

KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY,
KUMASI

DYNAMICS OF MULTI INFECTIONS DISEASE
(MALARIA-ELEPHANTIASIS-ZIKA VIRUS) TRANSMISSION IN MOSQUITO
ENDEMIC REGIONS

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BY

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This thesis submitted to the Department of Mathematics of the School of Physical Sciences, College of Agriculture and Natural Sciences, Kwame Nkrumah University of Science and Technology, in partial fulfilment of the requirements for the award of Doctor of Philosophy degree in Applied Mathematics

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DECLARATION

Candidate's Declaration

I hereby declare that this thesis is the result of my own original research and that no part of it has been presented for another degree in this university or elsewhere.

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Supervisors' Declaration

We hereby declare that the preparation and presentation of the thesis were supervised in accordance with the guidelines on supervision of thesis laid down by the Kwame Nkrumah University of Science and Technology.

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ABSTRACT

Mosquitoes are one of the deadliest insects in the world. Their ability to carry and spread disease to humans cause millions of deaths every year. The worldwide incidence of diseases caused by mosquitoes has risen 30-fold in the past 30 years, and more countries are reporting their first outbreaks of the mosquito caused diseases. Zika, Malaria, and Elephantiasis are all transmitted to humans by the *Aedes aegypti* mosquito. More than half of the world's population live in areas where this mosquito species are present. Sustained mosquito control efforts are important to prevent outbreaks from these diseases. There are several different types of mosquitoes and some have the ability to carry many different diseases. The study presents a multi-infections system model to study the transmission dynamics of Malaria, Zika-Virus and Elephantiasis in an endemic region such as Kedougou in the South Eastern part of Senegal and other parts of the world. This makes it possible to have multi-infections of the three diseases simultaneously. The main objective of this work was to study the dynamics of multi-infections (Malaria-Elephantiasis-Zika virus) and transmission through the use of mathematical model, to determine the stability of the multi-infections model, the co-infections model and also study the single models for individual diseases including Malaria, Zika and Elephantiasis. The disease-free equilibrium is performed and it was shown to be globally asymptotically stable when the associated threshold number known as the basic reproduction number for the model is $R_0 < 1$. Investigation on the existence and stability of equilibria was also derived, the model was found to exhibit backward bifurcation. Thus, R_0 less than unity is not sufficient to eradicate the disease from the population and there was the need to lower R_0 below a certain threshold for effective disease control. Sensitivity analysis was performed to determine parameters that have high influence on the basic

reproduction number. Optimal control policies was also used as measures to eradicate the diseases from the system.

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DEDICATION

This thesis is dedicated to God and my family

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CHAPTER ONE

INTRODUCTION

1.1 Background to the Study

Zika virus disease is mostly by mosquito (mosquitosurveillance, 2016; Gao et al., 2016; zika, 2016) which is also responsible for the spread of chikungunya and other disease. The disease was initially discovered in an animal in Uganda forest the year 1947 (Abushouk et al., 2016);(Nautiyal, 2017). However, much attention was not given to it until recently when it started causing harm to expectant mothers in the South and Central America. Mothers in these countries were producing microcephaly babies (children with abnormal small head and other neurological disorders), and this caught the attention of the World Health Organization (WHO). The incidence of Zika virus disease is spreading and this is partly due to the fact that there is neither cure nor vaccine.

As part of the mode of transmission of zika virus, only female aedes aegypti mosquito can cause an infection and this has to be done during the viremic stage. That is in the first several days of infection, when the virus is still circulating in the human blood. The mosquito takes up the virus, stores it in her gut and salivary glands, and then transmits it when she bites another uninfected human (Hennessey et al., 2016). As part of the mode of transmission, there has been an evidence that zika virus can be contracted through casual sex with an infected person according to Centre for Disease and preventive Control (CDC). In the light of this, the very key things in the spread should be known to come out with the measures to control the spread.

In another development, Malaria is an old disease that was first studied by Ross in the late 1800's (Kamal-Yanni et al., 2012). There are a number of mosquito species in the world, however only those species from female anopheles genus can transmit malaria (WHO1, 2015). The first disease is an infection obtained

from a female Anopheles mosquito. The species parasites include: plasmodium falciparum, plasmodium vivax, plasmodium ovale, plasmodium Malariae and plasmodium Knowlese (Olaniyi & Obabiyi, 2013). Among the parasites, plasmodium falciparum is considered as deadly (Geleta & Ketema, 2016). The disease continues to be a major problem in sub- sub-Sahara Africa, Asia, Central and South America and furthermore the Middle East. Almost 40% of the world's population settles in endemic areas (Mwamtobe et al., 2014). The disease is caused by parasite and is spread between people through contact. It kills many million people yearly, majority of whom are African children (N. Chitnis et al., 2006). The parasites develops into the body of human between 10–18 days. As time goes on the parasites find their way in the body and develop in the cells. At this stage the infected individuals symptoms include fever etc.

To add to the first two diseases is the third disease is also a vector borne disease. It is a neglected tropical disease primarily prevalent in poor population in 73 countries (Kastner et al., 2015). It is a disease which is caused by worms that are spread by the bite of mosquitoes (Medicalnewstoday, 2018). The skin becomes bigger than the normal size. There are three types of worms namely; Wuchereria Bancroft, Brugia Malayi and Brugia Timori. Wuchereria accounts for majority of the cases around the globe (Bhunu & Mushayabasa, 2012).

Multi-infection is an individual suffering from many infection. However, Coinfections are two diseases such as malaria and zika virus only or malaria and elephantiasis only etc. But, entomological survey conducted by Muturi et al. (2006) in some inland villages along the coast of Kenya showed that there is a common item for malaria, zika virus and other diseases. Mosquitoes were sampled by the use of spray sheet collection inside houses and were later sorted to species for examination using an enzyme-linked immunosorbent assay (ELISA). The result showed that there is the possibility of an individual being infected with all three diseases though the intensity of say malaria, zika

virus or elephantiasis by their respective mosquito species will be much higher compare to the other.

1.2 Statement of the Problem

Zika virus has been in many regions around the globe for couple of years and has been misdiagnosed and treated as malaria because of similarities in symptoms (WHO1, 2015).

As a result of this, the health care officials in diverse ways sampled out some patients who reported at the health facilities in Kadougou district, Senegal to test for arboviruses (Diagne et al., 2015).

It was confirmed that some of the patients were not only having arboviruses but were also co-infected with other diseases such as malaria and others (Sow et al., 2016). This has necessitated the research into multi infectious diseases in mosquito endemic regions where other vector borne diseases are common. As an example, Okongo (2015) developed a mathematical model involving a multi-infection system of differential equations of HIV/AIDS co-infected with TB and Malaria. From his study the susceptible human cannot simultaneously get infected with malaria, HIV/AIDS and TB since the transmission is different for the three diseases. His results showed that with an increase in mosquito biting rate the model exhibit a backward bifurcation phenomenon. However, a susceptible human can simultaneously be infected with Malaria, Zika virus and Elephantiasis even though the same vector but different species. It is against this backdrop that has necessitated the study into the multi-infection (Malaria, Zika virus and Elephantiasis) model.

1.3 Research Objectives

The main objective of this work was to study the dynamics of Malaria-Zika virus and Elephantiasis disease transmission through the use of a mathematical

model. In particular to put up a constructive model incorporating the important epidemiological parameters influencing the multi-infection state of these diseases as well as the spread of the epidemic and possible control strategies.

The objectives of the study were:

1. to develop a model for the human population as well as the mosquito population known to be the causative organism for these diseases.
2. to develop sub-models that investigate the possible impact of the co-infection of diseases.
3. to investigate the conditions under which the epidemics would persist or die out in the population.
4. to carry out sensitivity analysis so as to establish the key vital parameters in the model.
5. to use optimal control technique to examine the control measures and the most effective control measure.

1.4 Significance of the Study

Mathematical modelling over the years has been seen as the process of translating conceptualisation whose theoretical and numerical analysis provides a comprehensive ideas, solutions, and directions useful for the problem under consideration (Martcheva, 2015). It is seen as a tool that gives precision and direction for problem solution and also enables a thorough understanding of the system being modelled by preparing the way for better design to allow for good analysis. The understanding of the dynamics of several diseases has been achieved with the help of these models. This has led to

important measures and strategies being employed to check such diseases and also the eradication of most of the diseases.

This study would help support the World Health Organisation to obtain qualitative information on the progression from Zika-virus, malaria and elephantiasis infection to disease. The dynamics involve also provide further information to various stakeholders in order to make precise policy interventions which would go a long way to accelerate progress towards achieving of the Millennium Development Goals (MDGs) for disease eradication.

Lastly, the work would also aid research scientist, mathematicians, etc., to develop various suitable models in order to help public health professionals make better strategies for controlling the disease.

1.5 Limitation

In the light of the nature of the model used in this work, some of the items used did not have the backing of being clinically or experimentally determined. This is a problem for assessing the model.

1.6 Methodology

A model that examine the epidemiology of the multi-infections diseases (MalariaElephantiasis-Zika virus) using deterministic approach is obtained.

Explanations of the multi-infections model would be done with also the various co-infected sub-models as well as the single individual models would be taken into consideration. Qualitative analysis would be carried out to determine the existence of both disease free and endemic equilibria.

The basic reproduction number which is the threshold value which the health officials use in determining whether the disease would invade the population or the disease would die out would be determined. Routh-Hurwitz criterion would be employed to establish the existence for multi-infectious disease at locally asymptotically stable. Lyapunov function would be constructed to study the global stability of the system. Bifurcation analysis would be considered to examine the behaviour of the system whether the disease would persist if $R_0 < 1$ or $R_0 > 1$.

Sensitivity analysis would also be carried out to determine which parameter would have some serious impact on the multi-infections model. On the control of the spread of the multi-infections, the optimal control analysis would be employed using the principle of Pontryagin Maximum Principle.

1.7 Organisation of the Study

The thesis was arranged into five chapters. In addition to this chapter which describes the background of the research including the objectives, Chapter two was devoted to reviews related works which have been done by other researchers and also discussed various conclusions drawn from these works. Chapter Three explored the various qualitative analysis employed in this study and performed the sensitivity analysis. In Chapter Four, we used the programming tool to calibrate the model to derive numerical results in order to interpret and analyse the behaviour of the model.

Finally, Chapter Five captured the summary and conclusion of the thesis; discussing the results obtained from the analyses performed and making recommendations where necessary. Further work to be done in the area of this thesis would also be explored with all other conclusions clearly shown.

CHAPTER TWO
LITERATURE REVIEW

2.1 Introduction

This chapter emphasised on literature works on Malaria, Zika-virus and Elephantiasis (Multi-infections) that have been considered by other authors. The focus here is on the epidemiology and the history of the diseases in various countries where these disease are endemic. The clinical manifestation and the method of application of control strategies and options were also mention.

2.2 History and Epidemiologies

Malaria is endemic throughout most of the tropics. Almost ninety five countries and territories around the globe still experience transmission (mosquitosurveillance, 2016). In 2017, the World Health Organization (WHO) reported that, between 2016, substantial increase in cases of incidence occur in WHO regions of Americas and marginally in Southeast Asia, Western Pacific and African regions (Gao et al., 2016). Of the approximately 3.2 billion people living in the endemic countries 1.2 billion are at risk. This was stated by the WHO that there are 214 million people who are symptomatic malaria in 2015. The true magnitude of the mortality and morbidity accountable to malaria globally is at best a scientific assumption, even though it is not disputable that the greatest burden is in sub-Sahara Africa (zika, 2016). The risk of malaria attacks in residents of malaria endemic areas falls as they become older (Baird et al., 1991), suggesting that protection is a function of age.

On the other hand, elephantiasis which is described as a neglected tropical disease with serious economic and social consequence can affect people of all ages (Gelderblom, 1995; Remme et al., 1993; Bhunu & Mushayabasa, 2012). They are caused by three types of nematode namely *Wuchereria Bancrofti*,

Brugia Malayi and *Brugia timori*. Of these *Wuchereria Bancrofti* accounts for 90% of the infection while *Brugia Malayi* and *Brugia Timori* also account for 10% (Bhunu & Mushayabasa, 2012). Human beings are exclusive host of infection with *Wuchereria Bancroft* accounts for the greater percentage. Areas or regions where elephantiasis are common have higher incidence rate of poverty (Tan, 2003) making it a disease of the poor and also serve as an indicator of underdeveloped nation or country. It is estimated that 120 million people globally are affected with the disease (Bhunu & Mushayabasa, 2012).

In another development, Zika virus is also a vector borne disease which is caused by the bite of *Aedes aegypti* mosquitoes (Dick et al., 1952). The infection was first found in the Zika backwoods in rhesus monkeys in Uganda in the year 1947, be that as it may, the main human event was in Nigeria in 1954. (Gao et al., 2016). The main human out break of Zika virus occurred in Yap Island in 2007 in Micronesia but there was no casualties (Posen et al., 2016). In the past, the infection spread eastbound from tropical Africa and Asia to the Pacific islands during the late 2000s to 2010, attacked the Caribbean and Central and South America in 2015 and arrived at North America in 2016 (Song et al., 2017).

2.3 Malaria, Elephantiasis and Zika Virus in Ghana

Malaria has been one of the major causes of poverty and low productivity in the country and this has accounted for approximately 32.5 percent of all cases at the OPD attendances (Boadu et al., 2016). Malaria is considered among the major health and development challenges facing some of the poorest economics in the world (Asante, 2007). The malady represents a normal of 13.2% of all mortality cases in Ghana and 22% of all mortalities in kids under 5 years.

On account of pregnant ladies, out of the absolute number announcing at the wellbeing organizations, 13.8% experience the ill effects of jungle fever and 9.4% of the passings in pregnant ladies (Antwi & Marfo, 1998). As far as malaria elimination is concern, Ghana is categorized in the malaria control phase following the global malaria eradication program. As a result of several years of strategic policy development and control interventions, malaria specific mortality among children less than five years has reduced drastically from 14.4% in 2000 to 0.6% in 2012 (Awine et al., 2017).

Elephantiasis on its part becomes a permanent disability and a major source of worry to socio-economic development in many endemic and sub-tropical countries (Ramaiah et al., 2000). In recent times, close to 120 million people are infected in about 80 countries (Pothikasikorn et al., 2008). In Ghana, research on Elephantiasis has shown that the three Northern regions in the country exhibit greater prevalent compare to the Southern part of the country (J. O. Gyapong et al. (1996); de Souza et al. (2014); Dunyo et al. (1996)). The pattern of the disease manifestations reveal a preponderance of elephantiasis (1.7%), microfilaria(11.3%), hydrocele (20.3%) and breast lymphedema (6.6%) in the Northern Ghana as compared with the Southern part of the country where it is (0.3%, 0.6%, 5.2% and 6.1% respectively) (de Souza et al., 2014).

For Zika virus, since the *Aedes aegypti* mosquito species is not found in Ghana, no incidence has been reported, nevertheless, Ghana is among one of the African countries who are at risk of getting the disease if proper measures are not put in place. Since the disease can be transported through cargo ships and air planes it is possible for a country to acquire it if proper security measures are not put in place. Again since it can be transmitted sexually it is also possible that a partner from an endemic community can pass it on to his or her sex partner who is in Ghana. There was an incidence in Colorado where a scientist returned from Senegal an endemic region with the virus. After having an affair with the wife, it was later confirmed through Laboratory report that both of

them have the Zika virus through sexual intercourse (Zamani & Zamani, 2017). In 2011, it was accounted for that a tainted male has contaminated a female by having vaginal sex, even before the beginning of the side effects.

2.3.1 Mode of Transmission

Only female aedes aegypti mosquito bites an infected human. She has to bite during the viremic stage. That is in the first several days of infection, when the virus is still circulating in the humans blood. The mosquito takes up the virus, stores it in her gut and salivary glands, and then transmits it when she bites another uninfected human (consumerreport, 2016). As part of the mode of transmission, there has been an evidence that zika virus can be contracted through casual sex with an infected person according to CDC. In the light of this, it is very important to know the key parameters in the transmission of the disease and come out with the measures to control the spread. In another development, Malaria is an old disease that was first studied by Ross in the late 1800s (Barley et al., 2012). There are a number of mosquito species in the world, however only those species from female anopheles genus can transmit malaria (zikasituationreport, 2016). There are five species of parasites namely: plasmodium falciparum, plasmodium vivax, plasmodium ovale, plasmodium Knowlese and plasmodium malariae infect human and plasmodium Knowlese (Olaniyi & Obabiyi, 2013).

Among the parasites, plasmodium falciparum is considered as deadly (Geleta & Ketema, 2016). The disease continues to be a major problem in sub-Saharan Africa, Asia, Central and South America and furthermore the Middle East. Almost 40% of the world's population settles in endemic areas (Mwamtobe et al., 2017). The disease is caused by plasmodium parasite and is transmitted between humans through the bite of the female anopheles mosquito. It kills about 700,000 to 2.7 million people yearly, 75% of whom are African children

(N. R. Chitnis, 2005). The parasites develop into the body of human between 10–18 days then is passed on when the mosquito injects saliva while feeding. In the human body malaria parasites migrate to the liver, where they grow and multiply. As time goes on the parasites find their way in the blood stream and continue to develop in the red blood cells. At this stage the infected individuals begin to show symptoms like fever, chills, sweating, headaches and other flu-like conditions. The infection can sometimes produce even more severe reactions including kidney failure and death, especially if not treated for a period of time (mosquitosurveillance, 2016).

To add to the first two diseases is the third disease which is Elephantiasis also known as Lymphatic filariasis which is also a vector borne disease. It is a neglected tropical disease primarily prevalent in poor communities in 73 countries (Kastner et al., 2015). It is a tropical disease caused by parasitic worms that are spread by the bite of mosquitoes (Medicalnewstoday, 2018). The skin becomes bigger than the normal size. There are three types of worms namely; *Wuchereria Bancroft*, *Brugia Malayi* and *Brugia Timori*. *Wuchereria* accounts for 90% of the cases and is found almost tropical and subtropical areas around the globe (Bhunu & Mushayabasa, 2012). Unlike malaria whose main mode of transmission is through the bite of infected female anopheles mosquitoes, elephantiasis has several species of mosquitoes including *Aedes Aegypti* mosquitoes mainly in endemic islands in the Pacific which is responsible of transmitting (zika virus and chikungunya), *Anopheles* female mosquitoes which can also transmit malaria (Sciencegov, 2018) and *Culex* mosquitoes, widespread across urban and semi-urban areas which also transmit elephantiasis. Firstly, before one becomes infected, the person might have lived in endemic region or might have been bitten by such species for a long time. As the mosquitoes become infected with the roundworm larvae they take a blood meal from infected human. It then passes it on to any human that it bites passing the larvae into the bloodstream. Finally, the worm larvae

migrate to the lymphatics through the bloodstream and mature in the lymph system (Medicalnewstoday, 2018). The worms affect the lymphatic system in the body. The lymphatic system is responsible for removing toxic and waste. When the system gets blocked it becomes difficult to function well and as a result leads to back up of lymphatic fluid which causes swelling. Many different species of mosquitoes act as vector for transmission of elephantiasis (Close et al., 2014). Approximately 1.4 billion people in 73 countries globally are under threat by the disease of which 120 million individuals are infected (Mwamtobe et al., 2017).

2.3.2 Difference between Zika-Virus, Malaria and Elephantiasis

Zika virus and Malaria are both mosquito borne diseases. The rise of Zika first in Brazil and now extending to other parts of the world, has raised a lot of questions being asked as to the differences between Zika virus and Malaria. The major differences in the manner we combat the two diseases generate from the fact that they are spread by two different types of mosquitoes namely female anopheles for malaria and female aedes aegypti for zika virus. Female anopheles mosquito bite at night and at dawn and can transmit the malaria. This can be prevented by sleeping in mosquito insecticide nets. On the contrary, the aedes aegypti mosquito bite during the day time (zikaandmalaria, 2016) which makes prevention more complex to deal with. However, to avoid being bitten by the female aedes aegypti mosquito having the virus, the medical experts suggest that using insect repellent and protective clothing can also help in a way (zikapressrelease, 2016). Since Zika virus can be transmitted through sexual intercourse there is the need for us to abstain or consistently use condom (Oster, 2016). Elephantiasis on the other hand is a debilitating disease that affects the leg, arms, and genital organs such as scrotum

(hydrocele). This does not claim life like malaria and other vector borne disease but the stigmatization attached make it more embarrassing. Malaria and Elephantiasis cause the largest public health burden of all vector-borne diseases globally with around 350–500 million clinical episodes and 1 million deaths every year caused by malaria and more than 120 of them globally infected with Elephantiasis (Malaria, 2005). The disease are co-endemic in sub-Saharan Africa (Slater et al., 2013).

Elephantiasis can be transmitted through the bite of infected *Culex* female mosquitoes, *Aedes* mosquitoes and female *Anopheles* mosquitoes dependent on the geographical location of the vector.

2.4 Clinical Presentation

Intestinal sickness is a genuine tropical infection influencing individuals in sub-Saharan Africa, South and Central America, some portion of Middle East and Asia. It is transmitted to people through the nibble of a contaminated female *Anopheles* mosquitoes and brought into the circulatory system of people the parasite (Skeet, 2005). There are five types of parasitic plasmodium species namely; *Plasmodium falciparum*, *Plasmodium Vivax*, *Plasmodium Ovale*, *Plasmodium Malariae* and *Plasmodium Knowlesi*. Out of the five species *Plasmodium falciparum* is described as malignant form and is considered as more serious and can easily claim life. The remaining four which is described as benign form is generally not life threatening except in the infants, very old people and people with immunodeficiencies. Malaria can develop months or even years dependent on once immune system, and also dependent on the parasite causing it. The incubation period from the onset of being bitten to the appearance of clinical symptoms vary according to the species of mosquito.

Following the WHO report on 2005, it remains the leading cause of mortality and morbidity particularly among expectant mothers and children in sub-

Sahara Africa where at least 90% of the incidence of malaria death occurs (Kalinga et al., 2012). It can be categorized into two namely; uncomplicated and severe. In the case of uncomplicated malaria, this is diagnosed when symptoms are present, but there are no signs to indicate severe infection or dysfunction of the vital organs. Uncomplicated can be severe if left unattended to. Indications of uncomplicated jungle fever incorporate an impression of cold with shuddering, fever, cerebral pains, and regurgitating, seizures now and then happen in more youthful kids, sweats, trailed by an arrival to ordinary temperature, with tiredness (medicalnewstoday., 2017).

On the other hand, severe malaria shows clinical and laboratory evidence on vital organs dysfunction. Symptoms of severe malaria include fever and chills, impaired consciousness, prostration, or adopting a prone position, multiple convulsions. Severe malaria, that notwithstanding has recently occurred fairly common in older children in Ghana (33% in a recent series with cerebral malaria) (Kurtzhals et al., 1998). Neonatal malaria emerges as a result of combination of maternal and infant blood during the delivery process may not be so uncommon. On Clinical presentation in the case of elephantiasis is manifested in fever. The fever usually called filarial or elephantoid fever is immune-mediated and generally accompanies attacks of Lymphangitis (Obacha, 2016). Lymphangitis is an infection of the lymph channel, typically originating in the lymph node. Before individual is infected with the disease, that individual must have been bitten by mosquitoes infected with round worm several times, or that individual might have lived in endemic regions or tropical areas. As the infected female mosquito with roundworm bites you, the tiny larvae stays in the bloodstream and multiples in the lymph system. They can survive for many years and can cause harm to the lymphatic system (Medicalnewstoday, 2018). In adult men or boys the parasites settle is the scrotal lymphatics and in women and children are larger lymph vessels and lymph node draining to lower and upper limbs (Mand et al., 2004). The

development of a pathology depends on the presence of adult worm. The standard method for diagnosing active infection is the identification of microfilariae in the blood smear by microscopic examination and this test usually occurs at night since the microfilariae is very active during this period (WHO, 2013). Once an individual is infected with the elephantiasis disease, it affects his or her immune system thereby increases the risk of individual getting a secondary infection (Healthline, 2017).

In addition to the above, the clinical presentation of Zika-virus is similar to that of chikungunya and dengue. The common symptoms including mild fever, rash, headache, conjunctivitis arthralgia which appears usually between three days to twelve days after the bite of the infected aedes aegypti mosquito. To some people, the disease shows no symptoms while others experience the symptoms.



Figure 1: symptoms of Zika virus. Source: (Zikalmage, 2018a)

Similarly, the symptoms of Zika is just like other arboviruses such as dengue and chikungunya which means it could be mistaken considered as other illnesses. The clinical symptoms in the patients are low-grade fever, conjunctivitis transient arthritis or arthralgia. Complications associated with Zika virus infection at the expectant duration of a mother is a cause of microcephaly and other congenital malformations known as congenital Zika syndrome. Other complications also include the Guillian –Bare Syndrome and still birth.



Figure 2: Children with abnormal small head. Source: (Zika-Image, 2018b)

2.5 Treatment

The clinical aim of treating uncomplicated malaria is to ensure that it does not generate into severe type of malaria which can lead to kidney failure and eventually to death. In treating malaria, our attention is drawn to the elimination of plasmodium parasite from the patient's bloodstream. Individuals who do not have symptoms may be treated to avoid the risk of further transmission to uninfected population. In treating malaria, infected individual should ensure that the parasite is out of the blood, other than that it can hibernate and will reoccur few days after responding to treatment. To completely eradicate the disease from the population, White et al. (2009) explained the phases of eradication of an infectious disease as defined by (Molyneux et al., 2004) as follows:

- Elimination of disease: Reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate efforts. Continued interventions are required.

- Control: Reduction of disease incidence, prevalence, efforts morbidity or mortality to locally acceptable level as a result of deliberate efforts. Continued interventions are required to maintain the reduction.
- Elimination of infection: Reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts. Continued measures to prevent re-establishment of transmissions are required.
- Eradication: Permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts. Interventions measures are no longer needed.

Treatments for lymphatic filariasis differ depending on the geographical location of the endemic areas. In sub-Sahara Africa, albendazole is being used with ivermectin to treat the disease, whereas elsewhere in the world, albendazole is used with diethylcarbamazine.



(a)



(b)

Figure 3: Persons suffering from Elephantiasis. Source: (M. Gyapong, 2000)

Information of pathology of lymphatic filariasis and presence of the medications diethylcarbamazine and albendazole are important to treat lymphatic filariasis, it keeps on being a noteworthy general medical problem in

tropical and subtropical nations. These medications are to be taken once a year for five consecutive years. The medicine will not heal the disability or the disfigured part of the body but rather kill the microfilariae (immature larvae) to prevent further deterioration. Again, one of the primary goals of treating the influenced networks is to dispose of the microfilariae from the blood of the contaminated people so as to intrude on transmission of disease by mosquitoes. The medication has its own side effect like dizziness, fever and itching muscles. If the situation is detected early, surgical operation can be performed to get rid of the part that is showing disfigured.

On the treatment of Zika virus the current situation is such that there is neither a vaccine nor a cure to it. In view of this the only way to prevent Zika is to avoid the bite of *Aedes aegypti* mosquito and also use condom when having an affair with a Zika patient (Paixao et al., 2016). Owing to the fact that the symptoms such as fever, rash, or joint and muscle pain is common the health officials recommend that patients with Zika virus should have enough rest, drink fluids and treat pain and fever with ordinary pain killer medicines. Since the disease can be transmitted sexually, there is the need to protect your self-using condom especially when you are living in endemic regions. It is believed that once the person is infected with Zika virus, he or she becomes immune to it; thus he or she does not get it again (zikavirus-jhpiego, 2016).

2.6 Mathematical Model Framework

For a long time the flare-up and spread of illnesses have been detailed and contemplated. This has enabled scientists and researchers to evaluate inoculation plans which have had a significant effect on the mortality rate of particular epidemics. Daley & Gani (2001), surveyed the demonstrating of irresistible maladies to be a device which is utilized to consider the elements

by which infections spread, and furthermore to increase a knowledge that predicts the future course of a flare-up so as to assess systems to control a pestilence.

The beginning of scientific displaying of the spread of illness is accounted to have been completed by Daniel Bernoulli in 1766. In his model, Bernoulli protected the act of immunizing against smallpox (Hethcote, 2000) and he was able to use the model to calculate and predict that, there would be an increase in life expectancy from 26 years 7 months to 29 years 9 months as a result of universal inoculation against smallpox (Bernoulli & Blower, 2004). The work done by Daniel Bernoulli gave rise to the modern understanding of "game theory" and modern theoretical epidemiology began when Roland Ross researched into the spread of malaria. A. G. Mckendrick and W. O. Kermack followed immediately with their work on "A contribution to the Mathematical Theory of Epidemics" and this was published in 1927 (Kermack & McKendrick, 1933). In their work, a simple deterministic (compartmental) model was formulated and according to Brauer et al. (2001), the hypothetical record was fruitful in anticipating the conduct of flare-ups fundamentally the same as that saw in many recorded scourges. Such documentations could not be left out when dealing with modelling the multi-infection of malaria-zika virus and elephantiasis transmission dynamics in mosquitoes endemic regions.

In this subsection, we discuss some of the studies in relation to this thesis.

The Ross-MacDonald model as studied in Castillo-Chavez et al. (2002); CastilloChavez & Song (2004); Chachuat (2007); Clarke (1990); Diekmann et al. (2012) has been recorded as the earliest attempt to describe quantitatively the dynamics of the transmission of malaria at the population level. Given, the following differential equations

$$\frac{dI_h}{dt} = qx_1 I_m \frac{N_h - I_h}{N_h} - g_1 I_h,$$

$$\frac{dI_m}{dt} = q x_2 (M_m - I_m) \frac{I_h}{N_h} - g_2 I_m,$$

where N_h and M_m are the respective total populations for the human beings and female mosquitoes and the constant q the biting rate; x_1 and x_2 is the likelihood that a from an infective mosquito will cause disease of a vulnerable human and

vice versa respectively. The assumption that $\frac{1}{g_1}$ and $\frac{1}{g_2}$ is the average duration of infection for human beings and mosquitoes respectively. In their analysis, Ross and McDonald found out that the transmission of malaria could be eradicated without necessary killing all vector mosquitoes. This was however not in line with the traditional belief that malaria could be eliminated only by killing all the vector mosquitoes. Interestingly, the basic reproduction of their model which is given by

$$R_0 = \frac{a e_1 M q e_2}{d_1 N d_2},$$

indicates that any method that can lead to R_0 been less than 1 will eventually lead the disease to extinction. Although these measures were just an assertion made by Ross and McDonald recent models have included cost effective approaches in the quest to help curtailed the disease transmission.

For example, Okosun et al. (2013) investigated the effectiveness of three malaria preventive measure by incorporating the cost associated with those measures.

The controls applied were in line with the assertion made in the work of Ross and McDonald. They considered a mathematical model that incorporate this models. By calculating the basic reproduction number using a constant control

parameter, they showed that the existence and stability equilibria of the model exhibit a backward bifurcation. By the use of Pontryagin's Maximum Principle to derive necessary conditions for the control of the diseases they performed the calculation of the Infection Averted Ratio and the incremental cost ratio to establish the associated cost attached to those controls. They observed through their numerical simulation that the strategies will require that they give a 100% effort in the application of treatment for 20 days and also spraying of insecticides for 57 days. Their work did not however consider forces of infections in the form of a saturated incidence rates.

To cater for the gap in Okosun et al. (2013), Olaniyi & Obabiyi (2013) developed a malaria transmission model with nonlinear forces of infection in the form of a saturated incidence rate to investigate the transmission of *Plasmodium Falciparum* malaria. Their model made use of seven ordinary differential equations and their incidence rates was developed to capture the production of antibodies in response to the presence of parasite-causing malaria both in humans and female mosquito population. By applying the basic properties in epidemiology, their model showed that the disease-free is both locally and globally asymptotically stable. The results from their numerical simulations showed that increasing the proportions of antibodies in humans correspond positively in reducing the transmission of malaria infection. But no matter the proportions of antibodies in the system, when the mosquito biting rate exceeds the threshold, reducing its transmission becomes ineffective.

In a similar manner, Traore et al. (2017), developed a scientific model of the transmission of jungle fever with an organized vector populace and regularity. Their model considered the biting rate to be a periodic function which depends on climatic factors. The numerical result of their model showed that malaria can be controlled by fighting the proliferation of the mosquitoes, thus, the available breeder sites represented by KE and KL sites in their model should be

reduced. They did not factor the fact that to fight breeding sites then the transmission of malaria should be considered in a periodic environment.

In another work by the same authors to now make up the gap in their earlier work, Bakary et al. (2018) formulated a model that investigate intestinal sickness transmission in an occasional situation. In order to also move a little ahead of the work done by Okosun et al. (2013) and Olaniyi & Obabiyi (2013), their model incorporated an age structure for the vector populace and furthermore doled out a parameter to decide the occasional gnawing pace of female anopheles mosquitoes. The human populace in their model was divided into groups, that is those that are most vulnerable known as the non-immune group and those that are least vulnerable known as the semi-immune group; a situation that was not considered by Olaniyi & Obabiyi (2013) when determine the effect of antibodies in the transmission of malaria. By applying the theory of uniform persistence and the Floquet theory with the comparison principle, they showed the stability of the disease-free equilibrium and analyse the reproduction number of the system. Their model through the basic reproduction number indicated that the transmission of malaria was highly influenced by the biting rate. Their result showed that when prevention measures are employed, it is difficult for the required goal to be achieved but in the long run those measures are achievable making their numerical result to prove their assertion of mathematical attaining an R_0 which is all inclusive asymptotically stable at the ailment free state. The work done by Ross and Mcdonald and the success in the methods and prevention strategies employed in their work by policy makers has made researchers transfer the idea of developing mathematical models to cater for other diseases. For example, Bonyah et al. (2017) analysed an SEIR Zika virus transmission model by incorporating time dependent controls to ascertain its optimal effect of bed nets, treatment of infective and the application of insecticides sprays. The basic principles of mathematics were used to determine the local and global stability

of the model. By applying the center manifold theorem, they observed a backward bifurcation phenomenon in their work. The Pontryagin's Maximum Principle were used to establish the optimal control of the Zika virus. Their results showed that the best way to minimize the Zika virus transmission was to optimize all the three controls implemented in their model and as a result, the reduction of the disease could only be attained when all the controls are taken into consideration. However, their model did not consider the transmission of Zika virus through sexual means and as such their controls did not cater for that approach. Although, treatment as recorded in their model can provide a long term solution to that effect.

Goswami et al. (2018) studied a mathematical model that incorporated human to human transmission of the Zika virus disease which was not recorded in the work done by Bonyah et al. (2017). In their study, they introduced an inci-

dence rate $\frac{C I_h}{1+I_h}$, where $C I_h$ is the infected force of the virus and $\frac{1}{1+I_h}$ is the number of infected susceptible individuals when there is an increase in the infected compartment. They applied the Maximum principle as well in helping to find an optimal control strategies that will help reduce the number of infected Zika virus cases. Their result indicated that by applying two controls that is insecticide-treated bed nets and the use of repulsive lotions as well as other devices to reduce contact rate, the transmission of the disease will be curtailed.

In a similar manner, various mathematical models have been developed for elephantiasis. Some of the most reached articles on this disease includes the work done by (Bhunu & Mushayabasa, 2012). They developed an epidemiological model that check the spread of lymphatic filariasis; the causative agent for Elephantiasis. Their model incorporated treatment and they observed that treatment has the possibility of reducing lymphatic filariasis cases however, what their model could not record was the magnitude of those

reduction. But for an effective reduction of the disease, then treatment should be given to those displaying symptoms as well as applying chemoprophylaxis for exposed individuals.

In another work done by Nwadibia et al. (2018), a model for the transmission of genital Elephantiasis was developed and investigated. Their model made use of eight compartments with five for the human population and three for the vector population. By using the Lyapunov function technique, they found the stability of their to be globally asymptotically stable both at the disease-free and endemic equilibrium. Results from their numerical simulation showed that even when the individuals infected with elephantiasis are put on treatment, eradicating the disease will not be achieved. However, for an effective eradicating of the disease lie in treating individuals who are rather displaying symptoms of the disease.

Over the last decade, researchers have been hit with the situation of developing complex models to deal with individuals suffering from various forms of diseases ranging from single infection to multi-infection. By single infection; this refers to an individual suffering from one disease. Many of these works are recorded and published online, however much concentration are given to single infection diseases like HIV/AIDS, Tuberculosis, Human Papillomavirus, Syphilis, Malaria etc. Moreover, co-infections refer to an individual suffering from more than one disease and notably among them is Mutua et al. (2015), who developed a co-infected mathematical model of malaria and typhoid fever in Kenya. By analysing the model mathematically, they identified distinct features of typhoid and malaria infection dynamics that lead them to come out with relationship associated with their co-infection. By investigating two threshold and one threshold for malaria and typhoid respectively the global dynamics of the disease was determined. The numerical results by the use of data from the Eastern Province of Kenya depicted

illustrative graphs on what led to a possible false diagnosis that come out from this co-infection.

2.6.1 Multi-Infection Models

Multi-infections which is an emerging area is the process where an individual is suffering from more than two diseases. It is attracting an attention in the epidemiological world. Notable among them are Okongo et al. (2015) and AmoahMensah et al. (2019).

Okongo et al. (2015), built up a scientific model to decide the steadiness of an individual multi-contaminated with HIV/AIDS, Tuberculosis and Malaria. By characterizing an arrangement of twelve (12) differential conditions, the model was examined to acquire the conditions for the solidness of the equilibria focuses. The model was recognized to show a retrogressive bifurcation marvel; a scenario which pose serious as to how the multi-infected disease can be effectively controlled. To come with a convincing result, the model HIV/AIDS only model was analyzed to ascertain the stability of the equilibria so as to determine the role of both counselling and treatment in controlling how the disease spread. Their results show that increasing ARV treatment without incorporating effective counselling will increase the reproduction number and vice versa. Their work therefore suggested that for HIV/AIDS to be controlled then the emphasis should be on counselling rather than treatment. Furthermore, a complete success would be achieved if the reproduction number for the transmission of both malaria and tuberculosis is also brought to a number below unity.

But, when it comes to the development of multi-infection models, work has been done on the likes of diseases such as HIV/AIDS co-infection with other diseases like Tuberculosis; HPV etc with very few works done on the multi-infection of neglected tropical diseases which the zika-virus, elephantiasis and malaria are not excluded; a motivation for this work since all three disease are caused by the mosquito parasite.

2.7 Mathematical Tools

2.7.1 Basic Reproduction Number, R_0

The mathematical models use a threshold number that defines the most significant aspects of transmission for any infectious disease. This threshold number in this context is called the basic reproduction number which is defined as the average number of infected individual produced in a population when a single infective individual is introduced into a wholly susceptible population. It is denoted by R_0 . If $R_0 < 1$, then the disease will fade out of the population and $R_0 > 1$ implies that the disease will invade the population.

2.7.2 Bifurcation Analysis

Theorem 1

Consider a general system of ordinary differential equations with a parameter

θ^* .
 θ

$$\frac{dx}{dt} = f(x, \theta^*), f: \mathbb{R}^n \times \mathbb{R} \rightarrow \mathbb{R}^n \text{ and } f \in C^2(\mathbb{R}^n \times \mathbb{R}) \rightarrow \mathbb{R}, dt$$

where 0 is an equilibrium point of the system (that is, $f(0, \theta^) \equiv 0$ for all θ^*) and*

A1: $A = D_x f(0, 0) = \left(\frac{\partial f_i}{\partial x_j}(0, 0) \right)$ is the linearization matrix of the system around the equilibrium 0 and θ^ evaluated at 0. Zero is a simple eigenvalue of A and other eigenvalues of A have negative real parts.*

A2: Matrix A has a non-negative right eigenvalue w and a left eigenvector v corresponding to the zero eigenvalue.

Let f_k be the k^{th} component of f and

$$\frac{\partial^2 f_k}{\partial x^2}$$

$$a = \sum_{j=1}^n v_j w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0)$$

$$b = \sum_{j=1}^n v_j w_j \frac{\partial^2 f_k}{\partial x_i \partial \beta^*}(0,0).$$

Then the local dynamics of the system around 0 is totally determined by the signs of a and b

1. $a > 0, b > 0$. When $\beta^* < 0$ with $|\beta^*| \ll 1, 0$ is local asymptotically stable and there exist a positive unstable equilibrium; when $0 < \beta^* \ll 1, 0$ is unstable and there exists a negative, locally asymptotically stable equilibrium;
2. $a < 0, b < 0$. When $\beta^* < 0$ with $|\beta^*| \ll 1, 0$ is locally asymptotically stable, and there exists a positive unstable equilibrium.
3. $a > 0, b < 0$. When $\beta^* < 0$ with $|\beta^*| \ll 1, 0$ is stable and a positive unstable equilibrium appears;
4. $a < 0, b > 0$. When β^* changes from negative to positive, 0 changes its stability from stable to unstable. Corresponding a negative unstable equilibrium becomes positive and locally asymptotically stable. Particularly, if $a > 0$ and $b > 0$, then a sub-critical (backward) bifurcation occurs at $\beta^* = 0$.

2.7.3 Sensitivity Analysis

The parameter values and assumptions of any model are subject to changes and errors. Sensitivity analysis is broadly defined as the investigation of these potential changes and errors and their impacts on the conclusions to be drawn from the models. Sensitivity analysis therefore helps to establish confidence in

the model by studying the uncertainty associated with the parameters in the real world. It is derived by applying the definition below:

Definition 1

A sensitivity index is a number calculated by a defined procedure which gives information about the relative sensitivity of results to different parameters of the model.

Sensitivity indices allow us to measure the relative change in a variable when the parameter changes (Martcheva, 2015). The sensitivity index of a variable u that is dependent on the partial derivative of z is defined as

$$\varepsilon_z^u = \frac{\partial u}{\partial z} \times \frac{z}{u}.$$

Therefore, sensitivity indices of R_0 with respect a parameter v can be defined as

$$\varepsilon_{zR_0}^v = \frac{\partial R_0}{\partial v} \times \frac{v}{R_0}.$$

If the model is simple, it may be possible to take the derivative of the outcome with respect to each parameter in each of them. The derivatives are the rate of prediction with respect to the parameters.

