[R_0-\frac{ab_1\lambda_v\alpha}{\mu_v\lambda_h\bar{\gamma}}\right]\right\}$$
$$=\frac{\bar{\gamma}(\mu_h+\gamma)^2\mu_v^3\lambda_h\alpha}{ab_1\lambda_v}\left\{R_0-\frac{ab_1\lambda_v\alpha}{\mu_v\lambda_h\bar{\gamma}}\right\},$$

$$B=2\bar{\gamma}\alpha(\mu_h+\gamma)^2\mu_v^2\lambda_h-a\mu_hK\left\{\bar{\gamma}(\mu_h+\gamma)\mu_v\lambda_h+\lambda_v[(\mu_h+\gamma)(\mu_h+\alpha)+\mu_h\delta]\right\}$$
$$=\frac{\bar{\gamma}(\mu_h+\gamma)\mu_v^2\lambda_h}{ab_1\lambda_v}\left\{2ab_1\lambda_v\alpha(\mu_h+\gamma)-R_0[\bar{\gamma}(\mu_h+\gamma)\mu_v\lambda_h+\lambda_v[(\mu_h+\gamma)(\mu_h+\alpha)+\mu_h\delta]]\right\},$$

and

$$C = a\mu_h\lambda_v\lambda_h(\mu_h+\gamma)K - \bar{\gamma}(\mu_h+\gamma)^2\mu_v^2\lambda_h^2$$
$$= \frac{\bar{\gamma}(\mu_h+\gamma)^2\mu_v^2\lambda_h^2}{ab_1}\left[R_0 - 1\right].$$

Multiplying both sides of the quadratic equation by the term $\frac{ab_1\lambda_v}{\bar{\gamma}(\mu_h+\gamma)\mu_v^2\lambda_h}$ the above constants becomes;

$$A = \bar{\gamma}(\mu_h+\gamma)\mu_v\left\{R_0 - \frac{ab_1\lambda_v\alpha}{\mu_v\lambda_h\bar{\gamma}}\right\},$$

$$B = \{2ab_1\lambda_v\alpha(\mu_h+\gamma) - R_0[\bar{\gamma}(\mu_h+\gamma)\mu_v\lambda_h + \lambda_v[(\mu_h+\gamma)(\mu_h+\alpha)+\mu_h\delta]]\},$$

and

$$C = (\mu_h+\gamma)\lambda_h\lambda_v\left[R_0 - 1\right].$$

we now use the quadratic formula to find the roots of equation 9, that is;

$$\bar{I}_h = \frac{-B \pm \sqrt{B^2 - 4AC}}{2A}$$

from this we see that $-B$ is always positive when $R_0 > 1$ hence we take,

$$\bar{I}_h = \frac{-B + \sqrt{B^2 - 4AC}}{2A} \tag{10}$$

which is always positive for it to biologically realistic. Now from equations 5, 6, 8 and using this value of $\bar{I}_h$ we have in terms of parameters only;

$$\bar{A}_h = \frac{\delta}{(\mu_h + \gamma)}\bar{I}_h \tag{11}$$

$$\bar{N}_h = \frac{\lambda_h}{\mu_h} - \frac{\alpha}{\mu_h}\bar{I}_h \tag{12}$$

$$\bar{I}_v = \frac{a\mu_h\lambda_v K\bar{I}_h}{\mu_v^2(\mu_h+\gamma)\lambda_h + [a\mu_h\mu_v K - \mu_v^2(\mu_h+\gamma)\alpha]\bar{I}_h} = \frac{R_0\bar{\gamma}\lambda_v\lambda_h\bar{I}_h}{(\mu_v\bar{\gamma}\lambda_h R_0 - \alpha)\bar{I}_h + ab_1\lambda_v\lambda_h}. \tag{13}$$

Hence the endemic equilibrium points have been determined in terms of parameters in equations 10, 11, 12 and 13 above.

3.6.5 Local stability analysis of the endemic equilibrium EE, E_1

In this section we prove that if $R_0 > 1$, then the endemic equilibrium E_1 is locally asymptotically stable.