2.7.4 Optimal Control Method

Over the years optimal control has become an important mathematical tool in disease modelling. Optimal control is generated from calculus of variation and is very important in making a decision regarding difficult situations such as biological, finance, economic, ecology and many others. The behaviour of the differential equation of the model is explained by the state variable(s). The assumption is that there is a way to deal with the state variables say S_H , by

acting upon it with the suitable control. The main aim is to adjust the control u to minimize or maximize the objective functional $J(u(t), x(t), t)$ that attains the desired aim and the required cost to arriving at it. The optimal solution is then achieved when the required goal is achieved with reasonable cost. The functional is dependant on the control and the state variables. Various methods of computing optimal control are employed, but for the purpose of this thesis, the principle of Pontryagin Maximum Principle would be employed. This allows the computation of the optimal control for an ordinary differential equation model system with given constraints (Gerds, 2011).

2.7.5 The Pontryagin Maximum Principle

The principle states that the optimization problem $J(u(t), x(t), t)$ can be solved using Hamiltonian function H over a certain duration. That is, the principle converts the maximization or minimization of the objective functional J together with the state variable into maximizing or minimizing the pointwise the Hamiltonian with respect to the control (Gerds, 2011).

Theorem 2

Following Lenhart & Workman (2007) in order that $u^*(t)$ and $x^*(t)$ be an optimal problem, it is necessary that there exist a piecewise differential adjoint variable

$\gamma(t)$ for all $0 \leq t \leq T$ we have $\gamma(t) \neq 0$ such that for every $0 \leq t \leq T$,

$$H(t, x^*(t), u(t), \gamma(t)) \leq H(t, x^*(t), u^*(t), \gamma(t)),$$

for all controls at each time t , where H is

$$H = g(t, x(t), u(t)) + \gamma(t)f(t, x(t), u(t))$$

and

$$\frac{d}{dt} \frac{\partial H(t, x^*, u^*(t), \Upsilon(t))}{\partial x} = 0.$$

$$\Upsilon(t_f) = 0.$$

2.7.6 Necessary Condition

If $u^*(t)$ and $x^*(t)$ are optimal, then the following conditions hold: and

$$\frac{d}{dt} \frac{\partial H(t, x^*, u^*(t), \Upsilon(t))}{\partial x} = 0.$$

$$\Upsilon(t_f) = 0$$

$$\frac{\partial H(t, x^*(t), u^*(t), \Upsilon(t))}{\partial u} = 0.$$

2.7.7 Sufficient conditions

If all the functions f_i and g are jointly convex with respect to x and u and if $\Upsilon_i(t) \geq 0$ we have a set of sufficient conditions for optimality.

In this situation $\Upsilon(t)$ is the co-state variable which denotes the increase of the objective functional as a result of marginal increase in the state variables. At any particular moment the policy maker can apply the control variable to generate direct contributions to the objective functional (represented by the term $f(t, x(t), u(t), \Upsilon(t))$ in the Hamiltonian), can use the control variable to change the value of the state variables in order to generate contributions to the objective function in the future. The indirect contributions are measured by the term

$\Upsilon(t), g(t, x(t), u(t))$ in the Hamiltonian.

3.1 Introduction

Compartmental models have been described as strong and well established mathematical tools for explaining disease epidemics in the population. These models provide a suitable framework in which individuals in different compartments can be described in mathematical terms based on their relationships. The models assume that the population can be divided into compartments that are homogeneous in relation to a particular characteristics. They make it easy to determine prevalence and incidence of disease at various times from the mathematical equations derived.

In this chapter, a mathematical model to explain the transmission dynamics of a multi-infection disease that is Malaria-Zika-Elephantiasis model is developed. The next section presents the basic properties of the model. The analysis of the model where the basic reproduction number, the disease free equilibrium and endemic equilibrium states, as well as their stability for the equilibria were also investigated. The approach to perform the numerical simulation was discussed in the last section.

3.2 Model Formulation and Description

The proposed model subdivides the human population into eleven compartments namely: susceptible individual (S_h), infectious malaria individuals (I_m), infectious elephantiasis individuals (I_f), infectious zika virus individuals (I_z), individuals infected with both malaria and zika virus (I_{mz}), individuals infected with both malaria and elephantiasis (I_{mf}), individuals

infected with both zika virus and elephantiasis (I_{zf}), and individuals that are infected with all three diseases

(I_{mzf}) known as the multi-infection. Individuals that recover from malaria only are denoted by R_m , while those that recover from zika and elephantiasis only are denoted by (R_z) and (R_f) respectively.

The mosquito population is also partitioned into four compartments, that is, susceptible mosquitoes (S_m), female anopheles mosquitoes infected with malaria parasite (I_p), female Aedes aegypti mosquito infected with zika virus (I_a) and female culex mosquito infected with round worm (I_w).

Susceptible individuals were recruited into the population at the rate Π_h and susceptible mosquitoes were also recruited at the rate Π_m . Susceptible individuals get infected with malaria through a bite from infectious female Anopheles mosquitoes at the rate δ_m . Zika infection was also acquired through a bite from infectious female Aedes aegypti mosquito at the rate δ_z and Elephantiasis infection occurs through a bite from infectious female mosquito with worm infection at the rate δ_f . Individuals exit the population through natural death at the rate μ_h and the mosquito population is also reduced at a natural death rate denoted by μ_m . Individuals can also exit through malaria induced death rate η . For co-infection to occur, individuals with malaria infection can either get zika or elephantiasis infection when bitten by infectious female aedes mosquitoes with zika virus or female Culux mosquitoes respectively and vice versa.

The state variables and parameters describing the assumption upon which the flowchart as shown in Figure 4 was obtained for the transmission dynamics of the infection are presented in Table 1 and 2.

$I_z(t)$	Individuals infected with Zika virus,
$I_f(t)$	Individuals infected with Elephantiasis.
$I_{mz}(t)$	Individuals infected with both Malaria and Elephantiasis.
$I_{mf}(t)$	Individuals infected with both Zika virus and Elephantiasis.
$I_{zf}(t)$	Individuals infected with both Zika virus and Elephantiasis.
$I_{mzf}(t)$	Individuals infected with both Malaria, Zika virus and Elephantiasis (multi-infected individuals).
$R_m(t)$	Individuals recovered from Malaria.
$R_z(t)$	Individuals recovered from Zika virus.
$R_f(t)$	Individuals recovered from Elephantiasis.
S_m	Susceptible mosquitoes.
I_p	Anopheles female mosquito infected with malaria parasite.
I_a	Aedes aegypti mosquito infected with Zika virus.
I_w	Culex mosquito infected with worms that causes Elephantiasis.

Table 2: Description of model parameters.

Parameters	Description of Parameters
α_m	Rate at which one acquires malaria infection.
α_f	Rate at which one acquires Elephantiasis infection.
α_z	Rate at which one acquires Zika virus infection.

$$\begin{aligned}
\alpha_m &= \frac{\theta_m \delta_m (I_m + I_{mz} + I_{mf} + I_{mzf})}{N_h}, \alpha_f = \frac{\theta_f \delta_f (I_f + I_{mf} + I_{zf} + I_{mzf})}{N_h}, \alpha_z = \frac{\theta_z \delta_z (I_z + I_{mz} + I_{zf} + I_{mzf})}{N_h}, \\
\lambda_p &= \frac{\theta_p \delta_p (I_p + I_{pf} + I_{pz} + I_{pm})}{N_h}, \lambda_w = \frac{\theta_w \delta_w (I_w + I_{wf} + I_{wz} + I_{wm})}{N_h}, \\
\lambda_a &= \frac{\theta_a \delta_a (I_a + I_{af} + I_{az} + I_{am})}{N_h}
\end{aligned} \quad (3.2)$$

The associated total population for humans and mosquitoes are respectively;

$$N_h = S_h + I_m + I_f + I_z + I_{mz} + I_{mf} + I_{zf} + I_{mzf} + R_m + R_f + R_z, \quad (3.3)$$

and

$$N_m = S_m + I_p + I_w + I_a \quad (3.4)$$

and are subject to the following initial conditions $S_h(0) = S_h^0, I_m(0) = I_m^0, I_f(0) = I_f^0, I_z(0) = I_z^0, I_{mz}(0) = I_{mz}^0, I_{mf}(0) = I_{mf}^0, I_{zf}(0) = I_{zf}^0, I_{mzf}(0) = I_{mzf}^0, R_m(0) = R_m^0, R_f(0) = R_f^0, R_z(0) = R_z^0$ and $S_m(0) = I_p(0) = I_w(0) = I_a(0) = 0$. We therefore proceed by stating some important basic properties for the System

3.1.

3.3 Analysis of Multi-Infection Model

This section accounts for the basic properties as well as the stability analysis of the System (3.1).

3.3.1 Invariant region and Positivity

This is the domain in which the solution of the System (3.1) makes sense biologically while the positivity of the solution describes the non-negativity of the solution. It shows that all feasible solutions are uniformly bounded in the proper subset $\Omega = \Omega_h \times \Omega_m$. All the state variables and parameters for the System 3.1 are non-negative for all $t \geq 0$.

Theorem 3

The solutions of System 3.1 are contained in the region $\Omega = \Omega_h \times \Omega_m$.

To show that all feasible solutions are uniformly bounded in the proper subset Ω , Equations 3.3 and 3.4 are applied. Thus, from Equations 3.3 and 3.4, we respectively have:

$$\frac{dN_h}{dt} = \Pi_h - \mu_h N_h,$$

and

$$\frac{dN_m}{dt} = \Pi_m - \mu_m N_m.$$

Applying the approach in Birkhoff & Rota (1982) on differential inequality, it follows that:

$$\frac{dN_h}{dt} \leq \Pi_h - \mu_h N_h.$$

Integrating both sides gives:

$$\int_0^Z \frac{dN_h}{\Pi_h - \mu_h N_h} \leq \int_0^Z dt,$$

$$- \frac{1}{\mu_h} \ln(\Pi_h - \mu_h N_h) \leq t + c, \quad \mu_h \ln(\Pi_h - \mu_h N_h) \geq -\mu_h(t + c),$$

$$\Rightarrow \Pi_h - \mu_h N_h \geq e^{-\mu_h(t+c)},$$

$$\Pi_h - \mu_h N_h \geq A e^{-\mu_h t}, \quad (3.5)$$

where A is a constant. Substituting the initial condition into Equation 3.5 gives

$$\Pi_h - \mu_h N_h \geq [\Pi_h - \mu_h N_h(0)] e^{-\mu_h t}, \quad (3.6)$$

$$\Rightarrow N_h \leq \frac{1}{\mu_h} \left\{ \frac{\Pi_h - \mu_h N_h(0)}{e^{-\mu_h t}} \right\} = \frac{\Pi_h - \mu_h N_h(0)}{\mu_h} e^{\mu_h t}.$$

Thus as $t \rightarrow \infty$, the size of the population approaches

$$0 \leq N_h \leq \frac{\Pi_h}{\mu_h}$$

In a similar manner, same can be done for the mosquito population to obtain

$$\leq \frac{1}{\mu_m} \left\{ \frac{\Pi_m - \mu_m N_m(0)}{e^{-\mu_m t}} \right\} = \frac{\Pi_m - \mu_m N_m(0)}{\mu_m} e^{\mu_m t}.$$

Thus as $t \rightarrow \infty$, we have:

$$0 \leq N_m \leq \frac{\Pi_m}{\mu_m}$$

Hence, the feasible solutions for both human and mosquito population for System

(3.1) is given by

$$\Omega_h = \left\{ (S_h, I_m, I_f, I_z, I_{mz}, I_{mf}, I_{zf}, I_{mfz}, R_m, R_f, R_z) \in \mathbb{R}_{11}^+ : N_h(t) \leq \frac{\Pi_h}{\mu_h} \right\}$$

and

$$\Omega_m = \left\{ (S_m, I_p, I_w, I_a) \in \mathbb{R}_+^4 : N_m(t) \leq \frac{\Pi_m}{\mu_m} \right\}. \quad (3.8)$$

Hence the feasible solution set for the multi-infection model is given as

$$\Omega = \left\{ (S_h, I_m, I_f, I_z, I_{mz}, I_{mf}, I_{fz}, I_{mfz}, R_m, R_f, R_z, S_m, I_p, I_w, I_a) \in \mathbb{R}_+^{15} : \right. \\ \left. S_h, I_m, I_f, I_z, I_{mz}, I_{mf}, I_{fz}, I_{mfz}, R_m, R_f, R_z : N_h(t) \leq \frac{\Pi_h}{\mu_h}; S_m, I_p, I_w, I_a : N_m(t) \leq \frac{\Pi_m}{\mu_m} \right\} \quad (3.10)$$

Thus, System (3.1) is positively invariant and well posed in the domain Ω .

3.3.2 Positivity of State Variables

The variations in the population were studied under certain conditions in the model System. We assumed that the variables and parameters are positive entities for all time values $t \geq 0$. Since it is also irrational to have a negative population density, it is necessary to prove that all state variables are non-negative.

Hence, we apply the following lemma.

Lemma 1

If $S_h(0) > 0, I_m(0) \geq 0, I_f(0) \geq 0, I_z(0) \geq 0, I_{mz}(0) \geq 0, I_{mf}(0) \geq 0, I_{fz}(0) \geq 0, I_{mfz}(0) \geq 0, R_m(0) \geq 0, R_f(0) \geq 0, R_z(0) \geq 0, S_m(0) > 0, I_p(0) \geq 0, I_w(0) \geq 0$, and $I_a(0) \geq 0$, then the solution $S_h(t), S_m(t), I_m(t), I_f(t), I_z(t), I_{mz}(t), I_{mf}(t), I_{fz}(t), I_{mfz}(t), I_p(t), I_w(t), I_a(t), R_m(t), R_f(t)$, and $R_z(t)$ of System (3.1) are positive for all $t \geq 0$.

We define

$$t^* = \sup\{t > 0 : S_h(t) > 0, S_m(t) > 0, I_m(t) \geq 0, I_f(t) \geq 0, I_z(t) \geq 0, I_{mz}(t) \geq 0,$$

$$I_{mf}(t) \geq 0, I_{fz}(t) \geq 0, I_{mfz}(t) \geq 0, I_p(t) \geq 0, I_w(t) \geq 0, I_a(t) \geq 0, R_m(t) \geq 0, R_f(t) \geq 0, R_z(t) \geq 0\}.$$

This implies that

$$S_h(t), S_m(t), I_m(t), I_f(t), I_z(t), I_{mz}(t), I_{mf}(t), I_{fz}(t), I_{mfz}(t), I_p(t), I_w(t), I_a(t), R_m(t), R_f(t), R_z(t) > 0 \forall t \in [0, t^*).$$

Considering the first equation of System 93.1), we have:

$$\frac{dS_h}{dt} = \Pi_h + \psi R_m + \phi R_f - (\alpha_m + \alpha_z + \alpha_f + \mu_h) S_h.$$

Since Π_h , ψ and ϕ are positive, it implies that:

$$\begin{aligned} \frac{dS_h}{dt} &\geq -(\alpha_m + \alpha_z + \alpha_f + \mu_h) S_h, dt \\ Z \frac{dS_h}{S_h} &\geq -(\alpha_m + \alpha_z + \alpha_f + \mu_h) dt, \\ \ln S_h &\geq -(\alpha_m + \alpha_z + \alpha_f + \mu_h) t + c, \\ S_h &\geq Z e^{-(\alpha_m + \alpha_z + \alpha_f + \mu_h) t}, \end{aligned}$$

where, $Z = e^c$. At $t = 0, S_h(0) = Z$. Therefore, $S_h(0) e^{-(\alpha_m + \alpha_z + \alpha_f + \mu_h) t} \geq 0$.

Similarly, from the second equation of System (3.1), we have:

$$\begin{aligned} \frac{dI_m}{dt} &= \alpha_m S_h + \tau_f I_{mf} + \tau_z I_{mz} - (\tau_m + \eta + \alpha_f + \alpha_m + \mu_h) I_m, \\ \frac{dI_m}{I_m} &\Rightarrow \geq -(\mu_h + \eta + \tau_m + \alpha_f + \alpha_z) dt, \\ Z \frac{dI_m}{I_m} &\Rightarrow \geq -(\mu_h + \eta + \tau_m + \alpha_f + \alpha_z) dt, \end{aligned}$$

$$\ln I_m \geq -(\mu_h + \eta + \tau_m + \alpha_f + \alpha_z)t + c,$$

$$I_m \geq e^{-(\mu_h + \eta + \tau_m + \alpha_f + \alpha_z)t + c}.$$

Representing $A = e^c$ gives:

$$I_m \geq Ae^{-(\mu_h + \eta + \tau_m + \alpha_f + \alpha_z)t}.$$

At $t = 0$ and $I_m = I_m(0)$ gives:

$$I_m \geq I_m(0)e^{-(\mu_h + \eta + \tau_m + \alpha_f + \alpha_z)t} \geq 0.$$

The right hand side of System (3.1) is clearly positive. Thus, the solution of I_m will always be positive. In the same way, it can be shown that $I_f(t)$, $I_z(t)$, $I_{mz}(t)$, $I_{mf}(t)$, $I_{fz}(t)$, $I_{mzf}(t)$, $R_m(t)$, $R_f(t)$, $R_z(t)$, $S_m(t)$, $I_p(t)$, $I_w(t)$ and $I_a(t) > 0$ for all $t > 0$ and this completes the proof.

3.3.3 Disease Free Equilibrium (DFE) Points

The disease free equilibrium points denoted by E_{mzf} are the steady state solution where there are no malaria, zika virus and elephantiasis disease in the population. It can be determined by putting the right hand side of the infected compartment in Equation (3.1) to be equal to zero. That is

$$I_m = I_f = I_z = I_{mz} = I_{mf} = I_{fz} = I_{mzf} = I_p = I_w = I_a = 0.$$

Since no infection implies no recovery, it further implies that:

$$R_m = R_f = R_z = 0.$$

Hence, we obtain:

$$\Pi_h - \mu_h S_h = 0 \Rightarrow S_h = \frac{\Pi_h}{\mu_h} \quad (3.11)$$

$$\Pi_m - \mu_m S_m = 0 \Rightarrow S_m = \frac{\Pi_m}{\mu_m} \quad (3.12)$$

Therefore, the disease free equilibrium point for the multi-infection state is given as:

$$\begin{aligned} &= (S_h, I_m, I_f, I_z, I_{mz}, I_{mf}, I_{zf}, I_{mzf}, R_m, R_f, R_z, S_m, I_p, I_w, I_a) \\ &= \left(\frac{\Pi_h}{\mu_h}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, \frac{\Pi_m}{\mu_m}, 0, 0, 0 \right). \end{aligned}$$

3.3.4 Basic Reproduction Number R_0

In this subsection, we compute the basic reproduction number, R_0 . It is the expected number of secondary cases, taking into consideration the complete population of the susceptible individuals having an infected individual who serve as an index case during the entire period of infectiousness (Van den Driessche & Watmough, 2002). It is a very essential tool use in epidemiological modelling of diseases. It is used to determine whether the disease is invading the population or the disease is dying out of the population. When $R_0 = 1$, we have the point in which the generation of secondary cases are not adequate enough to sustain the infection within the human community. However, if $R_0 \leq 1$, then it means that the rate at which an individual infect another individual is slow and hence the disease will gradually fade out or can be eradicated out of the population. Furthermore, if $R_0 \geq 1$, then the rate at which an individual infect another is high and as a result the disease will be rampant in the population. The implication here is that in order for a population to completely eradicate the disease from the population, the value for the basic reproduction number should always be less than unity (one).

In order to compute R_0 , let us suppose that there are n compartments of which the first m compartments corresponds to infected individuals. Let $F_i(x)$ represents the rate of appearance of new infections in compartment i such that $V_i^+ = V_i^-(x) - V_i^+(x)$, where V_i^- and V_i^+ is the rate of individuals moving out of the i th compartment and the rate of transfer of individuals into compartment i by all available means respectively. It is assumed that each function is continuously differentiable at least twice in each variable. The disease transmission model is made up of positive initial conditions together with the following System of equations:

$$x' = g_i(x) = F_i(x) - V_i(x), i = 1, 2, \dots, n;$$

where n denotes the number of compartments with new infection.

Let

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0) \right] \quad \text{and} \quad V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x_0) \right] \quad \text{with} \quad 1 \leq (i, j) \leq m.$$

Here, F is non-negative and V is a non-singular matrix. However, both are $m \times m$ matrices, where m is the number of infected classes and x_0 is the disease free equilibrium point. Hence, R_0 is the largest eigenvalue of FV^{-1} .

In order to obtain an expression for the basic reproduction number, there is the need to rewrite System (3.1) starting from the infected classes and followed by the uninfected classes.

$$\begin{aligned} \frac{dI_m}{dt} &= \theta_m \delta m l_p S_h - \tau m l_m - (\mu_h + \eta) I_m + \tau_f l_{mf} - \theta_f \delta_f l_w l_m + \tau_z l_{mz} - \theta_z \delta_z l_a l_m. \\ \frac{dI_f}{dt} &= \theta_f \delta_f l_w S_h - (\mu_h + \tau_f) I_f - \theta_m \delta m l_p I_f + \tau m l_{mf} + \tau_z l_{zf} - \theta_z \delta_z l_a I_f. \end{aligned}$$

$$\begin{aligned}
\frac{dI_z}{dt} &= \theta_z \delta_z I_a S_h - (\tau_z + \mu_h) I_z - \theta_m \delta_m I_p I_z + \tau_m I_{mz} + \tau_f I_{zf} - \theta_f \delta_f I_w I_z, \\
\frac{dI_{mz}}{dt} &= \theta_z \delta_z I_a I_m - (\mu_h + \eta + \tau_m + \tau_z) I_{mz} + \tau_f I_{mzf} - \theta_f \delta_f I_w I_{mz} + \theta_m \delta_m I_p I_z, \\
\frac{dI_{mf}}{dt} &= \theta_f \delta_f I_w I_m - (\mu_h + \eta + \tau_m + \tau_f) I_{mf} + \tau_z I_{mzf} - \theta_z \delta_z I_a I_{mf} + \theta_m \delta_m I_p I_f, \\
\frac{dI_{zf}}{dt} &= \theta_z \delta_z I_a I_f - (\mu_h + \tau_f + \tau_z) I_{zf} + \tau_m I_{mzf} - \theta_m \delta_m I_p I_{zf} + \theta_f \delta_f I_w I_z, \\
\frac{dI_{mzf}}{dt} &= \theta_m \delta_m I_p I_{zf} - (\mu_h + \eta + \tau_m + \tau_f + \tau_z) I_{mzf} + \theta_f \delta_f I_w I_{mz} + \theta_z \delta_z I_a I_{mf}, \\
\frac{dI_p}{dt} &= \theta_m (I_m + I_{mzf}) S_m - \mu_m I_p, \\
\frac{dI_w}{dt} &= \theta_f (I_f + I_{mzf}) S_m - \mu_m I_w, \\
\frac{dI_a}{dt} &= \theta_z (I_z + I_{mzf}) S_m - \mu_m I_a, \\
\frac{dR_m}{dt} &= \tau_m I_m - (\mu_h + \psi) R_m, \\
\frac{dR_f}{dt} &= \tau_f I_f - (\mu_h + \phi) R_f, \\
\frac{dR_z}{dt} &= \tau_z I_z - \mu_h R_z, \\
\frac{dS_h}{dt} &= \Pi_h + \psi R_m + \phi R_f - \theta_m \delta_m I_p S_h - \mu_h S_h - \theta_z \delta_z I_a S_h - \theta_f \delta_f I_w S_h, \\
\frac{dS_m}{dt} &= \Pi_m - \mu_m S_m - \theta_m \delta_m (I_m + I_{mz} + I_{mf} + I_{mzf}) S_m - \theta_f \delta_f (I_f + I_{mf} + I_{zf} + I_{mzf}) S_m - \theta_z \delta_z (I_z + I_{mz} + I_{zf} + I_{mzf}) S_m.
\end{aligned} \tag{3.13}$$

We identify the matrices F and V for the new infection terms and the remaining transfer terms at the disease free equilibrium using the next generation operator method as described by Van den Driessche & Watmough (2002) respectively.

$$\begin{array}{ccc}
\frac{\partial}{\partial I_p} & \frac{\partial}{\partial I_w} & \frac{\partial}{\partial I_a} \\
\begin{array}{c} S_h - \\ h \end{array} & \begin{array}{c} I_m - \\ N_h \end{array} & \begin{array}{c} I_m - \\ N_h \end{array} \\
\frac{\partial}{\partial I_p} & \frac{\partial}{\partial I_w} & \frac{\partial}{\partial I_a}
\end{array}$$

$$\begin{bmatrix} (\mu_h + \eta + \tau_m)I_m - \tau_f I_{mf} - \tau_z I_{mz} \\ (\mu_h + \tau_f)I_f - \tau_m I_{mf} - \tau_z I_{zf} \\ (\tau_z + \mu_h)I_z - \tau \\ mI_{mz} - \tau_f I_{zf} \\ (\mu_h + \eta + \tau_m + \tau_z)I_{mz} - \tau \\ fI_{mzf} \end{bmatrix}$$

$$\begin{bmatrix} (\mu_h + \eta + \tau_m + \tau_f)I_{mf} - \tau_z I_{mzf} \\ \nabla = \begin{bmatrix} (\mu_h + \tau_f + \tau_z)I_{zf} - \tau \\ mI_{mzf} \end{bmatrix} \end{bmatrix}$$

$$\begin{bmatrix} (\mu_h + \tau_f + \tau_z)I_{zf} - \tau_m I_{mzf} \\ (\mu_h + \eta + \tau_m + \tau_f + \tau_z)I_{mzf} \\ \mu_{mlp} \\ \mu_{mlw} \\ \mu_{mla} \end{bmatrix}$$

The Jacobian matrix of F and V are given as

$$\begin{bmatrix} -a_{11} & 0 & 0 & 0 & 0 & 0 & 0 & a_{18} & -a_{19} & -a_{20} & -a_{29} & -a_{30} \\ 0 & -a_{22} & 0 & 0 & 0 & 0 & 0 & -a_{28} & a & 20 & -a_{60} \\ 0 & 0 & -a_{33} & 0 & 0 & 0 & 0 & -a_{38} & -a_{39} & a & 30 \end{bmatrix}$$

$$F = \begin{bmatrix} a_{41} & 0 & a_{43} & -a_{44} & 0 & 0 & 0 & a_{38} & -a_{49} & a \\ 0 & a_{41} & a_{44} & 0 & 0 & -a_{43} & 0 & -a_{68} & a_{39} & a \\ 0 & 0 & 0 & a_{44} & a_{41} & a_{43} & 0 & a_{68} & a_{49} & a_{60} \\ a_{81} & 0 & 0 & a_{84} & a_{85} & 0 & a_{87} & 0 & 0 & 0 \\ 0 & a_{92} & 0 & 0 & a_{95} & a_{96} & a_{97} & 0 & 0 & 0 \\ 0 & 0 & a_{103} & a_{104} & 0 & a_{106} & a_{107} & 0 & 0 & 0 \end{bmatrix}$$

where,

$$\begin{aligned} &= \left(\theta_f \delta_f + \vartheta_z \delta_z I_a \right), a_{18} = \frac{\vartheta_m \delta}{N_h} \frac{l_{wm} Sh}{N_h} \frac{\theta_f \delta_f l_m}{N_h} \frac{\theta_z \delta_z l_m}{N_h} a_{11} \\ &= \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22}, a_{19} = \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22}, a_{20} = \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22}, a_{21} = \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22} \\ &= \left(\frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22} + \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22} \right), a_{28} = \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22}, a_{29} = \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22} \\ &= \left(\frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22} + \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22} \right), a_{38} = \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22}, a_{39} = \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22}, a_{40} = \frac{\delta_f Sh}{N_h} \frac{\theta_z \delta_z l_f}{N_h} a_{22} \end{aligned}$$

$$\begin{aligned}
a_{41} &= \frac{\theta_z \delta_z l_a}{N_h}, a_{43} = \frac{\theta_m \delta_m l_p}{N_h}, a_{44} = \frac{\theta_f \delta_f l_w}{N_h}, a_{49} = \frac{\theta_f \delta_f l_{mz}}{N_h}, a_{60} = \frac{\theta_z \delta_z l_{mf}}{N_h}, \\
a_{78} &= \frac{\theta_m \delta_m l_{zf}}{N_h}, a_{81} = \frac{\theta_m \delta_m (l_{mz} + l_{mf} + l_{mzf})}{N_h}, a_{84} = \frac{\theta_m \delta_m (l_m + l_{mf} + l_{mzf})}{N_h} S_m, \\
a_{85} &= \frac{\theta_m \delta_m (l_m + l_{mz} + l_{mzf})}{N_h} S_m, a_{87} = \frac{\theta_m \delta_m (l_m + l_{mz} + l_{mf})}{N_h} S_m, \\
a_{92} &= \frac{\theta_f \delta_f (l_{mf} + l_{zf} + l_{mzf})}{N_h} S_m, a_{95} = \frac{\theta_f \delta_f (l_f + l_{zf} + l_{mzf})}{N_h} S_m, \\
a_{96} &= \frac{\theta_f \delta_f (l_f + l_{mf} + l_{mzf})}{N_h} S_m, a_{97} = \frac{\theta_f \delta_f (l_f + l_{mf} + l_{zf})}{N_h} S_m, \\
a_{103} &= \frac{\theta_z \delta_z (l_{mz} + l_{zf} + l_{mzf})}{N_h} S_m, a_{104} = \frac{\theta_z \delta_z (l_z + l_{zf} + l_{mzf})}{N_h} S_m, \\
a_{106} &= \frac{\theta_z \delta_z (l_z + l_{mz} + l_{mzf})}{N_h} S_m, a_{107} = \frac{\theta_z \delta_z (l_z + l_{mz} + l_{zf})}{N_h} S_m.
\end{aligned}$$

$$\begin{aligned}
& \begin{bmatrix} b_{11} & 0 & 0 & -b_{14} & -b_{15} & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \\
& \begin{bmatrix} 0 & b_{22} & 0 & 0 & -b_{25} & -b_{14} & 0 & 0 & 0 & 0 \end{bmatrix} \\
& \begin{bmatrix} 0 & 0 & b_{33} & -b_{25} & 0 & -b_{15} & 0 & 0 & 0 & 0 \end{bmatrix} \\
& \begin{bmatrix} 0 & 0 & 0 & b_{44} & 0 & 0 & -b_{15} & 0 & 0 & 0 \end{bmatrix} \\
& \begin{bmatrix} 0 & 0 & 0 & 0 & b_{55} & 0 & -b_{14} & 0 & 0 & 0 \end{bmatrix} \\
V &= \begin{bmatrix} \end{bmatrix},
\end{aligned}$$

$$\begin{array}{cccccccccccc}
 ? & 0 & 0 & 0 & 0 & 0 & b_{66} & -b_{25} & 0 & 0 & 0 & ? \\
 ? & & & & & & & & & & & ? \\
 ? & & & & & & & & & & & ? \\
 ? & 0 & 0 & 0 & 0 & 0 & 0 & b_{77} & 0 & 0 & 0 & ? \\
 ? & ? & ? & & & & & & & & & ? \\
 ? & & & & & & & & 88 & 0 & 0 & | \\
 ? & 0 & 0 & 0 & 0 & 0 & 0 & 0 & b & & & \\
 ? & ? & ? & & & & & & & & & \\
 ? & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & b_{88} & 0 & ? \\
 ? & & & & & & & & & & & ? \\
 ? & & & & & & & & & & & ? \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & b_{88} &
 \end{array}$$

where,

$$b_{11} = (\mu_h + \eta + \tau_m), b_{14} = \tau_z, b_{15} = \tau_f, b_{22} = (\mu_h + \tau_f), b_{25} = \tau_m, b_{33} = (\mu_h + \tau_z),$$

$$b_{44} = (\mu_h + \eta + \tau_m + \tau_z), b_{55} = (\mu_h + \eta + \tau_m + \tau_f), b_{66} = (\mu_h + \tau_f + \tau_z),$$

$$b_{77} = (\mu_h + \eta + \tau_m + \tau_f + \tau_z), b_{88} = \mu_m.$$

$$\begin{array}{cccccccccccc}
 ? & ? & c_{11} & 0 & 0 & -c_{14} & c_{15} & 0 & c_{17} & 0 & 0 & 0 \\
 ? & & & & & & & & & & & ? \\
 ? & & & & & & & & & & & ? \\
 ? & 0 & c_{22} & 0 & 0 & c_{25} & c_{26} & c_{27} & 0 & 0 & 0 & ? \\
 ? & & & & & & & & & & & ? \\
 ? & & & & & & & & & & & ? \\
 ? & 0 & 0 & c_{33} & c_{34} & 0 & c_{36} & c_{37} & 0 & 0 & 0 & ? \\
 ? & & & & & & & & & & & ? \\
 ? & & & & & & & & & & & ? \\
 ? & 0 & 0 & 0 & c_{44} & 0 & 0 & c_{47} & 0 & 0 & 0 & ? \\
 ? & & & & & & & & & & & ? \\
 ? & & & & & & & & & & & ? \\
 ? & & & & & & & & & & & ? \\
 V-1 = ? & ? & 0 & 0 & 0 & 0 & c_{55} & 0 & c_{57} & 0 & 0 & 0 \\
 & & & & & & & & & & & ? \\
 ? & & & & & & & & & & & ? \\
 ? & 0 & 0 & 0 & 0 & 0 & c_{66} & c_{67} & 0 & 0 & 0 & ? \\
 ? & & & & & & & & & & & ?
 \end{array}$$

$$\begin{array}{cccccccccccc}
? & & & & & & & & & & & ? \\
? & 0 & 0 & 0 & 0 & 0 & 0 & c_{77} & 0 & 0 & 0 & ? \\
? & & & & & & & & & & & ? \\
? & & & & & & & & & & & ? \\
? & & & & & & & & 88 & 0 & 0 & | \\
? & 0 & 0 & 0 & 0 & 0 & 0 & 0 & c & & & ? \\
? & & & & & & & & & & & ? \\
? & & & & & & & & & & & ? \\
? & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & c_{88} & 0 & ? \\
? & & & & & & & & & & & ? \\
? & & & & & & & & & & & ? \\
0 & & & & & & 0 & 0 & 0 & 0 & 0 & 0 \\
& & & & & & & 0 & 0 & c_{88} & &
\end{array}$$

where,

$$\begin{aligned}
c_{11} &= \frac{1}{(\mu_h + \eta + \tau_m)}, c_{14} = \frac{\tau_z}{(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_z)}, \\
c_{15} &= \frac{\tau_f}{(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_f)}, \\
c^{17} &= \frac{\tau_z \tau_f (\mu_h + \eta + \tau_m + \tau_z) + \tau_z \tau_f (\mu_h + \eta + \tau_m + \tau_f)}{(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
c_{22} &= \frac{1}{(\mu_h + \tau_f)}, c_{25} = \frac{\tau_m}{(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_f)}, c_{26} = \frac{\tau_z}{(\mu_h + \tau_f)(\mu_h + \tau_f + \tau_z)}, \\
c^{27} &= \frac{\tau_z \tau_m (\mu_h + \eta + \tau_m + \tau_f) + \tau_z \tau_m (\mu_h + \tau_f + \tau_z)}{(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
c_{33} &= \frac{1}{(\mu_h + \tau_z)}, c_{34} = \frac{\tau_m}{(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)}, c_{35} = \frac{\tau_f}{(\mu_h + \tau_z)(\mu_h + \tau_f + \tau_z)}, \\
c^{37} &= \frac{\tau_f \tau_m (\mu_h + \eta + \tau_m + \tau_z) + \tau_f \tau_m (\mu_h + \tau_f + \tau_z)}{(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
c^{44} &= \frac{1}{(\mu_h + \eta + \tau_m + \tau_z)},
\end{aligned}$$

$$c^{55} = \frac{1}{(\mu_h + \eta + \tau_m + \tau_f)},$$

$$C66 = \frac{1}{(\mu_h + \tau_f + \tau_z)}, C67 = \frac{\tau_m}{(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)},$$

$$c^{77} = \frac{1}{(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, c^{88} = \frac{1}{\mu_m}.$$

[illegible]

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0

0

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0

where,

$$\begin{aligned}
 d_1 &= \frac{\theta_f \delta_f l_w + \theta_z \delta_z l_a}{N_h(\mu_h + \eta + \tau_m)}, d_2 = \frac{\theta_f \delta_f l_w + \theta_z \delta_z l_a}{N_h(\mu_h + \eta + \tau_m)}, d_3 = \frac{\tau_f (\theta_f \delta_f l_w + \theta_z \delta_z l_a)}{N_h(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_f)}, \\
 d_4 &= \frac{(\theta_f \delta_f l_w + \theta_z \delta_z l_a) \tau_z \tau_f (\mu_h + \eta + \tau_m + \tau_z) + \tau_f \tau_z (\mu_h + \eta + \tau_m + \tau_f)}{N_h(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
 d_5 &= \frac{\tau_m(\theta_m \delta_m l - p + \theta_z \delta_z l_a)}{N_h(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_f)}, d_{10} = \frac{\tau_z(\theta_m \delta_m l_p + \theta_z \delta_z l_a)}{N_h(\mu_h + \tau_f)(\mu_h + \tau_f + \tau_z)}, \\
 d_{11} &= \frac{(\theta_m \delta_m l_p + \theta_z \delta_z l_a) \tau_z \tau_m (\mu_h + \eta + \tau_m + \tau_f) + \tau_z \tau_m (\mu_h + \tau_f + \tau_z)}{N_h(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
 d_{12} &= \frac{\theta_m \delta_m l_f}{N_h \mu_m}, d_{13} = \frac{\theta_f \delta_f S_h}{N_h \mu_m}, d_{14} = \frac{\theta_z \delta_z l_f}{N_h \mu_m}, d_{15} = \frac{\theta_m \delta_m l_p + \theta_f \delta_f l_w}{N_h(\mu_h + \tau_z)}, \\
 d_{16} &= \frac{\tau_m(\theta_m \delta_m l_p + \theta_f \delta_f l_w)}{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)}, d_{17} = \frac{\tau_f(\theta_m \delta_m l_p + \theta_f \delta_f l_w)}{N_h(\mu_h + \tau_z)(\mu_h + \tau_f + \tau_z)}, \\
 d_{18} &= \frac{\tau_f \tau_m ((\theta_m \delta_m l_p + \theta_f \delta_f l_w)(\mu_h + \eta + \tau_m + \tau_z) + (\mu_h + \tau_f + \tau_z))}{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
 d_{19} &= \frac{\theta_m \delta_m l_z}{N_h \mu_m}, d_{20} = \frac{\theta_f \delta_f l_z}{N_h \mu_m}, d_{21} = \frac{\theta_z \delta_z S_h}{N_h(\mu_h + \eta + \tau_m)}, d_{22} = \frac{\theta_z \delta_z l_a}{N_h(\mu_h + \tau_z)}, d_{23} = \frac{\theta_m \delta_m l_p}{\tau_m \theta_m \delta_m l_p}, \\
 d_{24} &= \frac{\tau_z \theta_z \delta_z l_a}{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)} - \frac{\tau_z \theta_z \delta_z l_a}{N_h(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_z)}
 \end{aligned}$$

$$\begin{aligned}
& - \frac{\theta_f \delta_f l_w}{N_h(\mu_h + \eta + \tau_m + \tau_z)}, d_{25} = \frac{\theta_z \delta_z l_a \tau_f}{N_h(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_f)}, \\
d_{26} &= \frac{\theta_m \delta_m l_p \tau_f}{N_h(\mu_h + \tau_z)(\mu_h + \tau_f + \tau_z)}, \\
d_{27} &= \frac{\theta_m \delta_m l_p \tau_z \tau_f ((\mu_h + \eta + \tau_m + \tau_z) + (\mu_h + \tau_f + \tau_z))}{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& + \frac{\theta_m \delta_m l_p \tau_f \tau_m ((\mu_h + \eta + \tau_m + \tau_z) + (\mu_h + \tau_f + \tau_z))}{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
& - \frac{\theta_f \delta_f l_w \tau_f}{N_h(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
d_{28} &= \frac{\theta_m \delta_m l_z}{N_h \mu_m N_h \mu_h N_h(\mu_h + \eta + \tau_m)}, d_{29} = - \frac{\theta_f \delta_f l_m z}{N_h \mu_m N_h \mu_h N_h(\mu_h + \eta + \tau_m)}, d_{30} = \frac{\theta_z \delta_z l_m}{N_h \mu_m N_h \mu_h N_h(\mu_h + \eta + \tau_m)}, d_{31} = \frac{\theta_f \delta_f l_w}{N_h \mu_m N_h \mu_h N_h(\mu_h + \eta + \tau_m)}, \\
d_{32} &= \frac{N_h \mu_m N_h \mu_h N_h(\mu_h + \eta + \tau_m) \theta_m \delta_m l_p \tau_a u z \theta_f \delta_f l_w}{N_h(\mu_h + \tau_f) N_h(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_z)}, \\
& \frac{\tau_f \theta_f \delta_f l_w}{N_h(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_f)} \theta_m \delta_m l_p \tau_m d_{34} = + \frac{\tau_z \theta_m \delta_m l_p}{N_h(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_f)}, \\
& - \frac{\theta_z \delta_z l_a}{N_h(\mu_h + \eta + \tau_m + \tau_f)}, d_{35} = \frac{\tau_z \theta_m \delta_m l_p}{N_h(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_f)}, \\
d_{36} &= \frac{\theta_f \delta_f l_w \tau_z \tau_f ((\mu_h + \eta + \tau_m + \tau_z) + (\mu_h + \eta + \tau_m + \tau_f))}{N_h(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& + \frac{\theta_m \delta_m l_p \tau_z \tau_m ((\mu_h + \eta + \tau_m + \tau_f) + (\mu_h + \tau_f + \tau_z))}{N_h(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
& - \frac{\tau_z \theta_z \delta_z l_a}{N_h(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)},
\end{aligned}$$