Theorem 3: *If $R_0 > 1$ then the endemic equilibrium of the system is locally asymptotically stable.*

The endemic equilibrium $E_1 = (\bar{I}_h, \bar{A}_h, \bar{I}_v, \bar{N}_h)$ is expressed in terms of R_0 with the components as in the above equations 10, 11, 12 and 13. It is noted from these equations that the system has no positive endemic equilibrium

point if $R_0 < 1$. This is because $\bar{I}_h, \bar{A}_h, \bar{I}_v$ will assume negative values which is not biologically realistic. Thus a positive endemic equilibrium point is achieved only when $R_0 > 1$. That is for existence of endemic equilibrium, $E_1 = (\bar{I}_h, \bar{A}_h, \bar{I}_v, \bar{N}_h)$,its coordinates should satisfy $\bar{I}_h > 0, \bar{A}_h > 0$, $\bar{I}_v > 0$ and $\bar{N}_h > 0$

Proof of theprem 3: The Jacobian matrix of the system

$$\dot{I}_h = \frac{dI_h}{dt} = ab_1 I_v \frac{S_h}{N_h} - \bar{\gamma} I_h,$$

$$\dot{A}_h = \frac{dA_h}{dt} = \delta I_h - (\mu_h + \gamma) A_h,$$

$$\dot{I}_v = \frac{dI_v}{dt} = ab_2 S_v \frac{I_h}{N_h} + ab_3 S_v \frac{A_h}{N_h} - \mu_v I_v.$$

$$\dot{N}_h = \frac{dN_h}{dt} = \lambda_h - \mu_h N_h - \alpha I_h$$

is given by;

$$J = \begin{bmatrix} -\bar{\gamma} & 0 & \frac{ab_1 S_h}{N_h} & 0 \\ \delta & -(\mu_h + \gamma) & 0 & 0 \\ \frac{ab_2 S_v}{N_h} & \frac{ab_3 S_v}{N_h} & -\mu_v & 0 \\ -\alpha & 0 & 0 & -\mu_h \end{bmatrix}$$

giving the Jacobian at the endemic equilibrium as,

$$J_{EE} = \begin{bmatrix} -\bar{\gamma} & 0 & \frac{ab_1(\bar{N}_h - \bar{I}_h - \bar{A}_h)}{\bar{N}_h} & 0 \\ \delta & -(\mu_h + \gamma) & 0 & 0 \\ \frac{ab_2(N_v^* - \bar{I}_v)}{\bar{N}_h} & \frac{ab_3(N_v^* - \bar{I}_v)}{\bar{N}_h} & -\mu_v & 0 \\ -\alpha & 0 & 0 & -\mu_h \end{bmatrix}$$

with the characteristic polynomial $P(\lambda)$ at endemic equilibrium given by,

$$P(\lambda) = |J_{EE} - \lambda I| = 0$$

or

$$P(\lambda) = |J_{EE} - \lambda I| =$$

$$\begin{bmatrix} -(\bar{\gamma} + \lambda) & 0 & \frac{ab_1(\bar{N}_h - \bar{I}_h - \bar{A}_h)}{\bar{N}_h} & 0 \\ \delta & -(\mu_h + \gamma + \lambda) & 0 & 0 \\ \frac{ab_2(N_v^* - \bar{I}_v)}{\bar{N}_h} & \frac{ab_3(N_v^* - \bar{I}_v)}{\bar{N}_h} & -(\mu_v + \lambda) & 0 \\ -\alpha & 0 & 0 & -(\mu_h + \lambda) \end{bmatrix} = 0$$

Expanding along the fourth row we have;

$$P(\lambda) = -\alpha \begin{vmatrix} 0 & \frac{ab_1(\bar{N}_h - \bar{I}_h - \bar{A}_h)}{\bar{N}_h} & 0 \\ -(\mu_h + \gamma + \lambda) & 0 & 0 \\ \frac{ab_3(N_v^* - \bar{I}_v)}{\bar{N}_h} & -(\mu_v + \lambda) & 0 \end{vmatrix}$$

$$-(\mu_h + \lambda) \begin{vmatrix} -(\bar{\gamma} + \lambda) & 0 & \frac{ab_1(\bar{N}_h - \bar{I}_h - \bar{A}_h)}{\bar{N}_h} \\ \delta & -(\mu_h + \gamma + \lambda) & 0 \\ \frac{ab_2(N_v^* - \bar{I}_v)}{\bar{N}_h} & \frac{ab_3(N_v^* - \bar{I}_v)}{\bar{N}_h} & -(\mu_v + \lambda) \end{vmatrix}$$