$$\begin{aligned}
& N_h(\mu_h + \eta + \tau_m + \tau_f)(\mu_h + \eta + \tau_m + \tau_f + \tau_z) \\
d_{37} &= \frac{\theta_m \delta m l f}{N_h \mu_m}, d_{38} = \frac{\theta_f \delta f l m}{N_h \mu_m}, d_{39} = \frac{\theta_z \delta z l m f}{N_h(\mu_h + \tau_f)}, d_{40} = \frac{\theta_z \delta z l a}{N_h(\mu_h + \tau_z)}, \\
d_{41} &= \frac{\tau_m \theta_f \delta f l w}{N_h(\mu_h + \tau_z)}, d_{42} = \frac{\tau_m \theta_f \delta f l w}{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)}, \\
d_{43} &= \frac{\tau_m \theta_z \delta z l a}{N_h(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_f)}, \\
d_{44} &= \frac{\tau_z \theta_z \delta z l a}{N_h(\mu_h + \tau_f)(\mu_h + \tau_f + \tau_z)} + \frac{\tau_f \theta_f \delta f l w}{N_h(\mu_h + \tau_z)(\mu_h + \tau_f + \tau_z)} - \frac{\theta_m \delta m l p}{N_h(\mu_h + \tau_f + \tau_z)}, \\
d_{45} &= \frac{\theta_z \delta z l a \tau_z \tau_m ((\mu_h + \eta + \tau_m + \tau_f) + (\mu_h + \tau_f + \tau_z))}{N_h(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
&+ \frac{\theta_f \delta f l w \tau_f \tau_m ((\mu_h + \eta + \tau_m + \tau_z) + (\mu_h + \tau_f + \tau_z))}{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
&- \frac{\tau_m \theta_m \delta m l p}{N_h(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
d_{46} &= \frac{\theta_m \delta m l z f}{N_m \mu_m}, d_{47} = \frac{\theta_f \delta f l z}{N_h \mu_m}, d_{48} = \frac{\theta_z \delta z l f}{N_h(\mu_h + \eta + \tau_m + \tau_z)}, d_{49} = \frac{\theta_f \delta f l w}{\theta_z \delta z l a}, \\
d_{50} &= \frac{\theta_m \delta m l p}{N_h(\mu_h + \eta + \tau_m + \tau_f)}, d_{51} = \frac{\theta_m \delta m l p}{N_h(\mu_h + \tau_f + \tau_z)}, \\
d_{52} &= \frac{\tau_f \theta_f \delta f l - w}{N_h(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
&+ \frac{\tau_z \delta z l a}{N_h(\mu_h + \eta + \tau_m + \tau_f)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}
\end{aligned}$$

$$\begin{aligned}
& + \frac{\tau_m \theta_m \delta_m l_p}{N_h(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
& \theta_m \delta_m l_z f \theta_f \delta_f l_m z \theta_z \delta_z l_m f d_{53} = \frac{\quad}{\quad}, d_{54} \\
& = \frac{\quad}{\quad}, d_{55} = \frac{\quad}{\quad}, N_h \mu_m N_h \mu_m N_h \mu_m \\
& \theta_m \delta_m (l_{mz} + l_{mf} + l_{mzf}) S_m d_{56} = \\
& \frac{N_h(\mu_h + \eta + \tau_m) \theta_m \delta_m (l_m + l_{mf} + l_{mzf}) S_m}{N_h(\mu_h + \eta + \tau_m + \tau_z)} - \frac{\tau_z \theta_m \delta_m (l_{mz} + l_{mf} + l_{mzf}) S_m}{N_h(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
& \theta_m \delta_m (l_{mz} + l_{mf} + l_{mzf}) S_m \quad \theta_m \delta_m (l_m + l_{mz} + l_{mzf}) S_m d_{58} = - \frac{\tau_f}{N_h(\mu_h + \eta + \tau_m + \tau_f)}, \\
& \tau_f \tau_z ((\theta_m \delta_m (l_{mz} + l_{mf} + l_{mzf}))(\mu_h + \eta + \tau_m + \tau_z) + (\mu_h + \eta + \tau_m + \tau_f)) S_m \\
& d_{59} = \frac{\quad}{N_h(\mu_h + \eta + \tau_m)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& \tau_f \theta_m \delta_m (l_m + l_{mf} + l_{mzf}) S_m \\
& + \frac{\quad}{N_h(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& \tau_z \theta_m \delta_m (l_m + l_{mz} + l_{mzf}) S_m \\
& + \frac{\quad}{N_h(\mu_h + \eta + \tau_m + \tau_f)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& \theta_f \delta_f (l_{mf} + l_{zf} + l_{mzf}) S_m d_{60} = \frac{\quad}{N_h(\mu_h + \tau_f)}, \\
& \tau_m \theta_f \delta_f (l_{mf} + l_{zf} + l_{mzf}) S_m \theta_f \delta_f (l_f + l_{mf} + l_{mzf}) S_m d_{61} = \frac{\quad}{N_h(\mu_h + \tau_f)(\mu_h + \tau_f + \tau_z)} + \frac{\quad}{N_h(\mu_h + \eta + \tau_m + \tau_f)}, \\
& \tau_z \theta_f \delta_f (l_{mf} + l_{zf} + l_{mzf}) S_m \theta_f \delta_f (l_f + l_{mf} + l_{mzf}) S_m d_{62} = \frac{\quad}{N_h(\mu_h + \tau_f)(\mu_h + \tau_f + \tau_z)} + \frac{\quad}{N_h(\mu_h + \tau_m + \tau_f)}, \\
& \tau_z \tau_m ((\theta_f \delta_f (l_{mf} + l_{zf} + l_{mzf}))(\mu_h + \eta + \tau_m + \tau_f) + (\mu_h + \tau_f + \tau_z)) S_m \\
& d_{63} = \frac{\quad}{N_h(\mu_h + \tau_f)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& \tau_z \theta_f \delta_f (l_f + l_{zf} + l_{mzf}) S_m
\end{aligned}$$

$$\begin{aligned}
& + \frac{\theta_f \delta_f \tau_m (I_f + I_{mf} + I_{mzf}) S_m}{N_h(\mu_h + \eta + \tau_m + \tau_f)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& + \frac{\theta_f \delta_f (I_f + I_{mf} + I_{zf}) S_m}{N_h(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}, \\
& \theta_z \delta_z (I_{mz} + I_{zf} + I_{mzf}) S_m d_{64} = \\
& \frac{N_h(\mu_h + \tau_z) \tau_m \theta_z \delta_z (I_{mz} + I_{zf} + I_{mzf}) S_m}{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)} \theta_z \delta_z (I_z + I_{zf} \\
& + I_{mzf}) S_m d_{65} = + \frac{N_h(\mu_h + \eta + \tau_m + \tau_z)}{\tau_f \theta_z \delta_z (I_{mz} + I_{zf} + I_{mzf}) S_m} \theta_z \delta_z (I_z + I_{mz} + I_{mzf}) S_m d_{66} = \\
& + \frac{N_h(\mu_h + \tau_z)(\mu_h + \tau_f + \tau_z)}{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)} \tau_f \tau_f (\theta_z \delta_z (I_{mz} + I_{zf} + I_{mzf}) (\mu_h + \eta + \tau_m + \tau_z) + (\mu_h + \tau_f + \tau_z)) S_m \\
& d_{67} = \frac{N_h(\mu_h + \tau_z)(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}{N_h(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& + \frac{\tau_f \theta_z \delta_z (I_z + I_{zf} + I_{mzf}) S_m}{N_h(\mu_h + \eta + \tau_m + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& + \frac{\tau_m \theta_z \delta_z (I_z + I_{mz} + I_{mzf}) S_m}{N_h(\mu_h + \tau_f + \tau_z)(\mu_h + \eta + \tau_m + \tau_f + \tau_z)} \\
& + \frac{\theta_z \delta_z (I_z + I_{zf} + I_{mz}) S_m}{N_h(\mu_h + \eta + \tau_m + \tau_f + \tau_z)}
\end{aligned}$$

By the use of the next generation matrix, and applying the method used to describe the reproduction number for multi-infection diseases in Okongo et al. (2015); the basic reproduction number was obtained as

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3.3.5 Local Stability for Disease-free Equilibrium

Theorem 4

To investigate the local stability at the disease free equilibrium, we linearize

[illegible]

$$\begin{array}{cccccccccccc}
0 & 0 & 0 & 0 & 0 & 0 & -b_{23} & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -b_{24} & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_h & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -b_{32} & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & b_{33}-\mu_m & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & b_{34} \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
b_{35} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0
\end{array}$$

where,

$$\begin{aligned}
b_1 &= \mu_h, b_2 = \theta_m \delta_m, b_3 = \theta_f \delta_f, b_4 = \theta_z \delta_z, b_6 = (\mu_h + \eta + \tau_m), b_9 = (\mu_h + \tau_f), b_{13} = (\mu_h + \tau_z), b_{15} = (\mu_h \\
&+ \eta + \tau_m + \tau_m), b_{18} = (\mu_h + \eta + \tau_m + \tau_f), b_{20} = (\mu_h + \tau_f + \tau_z), \\
b_{22} &= (\mu_h + \eta + \tau_m + \tau_f + \tau_z), b_{23} = (\mu_h + \psi), b_{24} = (\mu_h + \phi), b_{25} = \theta_f \delta_f \frac{\theta_m \delta_m \Pi_m \mu_h}{\Pi_h \mu_m}, \\
b_{26} &= \frac{\theta_z \delta_z \Pi_m \mu}{\Pi_h \mu_m}, b_{27} = \frac{\theta_z \delta_z \Pi_m \mu}{\Pi_h \mu_m}, b_{28} = \Pi_m \mu_h (\theta_m \delta_m + \theta_z \delta_z), \\
b_{29} &= \frac{\Pi_m \mu_h}{\Pi_h \mu_m} (\theta_m \delta_m + \theta_f \delta_f), b_{30} = \frac{\Pi_m \mu}{\Pi_h \mu_m} (\theta_z \delta_z + \theta_f \delta_f), \\
b_{31} &= \frac{\Pi_m \mu}{\Pi_h \mu_m} (\theta_m \delta_m + \theta_z \delta_z + \theta_f \delta_f), b_{32} = -\mu_m.
\end{aligned}$$

The stability of the multi-infections around E_{mfz} in J_{E_0} is established if all the eigenvalues have negative real parts. It is observed that the first, ninth, tenth, eleventh and twelfth columns have negative real parts given by $\lambda_1 = -\mu_h$, $\lambda_9 = -(\mu_h + \psi)$, $\lambda_{10} = -(\mu_h + \phi)$, $\lambda_{11} = -\mu_h$ and $\lambda_{12} = -\mu_m$ respectively. Hence, the stability of the disease free equilibrium is dependent on the eigenvalues of the sub-matrix of the Jacobian J_{E_1} .

$$\begin{bmatrix} a_{11} & -a_{12} \end{bmatrix} = \begin{bmatrix} \vartheta_m \delta_m \Pi_{\Pi_h \mu_m} - \mu & a_2 - (\mu_h + \tau_m + \eta) \theta_m \delta_m \end{bmatrix} \quad (3.15)$$

$$\begin{bmatrix} a_{14} & -a_{12} \end{bmatrix} = \begin{bmatrix} \vartheta_z \delta_z \Pi_{\Pi_h \mu} & -\mu_m \end{bmatrix} \quad (3.16)$$

From Equations (3.14), (3.15) and (3.16), we obtain the following respective characteristics polynomial;

$$x^2 + (\mu_h + \mu_m + \tau_f)x - \frac{\theta \delta \Pi \mu}{f} = 0, \quad \Pi_h \mu_m \quad (3.17)$$

$$y^2 + (\mu_h + \mu_m + \eta + \tau_m)y - \frac{\vartheta_m^2 \delta_m^2 \Pi_{\mu^h}}{\Pi_h \mu_m} + \tau_m \mu_m + \mu_h \mu_m = 0, \quad (3.18)$$

$$\lambda^2 + (\mu_h + \mu_m + \tau_z)\lambda - \frac{\vartheta_z^2 \delta_z^2 \Pi_{\mu^h}}{\Pi_h \mu_m} + \mu_h \mu_m + \tau_z \mu_m = 0, \quad (3.19)$$

By applying the Routh-Hurwitz criteria for order $n = 2$ requires that given a polynomial of the form:

$$b^2 + a_1 b + a_2 = 0,$$

the coefficient of a_1 and a_2 be greater than zero. Hence, applying the same principle, Equation (3.17) can be written in the form:

$$x^2 + f_1 x + f_2 = 0,$$

where,

$$f_1 = \mu_h + \mu_m + \tau_f,$$

$$f_2 = - \frac{\theta_f \delta_f \Pi_m \mu_h}{\pi h \mu_m} + \tau_f \mu_m + \mu_h \mu_m.$$

Since $f_1 > 0$, the criteria requires that $f_2 > 0$. Hence to achieve that we perform some algebraic manipulation to obtain:

$$f_2 = - \frac{(\mu_h + \tau_f) \Pi_h \mu_m^2 R_f}{\Pi_h \mu_m} + (\mu_h + \mu_m + \tau_f) + \mu_m (\mu_h + \tau_f),$$

$$= -R_f \mu_m (\mu_h + \tau_f) + \mu_m (\mu_h + \tau_f) + (\mu_h + \mu_m + \tau_f), = (\mu_h + \mu_m + \tau_f) + \mu_m (\mu_h + \tau_f) [1 - R_f].$$

It is observed that for f_2 to be greater than zero requires $R_f < 1$. Similarly, Equation (3.18) can be written in the form:

$$y^2 + m_1 y + m_2 = 0,$$

where,

$$m_1 = \mu_h + \mu_m + \eta + \tau_m,$$

$$m_2 = - \frac{\vartheta_m^2 \delta_m^2 \Pi_m \mu_h}{\pi h \mu_m} + \tau_m \mu_h + \mu_m (\mu_h + \tau_m).$$

It is seen that $m_1 > 0$ and after some manipulations the value for m_2 is obtained as:

$$m_2 = - \frac{(\mu_h + \eta + \tau_m) \Pi_h \mu_m^2 R_m}{\Pi_h \mu_m} + (\mu_h + \eta + \mu_m + \tau_m) + \mu_m (\mu_h + \tau_m) [1 - R_m].$$

Following the same approach, Equation (3.19) can be rewritten in the form:

$$\lambda^2 + q_1\lambda + q_2 = 0,$$

where,

$$q_1 = \mu_h + \mu_m + \eta + \tau_z,$$

$$q_2 = -\frac{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h}{\Pi_m \mu_m} + \tau \frac{z \mu_m + \mu_h \mu_m}{\Pi_m \mu_m}.$$

In order to make $q_2 > 0$ we have:

$$q_2 = (\mu_h + \mu_m + \tau_z) + \mu_m(\mu_h + \tau_z)[1 - R_z].$$

It is observed that for a_2 , f_2 and q_2 to be positive in order to satisfy RouthHurwitz criteria requires that R_f , R_m and R_z be less than unity. The condition that the various reproduction numbers be less than one indicates that the disease free equilibrium is locally asymptotically stable.

3.3.6 Global stability for Multi-Infection model at DFE

In this section, we prove the global stability of the disease-free equilibrium.

Theorem 5

The DFE of System of Equation (3.1) is globally asymptotically stable if $R_{mzf} < 1$ and unstable if $R_{mzf} > 1$.

We divide the model into two sub models that is infectious class and noninfectious class denoted by F and G respectively. The above description can be represented as:

$$\frac{dF}{dt} = \chi(F, G)$$

$$\frac{dG}{dt} = \gamma(F, G).$$

We define the two valued functions as $\chi(F, G)$ with $f \in \mathbb{R}^{10}_+$ and $\gamma(F, G)$ with $F \in \mathbb{R}^5_+$. The definition for $\chi(F, G)$ and $\gamma(F, G)$ are respectively given by

$$\chi(F, G) = \begin{bmatrix} \frac{\vartheta_m \delta_m I_p}{N_h} S_h - \tau_m I_m - (\mu_h + \eta) I_m + \tau_f I_{mf} - \frac{\vartheta_f \delta_f I_w}{N_h} I_m + \tau_z I_{mz} - \frac{\vartheta_z \delta_z I_a}{N_h} I_m \\ \frac{\vartheta_f \delta_f I_w}{N_h} S_h - (\mu_h + \tau_f) I_f - \frac{\vartheta_m \delta_m I_p}{N_h} I_f + \tau_m I_{mf} + \tau_z I_{zf} - \frac{\vartheta_z \delta_z I_a}{N_h} I_f \\ \frac{\vartheta_z \delta_z I_a}{N_h} S_h - (\tau_z + \mu_h) I_z - \frac{\vartheta_m \delta_m I_p}{N_h} I_z + \tau_m I_{mz} + \tau_f I_{zf} - \frac{\vartheta_f \delta_f I_w}{N_h} I_z \\ \frac{\vartheta_z \delta_z I_a}{N_h} S_h - (\mu_h + \eta + \tau_m + \tau_z) I_{mz} + \tau_f I_{mz} - \frac{\vartheta_f \delta_f I_w}{N_h} I_{mz} + \frac{\vartheta_m \delta_m I_p}{N_h} I_z \\ \frac{\vartheta_f \delta_f I_w}{N_h} I_m - (\mu_h + \tau_f + \tau_z) I_{zf} + \tau_m I_{mzf} - \frac{\vartheta_m \delta_m I_p}{N_h} I_{zf} + \frac{\vartheta_f \delta_f I_w}{N_h} I_z \\ \frac{\vartheta_m \delta_m I_p}{N_h} I_{zf} - (\mu_h + \eta + \tau_m + \tau_f + \tau_z) I_{mzf} + \frac{\vartheta_f \delta_f I_w}{N_h} I_{mz} + \frac{\vartheta_z \delta_z I_a}{N_h} I_{mf} \\ \frac{\vartheta_m \delta_m (I_m + I_{mzf})}{N_h} S_m - \mu_m I_p, \frac{\vartheta_f \delta_f (I_f + I_{mzf})}{N_h} S_m - \mu_m I_w, \\ \frac{\vartheta_z \delta_z (I_z + I_{mzf})}{N_h} S_m - \mu_m I_a \end{bmatrix}$$

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and

$$\gamma(F, G) = \begin{bmatrix} \tau_m I_m - (\mu_h + \psi) R_m \\ \tau_f I_f - (\mu_h + \phi) R_f \\ \tau_z I_z - \mu_h R_z \\ \Pi_h + \psi R_m + \phi R_f - \frac{\theta_m N \delta_m I_p S_h}{N_h} - \mu_h S_h - \frac{\theta_z \delta_z I_a S_h}{N_h} - \frac{\theta_f \delta_f I_w S_h}{N_h} \\ \Pi_m - \mu_m S_m - \frac{\theta_m \delta_m (I_m + I_{mz} + I_{mf} + I_{mzf})}{N_h} S_m \end{bmatrix}$$

$$\begin{aligned} & \theta_f \delta_f (I_f + I_{mf} + I_{zf} + I_{mzf}) \\ & - S_m - S_m N_h \quad N_h \end{aligned} \quad \theta_z \delta_z (I_z + I_{mz} + I_{zf} + I_{mzf})$$

where, T is the transpose. Now the reduced form of the System:

$$\begin{aligned} \frac{dG}{dt} &= \gamma(O, G) \\ \frac{dS}{dt} &= \Pi_h + \psi R_m + \phi R_f - \theta \frac{N_h}{N_h} m \delta m l p S_h - \mu_h S_h - \theta_z \delta_z l a S_h - \theta_f \delta_f l w S_h \\ &= \tau_m l_m - (\mu_h + \psi) R_m \\ \frac{dR_m}{dt} &= \tau_f l_f - (\mu_h + \phi) R_f \\ \frac{dR_z}{dt} &= \tau_z l_z - \mu_h R_z \\ \frac{dS_m}{dt} &= \Pi_m - \mu_m S_m - \frac{\theta_m \delta_m (I_m + I_{mz} + I_{mf} + I_{mzf})}{S_m} - \frac{\theta_f \delta_f (I_f + I_{mf} + I_{zf} + I_{mzf})}{N_h \theta_z \delta_z (I_z + I_{mz} + I_{zf} + I_{mzf})} \end{aligned} \quad (3.20)$$

$G^* = (S_h^*, R_m^*, R_f^*, R_z^*, S_m^*) = (\frac{\Pi_h}{\mu_m}, 0, 0, 0, \Pi_m)$ is globally asymptotically stable

for the reduced form of System $= \gamma(0, G)$. To see this we solve the second dt and third equations of (3.20) to yield the result $R_m(t) = R_m(0)e^{-(\mu_h + \psi)t}$ which turns to zero as $t \rightarrow \infty$ and $R_f(0)e^{-(\mu_h + \phi)t}$ also turns to zero as $t \rightarrow \infty$. It is

also observed that $S_m(t) = \frac{\Pi_m}{\mu_m} + \{S_m(0) - \frac{\Pi_m}{\mu_m}\}e^{-\mu_m t}$ which turns to $\frac{\Pi_m}{\mu_m}$ as $t \rightarrow \infty$.

Lastly substitute $S_h(t) = \Pi_h + \psi \{R_m(0)e^{-(\mu_h + \psi)t} + \phi \{R_f(0)e^{-(\mu_h + \phi)t} -$

$\mu_h \{ \frac{\Pi_m}{\mu_m} + [S_m(0) - \frac{\Pi_m}{\mu_m}] \} e^{-\mu_h t} \rightarrow \Pi_h$ as $t \rightarrow \infty$. This asymptotic dynamic is μ_h

independent of initial conditions in ω . Hence, the convergence of the solution

(3.20) is global in Ω . Truly $\chi(F, G)$ satisfies the following two conditions given as H_2 in Castillo-Chavez et al. (2002) namely;

$$\begin{aligned} 1. & \chi(0, G) = 0, \\ 2. & \chi(F, G) = TG - \chi^-(F, G), \chi^-(F, G) \geq 0, \quad \text{on } \Omega. \end{aligned} \quad (3.21)$$

[illegible]

where,

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 ?, where $i = 1, 2, 3, \dots, 10$.
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It is shown that $\chi'_4(F, G) < 0$, $\chi'_5(F, G) < 0$, $\chi'_6(F, G) < 0$, and $\chi'_7(F, G) < 0$. Hence, the conditions in 3.33 are not met. Hence, the DFE may not be globally asymptotically.

3.3.7 Existence of endemic equilibrium point of Multi-infections

Obtaining an implicit expression for the endemic equilibrium point of the multiinfection is not forthcoming due to the complex nature of the equations involved.

Therefore we assume that the endemic equilibrium may exist as

$$E_{mzf}^{**} = (S_h^{**}, I_m^{**}, I_z^{**}, I_f^{**}, I_{mz}^{**}, I_{mf}^{**}, I_{zf}^{**}, I_{mzf}^{**}, R_m^{**}, R_z^{**}, R_f^{**}, S_m^{**}, I_p^{**}, I_a^{**}, I_w^{**}).$$

Let us now determine the global stability of the endemic equilibrium as follows;

Theorem 6

*If $R_{mzf} > 1$, then the unique endemic equilibrium E_{mzf}^{**} of System (3.1) is globally stable in the interior of Ω .*

The global stability of the endemic equilibrium can be determined by constructing a common quadratic Lyapunov function $V(t)$ of the form:

$$\begin{aligned}
V(S_h, I_m, I_z, I_f, I_{mz}, I_{mf}, I_{fz}, I_{mfz}, R_m, R_f, R_z, S_m, I_p, I_w, I_a) = & \frac{1}{2} \{ (S_h - S_h^{**}) + (I_m - I_m^{**}) - \\
& + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) + (I_{fz} - I_{fz}^{**}) + (I_{mfz} - I_{mfz}^{**}) \\
& + (R_m - R_m^{**}) + (R_z - R_z^{**}) + (R_f - R_f^{**}) \}^2 + \frac{1}{2} \{ (S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**}) \\
& + (I_w - I_w^{**}) \}^2.
\end{aligned} \tag{3.23}$$

Differentiating Equation (3.23) gives;

$$\begin{aligned}
= & [(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) + (I_{fz} - I_{fz}^{**}) + (I_{mfz} - I_{mfz}^{**}) \\
& + (R_m - R_m^{**}) + (R_z - R_z^{**}) + (R_f - R_f^{**})] \times \\
& \frac{d}{dt} [S_h + I_m + I_z + I_f + I_{mz} + I_{mf} + I_{fz} + I_{mfz} + R_m + R_f + R_z] + [(S_m - S_m^{**}) + (I_p - I_p^{**}) \\
& + (I_a - I_a^{**}) + (I_w - I_w^{**})] \frac{d}{dt} [S_m + I_p + I_a + I_w] \tag{3.24}
\end{aligned}$$

The total population size of both humans and mosquitoes; N_h and N_m , can be defined by:

$$N_h = S_h + I_m + I_z + I_f + I_{mz} + I_{mf} + I_{fz} + I_{mfz} + R_m + R_f + R_z,$$

$$N_m = S_m + I_p + I_a + I_w,$$

such that:

$$\frac{dN_h}{dt} = \Pi_h - \mu_h N_h,$$

$$\frac{dN_m}{dt} = \Pi_m - \mu_m N_m.$$

Hence,

$$\begin{aligned}
\frac{d}{dt} [& \frac{1}{2} \{ (S_h - S_h^{**}) + (I_m - I_m^{**}) - \\
& - (I_m) + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) \} = (S_h \\
& - I_m) + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) = (S_h
\end{aligned}$$

$$\begin{aligned}
& \left. \frac{dN_h}{dt} = \left[(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) \right. \right. \\
& \left. \left. + (I_{zf} - I_{zf}^{**}) + (I_{mzf} - I_{mzf}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**}) + (R_f - R_f^{**}) \right] \times \right. \\
& \left. \left[\Pi_h - \mu_h (S_h + I_m + I_z + I_f + I_{mz} + I_{fz} + I_{mfz} + R_m + R_f + R_z) \right. \right. \\
& \left. \left. - \eta (I_m + I_{mz} + I_{mf} + I_{mzf}) \right] + [(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**}) + (I_w - I_w^{**})] \right. \\
& \left. \times [\Pi_m - \mu_m (S_m + I_p + I_a + I_w)] \right]
\end{aligned}$$

At the endemic equilibrium, we have the following relations:

$$\begin{aligned}
\Pi_h = & \mu_h (S_h^{**} + I_m^{**} + I_f^{**} + I_z^{**} + I_{mz}^{**} + I_{mf}^{**} + I_{zf}^{**} + I_{mzf}^{**} + R_m^{**} + R_f^{**} + R_z^{**}) + \eta (I_m^{**} + \\
& I_{mz}^{**} + I_{mf}^{**} + I_{mzf}^{**}).
\end{aligned}$$

$$\Pi_m = \mu_m (S_m^{**} + I_p^{**} + I_a^{**} + I_w^{**}).$$

We have:

$$\begin{aligned}
\frac{dV}{dt} = & \left[(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) \right. \\
& \left. + (I_{zf} - I_{zf}^{**}) + (I_{mzf} - I_{mzf}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**}) + (R_f - R_f^{**}) \right] \\
& \times [\mu_h (S_h^{**} + I_m^{**} + I_f^{**} + I_z^{**} + I_{mz}^{**} + I_{mf}^{**} + I_{zf}^{**} + I_{mzf}^{**} + R_m^{**} + R_f^{**} + R_z^{**}) + \eta (I_m^{**} + I_{mz}^{**} \\
& + I_{mf}^{**} + I_{mzf}^{**})] - \mu_h (S_h + I_m + I_z + I_f + I_{mz} + I_{mf} + I_{zf} + I_{mzf} + R_m + R_f + R_z) \\
& - \eta (I_m + I_{mz} + I_{mf} + I_{mzf}) + [(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**}) + (I_w - I_w^{**})]
\end{aligned}$$

$$\times [\mu_h(S_m^{**} + I_p^{**} + I_a^{**} + I_w^{**}) - \mu_m(S_m + I_p + I_a + I_w)]$$

Manipulating the right hand side of susceptible differential equations for both humans and mosquitoes at the endemic equilibrium points gives the relations

$$\Pi_h = \mu_h(S_h^{**} + I_m^{**} + I_f^{**} + I_z^{**} + I_{mz}^{**} + I_{mf}^{**} + I_{zf}^{**} + I_{mzf}^{**} + R_m^{**} + R_f^{**} + R_z^{**})$$

$$+ \eta(I_m^{**} + I_p^{**} + I_a^{**} + I_w^{**})$$

$$\Pi_m = \mu_m(S_m^{**} + I_p^{**} + I_a^{**} + I_w^{**})$$

$$\begin{aligned} \frac{\partial V^{**}}{\partial t} &= \left[\begin{aligned} & - (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) \\ & + (I_{zf} - I_{zf}^{**}) + (I_{mzf} - I_{mzf}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**}) + (R_f - R_f^{**}) \end{aligned} \right] \\ &\times \left[\begin{aligned} & \mu_h[(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) \\ & + (I_{zf} - I_{zf}^{**}) + (I_{mzf} - I_{mzf}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**}) + (R_f - R_f^{**})] - \eta[(I_m - I_m^{**}) \\ & + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) + (I_{mzf} - I_{mzf}^{**})] + [(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**}) \\ & + (I_w - I_w^{**})] \times \left[-\mu_m[(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**}) + (I_w - I_w^{**})] \right] \end{aligned} \right] \\ \Rightarrow \frac{\partial V}{\partial t} &= - \left[\begin{aligned} & (S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) \\ & + (I_{zf} - I_{zf}^{**}) + (I_{mzf} - I_{mzf}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**}) + (R_f - R_f^{**}) \end{aligned} \right] \\ &\times \left[\begin{aligned} & (S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_f - I_f^{**}) + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) \\ & + (I_{zf} - I_{zf}^{**}) + (I_{mzf} - I_{mzf}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**}) + (R_f - R_f^{**}) \end{aligned} \right] - \eta[(I_m - I_m^{**}) \\ & + (I_{mz} - I_{mz}^{**}) + (I_{mf} - I_{mf}^{**}) + (I_{mzf} - I_{mzf}^{**})] - \left[(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**}) \right. \\ & \left. + (I_w - I_w^{**}) \right] \left[\mu_m[(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**}) + (I_w - I_w^{**})] \right] \end{aligned}$$

By letting

$$A^1 = (S_h - S_h^{**}), A_2 = (I_m - I_m^{**}), A_3 = (I_z - I_z^{**}), A_4 = (I_f - I_f^{**}), A_5 = (I_{mz} - I_{mz}^{**}),$$

$$A_6 = (I_{mf} - I_{mf}^{**}), A_7 = (I_{zf} - I_{zf}^{**}), A_8 = (I_{mzf} - I_{mzf}^{**}), A_9 = (R_m - R_m^{**}), A_{10} = (R_z - R_z^{**}),$$

$$A_{11} = (R_f - R_f^{**}), A_{12} = (S_m - S_m^{**}), A_{13} = (I_p - I_p^{**}), A_{14} = (I_a - I_a^{**}), A_{15} = (I_w - I_w^{**}),$$

$$A_{16} = A_1 + A_2 + A_3 + A_4 + A_5 + A_6 + A_7 + A_8 + A_9 + A_{10} + A_{11},$$

$$A_{17} = A_2 + A_5 + A_6 + A_8, A_{18} = A_{12} + A_{13} + A_{14} + A_{15},$$

we substitute it to get:

$$-\frac{\partial V}{\partial t} - (\mu_h A_{216} + \eta A_{16} A_{17} + \mu_m A_{18}) \quad (3.25) =$$

It can be seen that $\frac{\partial V}{\partial t} \leq 0$ if $S_h \leq S^{**}, I_m \leq I_m^{**}, I_z \leq I_z^{**}, I_f \leq I_f^{**}, I_{mz} \leq I_{mz}^{**},$

$I_{mf} \leq I_{mf}^{**}, I_{zf} \leq I_{zf}^{**}, I_{mzf} \leq I_{mzf}^{**}, R_m \leq R_m^{**}, R_z \leq R_z^{**}, R_f \leq R_f^{**}, S_m \leq S_m^{**}, I_p \leq$

$I_p^{**}, I_a \leq I_a^{**}, I_w \leq I_w^{**}.$ Again, $\frac{\partial V}{\partial t} = 0$ if and only if $S_h = S_h^{**}, I_m = I_m^{**}, I_z = I_z^{**}, I_f = I_f^{**}, I_{mz} = I_{mz}^{**}, I_{mf} = I_{mf}^{**}, I_{zf} = I_{zf}^{**}, I_{mzf} = I_{mzf}^{**}, R_m = R_m^{**}, R_z = R_z^{**}, R_f = R_f^{**}, S_m = S_m^{**}, I_p = I_p^{**}, I_a = I_a^{**}, I_w = I_w^{**}.$ This leads to the following theorem;

Theorem 7

If a function $V(t)$ is positive definite on the entire state space and has the additional property that $|V(t) \rightarrow \infty|$ as $t \rightarrow \infty$ and its derivative $\frac{dV}{dt}$ is negative definite on the entire state space, then the equilibrium point at the origin is globally asymptotically stable.

Therefore $\frac{dL}{dt} \leq 0$ and by LaSalle's Extension, LaSalle (1976), it implies that the omega limit set of each solution lies in an invariant set contained in Ω . The only invariant set contained in Ω is the singleton E . This shows that each solution which intersects R^{15}_+ limits to the endemic equilibrium and that trivial equilibrium is globally asymptotically stable in the invariant feasible region. This completes the proof.

3.3.8 Bifurcation

In this subsection, we determine the stability of the endemic equilibrium by finding the eigenvalues of the Jacobian matrix computed at the endemic equilibrium. However, our mathematical model gave rise to multiple steady-states which show a bifurcation phenomena; a set of parameter values at which an equilibrium or fixed point of the System being considered changes stability, that is, either appears or disappears. There are two distinct bifurcation at $R_0 = 1$; forward and backwards bifurcation. A transcritical bifurcation brings about an exchange in stability between the disease free equilibrium, which exist for all values of R_0 and an endemic equation which only exist on one side of the bifurcation point. Hence, we apply the method of centre manifold theory used by Castillo-Chavez & Song (2004), to investigate the stability of endemic equilibrium.

To apply the method, System (3.1) can be rewritten in a dimensionless state variables of the multi-infection model as follows;

$$x_1 = S_h, x_2 = I_m, x_3 = I_f, x_4 = I_z, x_5 = I_{mz}, x_7 = I_{xf}, x_8 = I_{mfz}, x_9 = R_m, x_{10} = R_f, x_{11} = R_z, x_{12} = S_m, x_{13} = I_p, x_{14} = I_w, x_{15} = I_a.$$

The System (3.1) can be written in the vector form as

$$\frac{dX_i}{dt} = F(X_i),$$

where, $X_i = (x_1, x_2, x_3, \dots, x_{15})^T$, $F = (f_1, f_2, f_3, \dots, f_{15})^T$. Hence, we obtain the following;

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1 = \Pi_h + \psi x_9 + \phi x_{10} - \frac{\theta_m \delta_m x_{13}}{N_h} x_1 - \frac{\theta_z \delta_z x_{15}}{N_h} x_1 - \frac{\theta_f \delta_f x_{14}}{N_h} x_1, \\
\frac{dx_2}{dt} &= f_2 = \frac{\theta_m \delta_m x_{13}}{N_h} x_1 - (\mu_h + \eta + \tau_m) x_2 + \tau_f x_6 - \frac{\theta_f \delta_f x_{14}}{N_h} x_2 + \tau_z x_5 - \frac{\theta_z \delta_z x_{15}}{N_h} x_6, \\
\frac{dx_3}{dt} &= f_3 = \frac{\theta_f \delta_f x_{14}}{N_h} x_1 - \mu_h x_3 - \frac{\theta_m \delta_m x_{13}}{N_h} x_3 + \tau_m x_6 - \tau_f x_3 + \tau_f x_7 - \frac{\theta_z \delta_z x_{15}}{N_h} x_3, \\
\frac{dx_4}{dt} &= f_4 = \frac{\theta_z \delta_z x_{15}}{N_h} x_1 - \tau_z x_4 - \frac{\theta_m \delta_m x_{13}}{N_h} x_4 + \tau_m x_5 + \tau_f x_7 - \frac{\theta_f \delta_f x_{14}}{N_h} x_4 - \mu_h x_4, \\
\frac{dx_5}{dt} &= f_5 = \frac{\theta_z \delta_z x_{15}}{N_h} x_5 - \tau_z x_5 - (\mu_h + \eta) x_5 + \tau_f x_8 - \frac{\theta_f \delta_f x_{14}}{N_h} x_5 + \frac{\theta_m \delta_m x_{13}}{N_h} x_4 - \tau_m x_5, \\
\frac{dx_6}{dt} &= f_6 = \frac{\theta_f \delta_f x_{14}}{N_h} x_2 - \tau_f x_6 - (\mu_h + \eta) x_6 + \tau_z x_8 - \frac{\theta_z \delta_z x_{15}}{N_h} x_6 + \frac{\theta_m \delta_m x_{13}}{N_h} x_3 - \tau_m x_6, \\
\frac{dx_7}{dt} &= f_7 = \frac{\theta_z \delta_z x_{15}}{N_h} x_3 - \tau_f x_7 - \mu_h x_7 + \tau_m x_8 - \frac{\theta_m \delta_m x_{13}}{N_h} x_7 + \frac{\theta_f \delta_f x_{14}}{N_h} x_4 - \tau_z x_7, \\
\frac{dx_8}{dt} &= f_8 = \frac{\theta_m \delta_m x_{13}}{N_h} x_7 - \tau_m x_8 - (\mu_h + \eta) x_8 - \tau_f x_8 + \frac{\theta_f \delta_f x_{14}}{N_h} x_5 + \frac{\theta_z \delta_z x_{15}}{N_h} x_6 - \tau_z x_8, \\
\frac{dx_9}{dt} &= f_9 = \tau_f x_3 - (\mu_h + \phi) x_{10}, \\
\frac{dx_{10}}{dt} &= f_{10} = \tau_f x_3 - (\mu_h + \phi) x_{10}, \\
\frac{dx_{11}}{dt} &= f_{11} = \tau_z x_4 - \mu_h x_{11}, \\
\frac{dx_{12}}{dt} &= f_{12} = \Pi_m - \mu_m x_{12} - \frac{\theta_m \delta_m (x_6 + x_5 + x_7 + x_8)}{N_h} x_{12} - \frac{\theta_f \delta_f (x_3 + x_6 + x_7 + x_8)}{N_h} x_{12} - \frac{\theta_z \delta_z (x_4 + x_5 + x_7 + x_8)}{N_h} x_{12}, \\
\frac{dx_{13}}{dt} &= f_{13} = \frac{\theta_m \delta_m (x_2 + x_5 + x_6 + x_8)}{N_h} x_{12} - \mu_m x_{13}, \\
\frac{dx_{14}}{dt} &= f_{14} = \frac{\theta_f \delta_f (x_3 + x_6 + x_7 + x_8)}{N_h} x_{12} - \mu_m x_{14}, \\
\frac{dx_{15}}{dt} &= f_{15} = \frac{\theta_z \delta_z (x_4 + x_5 + x_7 + x_8)}{N_h} x_{12} - \mu_m x_{15}.
\end{aligned}
\tag{3.26}$$

$R_{ma} = 1$ gives

$\beta^* = v_m^2$ chosen as the bifurcation parameter and also

$R_{ma} = 1$ gives

$R_{ma} = 1$ gives

$R_{ma} = 1$ gives

$R_{ma} = 1$ gives

$$\begin{bmatrix}
 0 & 0 & 0 & 0 & 0 & 0 & -b_{23} & 0 & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & -b_{24} & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_h & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -b_{32} & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_m & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0
 \end{bmatrix}
 \begin{bmatrix}
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0
 \end{bmatrix}
 =
 \begin{bmatrix}
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0
 \end{bmatrix}$$

where,

$$\begin{aligned}
 b_1 &= \mu_h, b_2 = \theta_m \delta_m, b_3 = \theta_f \delta_f, b_4 = \theta_z \delta_z, b_6 = \mu_h + \eta + \tau_m, b_9 = \mu_h + \tau_f, b_{13} = \mu_h + \tau_z, b_{15} = \mu_h + \eta \\
 &+ \tau_m + \tau_z, b_{18} = \mu_h + \eta + \tau_m + \tau_f, b_{20} = \mu_h + \tau_f + \tau_z, b_{32} = -\mu_m, b_{22} = \mu_h + \eta + \tau_m + \tau_f + \tau_z, b_{23} = \mu_h + \psi, \\
 b_{24} &= \mu_h + \phi, \theta_m \delta_m \Pi_m \mu_h, \theta_f \delta_f \Pi_m \mu_h, \theta_z \delta_z \Pi_m \mu_h, b_{25} = \frac{\Pi_h \mu_m}{(\theta_m \delta_m + \theta_z \delta_z) \Pi_m \mu_h}, b_{26} = \frac{\Pi_h \mu_m}{(\theta_m \delta_m + \theta_f \delta_f) \Pi_m \mu_h}, b_{28} = \frac{\Pi_h \mu_m}{(\theta_z \delta_z + \theta_f \delta_f) \Pi_m \mu_h}, b_{29} = \frac{\Pi_h \mu_m}{(\theta_m \delta_m + \theta_z \delta_z + \theta_f \delta_f) \Pi_m \mu_h}, b_{30} = \frac{\Pi_h \mu_m}{\Pi_h \mu_m}, b_{31} = \frac{\Pi_h \mu_m}{\Pi_h \mu_h}
 \end{aligned}$$

The right eigenvector associated with the eigenvalues are given by:

$$\begin{bmatrix}
 1 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0 \\
 0
 \end{bmatrix}$$

Solving for the left eigenvector gives:

$$v_1 = 0,$$

$$v_2 = \frac{\theta_m \delta_m \Pi_m \mu_h v_{13}}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m \theta_f \delta_f \Pi_m \mu_h v_{14}}$$

$$v_3 = \frac{\theta_z \delta_z \Pi_m \mu}{(\mu_h + \tau_f) \Pi_h \mu_m}$$

$$v_4 = \frac{h v_{15}}{(\mu_h + \tau_z) \Pi_h \mu_m}$$

$$v_5 = 2 \theta_m \delta_m \Pi_m \mu_h v_{13} + \theta_z \delta_z \Pi_m \mu_h v_{15}, \tau_z v + \tau_m v_4 +$$

$$\frac{(\mu_h + \eta + \tau_m + \tau_z) \Pi_h \mu_m \tau_f v_2 + \tau_m v_3 + \theta_f \delta_f \Pi_m \mu_h v_{14} + \theta_z \delta_z \Pi_m \mu_h v_{15}}{(\mu_h + \eta + \tau_m + \tau_f) \Pi_h \mu_m} v_6 =$$

$$\frac{\tau_z v_3 + \tau_f v_4 + \theta_m \delta_m \Pi_m \mu_h v_{13} + \theta_f \delta_f \Pi_m \mu_h v_{14}}{(\mu_h + \tau_f + \tau_z) \Pi_h \mu_m} v_7 =$$

$$\frac{\tau_f v_5 + \tau_z v_6 + \tau_m v_7 + \theta_m \delta_m \Pi_m \mu_h v_{13} + \theta_f \delta_f \Pi_m \mu_h v_{14} + \theta_z \delta_z \Pi_m \mu_h v_{15}}{(\mu_h + \eta + \tau_m + \tau_f + \tau_z) \Pi_h \mu_m} v_8 =$$

$$v_9 = 0, v_{10}$$

$$= 0, v_{11} =$$

$$0, v_{12} = 0,$$

$$v_{13} = \frac{\theta_m \delta_m v_2}{\mu_m \theta_f}$$

$$\delta_f v_3 v_{14} =$$

$$\mu_m$$

$$= \frac{\theta_z \delta_z v_4 v_{15}}{\mu_m}$$

$$\mu_m$$

Computation of a and b

The associated non-zero second order partial derivatives at DFE are given by:

$$\begin{aligned}
 \frac{\partial^2 f_2}{\partial x_1 \partial x_{13}} &= \frac{\partial^2 f_2}{\partial x_{13} \partial x_1} = \theta_m \delta_m, & \frac{\partial^2 f_2}{\partial x_2 \partial x_{14}} &= \frac{\partial^2 f_2}{\partial x_{14} \partial x_2} = -\vartheta_f \delta_f \\
 \frac{\partial^2 f_3}{\partial x_1 \partial x_{13}} &= \frac{\partial^2 f_3}{\partial x_{13} \partial x_1} = \theta_m \delta_m, & \frac{\partial^2 f_3}{\partial x_2 \partial x_{14}} &= \frac{\partial^2 f_3}{\partial x_{14} \partial x_2} = -\vartheta_f \delta_f \\
 \frac{\partial^2 f_4}{\partial x_3 \partial x_{15}} &= \frac{\partial^2 f_4}{\partial x_{15} \partial x_3} = -\vartheta_m \delta_m, & \frac{\partial^2 f_4}{\partial x_4 \partial x_{12}} &= \frac{\partial^2 f_4}{\partial x_{12} \partial x_4} = \vartheta_m \delta_m \\
 \frac{\partial^2 f_5}{\partial x_4 \partial x_{13}} &= \frac{\partial^2 f_5}{\partial x_{13} \partial x_4} = \vartheta_m \delta_m, & \frac{\partial^2 f_5}{\partial x_2 \partial x_{14}} &= \frac{\partial^2 f_5}{\partial x_{14} \partial x_2} = \vartheta_f \delta_f \\
 \frac{\partial^2 f_6}{\partial x_3 \partial x_{13}} &= \frac{\partial^2 f_6}{\partial x_{13} \partial x_3} = \vartheta_m \delta_m, & \frac{\partial^2 f_6}{\partial x_3 \partial x_{15}} &= \frac{\partial^2 f_6}{\partial x_{15} \partial x_3} = \vartheta_z \delta_z \\
 \frac{\partial^2 f_7}{\partial x_4 \partial x_{14}} &= \frac{\partial^2 f_7}{\partial x_{14} \partial x_4} = \vartheta_f \delta_f, & \frac{\partial^2 f_7}{\partial x_2 \partial x_{12}} &= \frac{\partial^2 f_7}{\partial x_{12} \partial x_2} = \vartheta_m \delta_m \\
 \frac{\partial^2 f_{14}}{\partial x_3 \partial x_{12}} &= \frac{\partial^2 f_{14}}{\partial x_{12} \partial x_3} = \vartheta_f \delta_f, & \frac{\partial^2 f_{15}}{\partial x_4 \partial x_{12}} &= \frac{\partial^2 f_{15}}{\partial x_{12} \partial x_4} = \vartheta_z \delta_z
 \end{aligned}$$

Thus, the expression for a is given as:

$$\begin{aligned}
 a = & v_2 w_1 w_2 \left[\frac{\partial^2 f_2}{\partial x_1 \partial x_{13}} \right] + v_2 w_2 w_{14} \left[\frac{\partial^2 f_2}{\partial x_2 \partial x_{14}} \right] + v_3 w_1 w_{14} \left[\frac{\partial^2 f_3}{\partial x_1 \partial x_{14}} \right] \\
 & + v_3 w_3 w_{13} \left[\frac{\partial^2 f_3}{\partial x_3 \partial x_{13}} \right] + v_3 w_3 w_{15} \left[\frac{\partial^2 f_3}{\partial x_{15} \partial x_3} \right] + v_4 w_1 w_{15} \left[\frac{\partial^2 f_3}{\partial x_{15} \partial x_1} \right] \\
 & + v_4 w_4 w_{13} \left[\frac{\partial^2 f_4}{\partial x_4 \partial x_{13}} \right] + v_4 w_4 w_{14} \left[\frac{\partial^2 f_4}{\partial x_{14} \partial x_4} \right] + v_5 w_4 w_{13} \left[\frac{\partial^2 f_5}{\partial x_4 \partial x_{13}} \right] \\
 & + v_6 w_2 w_{14} \left[\frac{\partial^2 f_6}{\partial x_3 \partial x_{14}} \right] + v_6 w_3 w_{13} \left[\frac{\partial^2 f_6}{\partial x_3 \partial x_{13}} \right] + v_7 w_3 w_{15} \left[\frac{\partial^2 f_7}{\partial x_3 \partial x_{15}} \right] \\
 & + v_7 w_4 w_{14} \left[\frac{\partial^2 f_7}{\partial x_4 \partial x_{14}} \right] + v_{13} w_2 w_{12} \left[\frac{\partial^2 f_{13}}{\partial x_2 \partial x_{12}} \right] + v_{14} w_3 w_{12} \left[\frac{\partial^2 f_{14}}{\partial x_3 \partial x_{12}} \right]
 \end{aligned}$$

$$+v_{15}w_4w_{12}\left[\frac{\partial^2 f_{15}}{\partial x_4 \partial x_{12}}\right] > 0.$$

The non-zero partial derivatives of f associated with b is given as:

$$= \frac{\partial^2 f_2}{\partial \vartheta \partial \vartheta} = \delta_{m x_1} > 0 \quad b.$$

It is observed that for $a > 0$ and $b > 0$, the result satisfies Theorem 1. Thus, when $\beta < 0$ with $|\beta| \ll 1$, 0 , is locally asymptotically stable and there exists a positive unstable equilibrium; when $0 < \beta \ll 1$, 0 is unstable and there exists a negative and locally asymptotically stable equilibrium.