$$= -(\mu_h + \lambda) \begin{vmatrix} -(\bar{\gamma} + \lambda) & 0 & \frac{ab_1(\bar{N}_h - \bar{I}_h - \bar{A}_h)}{\bar{N}_h} \\ \delta & -(\mu_h + \gamma + \lambda) & 0 \\ \frac{ab_2(N_v^* - \bar{I}_v)}{\bar{N}_h} & \frac{ab_3(N_v^* - \bar{I}_v)}{\bar{N}_h} & -(\mu_v + \lambda) \end{vmatrix}$$

$$= 0$$

which gives $-(\mu_v + \lambda) = 0$, that is $\lambda_1 = -\mu_v$ or;

$$P(\lambda) = \begin{vmatrix} -(\bar{\gamma} + \lambda) & 0 & \frac{ab_1(\bar{N}_h - \bar{I}_h - \bar{A}_h)}{\bar{N}_h} \\ \delta & -(\mu_h + \gamma + \lambda) & 0 \\ \frac{ab_2(N_v^* - \bar{I}_v)}{\bar{N}_h} & \frac{ab_3(N_v^* - \bar{I}_v)}{\bar{N}_h} & -(\mu_v + \lambda) \end{vmatrix} = 0,$$

expanding this along the first row we have

$$P(\lambda) =$$

$$-(\bar{\gamma} + \lambda) \begin{vmatrix} -(\mu_h + \gamma + \lambda) & 0 \\ \frac{ab_3 \lambda_v \mu_h}{\mu_v \lambda_h} & -(\mu_v + \lambda) \end{vmatrix} + \frac{ab_1(\bar{N}_h - \bar{I}_h - \bar{A}_h)}{\bar{N}_h} \begin{vmatrix} \delta & -(\mu_h + \gamma + \lambda) \\ \frac{ab_2(N_v^* - \bar{I}_v)}{\bar{N}_h} & \frac{ab_3(N_v^* - \bar{I}_v)}{\bar{N}_h} \end{vmatrix} = 0$$

or

$$P(\lambda) = -(\bar{\gamma}+\lambda)(\mu_h+\gamma+\lambda)(\mu_v+\lambda) + \frac{ab_1(\bar{N}_h-\bar{I}_h-\bar{A}_h)}{\bar{N}_h}\left[\delta\frac{ab_3(N_v^*-\bar{I}_v)}{\bar{N}_h}+(\mu_h+\gamma+\lambda)\frac{ab_2(N_v^*-\bar{I}_v)}{\bar{N}_h}\right]=0$$

or

$$P(\lambda) = -(\bar{\gamma}+\lambda)[(\mu_h+\gamma)\mu_v+\lambda(\mu_h+\gamma+\mu_v)+\lambda^2]+a^2b_1b_3\delta(N_v^*-\bar{I}_v)\frac{(\bar{N}_h-\bar{I}_h-\bar{A}_h)}{\bar{N}_h^2} + a^2b_1b_2(\mu_h+\gamma+\lambda)(N_v^*-\bar{I}_v)\frac{(\bar{N}_h-\bar{I}_h-\bar{A}_h)}{\bar{N}_h^2}=0$$

or

$$P(\lambda) = \lambda^3+\lambda^2(\bar{\gamma}+\mu_h+\gamma+\mu_v)+\lambda\left[\bar{\gamma}(\mu_h+\gamma+\mu_v)+(\mu_h+\gamma)\mu_v-a^2b_1b_2P\right] \tag{14}$$

$$+\left[\bar{\gamma}(\mu_h+\gamma)\mu_v-a^2b_1P\right]=0 \tag{15}$$

where

$$P=(N_v^*-\bar{I}_v)\frac{(\bar{N}_h-\bar{I}_h-\bar{A}_h)}{\bar{N}_h^2}$$

in which equation 14 is equivalent to the cubic polynomial,

$$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

Where;

$$a_0 = 1$$

$$a_1 = (\bar{\gamma} + \mu_h + \gamma + \mu_v)$$

$$a_2 = [\bar{\gamma}(\mu_h + \gamma + \mu_v) + (\mu_h + \gamma)\mu_v - a^2 b_1 b_2 P]$$