3.3.9 Numerical Bifurcation

This is a qualitative change in behaviour of a dynamical System produced by varying a parameter in the equation. Backward bifurcation is an important phenomenon in compartmental epidemiological models. The existence of such a bifurcation suggests that the basic reproduction number itself is not sufficient enough to characterize or decide whether Malaria, Zika virus and Elephantiasis will prevail or not and if the disease will become endemic also depend on the initial sizes of the involved population. Thus it is important to identify the backward bifurcation and establish its threshold. We carry out bifurcation analysis to study the behaviour of the model System (3.1) based on the results in the endemic equilibrium of the model state variables through numerical simulation over chosen parameter values. It is important to note that the existence of the bi-stability is not easy to simulate numerically. This is because a small interval of R_0 is required for the occurrence of backward bifurcation and a very range of parameter has to be chosen. The qualitative backward bifurcation diagram describing the behaviour of R_0 is presented in Figure 5 where θ_m is taken as bifurcation parameter. The result indicates that reducing

the R_0 below the saddle-node bifurcation value which is less than 1 but greater than zero, may result in disease eradication.

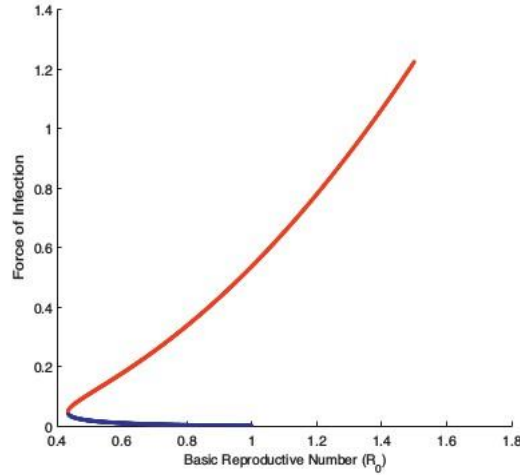


Figure 5: Description of the backward bifurcation of System (3.1) with θ_m as the chosen parameters.

Epidemiologically, Figure (5) implies that bringing R_0 below unity does not suffice for the eradication of multi-disease. From the analysis of the existence of the endemic equilibrium, we have established that the model System exhibits backward bifurcation when $R_0 < 1$. The existence of backward bifurcation indicates that in the neighbourhood of 1, for $R_0 < 1$, a stable disease free equilibrium coexists with two endemic equilibria, that is a smaller equilibrium (smaller number of infectious individuals) which is unstable and a larger equilibrium (with a large number of infectious individuals) which is stable. These two endemic equilibria disappear by saddle-node bifurcation when the basic reproduction number R_0 is decreased below the critical value which is less than one but greater than zero.

In order to achieve the epidemiological goal of disease eradication, R_0 must be brought below the critical value. The interpretation of this is that reducing the transmission rate or increasing treatment can lead to disappearance of the backward bifurcation curve and in this case lowering R_0 below unity is sufficient to eliminate the disease from the population; a situation that will lead to

forward bifurcation which is shown in Figure 6 and lowering R_0 below unity would be sufficient to make the disease free equilibrium globally stable.

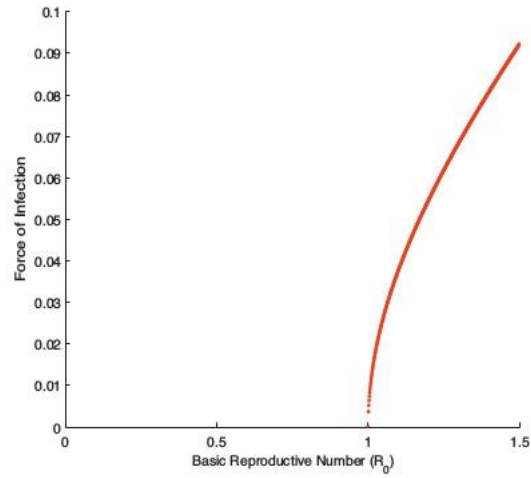


Figure 6: Description of the forward bifurcation of System (3.1).

3.4 Model co-infection states

In order to fully understand the dynamics of the multi-infection disease, we begin by gaining insight from the various co-infection sub-model that is derived from the System (3.1).

3.4.1 Malaria-Zika virus Sub-model

The following differential equations are derived for the Malaria-Zika virus submodel.

$$\begin{aligned}
 \frac{dS_h}{dt} &= \Pi_h - \mu_h S_h - \alpha_m S_h - \alpha_z S_h + \psi R_m, \\
 \frac{dI_m}{dt} &= \alpha_m S_h - \tau_m I_m - (\mu_h + \eta) I_m - \alpha_z I_m + \tau_z I_{mz}, \\
 \frac{dI_z}{dt} &= \alpha_z S_h - \tau_z I_z - \alpha_m I_z + \tau_m I_{mz} - \mu_h I_z, \\
 \frac{dI_{mz}}{dt} &= \alpha_z I_m - \tau_z I_{mz} - (\mu_h + \eta) I_{mz} + \alpha_m I_z - \tau_m I_{mz}, \\
 \frac{dR_m}{dt} &= \tau_m I_m - (\mu_h + \psi) R_m,
 \end{aligned} \tag{3.28}$$

$$\begin{cases} \frac{dR_z}{dt} = \tau_z I_z - \mu_h R_z, \\ \frac{dS_m}{dt} = \Pi_m - \mu_m S_m - \lambda_p S_m - \lambda_a S_m, \\ \frac{dI_p}{dt} = \lambda_p S_m - \mu_m I_p, \\ \frac{dI_a}{dt} = \lambda_a S_m - \mu_m I_a, \end{cases}$$

where,

$$\lambda_p = \frac{\theta_m \delta_m I_p}{N_h}, \lambda_a = \frac{\theta_m \delta_m (I_m + I_{mz})}{N_h}, \alpha_m = \frac{\theta_z \delta_z I_a}{N_h}, \alpha_z = \frac{\theta_z \delta_z (I_z + I_{mz})}{N_h} \quad (3.29)$$

3.4.2 Disease free equilibrium for Malaria-Zika Co-infection

The Malaria-Zika co-infection model of System (3.29) has a disease free equilibrium point when all the infectious states are set to zero. Thus, we have

$$E_{mz} = (S_h, I_m, I_z, I_{mz}, R_m, R_z, S_m, I_p, I_a) = \left(\frac{\Pi_h}{\mu_h}, 0, 0, 0, 0, 0, \frac{\Pi_m}{\mu_m}, 0, 0 \right). \quad (3.30)$$

3.4.3 Basic Reproduction Number for Malaria-Zika Co-infection

(R_{mz})

Rewriting System (3.28) starting from the infected states;

$$\begin{cases} \frac{dI_m}{dt} = \alpha_m S_h - \tau_m I_m - (\mu_h + \eta) I_m - \alpha_z I_m + \tau_z I_{mz}, \\ \frac{dI_z}{dt} = \alpha_z S_h - \tau_z I_z - \alpha_m I_z + \tau_m I_{mz} - \mu_h I_z, \\ \frac{dI_{mz}}{dt} = \alpha_z I_m - \tau_z I_{mz} - (\mu_h + \eta) I_{mz} + \alpha_m I_z - \tau_m I_{mz}, \end{cases}$$

$$\frac{dI}{dt} = \lambda_p S_m - \mu_m I_p,$$

$$\begin{aligned} \frac{dR_m}{dt} &= \lambda_a S_m - \mu_m I_a, \\ \frac{dR_z}{dt} &= \tau_m I_m - (\mu_h + \psi) R_m, \\ \frac{dS_m}{dt} &= \Pi_m - \mu_m S_m - \lambda_p S_m - \lambda_a S_m, \\ \frac{dS_h}{dt} &= \Pi_h - \mu_h S_h - \alpha_m S_h - \alpha_z S_h + \psi R_m; \end{aligned} \quad (3.31)$$

we identify matrices F and V for the new infection terms and the remaining transfer terms at the disease free equilibrium using the next generation operator method as described by Van den Driessche & Watmough (2002) respectively from equation (3.31).

$$F = \begin{bmatrix} \frac{\theta_m \delta_m I_p - \theta_z N \delta_h I_a}{S_h} & (\mu_h + \eta + \tau_m) I_m - \tau_z I_{mz} \\ \frac{\theta_z \delta_z I_a S_h - \theta_m N \delta_h m I_p}{S_h} & (\mu_h + \tau_z) I_z - \tau_m I_{mz} \end{bmatrix} \text{ and } V = \begin{bmatrix} \mu_m I_p & \theta_m \delta_m (I_m + I_{mz}) \\ \mu_m I_a & \theta_m \delta_m (I_m + I_{mz}) \end{bmatrix}.$$

The Jacobian matrix is given as

$$\frac{\partial}{\partial S_h} \left(\theta_z \delta_z I_a \right) - \theta_m \delta_m S_h - \theta_z N \delta_h I_m$$

$$\begin{aligned}
 & \begin{array}{cccc|c}
 -N_h & 0 & 0 & N_h & \\
 \hline
 0 & -\theta_m N \delta_{hm} \rho & 0 & -\theta_m N \delta_{hm} \rho & \theta_z N \delta_{zh} S_h \\
 \hline
 0 & \frac{\theta_z \delta_z S_m}{N_h} & \frac{\theta_z \delta_z S_m}{N_h} & 0 & 0 \\
 \hline
 (\mu_h + \eta + \tau_m) & 0 & 0 & -\tau_z & 0 \\
 \hline
 0 & (\mu_h + \tau_z) & -\tau_m & 0 & 0 \\
 \hline
 0 & 0 & (\mu_h + \eta + \tau_m + \tau_z) & 0 & 0 \\
 \hline
 0 & 0 & 0 & \mu_m & \mu_m \\
 \hline
 0 & 0 & 0 & 0 & 0
 \end{array} \\
 & V = \begin{array}{ccccc}
 0 & 0 & -\tau_z & 0 & 0 \\
 (\mu_h + \tau_z) & -\tau_m & 0 & 0 & 0 \\
 0 & 0 & (\mu_h + \eta + \tau_m + \tau_z) & 0 & 0 \\
 0 & 0 & 0 & \mu_m & \mu_m \\
 0 & 0 & 0 & 0 & 0
 \end{array} \\
 & F = \begin{array}{cccc|c}
 \theta_z N \delta_{zh} \rho & \theta_m N \delta_{hm} \rho & 0 & \theta_m N \delta_{hm} \rho & \theta_z N \delta_{zh} \rho \\
 \hline
 S_m & 0 & \theta_m N \delta_{hm} S_h & 0 & 0 \\
 \hline
 \theta_m \delta_m & N_h & & &
 \end{array} \text{ and }
 \end{aligned}$$

The basic reproduction number of co-infection model Malaria and Zika Virus is obtained by considering the dominant eigenvalue $R_{mz} = FV^{-1} = \{R_m, R_z\}$, where,

$$\begin{aligned}
 & = \left\{ 0, \pm \sqrt{\frac{\vartheta_m^2 \delta_m^2 \Pi_m \mu_h}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m^2}}, \pm \sqrt{\frac{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h}{(\mu_h + \tau_z) \Pi_h \mu_m^2}} \right\} \\
 & R_{mz} = \left\{ \sqrt{\frac{\vartheta_m^2 \delta_m^2 \Pi_m \mu_h}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m^2}}, \sqrt{\frac{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h}{(\mu_h + \tau_z) \Pi_h \mu_m^2}} \right\},
 \end{aligned}$$

$$R_m = \left\{ \sqrt{\frac{\vartheta_m^2 \delta_m^2 \Pi_m \mu_h}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m^2}} \right\} \quad \text{and} \quad R_z = \left\{ \sqrt{\frac{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h}{(\mu_h + \tau_z) \Pi_h \mu_m^2}} \right\}.$$

R_m is the average number of secondary malaria infections in human or female anopheles mosquito population caused by a single infective human or mosquito introduced into a wholly susceptible population. In the same way, R_z is the average number of secondary Zika virus infections in human or mosquito population caused by a single infective human or female aedes aegypti mosquito introduced into a wholly susceptible population.

3.4.4 Local Stability of Disease Free Equilibrium Point for Co-Infection

Malaria-Zika Model

To determine the local stability of the disease free equilibrium of the co-infection Malaria-Zika model of System (3.31), the following theorem is considered.

Theorem 8

The disease free equilibrium point is locally asymptotically stable if $R_0 < 1$, that is $R_m < 1$ and $R_z < 1$, and unstable otherwise.

The prove of Theorem 8 is done by linearising System (3.31) around the disease free equilibrium to obtain the Jacobian matrix J_{mz} .

$$\begin{array}{cccccccc|cc} \text{[?]} & & & & & & & & \text{[?]} & & \\ -\mu_h & 0 & 0 & 0 & \psi & 0 & 0 & -\theta_m \delta_m & -\theta_z \delta_z & 0 & -Q_1 \\ \text{[?]} & & & & & & & & & \text{[?]} & \\ & & & 0 & \tau_z & 0 & 0 & \theta_m \delta_m & 0 & \text{[?]} & \\ & & & & & & & & & \text{[?]} & \\ \text{[?]} & & & & & & & & & \text{[?]} & \\ \text{[?]} & 0 & 0 & -Q_2 & \tau_m & 0 & 0 & 0 & \theta_z \delta_z & \text{[?]} & \\ \text{[?]} & & & & & & & & & \text{[?]} & \\ \text{[?]} & & & & & & & & & \text{[?]} & \\ \text{[?]} & 0 & 0 & 0 & -Q_3 & 0 & 0 & 0 & 0 & \text{[?]} & \\ \text{[?]} & & & & & & & & & \text{[?]} & \\ \text{[?]} & & & & & & & & & \text{[?]} & \end{array}$$

$$J_{mz} = \begin{bmatrix} \tau_m & 0 & 0 & -Q_6 & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau_z & 0 & 0 & -\mu_h & 0 & 0 \\ -Q_7 - Q_8 - Q_9 & 0 & 0 & -\mu_m & 0 & 0 & 0 & 0 \\ 0 & Q_7 & 0 & Q_7 & 0 & 0 & 0 & \mu_m \\ 0 & 0 & Q_8 & Q_8 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_m \end{bmatrix}$$

where,

$$Q_1 = (\mu_h + \eta + \tau_m), Q_2 = (\mu_h + \tau_z), Q_3 = (\mu_h + \tau_m + \tau_z), Q_6 = (\mu_h + \psi), \\ Q_7 = \frac{\vartheta_m \delta_m \Pi_m \mu_h}{\Pi_h \mu_m}, Q_8 = \frac{\vartheta_z \delta_z \Pi_m \mu_m}{\Pi_h \mu_m}, Q_9 = \frac{(\theta_m \delta_m + \theta_z \delta_z) \Pi_m \mu_h}{\Pi_h \mu_m}$$

The DFE is locally stable if all eigenvalues of Jacobian J_{mz} are negative. The matrix has all eigenvalues negative only if the trace of $J_{mz} < 0$ and determinant of $J_{mz} > 0$. It is observed that the diagonal entries of J_{mz} are all negative, therefore, using the properties of matrix algebra J_{mz} can be reduced to obtain:

$$J_{mz}^* = \begin{bmatrix} -Q_1 & 0 & \tau_z & \theta_m \delta_m & 0 \\ 0 & -Q_2 & \tau_m & 0 & \vartheta_z \delta_z \\ 0 & 0 & -Q_3 & 0 & 0 \\ Q_7 & 0 & Q_7 - \mu_m & 0 & 0 \\ 0 & Q_8 & Q_8 & 0 & -\mu_m \end{bmatrix}$$

Applying the method in Abdulrahman & Abdulrahman (2013), we get:

$$J_{mz*0} = \begin{vmatrix} -Q_1 & 0 & \tau_z & \theta_m \delta_m & 0 \\ 0 & -Q_2 & \tau_m & 0 & 0 \\ 0 & \theta_z \delta_z & 0 & 0 & 0 \\ 0 & 0 & 0 & (Q_3 Q_7 \theta_m \delta_m - Q_3 Q_1 \mu_m) & 0 \\ 0 & 0 & 0 & 0 & (Q_3 Q_8 \theta_z \delta_z - Q_3 Q_2 \mu_m) \end{vmatrix}$$

The associated eigenvalues are derived as:

$$[-(Q_1 + \lambda_1)][-(Q_2 + \lambda_2)][-(Q_3 + \lambda_3)][(Q_3 Q_7 \theta_m \delta_m - Q_3 Q_1 \mu_m - \lambda_4)] \times$$

$$[(Q_3 Q_8 \theta_z \delta_z - Q_3 Q_2 \mu_m - \lambda_5)] = 0,$$

$$\Rightarrow \lambda_1 = -Q_1, \lambda_2 = -Q_2, \lambda_3 = -Q_3.$$

For λ_4 , the following manipulations are considered:

$$\begin{aligned} (Q_3 Q_7 \theta_m \delta_m - Q_3 Q_1 \mu_m - \lambda_4) &= 0, \\ \lambda_4 &= -Q_3 Q_1 \mu_m \left[1 - \frac{Q_3 Q_7 \theta_m \delta_m}{Q_3 Q_1 \mu_m} \right] \\ \lambda_4 &= -Q_3 Q_1 \mu_m [1 - R_m^2] \end{aligned}$$

Similarly for λ_5

$$\begin{aligned} (Q_3 Q_8 \theta_z \delta_z - Q_3 Q_2 \mu_m - \lambda_5) &= 0, \\ \lambda_5 &= -Q_3 Q_2 \mu_m \left[1 - \frac{Q_3 Q_8 \theta_z \delta_z}{Q_3 Q_2 \mu_m} \right] \\ \lambda_5 &= -Q_3 Q_2 \mu_m [1 - R_z^2] \end{aligned}$$

It can be seen that the disease free equilibrium point is locally asymptotically stable when $R_0 < 1$, that is $R_m < 1$ and $R_z < 1$.

3.4.5 Global Stability at the disease free equilibrium for coinfection model Malaria-Zika Virus

The proof of the global stability is done using the approach by (Castillo-Chavez & Song, 2004).

Theorem 9

The disease free equilibrium of System (3.31) is globally stable if $R_{mz} < 1$ and unstable if $R_{mz} > 1$.

We begin by dividing the System (3.31) into the uninfected class represented by A and infected class denoted by B. This is given as:

$$\begin{cases} \frac{dA}{dt} = \chi(A, B) \\ \frac{dB}{dt} = \Upsilon(A, B), \end{cases} \quad (3.32)$$

where we define the two valued functions as $\chi(A, B)$ (dimension 4) and $\Upsilon(A, B)$ (dimension 5) represented as:

$$\chi(A, B) = \begin{pmatrix} \Pi_h - \frac{\mu_h S_h}{N_h} - \frac{\theta_m \delta_m I_p S_h}{N_h} - \theta_z \delta_z I_a S_h + \psi R_m, \\ \Pi_m - \mu_m S_m - \theta_m \delta_m S_m (I_m + I_{mz}) - \theta_z \delta_z S_m N (I_h I_z + I_{mz}), \\ -(\mu_h + \psi) R_m, \\ \tau m I_m \\ \tau z I_z - \mu_h R_z \end{pmatrix} \quad (3.33)$$

$$\Upsilon(A, B) = \begin{pmatrix} \theta_m \delta_m N_m I_p S_h - \tau m I_m \theta_z \delta_z I_a I_m + \tau z I_m z, \\ -(\mu_h + \eta) I_m - \end{pmatrix}$$

$$\Upsilon(\mathbf{A}, \mathbf{B}) = \begin{pmatrix} \theta_z \delta_z l_a S_h - \tau_z l_z - \theta \frac{m \delta N m h l p l_z + \tau m l m z - \mu h l_z}{N_h} \\ \theta_z \delta_z S_m N(h l_z + l m z) - \mu m l a \\ \theta_m \delta_m (l N m + h l m z) S_m - \mu m l p, \\ \theta_z \delta_z S_m N(h l_z + l m z) - \mu m l a \end{pmatrix} \quad (3.34)_h$$

The proof of Theorem 9 will be complete if the following two conditions are satisfied:

$$\left\{ \begin{array}{l} 1. \chi(\mathbf{0}, \mathbf{B}) = 0 \\ 2. \Upsilon(\mathbf{A}, \mathbf{B}) = \mathbf{T}\mathbf{B} - \Upsilon^*(\mathbf{A}, \mathbf{B}), \Upsilon^*(\mathbf{A}, \mathbf{B}) \geq 0 \in \Omega. \end{array} \right. , \text{ is globally asymptotically stable} \quad (3.35)$$

The condition $\Gamma = D_T \Upsilon(\mathbf{A}, \mathbf{0})$ is an m-matrix (i.e off diagonal elements of Γ are nonnegative) and Ω is region where the System becomes biologically meaningful. Thus,

$$\Gamma = D_T \Upsilon(\mathbf{A}, \mathbf{0}) = \begin{pmatrix} -(\mu_h + \eta + \tau_m + \frac{\theta_z \delta_z l_a}{N_h}) & 0 & \tau_z & \theta_m \delta_m & \frac{\theta_z \delta_z l_a}{N_h} \\ 0 & -(\frac{\theta_z l_a}{N_h} + \mu_h + \tau_z) & \tau_m & -\frac{\theta_m \delta_m l_a}{N_h} & \theta_z \delta_z \\ \frac{\theta_z \delta_z l_a}{N_h} & \frac{\theta_m \delta_m l_a}{N_h} & -(\mu_h + \tau_m + \tau_z) & \frac{\theta_m \delta_m l_a}{N_h} & \frac{\theta_z \delta_z l_a}{N_h} \\ 0 & \frac{\theta_z \delta_z S_m}{N_h} & \frac{\theta_m \delta_m S_m}{N_h} & -\mu & 0 \\ \theta_m N \delta_m S_m & 0 & h & m & -\mu_m \end{pmatrix}$$

$$= \begin{pmatrix} -(\mu_h + \eta + \tau_z) & 0 & \tau_z & \theta_m \delta_m & \theta_z \delta_z \\ 0 & -(\mu_h + \tau_m) & \tau_m & 0 & 0 \\ 0 & -(\mu_h + \tau_m + \tau_z) & 0 & 0 & 0 \\ 0 & 0 & 0 & -\mu & 0 \\ 0 & 0 & 0 & 0 & -\mu_m \end{pmatrix}$$

$$0 \quad \theta_z N \delta_{zh} S_m \quad \theta_z N \delta_{zh} S_m \quad 0 \quad -\mu_m$$

This implies that:

$$\hat{\Upsilon}(\mathbf{A}, \mathbf{B}) = \begin{pmatrix} \hat{\Upsilon}_3(\mathbf{A}, \mathbf{B}) \\ \hat{\Upsilon}_4(\mathbf{A}, \mathbf{B}) \\ \hat{\Upsilon}_5(\mathbf{A}, \mathbf{B}) \end{pmatrix} = \begin{pmatrix} -(\alpha_m I_z + \alpha_z I_m) \\ \frac{\vartheta_m \delta_m (I_m + I_{mz})}{N_h} \left(1 - \frac{S_m}{N_h}\right) \\ \frac{\vartheta_z \delta_z (I_z + I_{mz})}{N_h} \left(1 - \frac{S_m}{N_h}\right) \end{pmatrix} \begin{pmatrix} \vartheta_m \delta_m I_p \left(1 - \frac{S_h}{N_h}\right) + \alpha_z I_m \\ \alpha \\ \alpha \end{pmatrix} \left(1 - \frac{S_h}{N_h}\right) + \alpha$$

Since $\hat{\Upsilon}_3(\mathbf{A}, \mathbf{B}) < 0$ and does not completely satisfy the two conditions in Equation (3.35), the disease free equilibrium may not be globally asymptotically stable.

3.4.6 Existence of endemic equilibrium point of co-infection Malaria and Zika virus

Endemic equilibrium point is the steady state solution where the disease (malaria and Zika virus) exists in the population. The endemic equilibrium point of the co-infection model is denoted by E_{mz}^* and is given by:

$$E_{mz}^* = (S_h^*, I_m^*, I_z^*, I_{mz}^*, R_m^*, R_z^*, S_m^*, I_p^*, I_a^*).$$

3.4.7 Global Stability of Endemic Equilibrium of Co-infection Malaria-Zika model

The prove of the global stability of the endemic equilibrium point is done using the following theorem;

Theorem 10

If $R_{mz} > 1$, then the unique endemic equilibrium E_{mz}^* of System (3.31) is globally stable in the interior of Ω .

The global stability of the endemic equilibrium can be determined by constructing a quadratic Lyapunov function $V(t)$ of the form:

$$V(S_h, I_m, I_z, I_{mz}, R_m, R_z, S_m, I_p, I_a) = \frac{1}{2} \left((S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_{mz} - I_{mz}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**}) \right)^2 + \frac{1}{2} \left((S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**}) \right)^2 \quad (S_m$$

Taking the time derivative gives:

$$\begin{aligned} \frac{\partial V}{\partial t} &= \left[(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_{mz} - I_{mz}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**}) \right] \\ &\quad \times \frac{d}{dt} [S_h + I_m + I_z + I_{mz} + R_m + R_z] + \left[(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**}) \right] \\ &\quad \times \frac{d}{dt} [S_m + I_p + I_a]. \quad dt \\ \frac{\partial V}{\partial t} &= \left[\mu_h [(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_{mz} - I_{mz}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**})] - \eta [(I_m - I_m^{**}) + (I_{mz} - I_{mz}^{**})] \right] \\ &\quad - [(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**})] \\ &\quad \times \mu_m [(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_a - I_a^{**})] \end{aligned}$$

Let

$$\begin{aligned} W_1 &= S_h - S_h^{**}, W_2 = I_m - I_m^{**}, W_3 = I_z - I_z^{**}, W_4 = I_{mz} - I_{mz}^{**}, W_5 = R_m - R_m^{**}, \\ W_6 &= R_z - R_z^{**}, W_7 = S_m - S_m^{**}, W_8 = I_p - I_p^{**}, W_9 = I_a - I_a^{**}, \end{aligned}$$

$$W_{10} = W_1 + W_2 + W_3 + W_4 + W_5 + W_6, W_{11} = W_2 + W_4, W_{12} =$$

$$W_7 + W_8 + W_9.$$

Thus, we obtain:

$$\frac{\partial V}{\partial t} = -[W_{10}^2 + \eta W_{10} W_{11} + \mu_m W_{12}^2].$$

It can be seen that $\frac{\partial V}{\partial t} \leq 0$ if $S_h \leq S^{**}, I_m \leq I_m^{**}, I_z \leq I_z^{**}, R_m \leq R_m^{**}, R_z \leq R_z^{**}, S_m \leq S_m^{**}, I_p \leq I_p^{**}, I_a \leq I_a^{**}$. Also, $\frac{\partial V}{\partial t} = 0$ if and only if $S_h = S_h^{**}, I_m = I_m^{**}, I_z = I_z^{**}, I_{mz} = I_{mz}^{**}, R_m = R_m^{**}, R_z = R_z^{**}, S_m = S_m^{**}, I_p = I_p^{**}, I_a = I_a^{**}$. Therefore, the endemic equilibrium of the co-infection Malaria-Zika sub-model is globally asymptotically stable.

3.4.8 Existence of Backward Bifurcation for Malaria-Zika virus sub-model

To the existence of a backward bifurcation phenomenon, System (3.31) can be rewritten as follows;

$$x_1 = S_h, x_2 = I_m, x_3 = I_z, x_4 = I_{mz}, x_5 = R_m, x_6 = R_z, x_7 = S_m, x_8 = I_p, x_9 = I_a.$$

It can further be expressed in a vector form as:

$$\frac{dx_i}{dt} = F(x_i),$$

where $x_i = (x_1, x_2, x_3, \dots, x_9)^T$ and $F = (f_1, f_2, f_3, f_4, \dots, f_9)^T$. Thus,

f

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1 = \Pi_h - \mu_h x_1 - \theta_m N \delta_{hm} x_8 x_1 - \theta_z N \delta_{hz} x_9 x_1 + \psi x_5, \\
\frac{dx_2}{dt} &= f_2 = \theta_m N \delta_{hm} x_8 x_1 - (\mu_h + \eta + \tau_m) x_2 - \theta_z N \delta_{hz} x_9 x_2 + \tau_z x_4, \\
\frac{dx_3}{dt} &= f_3 = \theta_z N \delta_{hz} x_9 x_1 - \tau_z x_3 - \theta_m N \delta_{hm} x_8 x_3 + \tau_m x_4 - \mu_h x_3, \\
\frac{dx_4}{dt} &= f_4 = \theta_m N \delta_{hm} x_8 x_3 - \tau_m x_4 + \theta_z N \delta_{hz} x_9 x_2 - (\mu_h + \eta + \tau_z) x_4 + \theta_m N \delta_{hm} x_8 x_3 - \tau_m x_4, \\
\frac{dx_5}{dt} &= f_5 = \tau_m x_2 - (\mu_h + \psi) x_5, \\
\frac{dx_6}{dt} &= f_6 = \tau_z x_3 - \mu_h x_6, \\
\frac{dx_7}{dt} &= f_7 = \Pi_m - dt \mu_m x_7 - \theta_m \delta_m N (x_{h2} + x_4) x_7 - \theta_z \delta_z (N x_{3h} + x_4) x_7, \\
\frac{dx_8}{dt} &= f_8 = \theta_m \delta_m N (x_{h2} + x_4) x_7 - \mu_m x_8, \\
\frac{dx_9}{dt} &= f_9 = \theta_z \delta_z (N x_{3h} + x_4) x_7 - \mu_m x_9.
\end{aligned} \tag{3.36}$$

The Jacobian matrix at the disease free equilibrium state is given as:

$$J_{E_0} = \begin{bmatrix}
0 & -(\mu_h + \eta + \tau_m) & 0 & \tau_z & 0 & 0 & 0 & -\vartheta_m \delta_m & -\vartheta_z \delta_z \\
0 & 0 & -(\mu_h + \tau_z) & \tau_m & 0 & 0 & 0 & \vartheta_m \delta_m & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \vartheta_z \delta_z \\
0 & \tau_m & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & \tau_z & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & -\frac{\theta_m \delta_m \Pi_m \mu_h}{\Pi_h \mu_m} & -\frac{\theta_z \delta_z \Pi_m \mu_h}{\Pi_h \mu_m} & 0 & 0 & 0 & 0 & \mu_m & 0 \\
0 & \frac{\theta_m \delta_m \Pi_m \mu_h}{\Pi_h \mu_m} & 0 & 0 & 0 & 0 & 0 & \mu_m & 0 \\
0 & -\mu_h & 0 & 0 & 0 & 0 & \psi & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_m
\end{bmatrix}$$

$$\begin{array}{ccccccc}
0 & -(\mu_h + \psi) & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & -\mu_h & & & & \\
-(\theta_m \delta_m'' + \theta_z \delta_z'') \Pi_m \mu_h & 0 & & & 0 & 0 & 0 \\
\Pi_h \mu_m & \theta_m \delta_m \Pi_m \mu & & & & & \\
h & 0 & 0 & 0 & & & \\
\Pi_h \mu_m & & & & & & \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\Pi_h \mu_m & & & & & & \\
\Pi_h \mu_m & & & & & &
\end{array}$$

To analyze the dynamics of Equation (3.36), we compute the eigenvectors of the Jacobian matrix J_{E_0} at the disease free equilibrium. We first of all consider the right and left eigenvectors represented by $W = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8, w_9)^T$ and $V = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8, v_9)^T$. Solving for the right eigenvector associated with the eigenvalue of the Jacobian J_{E_0} is given as;

$$\begin{aligned}
w_1 &= \frac{\psi w_5 - \theta_m \delta_m w_8 - \theta_z \delta_z w_9}{\mu_h}, & w_2 &= \frac{\theta_m \delta_m w_8}{(\mu_h + \eta + \tau_m)}, & w_3 &= \frac{\theta_z \delta_z w_9}{(\mu_h + \tau_z)}, \\
w_4 &= 0, & w_5 &= \frac{\tau_m w_2}{\mu_h}, & w_6 &= \frac{\tau_z w_3}{\mu_h}, & w_7 &= \frac{(\vartheta_m \delta_m w_2 + \vartheta_z \delta_z w_3) \Pi_m \mu_h}{2}, \\
w_8 &= \frac{\theta_m \delta_m \Pi_m \mu}{(\mu_h + \psi)}, & w_9 &= \frac{\theta_z \delta_z \Pi_m \mu}{\mu_h}, \\
w_8 &= \frac{\theta_m \delta_m \Pi_m \mu}{\Pi_h \mu_m}, & w_9 &= \theta \frac{z \delta_z \Pi_h \mu_m}{\Pi_h \mu_m}.
\end{aligned}$$

The solution for the associated left eigenvectors are as follows;

$$\begin{aligned}
v_2 &= \frac{\theta_m \delta_m \Pi_m \mu_h v_8}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m}, & v_3 &= \frac{\theta_z \delta_z \Pi_m \mu_h (v_9 - v_7)}{(\mu_h + \tau_z) \Pi_h \mu_m}, & v_1 &= 0, \\
v_4 &= \frac{(\tau_z v_2 + \tau_m v_m) \Pi_h \mu_m + (\theta_m \delta_m v_8 + \theta_z \delta_z v_9) \Pi_m \mu_h}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m}, & v_5 &= 0, & v_6 &= 0, v_7 = 0, \\
v_8 &= \frac{\theta_m \delta_m v}{\mu_m}, & v_9 &= \theta \frac{z \delta_z v_3}{\mu_m}.
\end{aligned}$$

Since we are dealing with a co-infection state, we consider the case when $R_{mz} =$

1 (assuming that $R_{ma} > R_{zv}$) and also consider the bifurcation parameter $\omega = \theta_m^2$.