$$a_3 = [\bar{\gamma}(\mu_h + \gamma)\mu_v - a^2 b_1 P]$$

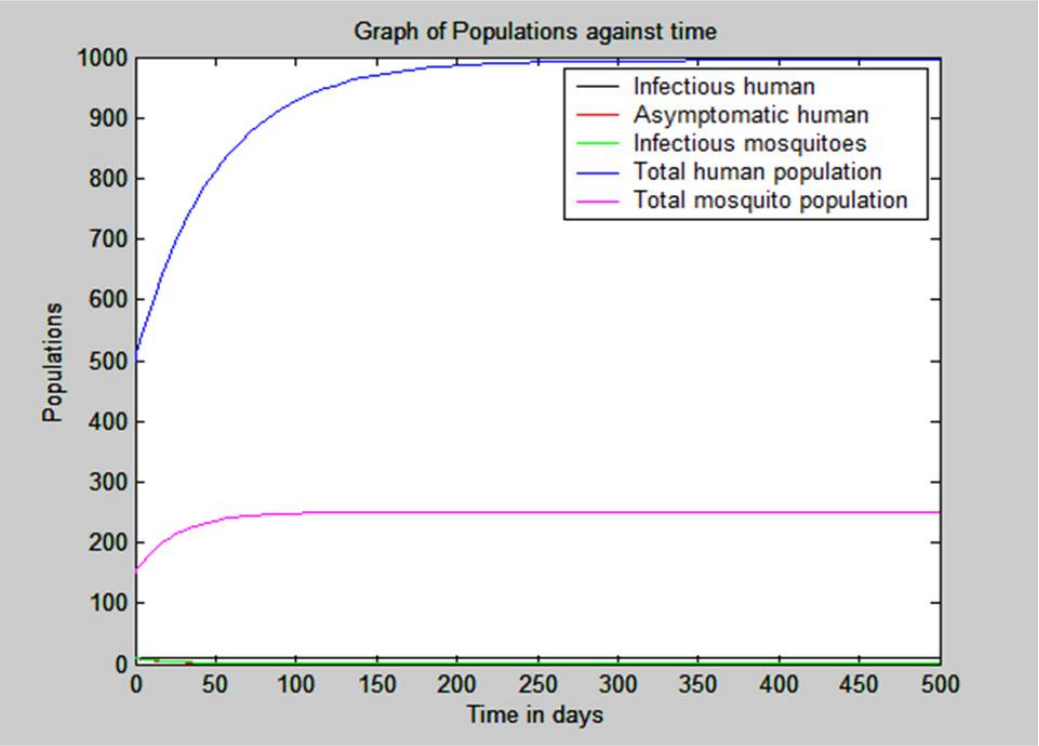
From above equations it is clearly seen that if $R_0 > 1$ we have $a_1 > 0$, $a_2 > 0$ and $a_3 > 0$ since p is always a small fraction. Now we find $a_1 a_2 - a_3 a_0$, that is;