Solving for ω from $R_m = R_z = 1$ gives:

$$\omega = \frac{(\mu_h + \eta + \tau_m)\Pi_h\mu_m^2}{\delta_m^2\Pi_m\mu_h}.$$

Computation of a and b

Here, the second partial derivative of all the state variables are computed to help obtain the value for both a and b. It follows that the value of a is given as:

$$\begin{aligned} \frac{\partial^2 f_1}{\partial x_1 \partial x_8} &= \frac{\partial^2 f_1}{\partial x_8 \partial x_1} = -\theta_m \delta_m, & \frac{\partial^2 f_1}{\partial x_1 \partial x_9} &= \frac{\partial^2 f_1}{\partial x_9 \partial x_1} = -\theta_z \delta_z, \\ \frac{\partial^2 f_2}{\partial x_1 \partial x_8} &= \frac{\partial^2 f_2}{\partial x_8 \partial x_1} = \theta_m \delta_m, & \frac{\partial^2 f_7}{\partial x_4 \partial x_7} &= \frac{\partial^2 f_7}{\partial x_7 \partial x_4} = -\theta_m \delta_m, \\ \frac{\partial^2 f_2}{\partial x_1 \partial x_8} &= \frac{\partial^2 f_2}{\partial x_8 \partial x_1} = -\theta_z \delta_z, & \frac{\partial^2 f_7}{\partial x_2 \partial x_7} &= \frac{\partial^2 f_7}{\partial x_7 \partial x_2} = -\theta_m \delta_m, \end{aligned}$$

$$\frac{\partial^2 f_7}{\partial x_4 \partial x_7} = \frac{\partial^2 f_7}{\partial x_7 \partial x_4} = -\theta_z \delta_z, \quad \frac{\partial^2 f_4}{\partial x_3 \partial x_8} = \frac{\partial^2 f_4}{\partial x_8 \partial x_3} = -\theta_m \delta_m$$

$$\frac{\partial^2 f_9}{\partial x_3 \partial x_7} = \frac{\partial^2 f_9}{\partial x_7 \partial x_3} = \theta_z \delta_z, \quad \frac{\partial^2 f_3}{\partial x_3 \partial x_8} = \frac{\partial^2 f_3}{\partial x_8 \partial x_3} = -\theta_m \delta_m, \quad \frac{\partial^2 f_1}{\partial x_4 \partial x_7} = \frac{\partial^2 f_1}{\partial x_7 \partial x_4} = \theta_z \delta_z$$

$$\frac{\partial^2 f_3}{\partial x_1 \partial x_9} = \frac{\partial^2 f_3}{\partial x_9 \partial x_1} = \theta_z \delta_z, \quad \frac{\partial^2 f_1}{\partial x_1 \partial x_8} = \frac{\partial^2 f_1}{\partial x_8 \partial x_1} = \theta_z \delta_z$$

$$\frac{\partial^2 f_7}{\partial x_1 \partial x_8} = \frac{\partial^2 f_7}{\partial x_8 \partial x_1} = \theta_z \delta_z, \quad \frac{\partial^2 f_9}{\partial x_1 \partial x_9} = \frac{\partial^2 f_9}{\partial x_9 \partial x_1} = \theta_z \delta_z$$

Thus, the expression for a is given as:

$$a = v_1 w_1 w_8 \left[\frac{\partial^2 f_1}{\partial x_1 \partial x_8} \right] + v_1 w_1 w_9 \left[\frac{\partial^2 f_1}{\partial x_1 \partial x_9} \right] + v_2 w_1 w_8 \left[\frac{\partial^2 f_2}{\partial x_1 \partial x_8} \right] + v_7 w_4 w_7 \left[\frac{\partial^2 f_7}{\partial x_4 \partial x_7} \right]$$

$$+ v_2 w_2 w_9 \left[\frac{\partial^2 f_2}{\partial x_2 \partial x_9} \right] + v_7 w_7 w_2 \left[\frac{\partial^2 f_7}{\partial x_7 \partial x_2} \right] + v_4 w_3 w_8 \left[\frac{\partial^2 f_4}{\partial x_3 \partial x_8} \right]$$

$$+ v_9 w_3 w_7 \left[\frac{\partial^2 f_9}{\partial x_3 \partial x_7} \right] + v_3 w_3 w_8 \left[\frac{\partial^2 f_3}{\partial x_3 \partial x_8} \right] + v_7 w_3 w_7 \left[\frac{\partial^2 f_7}{\partial x_3 \partial x_7} \right] + v_9 w_4 w_7 \left[\frac{\partial^2 f_9}{\partial x_4 \partial x_7} \right]$$

$$+ v_3 w_1 w_9 \left[\frac{\partial^2 f_3}{\partial x_1 \partial x_9} \right] + v_9 w_3 w_7 \left[\frac{\partial^2 f_9}{\partial x_3 \partial x_7} \right] + v_8 w_2 w_7 \left[\frac{\partial^2 f_8}{\partial x_2 \partial x_7} \right] > 0$$

From the left eigenvectors of the co-infection Malaria-Zika virus model, it follows that $v_1 = v_5 = v_6 = v_7 = 0$. Hence we do not consider the equations associated with f_1, f_5, f_6 and f_7 . Therefore, the value of b is obtained as follows;

$$\frac{\partial^2 f_2}{\partial x_8 \partial \theta_m} + \frac{\partial^2 f_3}{\partial x_8 \partial \theta_m} + \frac{\partial^2 f_4}{\partial x_8 \partial \theta_m} + \frac{\partial^2 f_8}{\partial x_7 \partial \theta_m} = \delta_m x_1 - \delta_m x_3 + \delta_m x_3 + \delta_m [x_2 + x_4],$$

$$= [\delta_m [x_1 + x_2 + x_4]] > 0.$$

Since $a > 0$ and $b > 0$, it shows that when $\omega < 0$ with $|\omega| \ll 1$, 0 is locally asymptotically stable and there exists a positive unstable equilibrium. Bifurcation

Diagram Co-infected Malaria-Zika virus sub-model

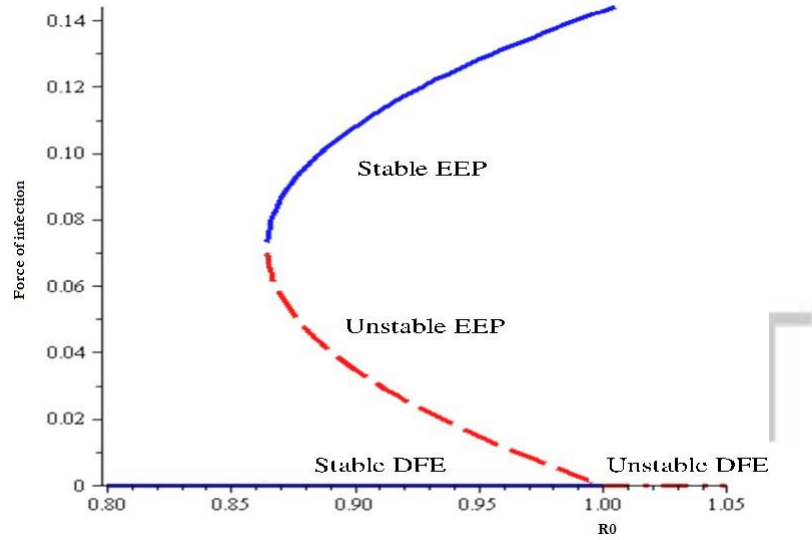


Figure 7: Description of the backward bifurcation of System (3.31).

The implication of the occurrence of backward bifurcation in this model is that, for the disease to be eradicated, it is no longer enough that the basic reproduction number R_0 should be less than one. In fact, to achieve eradication, additional efforts such as control measures and cost are required to bring R_0 below a critical value when $R_0 < 1$.

3.4.9 Malaria-Elephantiasis co-infection sub-model

In this subsection, we consider the Malaria-Elephantiasis sub-model given as:

$$\begin{aligned}
 \frac{dS_h}{dt} &= \alpha \Pi_m S_h - \psi R_m I_m - \phi R(\mu_{fh} + \alpha \eta_m) S I_{hm} - \mu \alpha_{hf} S I_{hm} + \alpha \tau_{ff} S I_{mfh}, \\
 \frac{dI_f}{dt} &= \alpha_f S_h - \mu_h I_f - \alpha m I_f - \tau_f I_f + \tau m I_{mf} dt \\
 \frac{dI_{mf}}{dt} &= \alpha_f I_m - (\mu_h + \eta + \tau_m + \tau_f) I_{mf} + \alpha m I_f, \\
 \frac{dR_f}{dt} &= \tau m I_m - (\mu_h + \psi) R_m,
 \end{aligned} \tag{3.37}$$

$$= \tau_f I_f - (\mu_h + \phi) R_f,$$

$\frac{d}{dt}$

$$dS_m$$

$$\frac{d}{dt} \Pi_m - \mu_m S_m - \lambda_p S_m - \lambda_w S_m =$$

$$\left\{ \begin{array}{l} dI_p \\ = \lambda_p S_m - \mu_m I_p, \end{array} \right.$$

$$\frac{d}{dt} \lambda_w m \mu_m w \frac{d}{dt} I_w = S - I,$$

where,

$$\lambda_p = \frac{\theta_m \delta m I_p}{N_h}, \lambda_w = \frac{\theta_f \delta f I_w}{N_h}, \alpha_m = \frac{\theta_m \delta m (I_m + I_{mf})}{N_h}, \alpha_f = \frac{\theta_f \delta f (I_f + I_{mf})}{N_h}$$

The disease-free equilibrium point for System (3.37) is obtained as

$$E_{mf} = \left(\frac{\Pi_h}{\mu_h}, 0, 0, 0, 0, 0, \frac{\Pi_m}{\mu_m}, 0, 0 \right).$$

Basic Reproduction Number for Malaria-Elephantiasis sub-model (R_{mf})

As defined in the preliminaries, the respective F and V for System (3.37) can be obtained as follows;

$$F = \left(\frac{\theta_f \delta f I_w S_h}{N_h} - \frac{\theta_m \delta m I_p I_f}{N_h}, \frac{\theta_f \delta f I_w I_m}{N_h} + \frac{\theta_m \delta m I_p I_f}{N_h}, \frac{\theta_m \delta m (I_m + I_{mf} S_m)}{N_h}, \frac{\theta_f \delta f S_m (I_f + I_{mf})}{N_h} \right) \text{ and } V = \left((\mu_h + \tau_f) I_f - \tau, (\mu_h + \eta + \tau_m + \tau_f) I_{mf} \right). \quad (3.38)$$

$\frac{d}{dt}$

$\frac{d}{dt}$

$\frac{d}{dt}$

$$\mu_m I_p$$

$$\mu_m I_w$$

Using the next generation method, the dominant eigenvalue of Equation ((3.38) given as FV^{-1} is obtained as

$$FV^{-1} = \left\{ \sqrt{\frac{\vartheta_m^2 \delta_m^2 \Pi_m \mu_h}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m^2}} \right\}, \left\{ \sqrt{\frac{\vartheta_f^2 \delta_m^2 \Pi_m \mu_h}{(\mu_h + \tau_f) \Pi_h \mu_m^2}} \right\}.$$

Therefore, the basic reproduction number is given as

$$R_{mf} = \left\{ \sqrt{\frac{\vartheta_m^2 \delta_m^2 \Pi_m \mu_h}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m^2}} \right\}, \left\{ \sqrt{\frac{\vartheta_f^2 \delta_m^2 \Pi_m \mu_h}{(\mu_h + \tau_f) \Pi_h \mu_m^2}} \right\}.$$

Local Stability of Disease Free Equilibrium for Co-Infection Malaria and Elephantiasis Sub-Model

To determine the local stability of the disease free equilibrium of System (3.37), the following theorem is considered.

Theorem 11

The DFE point is locally asymptotically stable if $R_0 < 1$ that is $R_{mf} < 1$ and unstable otherwise.

The Jacobian matrix $J_{E_{mf}}$ of System (3.37) at the disease free equilibrium state is:

$$J_{E_{mf}} = \begin{pmatrix} -T_1 & 0 & 0 & 0 & T_2 & T_3 & 0 & -T_4 & -T_5 \\ 0 & -T_7 & 0 & T_8 & 0 & 0 & 0 & T_4 & 0 \\ 0 & 0 & 0 & -T_{11} & T_{12} & 0 & 0 & 0 & 0 \\ 0 & T_{10} & T_6 & -T_{14} & 0 & 0 & 0 & T_{13} & T_9 \\ 0 & 0 & 0 & 0 & J_{E_{mf}} T_{12} & 0 & 0 & -T_{15} & 0 \\ 0 & 0 & 0 & 0 & 0 & -T_{16} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -T_{20} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$\begin{pmatrix}
? & ? & ? & ? & ? & ? & ? & ? & ? & ? \\
? & 0 & T_{17} & 0 & 0 & 0 & 0 & 0 & -T_{23} & 0 \\
? & 0 & 0 & T_{18} & 0 & 0 & 0 & 0 & 0 & -T_{23}
\end{pmatrix} \quad (3.39)$$

where,

$$T_1 = \mu_h, T_2 = \psi, T_3 = \varphi, T_4 = \theta_m \delta_m, T_5 = \theta_f \delta_f, T_7 = (\mu_h + \eta + \tau_m), T_8 = \tau_z$$

$$T_{11} = (\mu_h + \tau_f), T_{12} = \tau_m, T_{14} = (\mu_h + \eta + \tau_m + \tau_f), T_{15} = (\mu_h + \psi), T_{23} = \mu_m, T_{16} = (\mu_h + \varphi), T_{17}$$

$$= \theta_m \delta_m, T_{18} = \theta_f \delta_f, T_{19} = (\theta_m \delta_m + \theta_f \delta_f), T_{20} = \mu_m.$$

By applying matrix algebra it can be seen that all the trace of Equation (3.39) are all negative, thus the disease free equilibrium is locally asymptotically stable for $R_{mf} < 1$.

Global Stability of the DFE Co-Infection Malaria-Elephantiasis Sub-model

In this subsection, we prove the global stability of the disease free equilibrium for the co-infection Malaria-Elephantiasis sub-model by applying the following theorem

Theorem 12

The disease free equilibrium of System (3.37) is globally stable if $R_{mf} < 1$ and unstable otherwise.

The prove of the theorem is made possible by applying the idea in Theorem 1 with its putative explanation and approach applied in Theorem 5. By so doing we derived the following:

$$\begin{aligned}
U^*_1(A,B) &= \left(\vartheta_m \delta_m I_p \left(1 - \frac{S_h}{N_h} \right) + \alpha_f I_m \right) \left(1 - \frac{S_h}{N_h} \right) + \alpha_f I_m \\
U^*_2(A,B) &= \left(\frac{\vartheta_f \delta_f (I_f + I_{mf})}{N_h} \left(1 - \frac{S_h}{N_h} \right) \right) \\
U^*_3(A,B) &= \left(\frac{\vartheta_m \delta_m (I_m + I_{mf})}{N_h} \left(1 - \frac{S_m}{N_h} \right) \right) \\
U^*_4(A,B) &= \left(\frac{\vartheta_m \delta_m (I_m + I_{mf})}{N_h} \left(1 - \frac{S_m}{N_h} \right) \right) \\
U^*_5(A,B) &= \left(\frac{\vartheta_m \delta_m (I_m + I_{mf})}{N_h} \left(1 - \frac{S_m}{N_h} \right) \right)
\end{aligned}$$

From Castillo-Chavez & Song (2004), it can be seen that $U^*_3(A,B) < 0$ does not satisfy the condition. Thus, the disease free equilibrium of System (3.37) may not be globally asymptotically stable.

Existence of Endemic Equilibrium Point for System (3.37)

Due to the complex nature of the Malaria-Elephantiasis sub-model it was difficult to obtain an implicit solution for the endemic states. Thus, we assume and denote the endemic equilibrium point of System (3.37) by:

$$Emf^* = (Sh^{**}, Im^{**}, I^{**f}, Imf^{**}, R^{**m}, R^{**f}, Sm^{**}, Ip^{**}, lw^{**})$$

Global Stability of Endemic Equilibrium for System (3.37)

The global stability of the endemic equilibrium point is proved by applying the following theorem.

Theorem 13

If $R_{mf} > 1$, then the unique endemic equilibrium E_{mf}^{**} of System (3.37) is globally stable in the interior Ω .

The global stability of the endemic equilibrium can be determined by constructing a quadratic Lyapunov function $L(t)$ of the form:

$$L(S_h, I_m, I_f, I_{mf}, R_m, R_f, S_m, I_p, I_w) = \frac{1}{2} [(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_f - I_f^{**}) + (I_{mf} - I_{mf}^{**}) + (R_m - R_m^{**}) + (R_f - R_f^{**})]^2 - \frac{1}{2} [(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_w - I_w^{**})]^2$$

Taking the time derivative yields:

$$\begin{aligned} \frac{dL}{dt} &= [(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_f - I_f^{**}) + (I_{mf} - I_{mf}^{**}) + (R_m - R_m^{**}) + (R_f - R_f^{**})] \times \\ &\quad \times [\mu_h [(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_f - I_f^{**}) + (I_{mf} - I_{mf}^{**}) + (R_m - R_m^{**}) + (R_f - R_f^{**})]] \\ &\quad + \eta (I_m - I_m^{**}) + \eta (I_{mf} - I_{mf}^{**}) + [(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_w - I_w^{**})] \times \\ &\quad [\mu_m [(S_m - S_m^{**}) + (I_p - I_p^{**}) + (I_w - I_w^{**})]] \end{aligned}$$

Let

$$\begin{aligned} E_1 &= S_h - S_h^{**}, E_2 = I_m - I_m^{**}, E_3 = I_f - I_f^{**}, E_4 = I_{mf} - I_{mf}^{**}, E_5 = R_m - R_m^{**}, \\ E_6 &= R_f - R_f^{**}, E_7 = S_m - S_m^{**}, E_8 = I_p - I_p^{**}, E_9 = I_w - I_w^{**}, \\ E_{10} &= E_1 + E_2 + E_3 + E_4 + E_5 + E_6, E_{11} = \\ E_{12} &= E_7 + E_8 + E_9. \end{aligned}$$

Making the substitution gives:

$$\frac{\partial L}{\partial t} = [\mu_h E_{10} + \eta E_{10} E_{10} + \mu_m E_{12}]$$

It can be seen that $\frac{\partial L}{\partial t} \leq 0$ if $S_h \leq S_{h**}$, $I_m \leq I_{m**}$, $I_f \leq I_{f**}$, $I_m \leq I_{mf**}$, $R_m \leq R_{m**}$,

$R_f \leq R_{f**}$, $S_m \leq S_{m**}$, $I_f \leq I_{f**}$, $I_w \leq I_{w**}$. Again, $\frac{\partial L}{\partial t} = 0$ if and only if $S_h = S_{h**}$, $I_m = I_{m**}$, $I_f = I_{f**}$, $I_m = I_{mf**}$, $R_m = R_{m**}$, $R_f = R_{f**}$, $S_m = S_{m**}$, $I_f = I_{f**}$, $I_w = I_{w**}$.

Therefore, the endemic equilibrium of System (3.37) is globally asymptotically stable with reference.

Existence of Backward Bifurcation for System (3.37)

System (3.37) can be rewritten in a dimensionless state variables of the MalariaElephantiasis Co-infection model as follows:

$$x_1 = S_h, x_2 = I_m, x_3 = I_f, x_4 = I_{mf}, x_5 = R_m, x_6 = R_f, x_7 = S_m, x_8 = I_p, x_9 = I_w.$$

Writing it in the vector form yields:

$$\frac{dx_i}{dt} = F(X_i),$$

where $X_i = (x_1, x_2, x_3, \dots, x_9)^T$ and $F = (f_1, f_2, f_3, \dots, f_9)^T$. It follows that

$$\begin{aligned} \frac{dx_1}{dt} &= f_1 = \Pi_h + \psi x_5 + \varphi x_6 - \frac{\theta_m \delta_m x_8 x_1}{N_h} - \mu_h x_1 - \frac{\theta_f \delta_f x_9 x_1}{N_h}, \\ \frac{dx_2}{dt} &= f_2 = \frac{\theta_m \delta_m x_8 x_1}{N_h} - (\mu_h + \eta + \tau_m) x_2 - \frac{\theta_f \delta_f x_9 x_2}{N_h} + \tau_f x_4, \\ \frac{dx_3}{dt} &= f_3 = \frac{\theta_f \delta_f x_9 x_1}{N_h} - (\mu_h + \tau_f) x_3 - \frac{\theta_m \delta_m x_8 x_3}{N_h} + \tau_m x_4, \\ \frac{dx_4}{dt} &= f_4 = \frac{\theta_f \delta_f x_9 x_2}{N_h} - \tau_f x_4 + \frac{\theta_m \delta_m x_8 x_3}{N_h} \end{aligned}$$

$$\begin{aligned}
\frac{dx_4}{dt} &= f_4 = \frac{\tau_m x_2 - (\mu_h + \eta + \tau_f + \tau_m) x_4 + \theta_f \delta_f (x_3 + x_4) x_7}{N_h}, \\
\frac{dx_5}{dt} &= f_5 = \tau_m x_2 - (\mu_h + \psi) x_5, \\
\frac{dx_6}{dt} &= f_6 = \tau_f x_3 - (\mu_h + \phi) x_6, \\
\frac{dx_7}{dt} &= f_7 = \frac{\Pi_m \mu_m x_7}{N_h} - \frac{\theta_m \delta_m (x_2 + x_4) x_7}{N_h} - \frac{\theta_f \delta_f (x_3 + x_4) x_7}{N_h}, \\
\frac{dx_8}{dt} &= f_8 = \frac{\theta_m \delta_m (x_2 + x_4) x_7}{N_h} - \mu_m x_8, \\
\frac{dx_9}{dt} &= f_9 = \frac{\theta_f \delta_f (x_3 + x_4) x_7}{N_h} - \mu_m x_9.
\end{aligned}$$

The Jacobian at the disease free equilibrium point is given in Equation (3.39).

The associated right and left eigenvectors of the Jacobian matrix is respectively represented by $W = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8, w_9)^T$ and $V = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8, v_9)^T$, where T is the transpose. Solving for the right eigenvector with its associated zero eigenvalue yields;

$$\begin{aligned}
\psi w_5 + \phi w_6 - \theta_m \delta_m w_8 - \theta_f \delta_f w_9 &= 0, \\
\frac{\delta_f w_9}{\mu_h} &= w_2, \quad \frac{\theta_m \delta_m w_8}{(\mu_h + \eta + \tau_m)} = w_3, \quad \frac{\theta_f \delta_f w_9}{(\mu_h + \tau_z)} = w_1, \\
w_4 &= 0, \quad w_5 = \frac{\tau_m w_2}{(\mu_h + \psi)}, \quad w_6 = \frac{\tau_f w_3}{(\mu_h + \phi)}, \quad w_7 = -\frac{\theta_m \delta_m w_2 + \Pi \theta_h \mu_f \delta_m \tau_f w_3}{\Pi_m \mu_h}, \\
\frac{\theta_m \delta_m \Pi_m \mu_h w_2}{\Pi_h \mu_m} &= w_8, \quad \frac{\theta_f \delta_f \Pi_m \mu_h w_3}{\Pi_h \mu_m} = w_9.
\end{aligned}$$

The left eigenvector is also derived as:

$$\begin{aligned}
v_1 &= 0, \quad v_2 = \frac{\theta_m \delta_m \Pi_m \mu_h v_8}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m}, \quad v_3 = \theta \frac{\delta_f}{(\mu_h + \tau_z) \Pi_h \mu_m} \\
&\quad \Pi_m \mu_h (v_9 - v_7),
\end{aligned}$$

$$v_4 = \frac{(\tau_f v_2 + \tau_m v_3) \Pi_h \mu_m + (\theta_m \delta_m v_8 + \theta_f \delta_f v_9) \Pi_m \mu_h}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m}, \quad v_5 = 0, \quad v_6 = 0, \quad v_7 = 0,$$

$$\begin{aligned} \theta_m \delta_m v_2 \quad \theta_f \delta_f v_3 \quad v_8 = \\ \frac{\theta_m \delta_m v_2}{\mu_m}, \quad v_9 = \\ \frac{\theta_f \delta_f v_3}{\mu_m} \end{aligned}$$

Considering the case when $R_{mf} = 1$ and assuming that $R_m > R_f$ with the bifurcation parameter chosen as $\omega = \theta_m^2$ we solve for ω to obtain:

$$\omega = \frac{(\mu_h + \eta + \tau_m) \Pi_h \mu_m^2}{\delta_m^2 \Pi_m \mu_h}.$$

This is followed by the computation of a and b as described in (Castillo-Chavez & Song, 2004).

Computation of a and b: The associated non-zero partial derivatives at the DFE are given by:

$$\begin{aligned} \frac{\partial^2 f_1}{\partial x_1 \partial x_8} \quad \frac{\partial^2 f_1}{\partial x_8 \partial x_1} &= \frac{\partial^2 f_2}{\partial x_1 \partial x_8} = -\theta_m \delta_m, \quad \frac{\partial^2 f_2}{\partial x_8 \partial x_1} = \theta_m \delta_m, \\ \frac{\partial^2 f_1}{\partial x_1 \partial x_9} \quad \frac{\partial^2 f_1}{\partial x_9 \partial x_1} &= \frac{\partial^2 f_1}{\partial x_2 \partial x_9} = -\theta_f \delta_f, \quad \frac{\partial^2 f_1}{\partial x_9 \partial x_2} = -\theta_f \delta_f, \\ \frac{\partial^2 f_4}{\partial x_4 \partial x_8} \quad \frac{\partial^2 f_4}{\partial x_8 \partial x_4} &= \frac{\partial^2 f_7}{\partial x_4 \partial x_7} = -\theta_m \delta_m, \quad \frac{\partial^2 f_7}{\partial x_7 \partial x_4} = -\theta_f \delta_f, \\ \frac{\partial^2 f_7}{\partial x_2 \partial x_7} \quad \frac{\partial^2 f_7}{\partial x_7 \partial x_2} &= \frac{\partial^2 f_7}{\partial x_3 \partial x_7} = -\theta_m \delta_m, \quad \frac{\partial^2 f_7}{\partial x_7 \partial x_3} = -\theta_f \delta_f, \\ \frac{\partial^2 f_3}{\partial x_3 \partial x_8} \quad \frac{\partial^2 f_3}{\partial x_8 \partial x_3} &= \frac{\partial^2 f_8}{\partial x_2 \partial x_7} = \vartheta_m \delta_m, \quad \frac{\partial^2 f_3}{\partial x_1 \partial x_9} = \frac{\partial^2 f_3}{\partial x_9 \partial x_1} = \vartheta_f \delta_f, \\ &\quad \frac{\partial^2 f_9}{\partial x_2 \partial x_7} = \frac{\partial^2 f_9}{\partial x_7 \partial x_2} = \vartheta_m \delta_m, \quad \frac{\partial^2 f_9}{\partial x_1 \partial x_9} = \frac{\partial^2 f_9}{\partial x_9 \partial x_1} = \vartheta_f \delta_f \end{aligned}$$

$$\theta_m \delta_m \quad \frac{\partial x_3 \partial x_7}{\partial x_1 \partial x_8} \quad \frac{\partial x_7 \partial x_3}{\partial x_1 \partial x_9} \quad \theta_f \delta_f$$

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Thus, the expression for a is given as:

$$\begin{aligned} a = & v_1 w_1 w_8 \left[\frac{\partial^2 f_1}{\partial x_1 \partial x_8} \right] + v_2 w_1 w_8 \left[\frac{\partial^2 f_2}{\partial x_1 \partial x_8} \right] + v_1 w_1 w_9 \left[\frac{\partial^2 f_1}{\partial x_1 \partial x_9} \right] \\ & + v_2 w_2 w_9 \left[\frac{\partial^2 f_2}{\partial x_2 \partial x_9} \right] + v_4 w_4 w_8 \left[\frac{\partial^2 f_4}{\partial x_4 \partial x_8} \right] + v_7 w_4 w_7 \left[\frac{\partial^2 f_7}{\partial x_4 \partial x_7} \right] \\ & + v_7 w_2 w_7 \left[\frac{\partial^2 f_7}{\partial x_2 \partial x_7} \right] + v_7 w_7 w_4 \left[\frac{\partial^2 f_7}{\partial x_7 \partial x_4} \right] + v_7 w_3 w_7 \left[\frac{\partial^2 f_7}{\partial x_3 \partial x_7} \right] \\ & + v_7 w_4 w_7 \left[\frac{\partial^2 f_3}{\partial x_3 \partial x_8} \right] + v_9 w_4 w_7 \left[\frac{\partial^2 f_9}{\partial x_4 \partial x_7} \right] + v_8 w_3 w_7 \left[\frac{\partial^2 f_9}{\partial x_3 \partial x_7} \right] \\ & + v_8 w_2 w_7 \left[\frac{\partial^2 f_8}{\partial x_2 \partial x_7} \right] + v_3 w_1 w_9 \left[\frac{\partial^2 f_3}{\partial x_1 \partial x_9} \right] > 0 \end{aligned}$$

The value for b is also obtained as:

$$\begin{aligned} \frac{\partial^2 f_2}{\partial x_8 \partial \theta_m} + \frac{\partial^2 f_3}{\partial x_8 \partial \theta_m} + \frac{\partial^2 f_4}{\partial x_8 \partial \theta_m} + \frac{\partial^2 f_8}{\partial x_7 \partial \theta_m} &= \delta_m x_1 - \delta_m x_3 + \delta_m x_3 + \delta_m x_2, \\ &= [\delta_m (x_1 + x_2)] > 0. \end{aligned}$$

Since $a > 0$ and $b > 0$, it implies that there exist a positive unstable equilibrium which is locally stable.

Bifurcation Diagram for System (3.37)

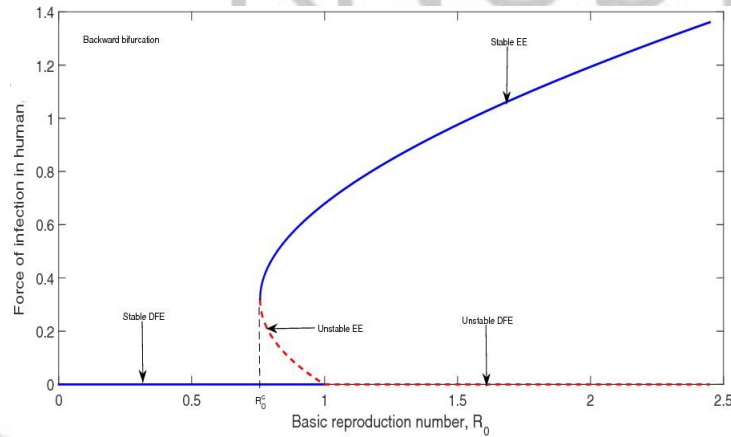


Figure 8: Description of the backward bifurcation of System (3.37).

The implication for occurrence of backward bifurcation for System (3.37) shows that the basic reproduction number is not sufficient to help eradicate the coinfection disease. Hence, eradication would be achieved if additional efforts such as control measures are applied.

3.4.10 Co-Infection Zika-Elephantiasis Sub-Model

Finally, for the Zika virus-Elephantiasis co-infection sub-model, we obtain the following differential equations;

$$\frac{dS_h}{dt} = \lambda - \beta I_h S_h - \mu S_h$$

$$\frac{d\Pi_h}{dt} = \Pi_h - \mu_h S_h - \alpha^2 S_h - \alpha^f S_h + \phi R_f, \quad \frac{dI_z}{dt}$$

$$= \alpha_z S_h - \tau_z I_z - \alpha_f I_z + \tau_f I_{zf} - \mu_h I_z,$$

$$\frac{dI_f}{dt}$$

$$= \alpha_f S_h - \mu_h I_f - \tau_f I_f + \tau_z I_{zf} - \alpha_z I_f,$$

$$\frac{dI_{zf}}{dt}$$

$$= \alpha_z I_f - \tau_f I_{zf} - \mu_h I_{zf} + \alpha_f I_z - \tau_z I_{zf},$$

$$\frac{dR_z}{dt}$$

$$= \tau_z I_z - \mu_h R_z, \quad (3.40) \quad \frac{dR_f}{dt}$$

$$= \tau_f I_f - (\mu_h + \phi) R_f,$$

$$\frac{dS_m}{dt}$$

$$\frac{dI_a}{dt} = \Pi_m - \mu_m S_m - \lambda_w S_m - \lambda_a S_m,$$

$$\frac{dI_w}{dt} = \lambda_a S_m - \mu_m I_a, \quad \frac{dI_w}{dt}$$

$$= \lambda_w S_m - \mu_m I_w, \quad dt$$

where,

$$\alpha_z = \frac{\theta_z \delta_z I_a}{N_h}, \quad \alpha_f = \frac{\theta_f \delta_f I_w}{N_h}, \quad \lambda_a = \frac{\theta_z \delta_z (I_z + I_{zf})}{N_h}, \quad \lambda_w = \frac{\theta_f \delta_f (I_f + I_{zf})}{N_h}$$

The disease free equilibrium point of System (3.40) is given as:

$$E_{zf} = \left(\frac{\Pi_h}{\mu_h}, 0, 0, 0, 0, 0, \frac{\Pi_m}{\mu_m}, 0, 0 \right).$$

Basic Reproduction Number for System (3.40)

The associated F and V matrices of System (3.40) is obtained as

$$F = \begin{bmatrix} \frac{\theta_f \delta_f I_w S_h}{N_h} - \frac{\theta_z \delta_z I_a I_f}{N_h} & -\tau_f I_{zf} & \frac{\theta_z \delta_z I_a S_h - \theta_f \delta_f I_w I_z}{(\mu_h + \tau_f) I_f - \tau} \\ \frac{\theta_z \delta_z I_a I_f}{N_h} + \frac{\theta_f \delta_f I_w I_z}{N_h} & 0 & 0 \\ \frac{\theta_z \delta_z (I_z + I_{zf}) S_m}{N_h} & I_{zf} & 0 \\ \frac{\theta_f \delta_f (I_f + I_{zf}) S_m}{N_h} & 0 & 0 \end{bmatrix}$$

$$\text{and } V = \begin{bmatrix} \mu_h & 0 & 0 \\ 0 & \mu_m & 0 \\ 0 & 0 & \mu_m \end{bmatrix}$$

Using the next generation matrix approach the basic reproduction number of System (3.40) is given as:

$$R_{zf} = \left\{ \sqrt{\frac{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h}{(\mu_h + \tau_z) \Pi_h \mu_m^2}}, \sqrt{\frac{\vartheta_m^2 \delta_f^2 \Pi_m \mu_h}{(\mu_h + \tau_f) \Pi_h \mu_m^2}} \right\}.$$

Local Stability of DFE Point for System (3.40)

To determine the local stability of the (DFE) point of System (3.40) the following theorem is considered.

Theorem 14

The DFE point of System (3.40) is locally asymptotically stable if $R_0 < 1$ that is

$R_{zf} < 1$ and unstable otherwise.

The Jacobian matrix $J_{E_{zf}}$ of System (3.40) is given by

$$J_{E_{zf}} = \begin{pmatrix} -Y_1 & 0 & 0 & 0 & 0 & Y_2 & 0 & -Y_3 & -Y_4 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & Y_3 & 0 & 0 \\ 0 & -Y_6 & 0 & Y_7 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -Y_{10} & Y_{11} & 0 & 0 & 0 & 0 & Y \\ 0 & 0 & Y_9 & Y_5 & -Y_{13} & 0 & 0 & 0 & Y_{12} & Y_8 \\ 0 & 0 & 0 & 0 & 0 & -Y_{14} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & Y_6 & 0 & 0 & -Y_{15} & 0 & 0 & 0 \end{pmatrix}$$

$$\begin{pmatrix}
0 & -Y_{16} - Y_{17} - Y_{18} & 0 & 0 & -Y_{19} & 0 & 0 \\
0 & Y_{16} & 0 & Y_{20} & 0 & 0 & 0 & -Y_{22} & 0 \\
0 & 0 & Y_{17} & Y_{23} & 0 & 0 & 0 & 0 & -Y_{22}
\end{pmatrix}
\quad (3.41)$$

where,

$$Y_1 = \mu_h, Y_2 = \phi, Y_3 = \theta_z \delta_z, Y_4 = \theta_f \delta_f, Y_6 = (\mu_h + \tau_z), Y_7 = \tau_f, Y_{10} = (\mu_h + \tau_f),$$

$$Y_{11} = \tau_z, Y_{13} = (\mu_h + \tau_z + \tau_f), Y_{14} = -\mu_h, Y_{15} = (\mu_h + \phi), Y_{16} = (\theta \frac{\delta_z \Pi_m \mu_h}{\Pi_h \mu_m}),$$

$$Y_{17} = (\theta \frac{f \delta_f \Pi_m \mu_h}{\Pi_h \mu_m}), Y_{18} = (\theta_z \delta_z \Pi_m \mu_h + \theta_f \delta_f \Pi_m \mu_h), Y_{19} = (\mu_m), Y_{20} = \theta_z \delta_z,$$

$$Y_{22} = (\mu_m), Y_{23} = \theta_f \delta_f.$$

Applying the concept of matrix algebra, a Jacobian matrix will be locally stable if its trace is negative. It can be seen that the Jacobian matrix $J_{E_{zf}}$ has all its trace being negative thus the disease free equilibrium is locally asymptotically stable for $R_{zf} < 1$.

Global Stability at the DFE for System (3.40)

The global stability of System (3.40) is shown using the method described in Castillo-Chavez & Song (2004) and explained and putatively analysed in Theorem 5. As a result we apply the following theorem;

Theorem 15

The DFE point of System (3.40) is globally stable if $R_{zf} < 1$ and unstable otherwise.

Applying the idea of Theorem 5, we have:

$$\begin{aligned} \hat{N}^*(A, B) &= \left| \hat{N}_3(A, B) \right| = \left| \begin{array}{c} \left(\hat{N}_1(A, B) \right) \left(\vartheta_z \delta_z I_a \left(1 - \frac{S_h}{N_h} \right) + \alpha_f I_z \right) \\ (A, B) \vartheta_z \delta_z I_a \left(1 - \frac{S_h}{N_h} \right) + \alpha_f I_z \\ 2 \\ -(\alpha_z I_f + \alpha_f I_z) \end{array} \right| \quad (3.42) \\ &= \left| \begin{array}{c} \left(\hat{N}_5(A, B) \right) \left(\frac{\vartheta_f \delta_f (I_f + I_{zf})}{N_h} \left(1 - \frac{S_m}{N_m} \right) \right) \\ 4(A, B) \left(\frac{\vartheta_z \delta_z (I_z + I_{zf})}{N_h} \left(1 - \frac{S_m}{N_m} \right) \right) \end{array} \right| \end{aligned}$$

The Castillo-Chavez & Song (2004) approach requires that $\hat{N}^*(A, B) > 0$, however, it can be seen from Equation (3.42) that $\hat{N}_3(A, B) < 0$ implying that $\hat{N}^*(A, B) < 0$. Therefore, System (3.40) does not completely satisfy the approach and thus the disease free equilibrium may not be globally asymptotically stable.

Existence of Endemic Equilibrium of System 3.40

The endemic equilibrium point is the steady state solution where the disease (Elephantiasis-Zika virus) exists in the population. We denote the endemic equilibrium point of System (3.40) by E_{zf} and due to the complexity nature to obtain an implicit solution we denote it by:

$$E_{zf**} = (S_h^{**}, I_f^{**}, I_z^{**}, I_{zf}^{**}, R_f^{**}, R_z^{**}, S_m^{**}, I_w^{**}, I_a^{**})$$

Global Stability of Endemic Equilibrium of System (3.40)

The endemic equilibrium point is solved using the following theorem.

Theorem 16

If $R_{zf} > 1$, then the unique endemic equilibrium E_{zf} of System (3.40) is globally stable in the interior of Ω .

The prove of the global stability of the endemic equilibrium is determined by constructing a quadratic Lyapunov function $V(t)$ of the form:

$$V(S_h, I_f, I_z, I_{zf}, R_f, R_z, S_m, I_w, I_a) = \frac{1}{2} [(S_h - S_h^{**}) + (I_f - I_f^{**}) + (I_z - I_z^{**}) + (I_{zf} - I_{zf}^{**}) + (R_f - R_f^{**}) + (R_z - R_z^{**})]^2 + \frac{1}{2} [(S_m - S_m^{**}) + (I_w - I_w^{**}) + (I_a - I_a^{**})]^2$$

Taking the time derivative of yields:

$$\begin{aligned} \frac{\partial V}{\partial t} &= [(S_h - S_h^{**}) + (I_f - I_f^{**}) + (I_z - I_z^{**}) + (I_{zf} - I_{zf}^{**}) + (R_f - R_f^{**}) + (R_z - R_z^{**})] \\ &\times \frac{d}{dt} [S_h + I_f + I_z + I_{zf} + R_f + R_z] + [(S_m - S_m^{**}) + (I_w - I_w^{**}) + (I_a - I_a^{**})] \\ &\times \frac{d}{dt} [S_m + I_w + I_a] \cdot dt \\ \frac{\partial V}{\partial t} &= [(S_h - S_h^{**}) + (I_f - I_f^{**}) + (I_z - I_z^{**}) + (I_{zf} - I_{zf}^{**}) + (R_f - R_f^{**}) + (R_z - R_z^{**})] \\ &\times [\mu_h [(S_h - S_h^{**}) + (I_f - I_f^{**}) + (I_z - I_z^{**}) + (I_{zf} - I_{zf}^{**}) + (R_f - R_f^{**}) + (R_z - R_z^{**})] \\ &+ \eta (I_f - I_f^{**})] - [(S_m - S_m^{**}) + (I_w - I_w^{**}) + (I_a - I_a^{**})] [\mu_m [(S_m - S_m^{**}) + (I_w - I_w^{**}) \\ &+ (I_a - I_a^{**})]] \end{aligned}$$

Let

$$\mathbb{Z}_1 = S_h - S_h^{**}, \mathbb{Z}_2 = I_f - I_f^{**}, \mathbb{Z}_3 = I_z - I_z^{**}, \mathbb{Z}_4 = I_{zf} - I_{zf}^{**}, \mathbb{Z}_5 = R_f - R_f^{**}$$

$$\mathbb{Z}_6 = R_z - R_z^{**}, \mathbb{Z}_7 = S_m - S_m^{**}, \mathbb{Z}_8 = I_w - I_w^{**}, \mathbb{Z}_9 = I_a - I_a^{**}$$

$$Z_{10} = Z_1 + Z_2 + Z_3 + Z_4 + Z_5 + Z_6, Z_{11} = Z_7 + Z_8 + Z_9.$$

We therefore obtain:

$$\frac{\partial V}{\partial t} = -[\mu_h Z_{10}^2 + \eta Z_2 Z_{10} + \mu_m Z_{11}^2] \quad (3.43)$$

We observe that $\frac{\partial L}{\partial t} \leq 0$ if

$$S_h \leq S^{**}, I_f \leq I_f^{**}, I_w \leq I_w^{**}, I_m \leq I_m^{**}, I_f \leq I_f^{**}, I_m \leq I_m^{**}, R_m \leq R_m^{**},$$

$R_f \leq R_f^{**}, S_m$. Again, 0 if and only if $S_h = S_h^{**}, I_m = I_m^{**}, I_f = I_f^{**}, I_m = I_m^{**}, R_m = R_m^{**}, R_f = R_f^{**}, S_m = S_m^{**}, I_f = I_f^{**}, I_w = I_w^{**}$. Hence, the endemic equilibrium of System (3.43) is globally asymptotically stable with reference.

Existence of Backward Bifurcation for System (3.40) We

rewrite System (3.40) such that:

$$\frac{dX_i}{dt} = F(X_i), dt$$

where $X_i = (x_1, x_2, x_3, \dots, x_9)^T$ and $F = (f_1, f_2, f_3, \dots, f_9)^T$. We assign $x_1 =$

$S_h, x_2 = I_z, x_3 = I_f, x_4 = I_{zf}, x_5 = R_z, x_6 = R_f, x_7 = S_m, x_8 = I_a, x_9 = I_w$. Thus, System (3.40) becomes:

$$\begin{aligned} \frac{dx_1}{dt} &= f_1 = \Pi_h - \mu_h x_1 - \frac{\theta_z \delta_z x_8 x_1}{N_h} - \frac{\theta_f \delta_f x_9 x_1}{N_h} \\ \frac{dx_2}{dt} &= f_2 = \frac{\theta_z \delta_z x_8 x_1}{N_h} - (\mu_h + \tau_z) x_2 - \frac{\theta_f \delta_f x_9 x_2}{N_h} + \tau_f x_4 \\ \frac{dx_3}{dt} &= f_3 = \frac{\theta_f \delta_f x_9 x_1}{N_h} - (\mu_h + \tau_f) x_3 + \tau_z x_4 \end{aligned}$$

$$\begin{aligned}
\frac{d}{dt} N_h &= N_h \frac{dx_4}{dt} - \theta_z \delta_z x_8 x_3 - \theta_f \delta_f x_9 x_2 \\
\frac{d}{dt} N_h &= f_4 = \frac{N_h dx_4}{dt} - (\mu_h + \tau_f + \tau_z) x_4 + \frac{\theta_f \delta_f (x_3 + x_4) x_7}{N_h} \\
\frac{d}{dt} N_h &= f_5 = \tau_z x_2 - \mu_h x_5 \\
\frac{d}{dt} N_h &= f_6 = \tau_f x_3 - (\mu_h + \phi) x_6 \\
\frac{d}{dt} N_h &= f_7 = \frac{\theta_f \delta_f (x_3 + x_4) x_7}{N_h} - \mu_m x_8 \\
\frac{d}{dt} N_h &= f_8 = \frac{\theta_z \delta_z (x_2 + x_4) x_7}{N_h} - \mu_m x_9 \\
\frac{d}{dt} N_h &= f_9 = \frac{\theta_f \delta_f (x_3 + x_4) x_7}{N_h} - \mu_m x_9
\end{aligned}$$

The Jacobian matrix $J_{E_{df}}$ given by Equation (3.41) is analyzed by computing its eigenvectors at the disease free equilibrium. The right and left eigenvectors are respectively denoted by $w = (w_1, w_2, w_3, w_5, w_6, w_7, w_8, w_9)^T$ and $v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8, v_9)^T$. Solving for the right eigenvector associated with its zero eigenvalue yields:

$$\begin{aligned}
w_1 &= \frac{\psi w_6 - \theta_z \delta_z w_8 - \theta_f \delta_f w_9}{\mu_h (\mu_h + \tau_z)}, \quad w_2 = \frac{\theta_z \delta_z w_8}{(\mu_h + \tau_z)}, \quad w_3 = \frac{\theta_f \delta_f w_9}{(\mu_h + \tau_z)}, \\
w_4 &= 0, \quad w_5 = \frac{\tau_z w_2 \tau_f w_3}{\mu_h (\mu_h + \tau_z)}, \quad w_6 = \frac{\tau_z w_2 \tau_f w_3}{\mu_h (\mu_h + \tau_z)}, \quad w_7 = \frac{\tau_z w_2 \tau_f w_3}{\mu_h (\mu_h + \tau_z)}, \\
w_8 &= \frac{\theta_z \delta_z \Pi_m \mu}{\Pi_h \mu_m}, \quad w_9 = \frac{\theta_f \delta_f \Pi_m \mu}{\Pi_h \mu_m}
\end{aligned}$$

For the left eigenvector we obtain:

$$\theta_z \delta_z \Pi_m \mu$$

$$v_1 = 0, \quad v_2 = \frac{h v_8}{(\mu_h + \tau_z) \Pi_h \mu_m}, \quad v_3 = \theta \frac{f \delta_f}{(\mu_h + \tau_f) \Pi_h \mu_m}$$

$$\Pi_m \mu_h (v_9 - v_7),$$

$$v_4 = \frac{(\tau_f v_2 + \tau_z v_3) \Pi_h \mu_m + (\theta_z \delta_z v_8 + \theta_f \delta_f v_9) \Pi_m \mu_h}{(\mu_h + \tau_f + \tau_z) \Pi_h \mu_m}, \quad v_5 = 0, \quad v_6 = 0,$$

$$v_7 = 0, \quad v_8 = \theta \frac{z \delta_z v_2}{\mu_m},$$

$$v_9 = \theta \frac{f \delta_f v_3}{\mu_m}.$$

Considering the case where $R_{zf} = 1$ and assuming that $R_z > R_f$, we choose $\sigma = \theta_z^2$ to be the bifurcation parameter. Solving for σ gives:

$$\sigma = \frac{(\mu_h + \eta + \tau_z) \Pi_h \mu_m^2}{\delta_2 \Pi_m \mu_h}.$$

Computing for a and b, the non-zero second partial derivatives of f associated with a is given by:

$$\frac{\partial^2 f}{\partial x_1 \partial x_8} = \theta_z \delta_z, \quad \frac{\partial^2 f}{\partial x_2 \partial x_9} = \theta_f \delta_f, \quad \frac{\partial^2 f}{\partial x_3 \partial x_8} = -\theta_z \delta_z,$$

$$\frac{\partial^2 f}{\partial x_2 \partial x_7} = \theta_z \delta_z, \quad \frac{\partial^2 f}{\partial x_3 \partial x_7} = \theta_f \delta_f,$$

$$\frac{\partial^2 f}{\partial x_1 \partial x_9} = -\theta_f \delta_f,$$

Hence, the expression of a is given as:

$$a = [v_2 w_1 w_8 [\theta_z \delta_z] + v_2 w_2 w_9 [-\theta_f \delta_f] + v_3 w_1 w_9 [\theta_f \delta_f] + v_3 w_3 w_8 [-\theta_z \delta_z]$$

$$+ v_8 w_2 w_7 [\theta_z \delta_z] + v_9 w_3 w_7 [\theta_f \delta_f]] > 0.$$

Similarly, the expression for b is given by:

$$b = v_2 w_8 [\delta_2 x_1] > 0.$$

Since $a > 0$ and $b > 0$, it implies that the established endemic equilibrium is locally asymptotically stable and there exists a positive unstable equilibrium.

Bifurcation Diagram for System (3.40)

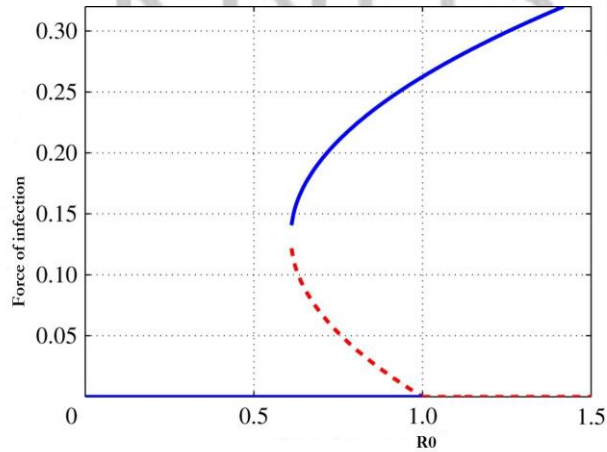


Figure 9: Description of the backward bifurcation of System (3.37).

Figure 10 shows the bifurcation graph for System (3.40). The implication here is that to achieve eradication, efforts that will help bring R_0 below the critical value when $R_0 < 1$ must be put considered.

3.4.11 Malaria Only Model

The Malaria only model is obtained by setting all the state variables and parameters related to Zika and Elephantiasis in System (3.1) to zero. Thus, we obtain:

$$\begin{aligned} \frac{dS_h}{dt} &= \Pi_h + \psi R_m - \alpha_m S_h - \mu_h S_h \\ \frac{dI_m}{dt} &= \alpha_m S_h - \tau_m I_m - (\mu_h + \eta) I_m \\ \frac{dR_m}{dt} &= \tau_m I_m - (\mu_h + \psi) R_m \end{aligned} \quad (3.44)$$

$$\begin{cases} \frac{dS_m}{dt} \\ \frac{dI_p}{dt} \end{cases} = \begin{cases} \Pi_m - \mu_m S_m - \lambda_p S_m \\ \lambda_p S_m - \mu_m I_p \end{cases}$$

where,

$$\alpha_m = \frac{\theta_m \delta_m I_p}{N_h}, \lambda_p = \frac{\theta_m \delta_m I_m}{N_h}$$

The disease free equilibrium of System (3.44) is given as:

$$E_m = \left(\frac{\Pi_h}{\mu_h}, 0, 0, \frac{\Pi_m}{\mu_m}, 0 \right)$$

Using the next generation method operator applied in Van den Driessche & Watmough (2002), the basic reproduction number of System (3.44) is derived as:

$$F_m = \begin{bmatrix} 0 & A_1 & A_3 & 0 \\ A_2 & 0 & 0 & A_4 \end{bmatrix} \text{ and } V_m = \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix},$$

where $A_1 = \theta_m \delta_m$, $A_2 = \frac{\theta_m \delta_m \Pi_m}{\mu_m \mu_h}$, $A_3 = (\mu_h + \eta + \tau_m)$, and $A_4 = \mu_m$. The spectral radius of $F_m V_m^{-1}$ which is the basic reproduction of System (3.44) is given by:

$$R_m = \sqrt{\frac{\vartheta_m^2 \delta_m^2 \Pi_m \mu_h}{(\mu_h + \eta + \tau_m) \Pi_h \mu_m^2}}$$

3.4.12 Local Stability of Disease Free Equilibrium Point for System (3.44)

Theorem 17

System (3.44) is locally stable if $R_m < 1$ and unstable otherwise.

The prove of the theorem is performed by linearising System (3.44). The Jacobian matrix J_{E_m} is given by:

$$J_{E_m} = \begin{pmatrix} -\mu_h & 0 & 0 & 0 & 0 \\ 0 & -(\mu_h + \eta + \tau_m) & 0 & 0 & 0 \\ 0 & \tau_m & -(\mu_h + \psi) & 0 & 0 \\ 0 & -m\delta_m \Pi_m \mu_h \theta & 0 & \vartheta_m \delta_m & 0 \\ 0 & 0 & 0 & \vartheta_m \delta_m & -\mu_m \end{pmatrix} \quad (3.45)$$

The diagonal entries μ_h , μ_m and $-(\mu_h + \psi)$ are the three of the eigenvalues of the Jacobian matrix J_{E_m} . Thus, Equation (3.45) can be reduced to obtain:

$$J_{E_m1} = \begin{pmatrix} -(\mu_h + \eta + \tau_m) & \vartheta_m \delta_m \\ \vartheta_m \delta_m \Pi_m \mu_h & -\mu_m \end{pmatrix} \quad (3.46)$$

For stability to be achieved, the determinant of Equation (3.46) must be positive and the trace must be negative. From Equation (3.46), we have:

$$\det(J_{E_m1}) = \mu_m(\mu_h + \eta + \tau_m) - \vartheta_m^2 \delta_m^2 \Pi_m \mu_h \quad (3.47)$$

$$\text{tr}(J_{E_m1}) = -(\mu_h + \eta + \tau_m + \mu_m) < 0.$$

Performing some algebraic manipulation Equation (3.47) becomes:

$$= \mu_m(\mu_h + \eta + \tau_m) - \vartheta_m^2 \delta_m^2 \Pi_m \mu_h^2 = 1 - R_m. \mu_m(\mu_h + \eta + \tau_m) (\mu_h + \eta + \tau_m) \Pi_h \mu_m$$

It is observe that if $R_m < 1$ the determinant will be positive. Hence, since the trace is negative and the determinant is positive if and only if $R_m < 1$, it implies that the disease free is locally asymptotically stable.

3.4.13 Global Stability of DFE for System (3.44)

Theorem 18

The DFE of System (3.44) is globally asymptotically stable if $R_m < 1$ and unstable otherwise.

Using the idea in explained in Theorem 1 and applied in Theorem 5, the solution to help obtained global stability is obtained as:

$$Q^*(V, W) = \begin{pmatrix} \hat{Q}_2(V, W) \\ \hat{Q}_1(V, W) \end{pmatrix} = \begin{pmatrix} \vartheta_m \delta_m I_m [1 - \frac{S_h}{N_m}] \\ \vartheta_m \delta_m I_p [1 - \frac{S_h}{N_h}] \end{pmatrix}.$$

Since the terms in $Q^*(V, W)$ are nonnegative and the conditions in Castillo-Chavez & Song (2004) are satisfied, we can conclude that the disease free equilibrium is globally asymptotically stable.

3.4.14 Existence of Endemic Equilibrium Point for System (3.44)

The endemic equilibrium point is the steady state solution where the disease (Malaria) is present in the population. It is given by:

$$E_{m^{**}} = (S_h^{**}, I_m^{**}, R_m^{**}, S_m^{**}, I_p^{**}),$$

where,

$$\begin{aligned}
 & ** \quad (N_h \vartheta_m^2 \delta_m^2 \mu_h (\mu_h + \psi)^2) - R_m \mu_m^2 (\mu_h + \psi) N_h \psi \tau_m + N_h \mu_m^2 (R_m - 1) (\mu_h + \psi) \\
 S^h = & \frac{\theta_m^2 \delta_m^2 \mu_h (\mu_h + \psi)^2 (R_m - 1) \Pi_h + \mu_h \mu_m N_h (G - R_m \mu_m \tau_m \psi)}{** (R_m - 1) (\mu_h + \psi) \mu_m \Pi_h I_m =} \\
 & \frac{(G - R_m \mu_m \tau_m \psi)}{** (R_m - 1) (\mu_h + \psi) \mu_m \tau_m \Pi_h R_{ma} =} \\
 S_m = & \frac{G - R_m \mu_m \tau_m \psi}{** \Pi_m (G - R_m \mu_m \tau_m \psi) - (R_m - 1) \theta_m \delta_m \Pi_m \mu_h (\mu_h + \psi)} \\
 I_p = & \frac{G - R_m \mu_m \tau_m \psi}{** (R_m - 1) (\mu_h + \psi) \theta_m \delta_m \Pi_m \mu_h} \\
 & \frac{H - R_m \mu_m^2 \tau_m \psi}{**}
 \end{aligned}$$

where,

$$\begin{aligned}
 G &= \frac{\vartheta_m^2 \delta_m^2 \mu_h \Pi_m}{\Pi \mu^2 (\mu + \psi)}, \\
 H &= \frac{\vartheta_m^2 \delta_m^2 \mu_h \Pi_m (\mu_h + \psi)}{\Pi_h}
 \end{aligned}$$

3.4.15 Global Stability of Endemic Equilibrium for System

(3.44)

Theorem 19

If $R_m > 1$, then there is a unique endemic equilibrium E_m^{**} for System (3.44) that is globally stable in the interior of ω .

The global stability of the endemic equilibrium can be determined by constructing a common quadratic Lyapunov function $V(t)$ of the form;

$$V(S_h, I_m, R_m, S_m, I_p) = \frac{1}{2} [(S_h - S_h^{**}) + (I_m - I_m^{**}) + (R_m - R_m^{**})]^2 + \frac{1}{2} [(S_m - S_m^{**}) + (I_p - I_p^{**})]^2 \quad 1$$

Taking the time derivative yields;

$$\begin{aligned} &= [(S_h - S_h^{**}) + (I_m - I_m^{**}) + (R_m - R_m^{**})] \frac{d}{dt} [(S_h + I_m + R_m)] \\ &\quad + [(S_m - S_m^{**}) + (I_p - I_p^{**})] \frac{d}{dt} [S_m + I_p]. \\ &= -[(S_h - S_h^{**}) + (I_m - I_m^{**}) + (R_m - R_m^{**})] [\mu_h (S_h - S_h^{**}) \\ &\quad + (\mu_h + \eta)(I_m - I_m^{**}) + \mu_h (R_m - R_m^{**})] \end{aligned}$$

Let $A_1 = S_h - S_h^{**}$, $A_2 = I_m - I_m^{**}$, $A_3 = R_m - R_m^{**}$, $A_4 = S_m - S_m^{**}$, $A_5 = I_p - I_p^{**}$, $A_6 = A_1 + A_2 + A_3$, and $A_7 = A_4 + A_5$. This gives:

$$\begin{aligned} \frac{\partial V}{\partial t} &= -[A_1 + A_2 + A_3] [\mu_h (A_1 + A_2 + A_3) + \eta A_2] + [A_4 + A_5] [\mu_m (A_4 + A_5)] \\ \frac{\partial V}{\partial t} &= -[\mu_h A_6 + \eta A_2 A_6 + \mu_m A_7] \end{aligned}$$

It is observed that $\frac{\partial V}{\partial t} \leq 0$ if $S_h \leq S_h^{**}$, $I_m \leq I_m^{**}$, $R_m \leq R_m^{**}$. Again $\frac{\partial V}{\partial t} = 0$ if and only if $S_h = S_h^{**}$, $I_m = I_m^{**}$, $R_m = R_m^{**}$, $S_m = S_m^{**}$ and $I_p = I_p^{**}$. Therefore, the endemic equilibrium of System (3.44) is globally asymptotically stable.

3.4.16 Bifurcation Analysis for System (3.44)

We rewrite System (3.44) in the form;

$$\frac{dX_i}{dt} = F(X_i), \quad dt$$

where $X_i = (x_1, x_2, x_3, x_4, x_5)^T$ and $F = (f_1, f_2, f_3, f_4, f_5)^T$. We also assigned the state variables as follows: $x_1 = S_h$, $x_2 = I_m$, $x_3 = R_m$, $x_4 = S_m$, $x_5 = I_p$. We therefore have the following;

$$\begin{aligned}
 \frac{dx_1}{dt} &= f_1 = \Pi_h + \psi_3 - \frac{\theta_m \delta_m x_5 x_1}{N_h} - \mu_h x_1 \\
 \frac{dx_2}{dt} &= f_2 = \frac{\theta_m \delta_m x_5 x_1}{N_h} - (\mu_h + \eta + \tau_m) x_2 \\
 \frac{dx_3}{dt} &= f_3 = \tau_m x_2 (\mu_h + \psi) x_3 \\
 \frac{dx_4}{dt} &= f_4 = \Pi_m - \mu_m x_4 - \frac{\theta_m \delta_m x_2 x_4}{N_h} \\
 \frac{dx_5}{dt} &= f_5 = \frac{\theta_m \delta_m x_2 x_4}{N_h} - \mu_m x_5
 \end{aligned}$$

Taking $\sigma^* = \vartheta_m^2$ as the bifurcation parameter for $R_m = 1$, System (3.44) is linearized at the disease free equilibrium point to obtain the Jacobian J_{E_m0} .

$$J_{E_m0} = \begin{bmatrix}
 \psi & 0 & 0 & 0 & 0 \\
 -\mu_h & 0 & 0 & \theta_m \delta_m & 0 \\
 0 & -(\mu_h + \psi) & 0 & \theta_m \delta_m & 0 \\
 0 & 0 & -\mu_m & 0 & 0 \\
 -(\mu_h + \eta + \tau_m) & 0 & 0 & 0 & -\mu_m \\
 \tau_m & 0 & 0 & 0 & 0 \\
 -\frac{\theta_m \delta_m \Pi_m \mu_h}{\Pi_h \mu_m} & 0 & 0 & 0 & 0 \\
 \frac{\theta_m \delta_m \Pi_m \mu_h}{\Pi_h \mu_m} & 0 & 0 & 0 & -\mu_m
 \end{bmatrix}$$

To analyze the dynamics of System (3.44), we compute the eigenvectors of the Jacobian J_{E_m0} . We consider the right and left eigenvectors represented by $W =$

$(w_1, w_2, w_3, w_4, w_5)^T$ and $V = (v_1, v_2, v_3, v_4, v_5)^T$. Solving the right eigenvector we obtain:

$$w_1 = \frac{\psi w_3 + \theta_m \delta_m w}{\mu_h}, \quad w_2 = \frac{\vartheta_m \delta_m w_5}{(\mu_h + \eta + \tau_m)}, \quad w_3 = \frac{\tau_m w - 2}{(\mu_h + \psi)},$$

$$w_4 = -\frac{\theta \delta \Pi \mu w}{h m}, \quad w_5 = -\frac{\theta \delta \Pi \mu w}{\Pi \mu^2}.$$

The left eigenvector is equally obtained as:

$$v_1 = 0, \quad v_2 = \frac{\theta_m \delta_m v}{\mu_h \eta + \tau_m}, \quad v_3 = \frac{\Pi \mu_m}{\mu_m}, \quad v_4 = 0, \quad v_5 = \frac{\theta_m \delta_m v}{\mu_m}.$$

The approach in Castillo-Chavez & Song (2004) is applied. As a result the nonzero second partial derivatives of f needed to compute the value for a is given as:

$$\frac{\partial^2 f_1}{\partial x_1 \partial x_5} = \frac{\partial^2 f_1}{\partial x_5 \partial x_1} = -\theta_m \delta_m, \quad \frac{\partial^2 f_2}{\partial x_1 \partial x_5} = \theta_m \delta_m, \quad \frac{\partial^2 f_4}{\partial x_2 \partial x_4} = \frac{\partial^2 f_5}{\partial x_4 \partial x_2} = \vartheta_m \delta_m,$$

Hence, the expression of a is given as:

$$a = v_1 w_1 w_5 \left[\frac{\partial^2 f_1}{\partial x_1 \partial x_5} \right] + v_2 w_1 w_5 \left[\frac{\partial^2 f_2}{\partial x_1 \partial x_5} \right] + v_4 w_2 w_4 \left[\frac{\partial^2 f_4}{\partial x_2 \partial x_4} \right] + v_5 w_2 w_4 \left[\frac{\partial^2 f_5}{\partial x_2 \partial x_4} \right] > 0.$$

Also, the non-zero second partial derivatives of f associated with b is given by:

$$b = + \frac{\frac{\partial^2 f_2}{\partial x_5 \partial \theta_m} + \frac{\partial^2 f_5}{\partial x_2 \partial \theta_m}}{(\theta_2 w_5 x_1 + v_5 w_2 x_4) \delta_m} > 0.$$

Since $a > 0$ and $b > 0$, it implies that there exist a positive unstable equilibrium.

3.4.17 Bifurcation Diagram for System 3.44

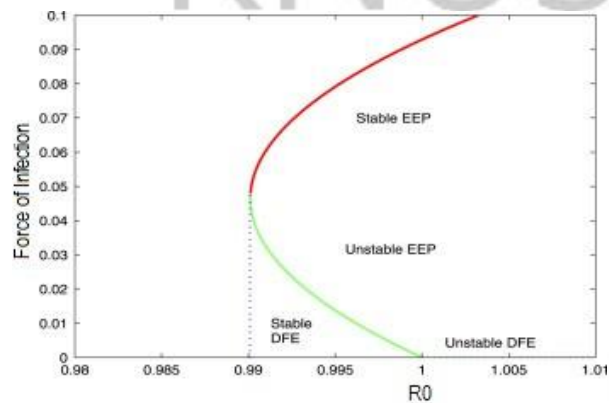


Figure 10: Depicts the backward bifurcation of System (3.44).

3.4.18 Zika Only Sub-Model

The Zika only model is obtained by setting all state variables and variables and parameters related to Malaria and Elephantiasis to zero that is ($I_f = I_m = I_{mz} = I_{mf} = I_{fz} = I_{mzf} = I_p = I_w = 0$) in the System (3.1) to get:

$$\begin{aligned} \frac{dS_h}{dt} &= \Pi_h - \mu_h S_h - \alpha_z S_h \\ \frac{dI_z}{dt} &= \alpha_z S_h - \tau_z I_z - \mu_h I_z \\ \frac{dR_z}{dt} &= \tau_z I_z - \mu_h R_z \\ \frac{dS_m}{dt} &= \Pi_m - \mu_m S_m - \lambda_a S_m \\ \frac{dI_a}{dt} &= \lambda_a S_m - \mu_m I_a \end{aligned} \quad (3.48)$$

where,

$$\alpha_z = \frac{\theta_z \delta_z I_a}{N_h}, \quad \lambda_a = \frac{\theta_z \delta_z I_z}{N_h}$$

The disease free equilibrium of System (3.48) is given as:

$$E_z = \left(\frac{\Pi_h}{\mu_h}, 0, 0, \frac{\Pi_m}{\mu_m}, 0 \right).$$

Using the next generation operator method of Van den Driessche & Watmough (2002), the basic reproduction number of System (3.48) is determined by first obtaining the values for F_z and V_z . Thus,

$$F_z \text{ and } V_z = \begin{pmatrix} 0 & \vartheta_z \delta_z \\ \frac{\vartheta_z \delta_z \Pi_m}{\Pi_h \mu_f} & 0 \end{pmatrix} \begin{pmatrix} \mu_h + \tau_z & 0 \\ 0 & \mu_z \end{pmatrix}$$

The basic reproduction number obtained as the spectral radius of $R_z = \{F_z V_z^{-1}\}$ is obtained as:

$$R_z = \sqrt{\frac{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h}{(\mu_h + \tau_z) \Pi_h \mu_h^2}}.$$

3.4.19 Local Stability of Disease free Equilibrium Point of System (11)

Theorem 20

The disease free equilibrium point of System (3.48) is locally asymptotically stable if $R_z < 1$ and unstable otherwise.

The prove is done by linearising System (3.48) to obtain the Jacobian matrix

J_{E_z} .

?

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$$J_{E_z} = \begin{pmatrix} 0 & -(\mu_h + \tau_z) & 0 & 0 & \vartheta_z \delta_z \\ 0 & -\frac{\vartheta_z \delta_z \Pi_m \mu_h}{\Pi_h \mu_m} & 0 & -\mu_m & 0 \\ 0 & \frac{\vartheta_z \delta_z \Pi_m \mu_h}{\Pi_h} & 0 & 0 & -\mu_m \end{pmatrix} \begin{pmatrix} -\mu_h & 0 & 0 \\ 0 & \theta_z \delta_z & 0 \end{pmatrix} \quad (3.49)$$

Applying matrix algebra requires that the trace of J_{E_z} be negative and the determinant be positive. It can be seen that the trace of $J_{E_z} < 0$. To determine the determinant we have:

$$\begin{aligned} \det(J_{E_z}) &= \mu_m(\mu_h + \tau_z) - \frac{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h}{\Pi_h \mu_m} \\ &= 1 - R_z \end{aligned}$$

It can be seen the $\det(J_{E_z}) > 0$ if and only if $R_z < 1$. Thus, System (3.48) is locally stable if $R_z < 1$.

3.4.20 Global Stability of DFE of System (3.48)

Theorem 21

The DFE of System (3.48) is globally asymptotically stable if $R_z < 1$ and unstable otherwise.

Applying Theorem 1 and the method in Castillo-Chavez & Song (2004), we have:

$$\hat{T}^*(V, W) = \begin{pmatrix} \hat{T}_1(V, W) \\ \hat{T}_2(V, W) \end{pmatrix} = \begin{pmatrix} \vartheta_z \delta_z I_a \left[1 - \frac{S_h}{N_h} \right] \\ \vartheta_z \delta_z I_z \left[1 - \frac{S_m}{N_m} \right] \end{pmatrix}$$

Since the terms in $T^*(V, W)$ are non-negative and the conditions given in Carlos et al. (2002) also satisfied, we can conclude that the disease free equilibrium of System (3.48) virus is globally stable.

3.4.21 Existence of Endemic Equilibrium Point for System (3.48)

The endemic equilibrium point of System (3.48) is given by $E_z = (S_h^{**}, I_z^{**}, R_z^{**}, S_m^{**}, I_a^{**})$ where,

$$\begin{aligned}
 S_h^{**} &= \frac{N_h \vartheta_z^2 \delta_z^2 \Pi_m \Pi_h \mu_h^3 \mu_m - R_z \mu_m^3 \mu_h N_h \Pi^2 \tau_z + N_h \tau_z (R_z - 1) \mu_m^3 \mu_h \Pi_h}{\vartheta_z^2 \delta_z^2 \Pi_m \Pi_h \mu_h^3 (R_z - 1) + N_h \mu_m \mu_h (\vartheta_z^2 \delta_z^2 \Pi_m \mu_h^2 - R_z \mu_m \tau_z \Pi_h)} \\
 I_z^{**} &= \frac{(R_z - 1) \mu_m \mu_h \Pi_h^2}{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h^2 - R_z \mu_m \tau_z \Pi_h} \\
 R_z^{**} &= \frac{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h^3 - (R_z^2 \mu_h \tau_z \Pi_h - 1) \mu_m^2 \mu_h \tau_z \Pi_h^2}{\vartheta_z^2 \delta_z^2 \Pi_m \mu_h^3 - R_z \mu_m} \\
 S_m^{**} &= \frac{\Pi_m (\vartheta_z^2 \delta_z^2 \Pi_m \mu_h^2 - R_z \mu_m^2 \tau_z \Pi_h) - (R_z - 1) \vartheta_z \delta_z \Pi_m \Pi_h \mu_h^2 \mu_m^2}{\theta_2 \delta_z^2 \Pi_m \mu_h^3 - R_z \mu_m^2 \mu_h \tau_z \Pi_h} \\
 I_a^{**} &= \frac{(R_z - 1) \vartheta_z \delta_z \Pi_m \Pi_h^2 \mu_h^2}{2 \theta_2 \delta_z^2 \Pi_m \mu_h - R_z \mu_m^2 \tau_z \Pi_h}
 \end{aligned}$$

3.4.22 Global Stability of Endemic Equilibrium of System (3.48)

Theorem 22

If $R_z > 1$, then the unique endemic equilibrium of System (3.48) is globally stable in the interior of Ω .

The global stability of the endemic equilibrium can be determined by constructing a common quadratic Lyapunov function $L(t)$ of the form;

$$V(S_h, I_z, R_z, S_m, I_a) = \frac{1}{2} [(S_h - S_h^{**}) + (I_z - I_z^{**}) + (R_z - R_z^{**})]^2 + \frac{1}{2} [(S_m - S_m^{**}) + (I_a - I_a^{**})]^2$$

The time derivative of $V(t)$ is given by:

$$\begin{aligned} \frac{\partial V}{\partial t} &= [(S_h - S_h^{**}) + (I_z - I_z^{**}) + (R_z - R_z^{**})] \frac{d}{dt} [(S_h - S_h^{**}) + (I_z - I_z^{**}) + (R_z - R_z^{**})] \\ &\quad + [(S_m - S_m^{**}) + (I_a - I_a^{**})] \frac{d}{dt} [(S_m - S_m^{**}) + (I_a - I_a^{**})] \\ &= -[(S_h - S_h^{**}) + (I_z - I_z^{**}) + (R_z - R_z^{**})] \times [(S_h - S_h^{**}) + (I_z - I_z^{**}) + (R_z - R_z^{**})] \\ &\quad - [(S_m - S_m^{**}) + (I_a - I_a^{**})] [\mu_m(S_m - S_m^{**}) + \mu_m(I_a - I_a^{**})] \end{aligned}$$

Let $B_1 = S_h - S_h^{**}, B_2 = I_z - I_z^{**}, B_3 = S_m - S_m^{**}, B_4 = I_a - I_a^{**}, B_5 = B_1 + B_2 + B_3$ and $B_7 = B_4 + B_5$. Thus,

$$\begin{aligned} \frac{\partial V}{\partial t} &= -[B_1 + B_2 + B_3] [\mu_h(B_1 + B_2 + B_3)] - [B_4 + B_5] [\mu(B_4 + B_5)] \\ \frac{\partial V}{\partial t} &= -[\mu_h B_5 + \mu B_7] \end{aligned}$$

It is observed that $\frac{\partial V}{\partial t} \leq 0$ if $S_h \leq S_h^{**}, I_z \leq I_z^{**}, R_z \leq R_z^{**}, S_m \leq S_m^{**}$ and $I_a \leq I_a^{**}$.

Again, $\frac{\partial V}{\partial t} = 0$ if and only if $S_h = S_h^{**}, I_z = I_z^{**}, R_z = R_z^{**}, S_m = S_m^{**}$ and $I_a = I_a^{**}$.

Therefore, the endemic equilibrium of System (3.48) is globally asymptotically stable in the interior Ω .

3.4.23 Bifurcation of System (3.48)

System (3.48) can be rewritten in the form:

$$x_1 = S_h, \quad x_2 = I_z, \quad x_3 = R_z, \quad x_4 = S_m, \quad x_5 = I_a.$$

It can be written in the vector form as:

$$\frac{dX_i}{dt} = F(X_i),$$

where, $X_i = (x_1, x_2, x_3, x_4, x_5)^T$ and $F = (f_1, f_2, f_3, f_4, f_5)^T$. The System (11) becomes:

$$\begin{aligned} \frac{dx_1}{dt} &= f_1 = \Pi_h - \mu_h x_1 - \frac{\theta_z \delta_z x_5 x_1}{N_h dx_2} \\ \frac{dx_2}{dt} &= f_2 = \frac{N_h dx}{N_h dx} - (\tau_z + \mu_h) x_2 \\ \frac{dx_3}{dt} &= f_3 = \tau_z x_2 - \mu_h x_3 \\ \frac{dx_4}{dt} &= f_4 = \Pi_m - \mu_m x_4 - \frac{\theta_z \delta_z x_2 x_4}{N_h dx_5} \\ \frac{dx_5}{dt} &= f_5 = \frac{N_h dx}{N_h} - \mu_m x_5. \end{aligned}$$

Taking the bifurcation parameter to be θ_z^2 at the point where $R_z = 1$, we have:

$$\theta_z^2 = \frac{(\mu_h + \tau_z) \Pi_h \mu_m^2}{2 \Pi_m \mu_h \delta_z}.$$

The Jacobian matrix of Equation (3.49) is evaluated at the DFE point at $R_z = 1$ by computing the right and left eigenvector. The right eigenvector is represented by $w = (w_1, w_2, w_3, w_4, w_5)^T$ and the left eigenvector is represented v =

$(v_1, v_2, v_3, v_4, v_5)^T$. Solving the right eigenvector associated with the Jacobian matrix (3.49) is obtained as:

$$\begin{aligned}
w_1 &= \frac{\theta_z \delta_z w_5}{\mu h}, \quad w_2 = \frac{\theta_z \delta_z w_5 \tau_z w_2}{(\mu h + \tau_z)}, \quad w_3 = \frac{\theta_z \delta_z w_5 \tau_z w_2}{(\mu h + \tau_z)}, \\
w_4 &= \frac{\theta_z \delta_z w_5}{\mu h}, \quad w_5 = \frac{\theta_z \delta_z \Pi m \mu h w_2}{\Pi h \mu m^2}
\end{aligned}$$

The associated eigenvector for v is given by:

$$\begin{aligned}
v_1 &= 0, \quad v_2 = \frac{\theta_z \delta_z \Pi m \mu h w_2}{\mu h}, \quad v_3 = 0, \quad v_4 = 0, \quad v_5 = \frac{\theta_z \delta_z \Pi m \mu h w_2}{\mu h}
\end{aligned}$$

Here, the method by Castillo-Chavez & Song (2004) is applied. The non-zero second partial derivative of f is derived to help compute the value for a . This gives:

$$\begin{aligned}
\frac{\partial^2 f}{\partial x_1 \partial x_5} &= \frac{\partial^2 f}{\partial x_5 \partial x_1} = -\vartheta_z \delta_z \frac{\partial^2 f_1}{\partial x_1 \partial x_5} = \theta_z \delta_z, \\
\frac{\partial^2 f}{\partial x_2 \partial x_4} &= -\vartheta_z \delta_z, \quad \frac{\partial^2 f}{\partial x_2 \partial x_4} = \frac{\partial^2 f_5}{\partial x_4 \partial x_2} = \vartheta_z \delta_z
\end{aligned}$$

Hence, the expression of a is given as:

$$\begin{aligned}
a &= v_1 w_1 w_5 \left[\frac{\partial^2 f_1}{\partial x_1 \partial x_5} \right] + v_2 w_1 w_5 \left[\frac{\partial^2 f_2}{\partial x_1 \partial x_5} \right] + v_4 w_2 w_4 \left[\frac{\partial^2 f_4}{\partial x_2 \partial x_4} \right] \\
&+ v_5 w_2 w_4 \left[\frac{\partial^2 f_5}{\partial x_2 \partial x_4} \right] > 0
\end{aligned}$$

Also, the non-zero second partial derivatives of f associated with b is given by:

$$b = + \frac{\partial^2 f_2}{\partial x_5 \partial \theta_z} + \frac{\partial^2 f_5}{\partial x_2 \partial \theta_z} > 0$$

Since $a > 0$ and $b > 0$, it satisfies one of the conditions and thus it is locally asymptotically stable and there exist a positive unstable equilibrium.

3.4.24 Bifurcation Diagram of System (3.48)

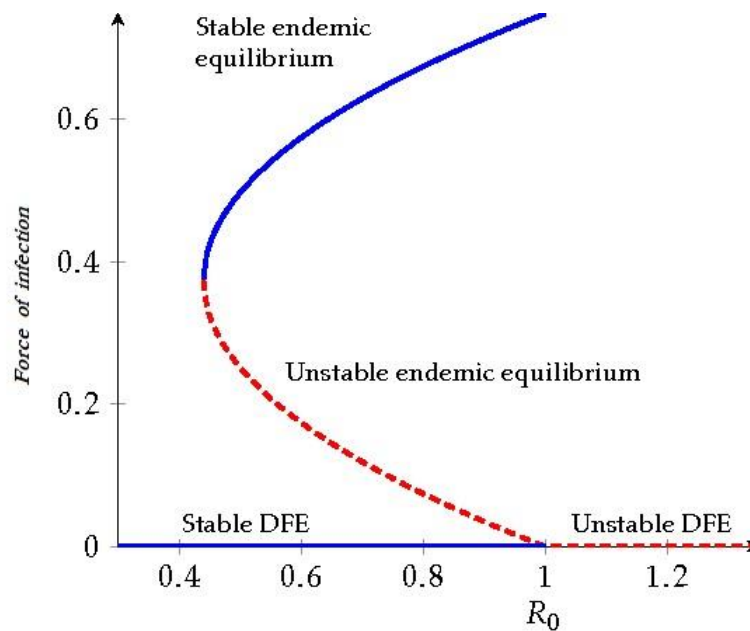


Figure 11: Depicts the backward bifurcation of System (3.48).

Figure 11 (Zika-virus only model) also exhibits a backward bifurcation curve. The implication is that the basic reproduction number less than unity is not sufficient to help eradicate the diseases. In fact, to achieve eradication, additional efforts such as control measures are required to bring R_0 below a critical value

$$R_0 < 1.$$

3.4.25 Elephantiasis Only Sub-Model

The Elephantiasis only sub-model is also obtained by setting the state variables and parameters related to Malaria and Zika virus to zero. By doing so we get:

$$\begin{aligned} \frac{dS_h}{dt} &= \Pi_h - \mu_h S_h - \alpha_f S_h \\ \frac{dI_f}{dt} &= \alpha_f S_h - \mu_h I_f - \tau_f I_f \\ \frac{dR_f}{dt} &= \tau_f I_f - \mu_h R_f \end{aligned} \quad (3.50)$$

$$\frac{dS_m}{dt} = \Pi_m - \mu_m S_m - \lambda_m S_m I_w$$

$$\frac{dI_w}{dt} = \lambda_m S_m - \mu_m I_w,$$

where,

$$\lambda_w = \frac{\theta_f \delta_f I_w}{N_h}, \quad \alpha_f = \frac{\theta_f \delta_f I_f}{N_h}$$

The disease free equilibrium of System (3.50) is given as:

$$E_f = \left(\frac{\Pi_m}{\mu_h}, 0, 0, \frac{\Pi_m}{\mu_m}, 0 \right).$$

Applying the next generation operator method as applied for the multi-infection as well as the various co-infection model, we do same for System (3.50). We derive our F_f and V_f matrix as

$$F_f = \begin{pmatrix} 0 & \theta_f \delta_f & (\mu_h + \tau_f) & 0 \\ \vartheta_f \delta_f & \Pi & \mu_h & \mu_f \end{pmatrix} \text{ and } V_f = \begin{pmatrix} \mu_h & 0 & 0 & 0 \\ 0 & \mu_m & 0 & 0 \end{pmatrix}$$

Therefore applying Van den Driessche & Watmough (2002), the basic reproduction number which is the spectral radius of $F_f V_f^{-1}$ is given by

$$R_f = \sqrt{\frac{\vartheta_f^2 \delta_f^2 \Pi_m \mu_h}{(\mu_h + \tau_f) \Pi_h \mu_m^2}}$$

3.4.26 Local Stability of DFE Point of System (3.50)

Theorem 23

The disease free equilibrium point of System (3.50) is locally asymptotically stable if $R_f < 1$ and unstable otherwise.

We linearise System (3.50) to obtain the Jacobian matrix J_{E_f} .

$$J_{E_f} = \begin{pmatrix} -\mu_h & 0 & \theta_f \delta_f \\ 0 & -(\mu_h + \tau_f) & -\mu_h \\ \tau_f & -\theta_f \delta_f \Pi_m \mu_m & -\mu_m \end{pmatrix}$$

The proof of local stability requires the trace be negative and determinant be positive (Mwamtobe et al., 2014). Thus,

$$\det(J_{E_f}) = \mu_m(\mu_h + \tau_f) - \frac{\theta_f \delta_f \Pi_m \mu_h}{\Pi_h \mu_m} \quad (3.51)$$

$$\text{tr}(J_{E_f}) = -(\mu_h + \tau_f + \mu_m) < 0.$$

From Equation (3.51) we observe that:

$$\det(J_{E_f}) = 1 - \frac{\theta_f \delta_f \Pi_m \mu_h}{(\mu_h + \tau_f) \Pi_h \mu_m} = 1 - R_f;$$

Thus, if $R_f < 1$, then the determinant is greater than zero which shows that the disease free equilibrium is locally stable.

3.4.27 Global Stability of DFE for System (3.50)

Theorem 24

The DFE of System (3.50) is globally asymptotically stable if $R_f < 1$ and unstable otherwise.

The prove is established by applying Theorem 1 and the method in CastilloChavez & Song (2004) to obtain:

$$(V, W) = \begin{pmatrix} \hat{G}_1(V, W) \\ \hat{G}_2(V, W) \end{pmatrix} = \begin{pmatrix} \vartheta_f \delta_f I_w \left[1 - \frac{S_h}{N_h} \right] \\ \vartheta_f \delta_f I_f \left[1 - \frac{S_h}{N_h} \right] \end{pmatrix} G^{\wedge}.$$

Since the terms in $G^{\wedge}(V, W)$ are nonnegative and the conditions in Castillo-Chavez & Song (2004) are satisfied, we can conclude that the disease free equilibrium of System (3.50) is globally asymptotically stable.