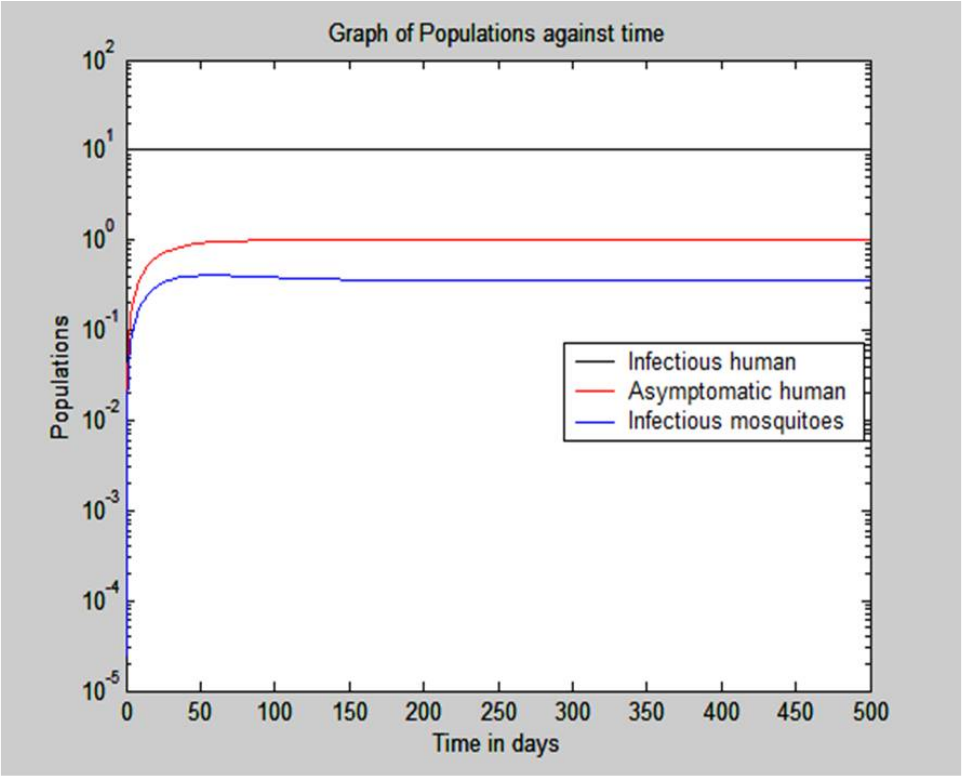
$$\begin{aligned}
& a_1 a_2 - a_3 a_0 \\
= (\bar{\gamma} + \mu_h + \gamma + \mu_v)[\bar{\gamma}(\mu_h + \gamma + \mu_v) + (\mu_h + \gamma)\mu_v - a^2 b_1 b_2 P] & \\
-[\bar{\gamma}(\mu_h + \gamma)\mu_v - a^2 b_1 P] & \\
= \bar{\gamma}(\mu_h + \gamma + \mu_v) & \\
+(\mu_h + \gamma + \mu_v)[(\mu_h + \gamma + \mu_v) + (\mu_h + \gamma)\mu_v] & \\
+a^2 b_1 P - (\bar{\gamma} + \mu_h + \gamma + \mu_v) a^2 b_1 b_2 P &
\end{aligned}$$

Which is clearly greater than zero when $R_0 > 1$. Thus, according to Hurwitz Criterion, the cubic polynomial has only roots with negative real parts and the endemic equilibrium is locally asymptotically stable; otherwise, if $R_0 < 1$ it may have atleast one positive root hence the endemic equilibrium is unstable. Hence the theorem above is proved.

3.7 Numerical simulations

The graphs of population agaist time was plotted. The following numerical values were used: $a = 0.01, b_1 = 0.2, b_2 = b_3 = 0.5, \delta = 0.005, \gamma = 0.03, \alpha = 0.01, \mu_v = 0.04, \mu_h = 0.02, \lambda_v = 10$ and $\lambda_h = 20$ with initial conditions $N_h(0) = 520, N_v(0) = 150, I_h(0) = 10, A_h(0) = 0$ and $I_v(0) = 0$ giving $R_0 = 0.001058$. In the first graph all compartments populations were plotted against time and it was clear that populations increased with time leveling off in the long-run. In the second figure only the disease compartment populations were considered.


Graph of Populations against time
Infectious human
Asymptomatic human
Infectious mosquitoes
Total human population
Total mosquito population
Populations
Time in days
0
100
200
300
400
500
600
700
800
900
1000
0
50
100
150
200
250
300
350
400
450
500


Graph of Populations against time
Populations
Time in days
Infectious human
Asymptomatic human
Infectious mosquitoes
10^{2}
10^{1}
10^{0}
10^{-1}
10^{-2}
10^{-3}
10^{-4}
10^{-5}
0
50
100
150
200
250
300
350
400
450
500

4 CONCLUSION

We modeled malaria as a 5-dimensional system of ordinary differential equations. We showed the existence and uniqueness of a domain where the model is epidemiologically and mathematically well-posed. The model was analysed for the disease free equilibrium and endemic equilibrium. We defined the reproduction number in terms of the parameters. It was also established that for the basic reproduction number, $R_0 \leq 1$, the disease free equilibrium point is asymptotically stable so that the disease dies out after some period of time and if $R_0 > 0$, the disease free equilibrium is unstable. We also established that when $R_0 > 1$ then the endemic equilibrium is locally asymptotically stable, and unstable if $R_0 < 1$. From the numerical simulations it is clear that populations increase with time and finally leveling off in the long run when carrying capacity is reached.

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