3.4.28 Existence of Endemic Equilibrium Point for System (3.50)

The endemic equilibrium point of System (3.50) is given by $E_f^{**} = (S_h^{**}, I_f^{**}, R_f^{**}, S_m^{**}, I_w^{**})$

where,

$$\begin{aligned} S_h^{**} &= \frac{\vartheta_f^2 \delta_f^2 \Pi_m \Pi_h \mu_h^3 \mu_m - N_h R_f \mu_m^3 \mu_h N_h \Pi_h^2 \tau_f + N_h \tau_f (R_f - 1) \mu_m^3 \mu_h \Pi_h}{\theta_f \delta_f \Pi_m \Pi_h \mu_h^3 (R_f - 1) + N_h \mu_m \mu_h (\theta_f \delta_f \Pi_m \mu_h^2 - R_f \mu_m \tau_f \Pi_h) - \Pi_h^2} \\ &= \frac{\vartheta_f^2 \delta_f^2 \Pi_m \mu_h^2 - (R_f - 1) \mu_m \mu_h}{I_f} \\ &= \frac{R_f \mu_m \Pi_h - 1) \mu_m^2 \mu_h \tau_f \Pi_h^2}{(R_f - 1) \mu_m \mu_h} \\ R_f &= \frac{\theta_f \delta_f \Pi_m \mu_h^3 - R_f \mu_m^2 \mu_h \tau_f \Pi_h}{\Pi_m (\vartheta_f^2 \delta_f^2 \Pi_m \mu_h^2 - \tau_f \Pi_h - (R_f - 1) \vartheta_f \delta_f \Pi_m \Pi_h \mu_h^2 \mu_m^2)} \\ S_m &= \frac{2 \tau_f \Pi_h - (R_f - 1) \vartheta_f \delta_f \Pi_m \Pi_h \mu_h^2}{2 \tau_f \Pi_h - (R_f - 1) \vartheta_f \delta_f \Pi_m \Pi_h \mu_h^2} \\ I_w^{**} &= \frac{\theta_f \delta_f \Pi_m \mu_h - \mu_m^2 \tau_f \Pi_h - R_f \mu_m^2 \mu_h \tau_f \Pi_h}{\theta_f \delta_f \Pi_m \mu_h - \mu_m^2 \tau_f \Pi_h - R_f \mu_m^2 \mu_h \tau_f \Pi_h} \end{aligned}$$

3.4.29 Global Stability of Endemic Equilibrium of Elephantiasis Only Sub-Model

Theorem 25

If $R_f > 1$, then the unique endemic equilibrium E_f^{**} of System (3.50) is globally stable in the interior of Ω .

The global stability of the endemic equilibrium can be obtained by constructing a common quadratic Lyapunov function $L(t)$ as in

$$L(S_h, I_f, R_f, S_m, I_w) = \frac{1}{2} [(S_h - S_h^{**}) + (I_f - I_f^{**}) + (R_f - R_f^{**})]^2 + \frac{1}{2} [(S_m - S_m^{**}) + (I_w - I_w^{**})]^2.$$

The time derivative of $\frac{\partial L}{\partial t}$ is given by:

$$\begin{aligned} \frac{\partial V}{\partial t} &= [(S_h - S_h^{**}) + (I_f - I_f^{**}) + (R_f - R_f^{**})] \frac{d}{dt} [(S_h - S_h^{**}) + (I_f - I_f^{**}) + (R_f - R_f^{**})] \\ &\quad + [(S_m - S_m^{**}) + (I_w - I_w^{**})] \frac{d}{dt} [(S_m - S_m^{**}) + (I_w - I_w^{**})] \\ &= -[(S_h - S_h^{**}) + (I_f - I_f^{**}) + (R_f - R_f^{**})] [\mu_h [(S_h - S_h^{**}) + (I_f - I_f^{**}) + (R_f - R_f^{**})] - (\mu_h (S_h - S_h^{**}) + \mu_f (I_f - I_f^{**}) + \mu_r (R_f - R_f^{**}))] \\ &\quad - [(S_m - S_m^{**}) + (I_w - I_w^{**})] [\mu_m (S_m - S_m^{**}) + \mu_w (I_w - I_w^{**})] \end{aligned}$$

We let $D_1 = S_h - S_h^{**}$, $D_2 = I_f - I_f^{**}$, $D_3 = R_f - R_f^{**}$, $D_4 = S_m - S_m^{**}$, $D_5 = I_w - I_w^{**}$, $D_6 = D_1 + D_2 + D_3$, $D_7 = D_4 + D_5$.

$$\begin{aligned} \frac{\partial V}{\partial t} &= -[D_1 + D_2 + D_3] [\mu_h (D_1 + D_2 + D_3)] - [D_4 + D_5] [\mu_m (D_4 + D_5)] \\ &= -[\mu_h D_6^2 + \mu_m D_7^2] \end{aligned}$$

It is observed that $\frac{\partial V}{\partial t} \leq 0$ if $S_h \leq S_h^{**}$, $I_f \leq I_f^{**}$, $R_f \leq R_f^{**}$, $S_m \leq S_m^{**}$ and $I_w \leq I_w^{**}$.

I_w^{**} . Moreover, $\frac{dI_w}{dt} = 0$ if and only if $S_h = S_h^{**}$, $I_f = I_f^{**}$, $R_f = R_f^{**}$, $S_m = S_m^{**}$ and $I_w = I_w^{**}$. Therefore the endemic equilibrium of System (3.50) is globally asymptotically stable.

3.4.30 Bifurcation Theorem for Elephantiasis Only Sub-Model

The System (3.50) is rewritten by assigning the state variables as follows:

$$x_1 = S_h, x_2 = I_f, x_3 = R_f, x_4 = S_m, x_5 = I_w.$$

Therefore, writing System (3.50) in the vector form is obtained as:

$$\frac{dx_i}{dt} = F(X_i),$$

where $X_i = (x_1, x_2, x_3, x_4, x_5)^T$ and $F = (f_1, f_2, f_3, f_4, f_5)^T$. Thus,

$$\begin{aligned} \frac{dx_1}{dt} &= f_1 = \Pi_h + \phi x_3 - \mu_h x_1 - \frac{\theta_f \delta_f x_5 x_1}{N_h} \\ \frac{dx_2}{dt} &= f_2 = \frac{\theta_f \delta_f x_5 x_1}{N_h} - (\mu_h + \tau_f) x_2 \\ \frac{dx_3}{dt} &= f_3 = \tau_f x_2 - (\mu_h + \phi) x_3 \\ \frac{dx_4}{dt} &= f_4 = \Pi_m - \mu_m x_4 - \frac{\theta_f \delta_f x_2 x_4}{N_h} \\ \frac{dx_5}{dt} &= f_5 = \frac{\theta_f \delta_f x_2 x_4}{N_h} - \mu_m x_5 \end{aligned}$$

Choosing the bifurcation parameter to be $\beta^* = \theta_f^2$ at the point $R_f = 1$ we have:

$$\beta^* = \frac{(\mu_h + \tau_f) \Pi_h \mu_m^2}{\delta_f \Pi_m \mu_h}.$$

The Jacobian matrix evaluated at the disease free equilibrium point for the chosen bifurcation parameter is given by:

$$J_{\beta^*} = \begin{pmatrix} 0 & 0 & \beta^* & 0 & 0 \\ -\mu_h & \phi & \delta_f & 0 & 0 \\ 0 & 0 & \beta^* \delta_f & 0 & 0 \\ -\frac{\beta^* \delta_f \Pi_m}{\Pi_h \mu_m} & J \tau_f & -(\mu_h + \phi) & 0 & 0 \\ \frac{\beta^* \delta_f \Pi_h \mu_h}{\Pi} & 0 & 0 & 0 & 0 \end{pmatrix} \quad (3.52)$$

To analyze the dynamics of System (3.50), we compute the eigenvectors of Equation (3.52). The right and left eigenvectors denoted by $w = (w_1, w_2, w_3, w_4, w_5)^T$ and $v = (v_1, v_2, v_3, v_4, v_5)^T$ respectively are considered. Solving the right eigenvector associated with the zero eigenvalue of Equation (3.52) gives:

$$w_1 = \frac{\phi w_3 + \beta^* \delta_f w_5}{\mu_h}, \quad w_2 = \frac{\beta^* \delta_f w_5}{(\mu_h + \tau_f)}, \quad w_3 = \frac{\tau_f w_2}{(\mu_h + \phi)}$$

$$w_4 = \frac{\beta^* \delta_f \Pi_h \mu_h w_5}{\Pi_h \mu_m \mu_2 h w_2}, \quad w_5 = -\beta^* \delta_f \Pi_f$$

For the left eigenvector, we transpose Equation (3.52) and solve to obtain:

$$v_1 = 0, \quad v_2 = -\frac{\beta^* \delta_f \Pi}{\mu_h \mu_m (\mu_h + \tau_f)}, \quad v_3 = 0, \quad v_4 = 0, \quad v_5 = \mu_m$$

Computing for the signs of a and b, we derive the non zero second partial derivative of f associated with a to be:

$$\frac{\partial^2 f_1}{\partial x_1 \partial x_5} = \frac{\partial^2 f_1}{\partial x_5 \partial x_1} = \frac{\partial^2 f_2}{\partial x_1 \partial x_5} = \frac{\partial^2 f_2}{\partial x_5 \partial x_1} = -\theta_f \delta_f, \quad = \quad = \theta_f \delta_f,$$

$$\frac{\partial^2 f}{\partial x_2 \partial x_4} = \frac{\partial^2 f}{\partial x_4 \partial x_2} = -\vartheta_f \delta$$

$$f, \frac{\partial^2 f}{\partial x_2 \partial x_4} = \frac{\partial^2 f}{\partial x_4 \partial x_2} = \theta_f \delta_f.$$

Hence, the expression of a is given as:

$$a = v_1 w_1 w_5 \left[\frac{\partial^2 f_1}{\partial x_1 \partial x_5} \right] + v_2 w_1 w_5 \left[\frac{\partial^2 f_2}{\partial x_1 \partial x_5} \right] + v_4 w_2 w_4 \left[\frac{\partial^2 f_4}{\partial x_2 \partial x_4} \right] + v_5 w_2 w_4 \left[\frac{\partial^2 f_5}{\partial x_2 \partial x_4} \right] > 0$$

Also, the non-zero second partial derivative of f associated with b is given by:

$$b = \frac{\partial^2 f_2}{\partial x_5 \partial \theta_*} + \frac{\partial^2 f_5}{\partial x_2 \partial \theta_*} = \delta_f x_1 + \delta_f x_4 > 0.$$

We realise $a > 0$ and $b > 0$, hence it is locally asymptotically stable and there exist a positive unstable equilibrium.

3.4.31 Bifurcation Diagram for Elephantiasis only Sub-model

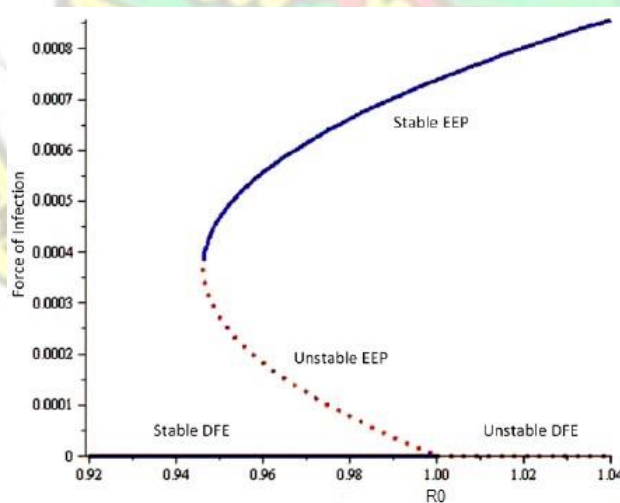


Figure 12: Depicts the backward bifurcation of System (3.50).

The Elephantiasis only sub-model of System (3.50) also exhibit a backward bifurcation curve indicating that in order to attain full eradication other control measures are needed to bring $R_0 < 1$.

3.5 Sensitivity Analysis

We perform sensitivity analysis on the parameters of the model to determine which parameter will increase or decrease the basic reproduction number R_0 when it is perturb by a small margin. It is computed using the normalized forward sensitivity index. In terms of differentiable expression, it is defined as follows

$$S = \frac{\partial R_0}{\partial P} \times \frac{P}{R_0},$$

where P is the parameter under consideration. Positive sensitivity index means an increase in that parameter will lead to a corresponding increase in the basic reproduction number. However, negative sensitivity index means an increase in parameter will lead to a decrease in the basic reproduction number. The sensitivity indices for the various Malaria, Zika virus and Elephantiasis sub-model only are given in Table 3.

Table 3: Sensitivity index for the various model parameters

Malaria Only	Parameter Value	Sensitivity Index
Π_h	800	-0.4655
Π_m	1000	0.4857
μ_h	0.00004	0.4857
μ_m	0.1429	-0.9107
Θ_m	0.034	0.9974

Δm	0.6502	0.9974
T_m	0.05	-0.4655
H	0.05	-0.2428
Zika Virus Only	Parameter Value	Sensitivity Index
Π_h	800	-0.4350
Θ_z	0.40	1.00
Δ_z	0.12	0.10012
T_z	0.02	-0.4350
Π_m	1000	0.4887
μ_h	0.00004	0.4887
μ_m	0.1429	0.8337
Elephantiasis Only	Parameter Value	Sensitivity Index
Π_h	800	-0.4363
Π_m	1000	0.4848
μ_h	0.00004	0.4880
μ_m	0.1429	-0.8337
Θ_f	0.034	0.9987
Δ_f	0.6502	0.9987
T_f	0.125	-0.4363

The graph of the sensitivity analysis is also performed using the Latin Hypercube Sampling (LHS); a stratified Monte Carlo sampling scheme applicable to many parameters from a multi-dimensional distributions.

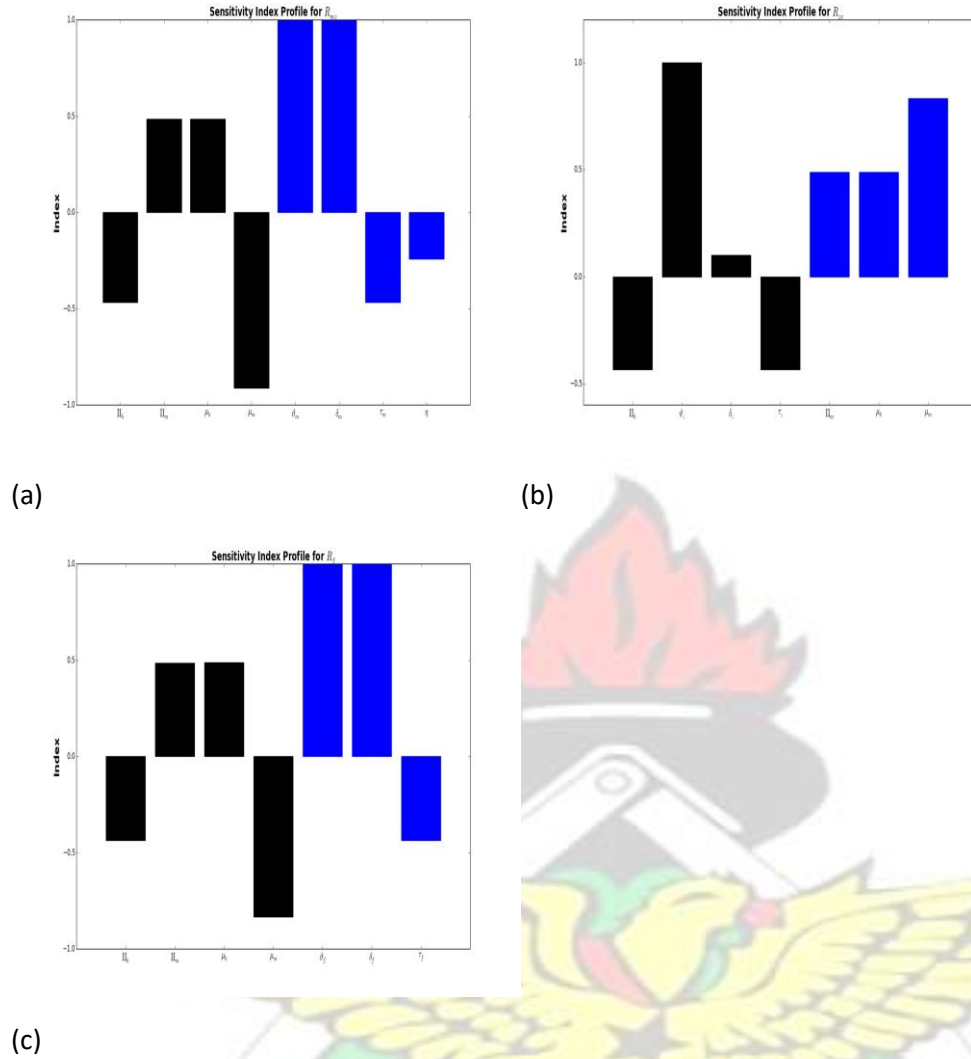


Figure 13: Simulation graph for the effect of parameter values of (a) Malaria only sub-model; (b) Zika virus only sub-model and (c) Elephantiasis only sub-model on R_0 .

Figure 13 shows the tornado plots of partial rank correlation coefficients (PRCCs) of parameters that influence the basic reproduction number R_0 for the input using values in Table 3. Parameters with $PRCC > 0$ increases R_0 when they are increased and those with $PRCC < 0$ decreases when the R_0 is increased.

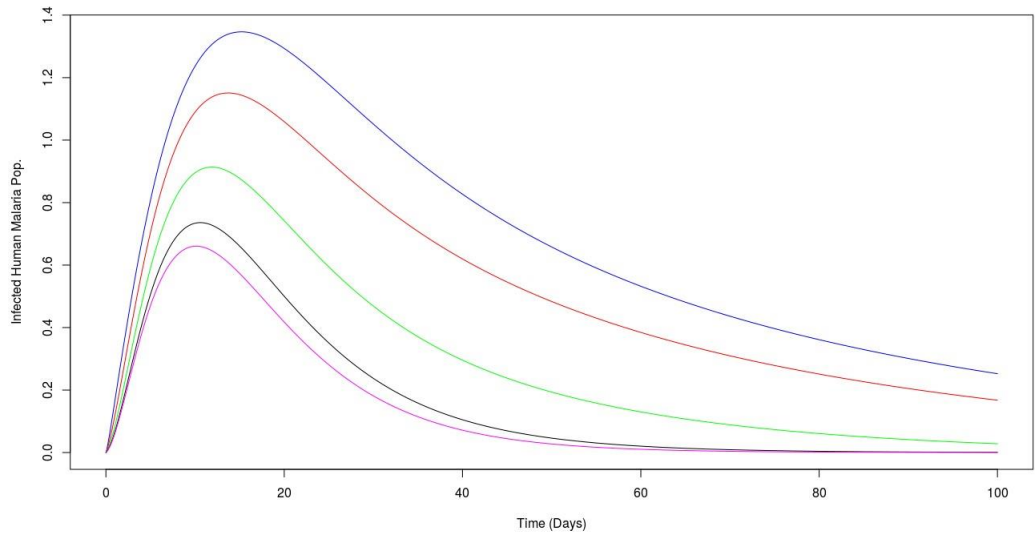


Figure 14: Depicts the changes in the number of individuals with malaria for different values of θ_m and δ_m .

Figure 14 track the changes in the population of individuals infected with malaria. It was observed that the infected human population with malaria would increase if the probability of transmission of infection from a mosquito with parasite infection to a susceptible human given that a contact between the two occurs. It also increases as well as if there is also an increase in the number of bites of humans per Anopheles mosquito per unit time. With parameter values shown in Table 3 and also using the following values for the state variables; $S_h = 0.30$,

$I_m = 0.2, I_f = 0.2, I_z = 0.2, I_z = 0.2, I_{mz} = 0.2, I_{mf} = 0.2, I_z f = 0.2, I_{mfz} = 0.2, R_m = 0, R_f = 0, R_z = 0, S_m = 0.40, I_p = 0.1, I_w = 0.1, I_a = 0.1$, we observe that when we set the values for both θ_m and δ_m to 0.1 the graph settles at the disease free equilibrium shown by the magenta colour and this is due to the small probability of transmission as well as the low occurrence of bites of humans by anopheles mosquito. But if the values of θ_m and δ_m is increased to 0.3, 0.5, 0.7, and 0.9, the infected human population with malaria also increase as respectively shown by the black, green, red and blue line in the graph. Therefore, for an increases in probability of transmission and the number of

bites of humans by anopheles mosquito there will be a corresponding increase in the number of individuals infected with malaria.

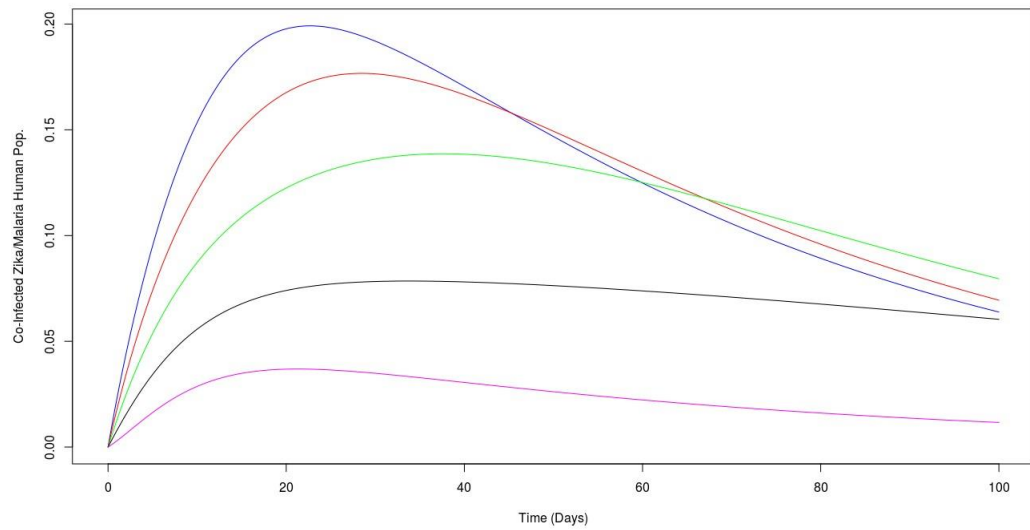


Figure 15: shows the changes in the number of individuals with Malaria and Zika virus for different values of θ_m , θ_z , δ_m and δ_z .

For the given parameter values shown in Table 3 and using the values for the state variables shown in the explanation of Figure 14 and also varying the values for θ_m , θ_z , δ_m and δ_z we determine their effect on the co-infected malaria and Zika compartment. It was noticed that if the probability of transmission of both θ_m and θ_z are high and relate positively with also a high number of bites of humans by mosquito (that is a corresponding high values of θ_m and θ_z) then the probability of one being infected with both disease is very high. In Figure 15 it was observed that when we set $\theta_m = \theta_z = \delta_m = \delta_z = 0.1$ respectively the magenta line, the level of transmission is not effective and the individuals in the co-infected population tends to zero. However, the number of individuals in the co-infected population increases when the values are increased to 0.3, 0.5, 0.7 and 0.9 shown by their respective colours black, green, red and blue. In the case of the multi-infected compartment, it was observed that the value of the state variable (I_{mfz}) has more effect on the compartment compared to the major transmission parameters that has to do with the multi-infected

differential equation $(\theta_m, \theta_f, \delta_m, \delta_f \text{ and } \delta_z)$ as shown in Figures 16 and 17 respectively.

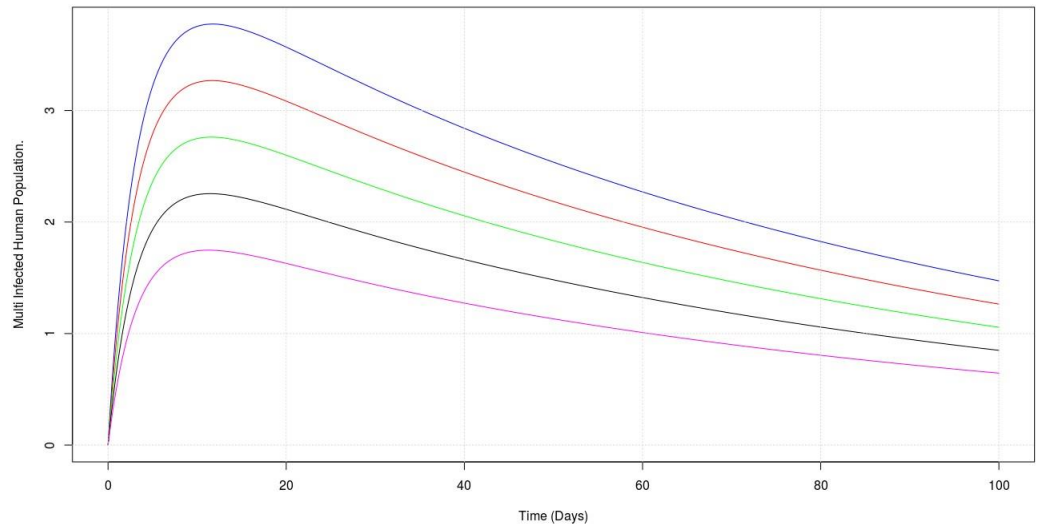


Figure 16: Simulation graph for the effect of varying values of the state variables on the multi-infected population.

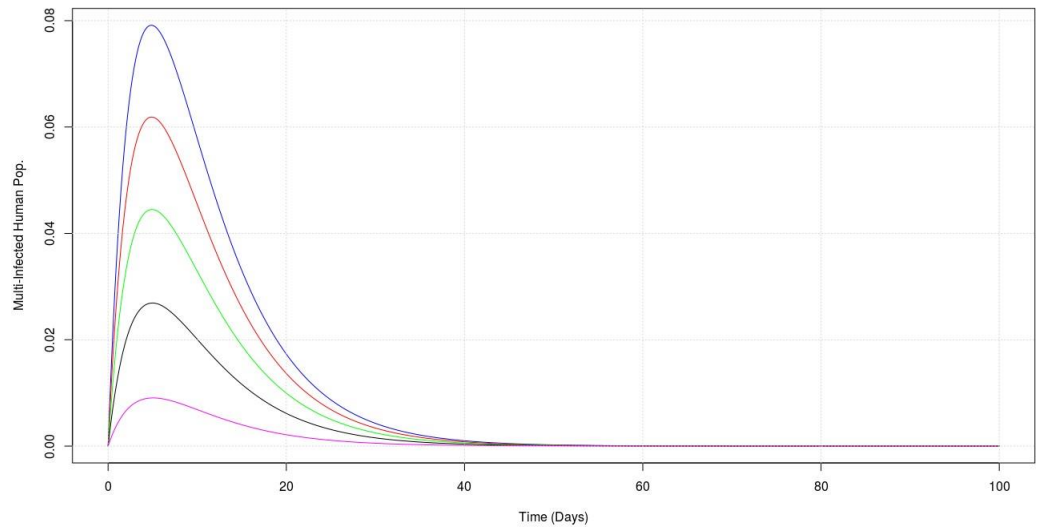


Figure 17: Simulation graph for the effect of varying parameter values on the multi-infected population.

From Figure 16, it is observed that when you set the value of the state variable of the multi-infected compartment (I_{mzf}) to 70, the disease settles at the endemic state and this increases when the value is further increased from 70 to 90, 110, 130 and 150 as represented by the respective magenta, black, green,

red and blue line. However, in Figure 17, it is observed that no matter how much you increase the corresponding values for the transmission parameters for the various disease (that is malaria, elephantiasis and Zika) indicated by $(\theta_m, \theta_f$ and $\theta_z)$ from 0.1, 0.3, 0.5, 0.7 and 0.9 together with an increase in their corresponding number of bites per unit time $(\delta_m, \delta_f$ and $\delta_z)$ also from 0.1, 0.3, 0.5, 0.7 and 0.9 shown by the magenta, black, green, red and line respectively, the graph tends to zero.

In conclusion, multi-infection model was formulated. Through the various submodels namely co-infected Malaria and Elephantiasis only; con-infected Malaria and Zika virus only; co-infected Zika virus and Elephantiasis only; Malaria only, Elephantiasis only and Zika virus only were derived. Through the various sub models stability analysis were examined and they were showed to exhibit a backward bifurcation. Sensitivity analysis were also performed using the Latin hypercube sampling Monte Carlo Sampling (LHS) scheme applicable to many parameters from a multi-dimensional distribution. From the analysis it was observed that parameters with $PRCC > 0$ increases the basic reproduction number when they are increased and vice versa.

CHAPTER FOUR
OPTIMAL CONTROL ON MULTI-INFECTION MODEL
(MALARIA-ZIKA VIRUS AND ELEPHANTIASIS)

4.1 Optimal Control Problem

In this section the optimal control of the model is discussed by minimizing the spread of the multi-infection Malaria-Zika virus and Elephantiasis using control parameters u_1, u_2, u_3, u_4, u_5 and u_6 . The description of the control parameters are such that

- u_1 ; represents the effort to reduce acquisition of malaria through the use of such measures as insecticide treated nets.
- u_2 ; represents the individual protecting themselves from female *Aedes aegypti* mosquitoes through the wearing of long sleeves, individual applying insecticides.
- u_3 ; represents individual applying insecticides to increase the death rate of the *Culex* mosquito in order to reduce its contact rate with humans.
- u_4 ; represents providing treatment controls to curtail the transmission of malaria.
- u_5 ; represents using condoms during sexual intercourse that helps to reduce the transmission of Zika virus.
- u_6 ; represents the drug that lower microfilariae in the bloodstream of elephantiasis infected people.

The general formulation and the derivation of the Euler-Lagrange optimality conditions for an Optimal Control Problem can be presented using the following control induced System:

$$\frac{dv}{dt} = f(x, u, t), x(0) = x_0, \quad (4.1)$$

where $x(t)$ is the state variable, $u(t)$ stands for the control parameter and t is the time. System (3.1) is modified by fixing in the control parameters to obtain;

$$\begin{aligned} \frac{dS_h}{dt} &= -(\pi_1 \theta_m \delta_{mlp} + u_3 \psi) R \theta_{mf} \delta + f I \phi_w R S_{hf} - (1-u_1) N_h S_h - \mu_h S_h \\ \frac{dI_m}{dt} &= (1-u_1) \frac{N_h}{\theta_m \delta_{mlp}} S_h - (\mu_h + \eta + \tau_m) I_m + \tau_f I_{mf} + \tau_z I_{mz} dt \\ \frac{dI_{mf}}{dt} &= ((\tau_1 m I_{mf} - m f u u_2 + \tau_3)) \theta \tau_{fz} N I \delta_{fz} N \delta_{hz} I_{hf} - a I_w I_m (S_{1-h} - (u_1 (2-\mu)_h \theta u + z_3 N \delta)_h \tau_z \theta I_{fa}) f N I I \delta_{fz} I_{hf} - I_w (1-u_1) \theta m N \delta_{hmlp} I_f \\ \frac{dI_{mz}}{dt} &= (1-u_2) \frac{\theta_z \delta_{zla}}{N_h} S_h - (\tau_z + \mu_h) I_z - (1-u_1) \frac{\theta_m \delta_{mlp}}{\theta_f \delta_f I_{wlz}} I_z dt \\ \frac{dI_{mf}}{dt} &= (1-u_3) \frac{\theta_f \delta_f I_w}{N_h} I_m - (\mu_h + \eta + \tau_m + \tau_f) I_{mf} + \tau_z I_{mzf} dt \end{aligned}$$

$$\frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) = \left(\frac{1}{N} \frac{dN}{dt} \right) \theta \theta$$

$$\theta_{zm} N_z N \delta N \delta h_z h_z m l l a l a l p l m f l f_z - + (+ (\mu_1 h_1 - + - \tau \tau u_1 f_3)) + \theta \theta m \tau N f_z \delta N \delta) h m h l f_z f l l p w + l f_z, \tau m l m z f$$

KNUST (4.2)

$$\frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) = (1 - u_1) \frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) - (\mu_h + \eta + \tau_m + \tau_f + \tau_z) l m z f$$

$$\left. \begin{aligned} & + (1 - u_2) \theta_z \delta_z l a l m f, \\ & \frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) \\ & \frac{dR_m}{dt} = \tau_m u_4 l_m - (\mu_h + \psi) R_m, \end{aligned} \right\} \frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) + (1 - u_3) \theta_f \delta_f l w l m z$$

$$\frac{dR_f}{dt} = \tau_f u_6 l_f - (\mu_h + \phi) R_f,$$

$$\frac{dR_z}{dt} = \tau_z u_5 l_z - \mu_h R_z,$$

$$\frac{dS}{dt} = \Pi_m - \mu_m S_m - (1 - u_1) \theta \frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) - m \delta_m (l_m + l_m z N_h + l_m f + l_m z f) S_m$$

(4.3)

$$\frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) - (1 - u_2) \theta \frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) - z \delta_z (l_z + l_m z N_h + l_z f + l_m z f) S_m$$

$$\theta \frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) - (1 - u_3) \theta \frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) - f \delta_f (l_f + l_m f N_h + l_z f + l_m z f) S_m$$

$$\frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) \frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) = (1 - u_1) \theta \frac{d}{dt} \left(\frac{1}{N} \frac{dN}{dt} \right) - m \delta_m (l N_m h + l_m z f) S_m - \mu_m l p$$

$$\begin{aligned} \frac{dI_w}{dt} &= (1-u_3)\theta \frac{f \delta_f (I N_f h + I m z f)}{N_h} S_m - \mu m l w \\ \frac{dI_a}{dt} &= (1-u_2)\theta \frac{z \delta_z (I z + I m z f)}{N_h} S_m - \mu m l a. \end{aligned}$$

It is important to note that the control variables are bounded and measured with Lebesgue measurable on $[0,1]$ such that when u_i for $i = 1,2,3,4,5,6$ equals zero then the control is not effective in helping to eradicate the disease whiles for $u_i = 1$ implies that the controls are effective in eradicating the disease. To apply the method, the following objective function is considered;

$$J(u_1, u_2, u_3, u_4, u_5, u_6) = \int_0^T [Y_1 I_m + Y_2 I_f + Y_3 I_z + Y_4 I_{mz} + Y_5 I_{mf} + Y_6 I_{zf} + Y_7 I_{mzf} + Y_8 N_m + \frac{1}{2} (Z_1 u_1^2 + Z_2 u_2^2 + Z_3 u_3^2 + Z_4 u_4^2 + Z_5 u_5^2 + Z_6 u_6^2)] dt. \quad (4.4)$$

In Equation (4.4), T is the final time, Y_i for $i = 1,2,3,4,5,6,7$ are the cost associated with minimizing the infected human population and Y_8 represent the cost associated with minimizing the infected vector (mosquito) population. The functional objective also includes $\frac{1}{2}(Z_i u_i^2)$ for $i = 1,2,3,4,5,6$ which relates to the use of insecticides treated nets; individuals protecting themselves through the wearing of long sleeves; applying insecticides to increase death rate of Culex mosquito to reduce its contact with humans; providing treatment controls to curtail the transmission of malaria; using condoms during sexual intercourse that helps to reduce the transmission of Zika virus; and providing drug that lower microfilariae in the bloodstream of elephantiasis infected individuals. Again, the total mosquito population represented as $N_m = I_p + I_w + I_a$ is included in the objective function. Thus,

$$J(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*) = \min J(u_1, u_2, u_3, u_4, u_5, u_6)$$

where $U = \{u = (u_1, u_2, u_3, u_4, u_5, u_6) \mid u_i(t) \text{ is Lebesgue Measurable, } 0 \leq u_i(t) \leq u_{i\max}(t) \leq 1 \text{ for } t \in [0, T] \rightarrow [0, 1], i = 1, 2, 3, 4, 5, 6\}$ is the control set subject to Systems (4.2) and (4.3) together with appropriate initial conditions.

The necessary condition for the application an optimal solution is applied in (Pontryagin et al., 1962). The Pontryagin principle converts Systems (4.2), (4.3) as well as Equation (4.4) into a problem of minimizing point wise Lagrangian L and Hamiltonian H with respect to u_i for $i = 1, 2, 3, 4, 5, 6$. The Lagrange of the control problem which is the Hamiltonian augmented with penalty terms for control constraints consists of the integrand of the objective functional and is given by:

$$L = Y_1 I_m + Y_2 I_f + Y_3 I_z + Y_4 I_{mz} + Y_5 I_{mf} + Y_6 I_{zf} + Y_7 I_{mzf} + Y_8 N_m + (z_1 u_1^2 + Z_2 u_2^2 + Z_3 u_3^2 + Z_4 u_4^2 + Z_5 u_5^2 + Z_6 u_6^2). \quad (4.5)$$

That is to say the Hamiltonian H , is the combination of the Lagrange together with the right hand side of Systems (4.2), (4.3) and the co-state variables or the adjoint variable. Hence,

$$\begin{aligned} H = & L + Y_{Sh} \frac{dS_h}{dt} + Y_{Im} \frac{dI_m}{dt} + Y_{If} \frac{dI_f}{dt} + Y_{Iz} \frac{dI_z}{dt} + Y_{Imz} \frac{dI_{mz}}{dt} + Y_{Imf} \frac{dI_{mf}}{dt} \\ & + Y_{Izf} \frac{dI_{zf}}{dt} + Y_{Imzf} \frac{dI_{mzf}}{dt} + Y_{Rm} \frac{dR_m}{dt} + Y_{Rf} \frac{dR_f}{dt} + Y_{Rz} \frac{dR_z}{dt} + Y_{Sm} \frac{dS_m}{dt} \\ & + Y_{Ip} \frac{dI_p}{dt} + Y_{Iw} \frac{dI_w}{dt} + Y_{Ia} \frac{dI_a}{dt} \\ = & Y_1 I_m + Y_2 I_f + Y_3 I_z + Y_4 I_{mz} + Y_5 I_{mf} + Y_6 I_{zf} + Y_7 I_{mzf} + Y_8 N_m \end{aligned}$$

$$\begin{aligned}
& + \frac{1}{2} (Z_1 u_1^2 + Z_2 u_2^2 + Z_3 u_3^2 + Z_4 u_4^2 + Z_5 u_5^2 + Z_6 u_6^2) \left(\begin{array}{c} + \quad + \quad - \quad - \quad \frac{\theta_m \delta_{mlp}}{\theta_z \delta_{zla}} \\ + Y_{Sh} \Pi_h \psi R_m \phi R_f \end{array} \right) + \left(\begin{array}{c} - \quad 1 \quad u_1 \end{array} \right) \frac{S_h - \mu_h S_h}{N_h N_h} \\
& - (1 - u_2) \frac{\theta_f \delta_f l_w \theta_m \delta_{mlp}}{N_h N_h} \\
& - (1 - u_3) \frac{S_h}{N_h N_h} Y_{lm} \frac{1}{N_h} \frac{u_1}{N_h} \frac{S_h - (\mu_h + \eta + \tau_m) l_m + \tau_f l_{mf}}{N_h} \\
& + \tau_z l_{mz} - (1 - u_2) \theta \frac{z \delta_{zla} l_m}{N_h} - (1 - u_3) \theta \frac{f \delta_f l_w + Y_{lf} (1 - u_3)}{N_h N_h} \frac{\theta_f \delta_f l_w S_h}{N_h} \\
& - (\mu_h + \tau_f) l_f - (1 - u_1) \frac{\theta_m \delta_{mlp}}{N_h} \frac{l_f + \tau_m l_{mf} + \tau_z l_{zf} - (1 - u_2)}{N_h} \frac{\theta_z \delta_{zla}}{N_h} l_f \\
& + Y_{lz} \left(\begin{array}{c} - u \end{array} \right) \frac{\theta_z \delta_{zla}}{N_h} \frac{\theta_m \delta_{mlp}}{N_h} \frac{1}{N_h} \frac{2}{N_h} \frac{S_h - (\tau_z}{N_h} \\
& + \mu_h) l_z - (1 - u_1) \frac{Y_{lf}}{N_h} \left(\begin{array}{c} - u \end{array} \right) \frac{l_z + \tau_m l_{mz} + \tau_f l_{zf}}{N_h} \frac{1}{N_h} \frac{2}{N_h} \frac{S_h - (\tau_z}{N_h} \\
& - (1 - u_3) \theta \frac{f \delta_f}{N_h N_h} \frac{\theta_z \delta_{zla} l_m - (\mu_h + \eta + \tau_m + \tau_z) l_{mz} + \tau_f l_{mzf}}{N_h N_h} \\
& - (1 - u_3) \theta \frac{f \delta_f l_w l_{mz}}{N_h} \frac{1}{N_h} \frac{u_1}{N_h} \frac{\theta_m \delta_{mlp} l_z Y_{lmf}}{N_h N_h} \frac{(1 - u_3) \theta}{N_h} \frac{f \delta_f l_w l_m}{N_h} \\
& - (\mu_h + \eta + \tau_m + \tau_f) l_{mf} + \tau_z l_{mzf} - (1 - u_2) \frac{\theta_z \delta_{zla}}{N_h} \frac{l_{mf} + (1 - u_1)}{N_h} \frac{\theta_m \delta_{mlp}}{N_h} l_f \\
& + Y_{lzf} \left(\begin{array}{c} - u \end{array} \right) \frac{\theta_z \delta_{zla}}{N_h} \frac{\theta_m \delta_{mlp}}{N_h} \frac{1}{N_h} \frac{2}{N_h} \frac{S_h - (\tau_z}{N_h} \\
& + \tau_z) l_{zf} + \tau_m l_{mzf} \left(\begin{array}{c} - (1 - u_1) \end{array} \right) \frac{1}{N_h} \frac{2}{N_h} \frac{S_h - (\tau_z}{N_h} \\
& + Y_{R_z} \left(\tau_f u_6 l_f - (\mu_h + \phi) R_f \right) + Y_{R_z} \left(\tau_z u_5 l_z - \mu_h R_z \right) + Y_{S_m} \left(\Pi_m - \mu_m S_m \right)
\end{aligned}$$

$$\begin{aligned}
& -\frac{(1-u_1)\theta}{N_h} \frac{m\delta m(l_m + l_{mz} + l_{mf} + l_{mzf})}{z\delta z(l_z + l_{mz} + l_{zf} + l_{mzf})} S_m - \frac{(1-u_2)\theta}{N_h} \\
& -\frac{(1-u_3)\theta}{Y_{lp}} \frac{f\delta f(l_f)}{\left((1-u_3) \right)} + \left(\left(- \right) + l_{mf} + l_{zf} + l_{mzf} \right) \\
&) S_m + Y_{la} \left((1-u_2) \right) \frac{N_h}{1u_1\theta} \frac{m\delta m(l_m + l_{mzf})}{N_h N_h} \\
& -\mu m l_p \\
& + Y_{lw} \frac{\theta_f \delta f(l_f + l_{mzf})}{S_m - \mu m l_w} - \frac{\theta_z \delta z(l_z + l_{mzf})}{S_m - \mu m l_a}, \text{ where,}
\end{aligned}$$

$$Y_{Sh}, Y_{lm}, Y_{lf}, Y_{lz}, Y_{lmz}, Y_{lmf}, Y_{lzf}, Y_{lmzf}, Y_{Rm}, Y_{Rf}, Y_{Sm}, Y_{lp}, Y_{lw}, Y_{la}$$

are the adjoint variables or co-state variables. The System of equations is found by taking the appropriate partial derivatives of the Hamiltonian with respect to the associated state variables.

Theorem 26

Given optimal controls $u_1, u_2, u_3, u_4, u_5, u_6$ and solutions $S_h, l_m, l_f, l_z, l_{mz}, l_{mf}, l_{zf}, l_{mzf}, R_m, R_f, S_m, l_p, l_w, l_a$ of the corresponding state of Systems (4.2) and (4.3) and the Hamiltonian that minimizes $J(u_1, u_2, u_3, u_4, u_5, u_6)$ over U , then there exist adjoint variables $Y_{Sh}, Y_{lm}, Y_{lf}, Y_{lz}, Y_{lmz}, Y_{lmf}, Y_{lzf}, Y_{lmzf}, Y_{Rm}, Y_{Rf}, Y_{Sm}, Y_{lp}, Y_{lw}, Y_{la}$ satisfying:

$$\frac{dY_i}{dt} = -\frac{\partial H}{\partial i}$$

with transversality conditions:

$$\begin{aligned}
Y_{Sh}(T) &= Y_{lm}(T) = Y_{lf}(T) = Y_{lz}(T) = Y_{lmz}(T) = Y_{lmf}(T) = Y_{lzf}(T) = Y_{lmzf}(T) = Y_{Rm}(T) = Y_{Rf}(T) \\
&= Y_{Sm}(T) = Y_{lp}(T) = Y_{lw}(T) = Y_{la}.
\end{aligned}$$

$$\left(\left[(1-u_1) \frac{\vartheta_m \delta}{N_h^2} \frac{\theta_z \delta_{zla}}{S_h} + (1-u_2) \frac{\theta_f \delta_{flw}}{N_h^2} + (1-u_3) \frac{\theta_f \delta_{flw}}{N_h^2} S_h \right] \right. \\ \left. + \left[-(1-u_1) \frac{\vartheta_m \delta}{N_h^2} \frac{\theta_z \delta_{zla}}{Y_{Sh} + Y_{1mlp}} \right] \right) S$$

$$\left[\frac{\theta_z \delta_{zla} I_m - (1-u_3) \theta_f \delta_{hf-lw} + (\mu_h + 1 - \eta u + 3) \tau \theta_m}{N_h^2} \right] Y_{Im} + \left[\frac{u_2}{N_h^2} \frac{N_h}{f} \frac{I_f}{I_f} + (1-u) \frac{\vartheta_z \delta_z I_a}{N_h^2} I \right] Y + \left[-(1-u) \frac{N_h^2}{N_h^2} \right] \\ \frac{\theta_z N_f N \delta \delta_{h2z} h_2 f l l a w S S_{hh} + (\theta + (z1 \delta 1 z - l - a u u)) \theta \theta_m N m \delta_h \delta m m l p l p l z l}{N_h^2} \\ + (1-u) \frac{\vartheta_f \delta_f I_w}{N_h^2} I \left] Y + \left[(1-u) \frac{\theta_f \delta_{flw}}{N_h^2} \theta_m \delta_{mlp} \theta_{u2z} N \right) \delta_{hzla} \right] \\ \left[-(1-u_2) \frac{I_m + (1-u_3) I}{N_h^2} \right]$$

$$S_m \left[Y_{I_p} - \left[(1-u_3) \frac{N_h^2}{N_h^2} \right] \frac{m \delta_m (I_m + I_{mzf})}{N_h^2} \right] \frac{\theta_f \delta_f}{N_h^2} \\ (I_f + I_{mzf}) S_m \left[Y_{I_w} \right]$$

$$I_{mzf}) \frac{Y_{I_{\alpha^*}}}{N_h^2}$$



$$\begin{aligned}
& - \frac{\theta_m \delta m l p}{l_{zf}} = dt m p \theta_f \delta f l w \theta_m \delta m l p \\
& \frac{\theta_z \delta z l a}{N_h^2 Y_{l_{zf}}} \frac{\theta_f \delta f l w}{N_{h2} l_{zf}} \\
& + (1 - u_2) \frac{N_h^2 \theta}{l_{mf} + l_{mzf}} \left| \frac{N_h^2}{S_m + (1 - u_2)} \right| + \left[(1 - u_1) \vartheta_m \delta_m (I_m + I_{mz} + z \delta z l a l_{mf} Y_{l_{mzf}} + \left[\tau_f u_6 \right] Y_{R_f} \right. \\
& \left. \frac{\theta_f \delta f l w l_{mz}}{N_h^2} \right] \\
& \left[\frac{\theta_z \delta z (l_z + l_{mz} N_h + 2 l_{zf} + l_{mzf})}{N_h^2} \right] \frac{S}{Y} \frac{S}{Y} \\
& - \left[(1 - u_3) \frac{\vartheta_f \delta}{N_h} \right] \frac{S}{Y} + \left[- (1 - \right. \\
& \left. \vartheta_z \delta_z (I_z + S_m) \right] - \left[(1 - u_1) \vartheta_m \delta_m (I_m + \right. \\
& \left. N_{h2} l_{mzf}) S_m Y_{lp} \right] \\
& \frac{f}{S_m} + (1 - u_3) \frac{\theta_f \delta f (l_f + l_{mzf})}{N_h^2} \frac{m}{l_w u_2) \\
& \left(\frac{N_h^2}{Y_{l_{\alpha}}} \right) \left[(1 - u_1) \frac{N_h^2 \theta_m \delta m l p}{\theta_z \delta z l a} + (1 - u_1) \frac{S}{\theta \delta l} \right]
\end{aligned}$$

$$\begin{aligned}
& \frac{\theta_m \delta m l p}{I_{zf} + (1 - u_3)} - \frac{\theta_z \delta z l a}{N_h} - \frac{\theta_f \delta f l w}{N_h^2} \\
& - (1 - u_3) \frac{\theta_f \delta f l w m l p}{N_h^2} - \frac{\theta_f \delta f l w}{Y_{lzf} - (1 - u_1)} - \frac{\theta_f \delta f l w}{I_{zf} + (1 - u_3)} - \frac{\theta_f \delta f l w}{I} \\
& \frac{(\theta_m l \delta - m(u l m_2) + \theta_z N_h^2 l \delta m_z N_{zh} l_2 + a l m f l m f + Y_{l m z f} l m z f) S_m}{- (1 - u_2) \theta_{Nz} \delta_{hz} u S_{1m}) + (1 - u_2) N_{h2} m_z} \\
& \left| \frac{\theta_z \delta z (l_z + l_{mz} + l_{zf} + l_{mzf})}{S_m^3} - \frac{\theta_f \delta f (l_f + l_{mf} + l_{zf} + l_{mzf})}{N_h^2 + (1 - u)} \right. \\
& \left. \frac{S_m Y_{S_m}}{S_m Y_{S_m}} \right| \\
& \left[+ (1 - u_2) \frac{\vartheta_z \delta}{N_h} - (1 - u_1) \frac{N_h^2 N \theta_{mh2} \delta_m (l_m + l_{mzf})}{N_h^2 \theta_f \delta_f (l_f + l_{mzf})} \right] Y_{I_p} - \left[(1 - u_3) \frac{S_m}{Y_{I_w}} \right] \\
& \frac{z}{S_m - (1 - u_2)} - \frac{\theta_z \delta z (l_z + l_{mzf})}{N_{h62}} - \frac{S_m Y_{I_a}}{S_m Y_{I_a}}
\end{aligned}$$

$$\begin{aligned} & \left[\begin{array}{c} \theta_m \delta_{mlp} \\ \vartheta_m \delta_{mlp} \end{array} \right] \begin{array}{c} \theta_f \delta_f l_w \\ \theta_f \delta_f l_w \end{array} \begin{array}{c} \theta_z \delta_z l_a \\ \theta_z \delta_z l_a \end{array} \begin{array}{c} \theta_f \delta_f l_w \\ \theta_f \delta_f l_w \end{array} \\ & \theta N_{h2} l_{zf} \quad N_h^2 \quad Y_{lzf} \quad N_h^2 \quad l_{zf} + (1-u_3) \end{aligned}$$

$$\begin{aligned} & f N \delta_{hf} l_w \quad -(1-u_3) \theta_{l_{fm}} N_h^2 \delta_{+f} \\ & l_w l_{mz} l_{mz} + - l_{mf} (1 + - l_{umzf})^2 N_h^2 \theta_z \delta_z l_a l_{mf} Y_{l_{mzf}} \theta_z + \left[- (1 - \delta_z \right. \end{aligned}$$

$$\begin{aligned} & \theta_m \delta_m \quad h \quad N_{h2} \quad m \quad -(1-u_2) \quad N_h \quad S_m \quad N \quad S_m \quad + (1-u_1) \\ & + (1 - \frac{S}{S_m}) \quad - \left[(1-u_1) \quad N_h^2 \quad + l_{zf} \right. \\ & \left. \theta_z \delta_z (l_z + l_{mz} + l_{mzf}) \theta_m \delta_m (l_m + l_{mzf}) u_2 \right) Y_{S_m} \end{aligned}$$

$$\begin{aligned} & S_m \quad Y_{I_p} - \left[(1-u_3) \quad N_h^2 \theta_f \delta_f \right. \\ & + l_{mzf}) S_m \left] Y_{I_w} - \left[(1-u_2) \quad N_h^2 \theta_z \delta_z (l_z + l_{mzf}) \quad S_m \right] Y_{I_a} \end{aligned} \quad (I_f)$$

$$\begin{aligned}
 & \left[5 I_{mf} + \left[(1 - u_1) \frac{N_h^2}{Y N} \right] \right. \\
 & + (1 - u_3) \frac{2 S_h Y S_h}{Y N} \\
 & + \left[- (1 - u_1) \frac{N_h^2}{Y N} \tau_f \right. \\
 & + \left[- (1 - u_3) \frac{N_h^2}{Y N} \tau_m \right. \\
 & + \left[- (1 - u_2) \frac{N_h^2}{Y N} \tau_{hh} \right. \\
 & + \left[- (1 - u_2) \frac{N_h^2}{Y N} \tau_{hh} \right. \\
 & + \left[- (1 - u_3) \frac{N_h^2}{Y N} \tau_{hh} \right. \\
 & = \left\{ \begin{aligned} & + (1 - u_2) \frac{N_h^2}{Y N} \tau_{hh} \\ & + (1 - u_3) \frac{N_h^2}{Y N} \tau_{hh} \end{aligned} \right\} \\
 & \theta \theta \theta \theta \theta_{zmz} \\
 & f f \delta \delta \delta \delta \delta_{zzm} f f l l l a a l w w S l p m l S_h S_{mh} + (+ (h - + + 1 (1 \mu - -_h + (+ (u + u) \eta) 1 1 \theta \theta - - + m f \\
 & u \delta u \delta \tau_{mf m})) l l w + \theta \theta p l m z l m z \tau_z \delta \delta_{f z m}) l a - l p l m l (1_f + (- 1 u_2 - \theta) \theta_f \theta u m \delta z N \delta f) \delta l m_h \theta z w l \theta l a f p z \delta + (\delta f z Y l l \\
 & w l Y a 1_z l l m z - m u Y Y 2 l l f)_m \\
 & d Y l_{mf} \theta_z \delta z l a \quad \theta_m \delta m l p \quad \theta_z \delta z l a
 \end{aligned}$$

[illegible]

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$\theta \theta \theta \theta m m z f f \delta \delta \delta \delta z z m f f l l l l a N l a w w l p h_2 S m l S S_{m h h} + (h + (+ (+ (S h 1 1 1 1 + (-----u 1 u u u -) 2))) \theta \theta u \theta \theta$
 $\theta_f N_2 m z m \delta_z) \delta_h \delta \delta \delta_f z 6 2 m z l m l l w a l a l p l l p m f m z l m l f f S - h (+ (1 - 1 u - 3$
 $) u \theta \theta \theta_3 N) f m m h \delta \delta \delta 6 2 f m m l N \theta \theta w l l h z_2 f p - \delta \delta m l z f f l p l S a Y w Y h l m l m f Y Y Y S l Y m z h l f z$

$$\begin{aligned} & dY_{l_z} \theta_z \delta_{zla} \\ & \frac{-l_f - (\mu_h + \tau_f)}{N_h^2} + \tau_z - (1 - u_1) + (1 - u_1) \frac{\theta_m \delta_{mlp}}{dt N_h} \\ & - (1 - u) \left[\frac{\vartheta_f \delta_f l_w}{I} \right] + \left[(1 - u)_3 \frac{N_h^2}{z} \right. \\ & \left. \frac{\theta_m N \delta_{h2mlplzf} Y_{l_z f1} \theta_m N \delta_{hmlp} - (1 - u_1)}{N_h^2} + \left[(1 - \right. \right. \\ & \left. \left. \frac{\theta_m \delta_{mlp}}{N_h^2} \frac{\theta_f \delta_f l_w}{N_h^2} \frac{\theta_z \delta_{zla}}{N_h^2} l_z f - (1 - u) l_{mz} \right. \right. \\ & \left. \left. - (1 - u) l_{mf} Y_{l_{mzf} u_1} \theta_m \delta_m (l_m + l_{mz} + l_{mf} + l_{mzf}) \theta_z \delta_z \right. \right. \\ & \left. \left. \frac{S_m}{N_{h2}} - (1 - u_2) \frac{S_m + (1 - u_2)}{N_h} \right] \right] \end{aligned}$$

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$$\begin{aligned}
 & \left[\begin{array}{c} \theta_f \delta_f (I_f + I_{mf}) \\ \theta_m \delta_m (I_m + I_{mzf}) \end{array} \right] \left[\begin{array}{c} - (1 - u_3) \theta N_f \delta_h f S_m + (1 - u_3) \\ S_m \end{array} \right] Y_{S_m} - \left[\begin{array}{c} (1 - u_1) \\ N_h^2 \end{array} \right] S_m \Bigg] \\
 & \quad \quad \quad \theta_z \delta_z (I_z + I_{mz} + 2 I_{zf} + I_{mzf}) S_m \\
 & \quad \quad \quad Y_l \\
 & \left[\begin{array}{c} \theta_f \delta_f I_w \\ Y_l I_{mzf} \\ S_h Y_{Sh} \end{array} \right] \left[\begin{array}{c} - \left[(1 - u_3) \theta_f \delta_f (I_f + I_{mf}) + (1 - u_1) N_h^2 \right] \\ + \left[(1 - u_1) N_h^2 \right] \end{array} \right] Y_{I_w} - \left[\begin{array}{c} (1 - u_2) \\ N_h^2 \end{array} \right] S_m \Bigg] \\
 & \quad \quad \quad \theta_z \delta_z (I_z + I_{mz} + 2 I_{zf} + I_{mzf}) Y_{I_w} \\
 & \quad \quad \quad \theta_m \delta_m I_p \\
 & \quad \quad \quad S_h + (1 - u^2) N_h^2 \\
 & \quad \quad \quad S_h + (1 - u^3) N_h^2 \\
 & \quad \quad \quad N_h^2
 \end{aligned}$$

$$\begin{aligned}
 & + (1 - u) \frac{1}{N_h^2} I \Big] + \Big[- (1 - u_3) \frac{1}{N_h^2} + \Big[- (1 - u_1) \frac{1}{N_h^2} \frac{2}{N_h^2} \frac{1}{N_h^2} \frac{3}{N_h^2} \frac{2}{N_h^2} \frac{1}{N_h^2} \frac{f}{N_h^2} \\
 & \quad \frac{1}{N_h^2} \frac{z}{N_h^2} + \Big[- (1 - u_2) \frac{1}{N_h^2} \tau_f \frac{3}{N_h^2} - (1 - u) \frac{1}{N_h^2} I \Big] \frac{1}{N_h^2} \\
 & \quad + \Big[- (1 - u_3) \frac{1}{N_h^2} \tau_z \frac{2}{N_h^2} \frac{1}{N_h^2} \\
 & \quad + \Big[- (1 - u_2) \frac{1}{N_h^2} \tau_m \frac{1}{N_h^2} \frac{3}{N_h^2} \\
 & \quad \Big\} + \Big[- (1 - u_1) \frac{1}{N_h^2} \\
 & \quad \frac{2}{N_h^2} \Big[\vartheta_m \delta \\
 & \quad + \Big[- (1 - u_2) \frac{\vartheta_z \delta_z}{N_h^2} \\
 & \quad \theta \theta \theta \theta z z m f f \delta \delta \delta \delta h z z m f f l l l l a a a l w w S l p m S l h S m h + + + (h + + + (111 + (+ (- + (- - u 11 u \frac{1}{N_h^2} \\
 & \quad + (1 - u) \frac{1}{N_h^2} I \Big] \\
 & \quad u 1) - - -) \theta) \theta u u \theta m u m z \delta) \delta \delta m) \theta \theta z m \theta l l m p a f l z \delta p \delta \delta l l m z l m f z \\
 & \quad f l l + (l a w p l l l m f m z f 1 - - - u ((\frac{3}{N_h^2} \frac{z}{N_h^2} \\
 & \quad 11) \theta - - \theta \theta f u u f \delta z \delta \delta f)) f z l l \theta \theta l \theta w w a m m f l \delta \delta \delta m m m f Y Y l l l Y l w z l p p l f m l l z f Y Y Y l l m z m f \\
 & \quad l \\
 & \quad l_f \\
 & \quad d Y l m z f z f \\
 & \quad - \frac{1}{dt} \theta_m \delta m l p \theta_m \delta f l w \\
 & \quad \frac{1}{S} \Big] Y + \Big[(1 - u) \frac{\vartheta_z \delta}{N_h^2} \frac{1}{S} \Big]
 \end{aligned}$$

$$z^m(\delta_1\delta_{z-m}(I(zu^l+m)+I\theta_{mz}N|zmz\delta_Nh+2z_2h_2l+|a_zf|lmfmf+|+Y_{mzf}|mzf|lmzf)S+m)S-m-(-1(1(-1-u-u_{31})u)\theta_2N)f$$

$$\theta N \delta_h N_{zhf} \delta_{hm} S_{zm} S_{mm} + (+ (+ (11 - 1 - - u_3 u u)_{12}))$$

$$\left[\begin{pmatrix} S \\ Y \end{pmatrix} + \left[(1-u)^{\vartheta_f \delta} mzf_m + l_{wl} l_p mzf \right] mY_{S2m3} - N N_h h_S f \right]$$

$$\begin{aligned}
& \left[\frac{\theta_f \delta_f l_w}{N_h^2} \left(\left[\psi + (1-u_1) \frac{\vartheta_m \delta}{N_h^2} \right] + \left[- (1-u_1) \frac{\vartheta_m \delta}{N_h^2} \right] + \left[- (1-u_3) \frac{\vartheta_f \delta_f}{N_h^2} \frac{S_h}{S_h} \frac{\vartheta_z \delta_z I_a}{\vartheta_z \delta_z I_a} \right] + (1-u_2) \frac{\vartheta_z \delta_z}{N_h^2} \frac{S_h Y_{Sh}}{S_h Y_{Sh}} + (1-u) \frac{I}{I} \right) \right. \\
& \left. + \left[- (1-u_2) \frac{\vartheta_z \delta_z}{N_h^2} \frac{S_h Y_{Sh}}{S_h Y_{Sh}} + (1-u) \frac{I}{I} \right] + \left[- (1-u_2) \frac{\vartheta_z \delta_z}{N_h^2} \frac{S_h Y_{Sh}}{S_h Y_{Sh}} - (1-u) \frac{I}{I} \right] \frac{m l_p}{\theta_z \delta_z l_a} \right. \\
& \left. + \left[- (1-u_3) \frac{\vartheta_f \delta_f I}{N_h^2} \frac{S_h + (1-u)^2 N_h^2}{S_h + (1-u)^2 N_h^2} - (1-u) \frac{I}{I} \right] + \left[- (1-u_2) \frac{\vartheta_z \delta_z}{N_h^2} \frac{S_h + (1-u)^2 N_h^2}{S_h + (1-u)^2 N_h^2} \right] \frac{1}{3} \frac{N_h^2}{N_h^2} \right. \\
& \left. - \left[(1-u_1) \frac{\vartheta_m \delta}{N_h^2} \frac{I_m Y_{Im}}{I_m Y_{Im}} - \left[\mu_h + \psi \right] + \left[(1-u_1) \frac{l_w}{N_h^2} \frac{\theta_m \delta m l_p}{S_h + (1-u)^2 N_h^2} \right] \right. \right. \\
& \left. \left. + (1-u) \frac{S}{S} \right] - \left[(1-u_1) \frac{\vartheta_m \delta_m (I_m + S_m)}{N_h^2} Y_{Ip} - \left[(1-u_3) \frac{N_h^2}{N_h^2} \frac{S_m}{S_m} \right] \right. \right. \\
& \left. \left. - \left[(1-u_2) \frac{\vartheta_z \delta_z (I_z + S_m)}{N_h^2} \right] \frac{I}{I} Y_{If} \right] \right. \\
& \left. \frac{l_a}{l_a} \frac{\theta_m \delta m l_p \theta_f \delta_f l_w}{\theta_m \delta m l_p \theta_f \delta_f l_w} \frac{S_h + (1-u)^2 N_h^2}{S_h + (1-u)^2 N_h^2} \frac{1}{3} \frac{N_h^2}{N_h^2} \frac{z}{z} Y_{Iz} \right. \\
& \left. \frac{l_a}{l_a} \frac{\theta_f \delta_f l_w \theta_m \delta m l_p}{\theta_f \delta_f l_w \theta_m \delta m l_p} \frac{I_m + (1-u)^3 N_h^2}{I_m + (1-u)^3 N_h^2} \frac{1}{3} \frac{N_h^2}{N_h^2} \frac{z}{z} Y_{Imz} \right. \\
& \left. \frac{l_a}{l_a} \frac{\theta_m \delta m l_p}{\theta_m \delta m l_p} \frac{w}{w} \frac{\theta_z \delta_z}{\theta_z \delta_z} \frac{I_m + (1-u)}{I_m + (1-u)} \frac{I_{mf} - (1-u)}{I_{mf} - (1-u)} \frac{I_f Y_{Imf}}{I_f Y_{Imf}} \right. \\
& \left. - \frac{dY_{Rm}}{dt l_a} = \frac{dt l_a}{dt l_a} \frac{1}{I_f + (1-u)^2 N_h^2} \frac{\theta_m \delta m l_p}{I_{zf}} \frac{3}{N_h^2} \frac{z}{z} Y_{Izf m l_p} \frac{\theta_f \delta_f l_w}{\theta_f \delta_f l_w} \frac{\theta_z \delta_z l_a}{\theta_z \delta_z l_a} \right. \\
& \left. \frac{I_{mf} Y_{Imzf}}{I_{mf} Y_{Imzf}} \frac{I_{zf} + (1-u)^3 N_h^2}{I_{zf} + (1-u)^3 N_h^2} \frac{I_{mz} + (1-u)^2 N_h^2}{I_{mz} + (1-u)^2 N_h^2} \right. \\
& \left. \theta_m \delta_m (I_m + I_{mz} + I_{mf} + I_{mzf}) \right.
\end{aligned}$$

$$\begin{aligned}
& - \left[(1 - u_1) \right. \\
& \quad \left. - \left[\mu_h \right] Y_{R_f} + \left[(1 - u_1) \right. \right. \\
& \quad \left. \left. + (\theta_z \delta_{1z} - I_a u Y_2) I_{mzf} \right. \right. \\
& \quad \left. \left. N_h^2 \theta_m \delta_{m l p l z f} + (\theta_m \delta_{1m} - (I u m^3 \right. \right. \\
& \quad \left. \left. N_h^2 \right) + \theta I f m z \delta_f + I w I m f I m z + I m z f \right) S_m^2 \right. \\
& \quad \left. N_h^2 \right.
\end{aligned}$$

$$\begin{aligned}
& \frac{\theta_z \delta_z (I_z + I_{mz} + I_{zf} + I_{mzf})}{S^m} \\
& \frac{\theta_f \delta_f (I_f + I_{mf} + I_{zf} + I_{mzf})}{N_h^2 + (1 - u)}
\end{aligned}$$

$$\begin{aligned}
& - \left[(1 - u_2) \right. \\
& \quad \left. N_h^2 \right. \\
& \quad \left. S_m \right] Y_{I_p} - \left[(1 - u_3) \right. \\
& \quad \left. N_h^2 Y_{I_w} \right. \\
& \quad \left. \theta_f \delta_f (I_f + I_{mzf}) \right] Y_{I_w S_m}
\end{aligned}$$

$$\begin{aligned}
& \left(- \left[\mu_m + (1 - u_1) \right. \right. \\
& \quad \left. \left. \vartheta_m \delta_m (I_m + I_{mz} + \right. \right. \\
& \quad \left. \left. N_h \right. \right. \\
& \quad \left. \left. I_{mf} + I_{mzf}) \right. \right. \\
& \quad \left. \left. + (1 - u_2) \right. \right. \\
& \quad \left. \left. \theta_z \delta_z (I_z \right. \right. \\
& \quad \left. \left. + I_{mz} + I_{zf} + I_{mzf}) \theta_f \delta_f (I_f + I_{mf} + I_{zf} + I_{mzf}) \right. \right. \\
& \quad \left. \left. S \right. \right. \\
& \quad \left. \left. N_h \right. \right. \\
& \quad \left. \left. m + (1 - u_3) \right. \right. \\
& \quad \left. \left. N_h \right. \right. \\
& \quad \left. \left. S_m Y_{S_m} \right. \right. \\
& \quad \left. \left. + \left[(1 - u_1) \right. \right. \right. \\
& \quad \left. \left. N_h \right. \right. \left. \right] Y_{I_p} + \left[(1 - u_3) \right. \\
& \quad \left. \left. N_h \right. \right. \\
& \quad \left. \left. dt \right. \right. \\
& \quad \left. \left. + \left[(1 - u_2) \right. \right. \right. \\
& \quad \left. \left. \vartheta_z \delta_z (I_z + \right. \right. \\
& \quad \left. \left. N_h \right. \right. \\
& \quad \left. \left. \theta_m \delta_m (I_m + I_{mzf}) \right. \right. \\
& \quad \left. \left. \theta_f \delta_f (I_f \right. \right. \\
& \quad \left. \left. Y_{I_w} \right. \right.
\end{aligned}$$

$$\begin{aligned}
& \frac{I_{mzf})}{Y_{I_w}} \\
& \left(\left[- (1 - u_1) \frac{\vartheta_m \delta_m}{N_h} S_h \right] Y_{S_h} + \left[(1 - u_1) \frac{\vartheta_m \delta_m}{N_h} S_h \right] Y_{I_m} - \left[(1 - u_1) \frac{\vartheta_m \delta_m}{N_h} I_f \right] Y_{I_f} \right)
\end{aligned}$$

$$\left\{ - \left[(1-u_1) \frac{\vartheta_m \delta_m}{N_h} I_{zf} \right] \right\} - \left[(1-u_1) \frac{\vartheta_m \delta_m}{N_h} I_z \right] Y_{I_z} + \left[(1-u_1) \frac{\vartheta_m \delta_m}{N_h} I_z \right] Y_{I_{zf}} + \left[(1-u_1) \frac{\vartheta_m \delta_m}{N_h} I_f \right] Y_{I_{mf}} - \left[\mu_m Y_{I_p} \right]$$

$$\begin{aligned} & \left\{ - \left[(1-u_3) \frac{\vartheta_f \delta_f}{N_h} S_h \right] Y_{S_h} - \left[(1-u_3) \frac{\vartheta_f \delta_f}{N_h} I_m \right] Y_{I_m} + \left[(1-u_3) \frac{\vartheta_f \delta_f}{N_h} S_h \right] Y_{I_f} \right. \\ & = \left\{ - \left[(1-u_3) \frac{\vartheta_f \delta_f}{N_h} I_m \right] Y_{I_{-z}} - \left[(1-u_3) \frac{\vartheta_f \delta_f}{N_h} \right] + \left[(1-u) \right] I \\ & + \left[(1-u_3) \frac{\vartheta_f \delta_f}{N_h} \right] Y_{I_{mf}} - \left[\mu_m \right] Y_{I_{mf}} \end{aligned}$$

$$\begin{aligned} -dY & = \left\{ - \left[(1-u_2) \frac{\vartheta_z \delta_z}{N_h} S_h \right] Y_{S_h} - \left[(1-u_2) \frac{\vartheta_z \delta_z}{N_h} I_m \right] Y_{I_m} - \left[(1-u_2) \frac{\vartheta_z \delta_z}{N_h} I_f \right] Y_{I_f} \right. \\ & + \left[(1-u_2) \frac{\vartheta_z \delta_z}{N_h} S_h \right] Y_{I_z} + \left[(1-u_2) \frac{\vartheta_z \delta_z}{N_h} I_m \right] Y_{I_{mf}} - \left[(1-u_2) \frac{\vartheta_z \delta_z}{N_h} I_a \right] Y_{I_{mf}} \\ & + \left[(1-u_2) \frac{\vartheta_z \delta_z}{N_h} I_f \right] Y_{I_{zf}} + \left[(1-u_2) \frac{\vartheta_z \delta_z}{N_h} I_{mf} \right] Y_{I_{mf}} - \left[\mu_m \right] Y_{I_a} \end{aligned}$$

To determine the optimal control parameters, we differentiate the Hamiltonian with respect to each control and equate it to zero. Thus,

For u_1

$$\begin{aligned} \frac{\partial H}{\partial u_1} & = Z_1 u_1 + \frac{\theta_m \delta_m I_p}{N_h} S_h Y_{S_h} - \frac{\theta_m \delta_m I_p}{N_h} S_h Y_{I_m} + \frac{\theta_m \delta_m I_p}{N_h} I_f Y_f + \frac{\theta_m \delta_m I_p}{N_h} I_z Y_{I_z} \\ & - \theta \frac{m \delta_m I_p I_z Y_{I_{mf}}}{N_h} - \theta \frac{m \delta_m I_p I_f Y_{I_{mf}}}{N_h} + \theta \frac{m \delta_m I_p I_z Y_{I_{zf}}}{N_h} - \theta \frac{m \delta_m I_p I_z Y_{I_{mf}}}{N_h} \\ & \theta_m \delta_m (I_m + I_{mz} + I_{mf} + I_{mzf}) \quad \theta_m \delta_m (I_m + I_{mzf}) \end{aligned}$$

$$+ \frac{S_m Y_{S_m}}{N_h} - \frac{S_m Y_{I_p}}{N_h} = 0.$$

$$u^* = \frac{1}{Z_1 N_h} \left[\vartheta_m \delta_m I_p \left[(Y_{I_m} - Y_{S_h}) S_h + (Y_{I_{mf}} - Y_{I_f}) I_f + (Y_{I_{mz}} - Y_{I_z}) I_z \right. \right. \\ \left. \left. + (Y_{I_{mzf}} - Y_{I_{zf}}) I_{zf} \right] \right] \\ + \frac{1}{Z_1 N_h} \left[\vartheta_m \delta_m \left[S_m (I_m + I_{mzf}) Y_{I_p} - S_m (I_m + I_{mz} + I_{mf} + I_{mzf}) Y_{S_m} \right] \right]$$

For u_2

$$\frac{\partial H}{\partial u_2} = Z_u u_2 + \frac{\theta_z \delta_z I_a}{N_h} S_h Y_{S_h} + \frac{\theta_z \delta_z I_a}{N_h} I_m Y_{I_m} + \frac{\theta_z \delta_z I_a}{N_h} I_f Y_{I_f} - \frac{\theta_z \delta_z I_a}{N_h} S_h Y_{I_z} \\ - \theta \frac{z \delta_z I_a I_m Y_{I_{mz}}}{N_h} + \theta \frac{z \delta_z I_a I_{mf} Y_{I_{mf}}}{N_h} - \theta \frac{z \delta_z I_a I_f Y_{I_{zf}}}{N_h} - \theta \frac{z \delta_z I_a I_{mf} Y_{I_{mzf}}}{N_h} \\ + \frac{\theta_z \delta_z (I_z + I_{mz} + I_{zf} + I_{mzf})}{N_h} S_m Y_{S_m} - \frac{\theta_z \delta_z (I_z + I_{mzf})}{N_h} S_m Y_{I_a} = 0.$$

$$u = \frac{1}{Z_2 N_h} \left[\vartheta_z \delta_z S_m \left[(Y_I - Y_S) S_h + (Y_{I_{mz}} - Y_{I_m}) I_m + (Y_{I_{mf}} - Y_{I_f}) I_f + (Y_{I_{mzf}} - Y_{I_{mf}}) I_{mf} \right] \right] \\ + \frac{1}{Z_2 N_h} \left[\vartheta_z \delta_z S_m \left[(I_z + I_{mzf}) Y_{I_a} - (I_z + I_{mz} + I_{zf} + I_{mzf}) Y_{S_m} \right] \right]$$

For u_3

$$\frac{\partial H}{\partial u_3} = Z_3 u_3 + \frac{\theta_f \delta_f I_w}{N_h} S_h Y_{S_h} + \frac{\theta_f \delta_f I_w}{N_h} I_m Y_{I_m} - \frac{\theta_f \delta_f \delta_f I_w}{N_h} S_h Y_{I_f} + \frac{\theta_f \delta_f I_w}{N_h} I_z Y_{I_z} \\ + \frac{I_{mz} Y_{I_{mz}}}{N_h} - \frac{I_m Y_{I_{mf}}}{N_h} - \frac{I_z Y_{zf}}{N_h} - \frac{I_{mz} Y_{I_{mzf}}}{N_h} \\ + \frac{\theta_f \delta_f (I_f + I_{mf} + I_{zf} + I_{mzf})}{N_h} S_m Y_{S_m} - \frac{\theta_f \delta_f (I_f + I_{mzf})}{N_h} S_m Y_{I_w} = 0.$$

$$u = \frac{1}{Z_3 N_h} \left[\vartheta_f \delta_f I_w \left[(Y_I - Y_S) S_h + (Y_{mf} - Y_{I_m}) I_m + (Y_{I_z} - Y_{I_z}) I_z + (Y_{I_{mzf}} - Y_{I_{mz}}) I_{mz} \right] \right] \\ + \frac{1}{Z_3 N_h} \left[\vartheta_f \delta_f S_m \left[(I_f + I_{mzf}) Y_{I_w} - (I_f + I_{mf} + I_{zf} + I_{mzf}) Y_{S_m} \right] \right]$$

For u_4

$$\frac{\partial H}{\partial u_4} = Z_4 u_4 + \tau_m I_m Y_{R_m} = 0. \quad \frac{\partial u_4}{\partial u_4} = -\frac{\tau_m}{Z_4}$$

For u_5

$$\frac{\partial H}{\partial u_5} = Z_5 u_5 + \tau_z I_z Y_{R_z} = 0. \quad \frac{\partial u_5}{\partial u_5} = -\frac{\tau_z I_z Y_{R_z}}{Z_5}$$

For u_6

$$\frac{\partial H}{\partial u_6} = Z_6 u_6 + \tau_f I_f Y_{R_f} = 0. \quad \frac{\partial u_6}{\partial u_6} = -\frac{\tau_f I_f Y_{R_f}}{Z_6}$$

Hence the optimal control is given as:

$$u_1^* = \max \left\{ 0, \min \left(1, \frac{1}{Z_1 N_h} \left[\vartheta_m \delta_m I_p \left[(Y_{I_m} - Y_{S_h}) S_h + (Y_{I_{mf}} - Y_{I_f}) I_f + (Y_{I_{mz}} - Y_{I_z}) I_z + (Y_{I_{zf}} - Y_{I_z}) I_{zf} \right] - Y_{I_{zf}} I_{zf} \right] + \frac{1}{Z_1 N_h} \left[\vartheta_m \delta_m \left[(Y_{I_{mf}} - Y_{I_f}) I_f + (Y_{I_{mz}} - Y_{I_z}) I_z + (Y_{I_{zf}} - Y_{I_z}) I_{zf} \right] - Y_{I_{zf}} I_{zf} \right] \right] \right\}$$

$$u_2^* = \max \left\{ 0, \min \left(1, \frac{1}{Z_2 N_h} \left[\vartheta_z \delta \left[(Y_{I_m} - Y_{S_h}) S_h + (Y_{I_{mf}} - Y_{I_f}) I_f + (Y_{I_{mz}} - Y_{I_z}) I_z + (Y_{I_{zf}} - Y_{I_z}) I_{zf} \right] - Y_{I_{zf}} I_{zf} \right] \right] \right\}$$

$$\begin{aligned}
& -1 - \max \left\{ 0, \min \left(1, \frac{1}{Z_1 N_h} \vartheta_m \delta_m \left[\begin{aligned} & -\mu_h S_h l_p (Y_{lmf} - Y_{lf}) \\ &) l_f \end{aligned} \right] \right. \right. \\
& \left. \left. \begin{aligned} & + I_p \\ & (Y_{lmz} - Y_{lz}) l_z + l_p (Y_{lmzf} - Y_{lzf}) l_{zf} + l_m (l_m + l_{mzf}) Y_{lp} \\ & - S_m (l_m + l_{mz} + l_{mf} + l_{mzf}) Y_{lp} \end{aligned} \right] \right\} \vartheta_m \delta_m \\
& S_h \left[I_a (Y_{lz} - Y_{S_h}) S_h + I - a \right] - 1 - \max \left\{ 0, \min \left(1, \frac{1}{h Z_2 N_h} \theta_z \delta_z \right. \right. \\
& \left. \left. \begin{aligned} & + I_a (Y_{lmzf} - Y_{lmf}) l_{mf} + S_m (l_z + l_{mzf}) Y_{la} - S_m (l_z + l_{mz} + l_{zf} \\ & (Y_{lmz} - Y_{lm}) l_m + I_a (Y_{lzf} - Y_{lf}) l_f \end{aligned} \right) \right\} \vartheta_z \delta_z + \\
& \begin{aligned} & l_{mzf}) Y_{S_m} \end{aligned} \frac{S_h - 1 - \max \left\{ 0, \min \left(1, \frac{1}{N_h Z_3 N_h} \theta_f \delta_f \right. \right. \\
& \left. \left. \begin{aligned} & I_w (Y_{lf} - Y_{S_h}) S_h + I_w \\ & (Y_{lmf} - Y_{lm}) l_m + I_w (Y_{lzf} - Y_{lz}) l_z \\ & + I_w \\ & (Y_{lmzf} - Y_{lmz}) l_{mz} + S_m (l_f + l_{mzf}) Y_{lw} - S_m (l_f + l_{mf} + l_{zf} \\ & + \theta_f \delta_f l_w \\ & l_{mzf} Y_{S_m}) \end{aligned} \right\} S_h}{N_h} \\
& f l_{mf} \left[\begin{aligned} & -(\mu_h + \eta + \tau_m) I_m + \tau \\ & 1 \end{aligned} \right] \left\{ \begin{aligned} & + \tau_z l_{mz} - 1 - \max \\ & 0, \min \left(1, \frac{1}{Z_1 N_h} \theta_m \delta_m \right. \right. \\ & \left. \left. \begin{aligned} & I_p (Y_{lm} - Y_{S_h}) + I_p \\ & (Y_{lmf} - Y_{lf}) l_f + l_p (Y_{lmz} - Y_{lz}) l_z + l_p (Y_{lmzf} - Y_{lzf}) l_{zf} \end{aligned} \right] \right\} \\
& + S_m (l_m + l_{mzf}) Y_{lp} - S_m (l_m + l_{mz} + l_{mf} + l_{mzf}) Y_{S_m} \theta_m N \delta_m l_p S_h \\
& \left\{ 0, \min \left(1, \frac{1}{z_2 N_h} \vartheta_z \delta_z \right. \right. \\
& \left. \left. \begin{aligned} & -1 - \max \\ & I_a (Y_{lz} - Y_{S_h}) S_h + I_a (Y_{lmz} - Y_{lm}) l_m + I_a (Y_{lzf} \end{aligned} \right) \right\}
\end{aligned}$$

$$\frac{dI_m}{dt}$$

$$dt - Y_{lf})I_f + I_a(Y_{lmz} - Y_{lmf})I_{mf} + S_m(I_z + I_{mzf})Y_{la}$$

$$\begin{aligned} & \left| \begin{aligned} & -S_m(I_z + I_{mz} + I_{zf} + \frac{\theta_f \delta_f I_w}{N_h})Y_{S_m} \\ & -1 - \max \left\{ 0, \min \left(1, \frac{1}{Z_3 N_h} \vartheta_f \delta_f \left[I_w(Y_{lf} - Y_{Sh})S_h + I_w(Y_{lmf} - Y_{lm})I_m \right. \right. \right. \\ & \left. \left. \left. + I_w(Y_{Izf} - Y_{Iz})I_z + I_w(Y_{lmz} - Y_{lm})I_{mz} + S_m(I_f + I_{mzf})Y_{lw} \right] \right\} \right. \\ & \left. -S_m(I_f + I_{mzf})Y_{S_m} \right. \\ & \left. \frac{S_h}{N_h} \right. \end{aligned} \right| \end{aligned}$$

?

$$\frac{-(\mu_h + \tau_f)I_f + \tau_m I_{mf} + \tau_z I_{zf}}{1 - Z_1 N_h \theta_m \delta_m} \left\{ \begin{aligned} & \left(\frac{1}{-1 - \max \left\{ 0, \min \left(1, \frac{1}{Z_3 N_h} \vartheta_f \delta_f \left[I_w(Y_{lf} - Y_{Sh})S_h + I_w(Y_{lmf} - Y_{lm})I_m \right. \right. \right. \right. \right. \right. \\ & \left. \left. \left. + I_w(Y_{Izf} - Y_{Iz})I_z + I_w(Y_{lmz} - Y_{lm})I_{mz} + S_m(I_f + I_{mzf})Y_{lw} \right] \right\} \right) \end{aligned} \right. \quad 0 \min$$

$$\begin{aligned} & \left| \begin{aligned} & \left[I_p(Y_{Im} - Y_{Sh})S_h + I_p(Y_{lmf} - Y_{lf})I_f + I_p(Y_{lmz} - Y_{Iz})I_z \right. \\ & \left. + I_p(Y_{lmz} - Y_{Izf})I_{zf} + S_m(I_m + I_{mzf})Y_{Ip} \right. \\ & \left. + \theta_m \delta_m I_p \right. \\ & \left. \left[I_a(Y_{Iz} - Y_{Sh})S_h + I_a(Y_{lmz} - Y_{lm})I_m + I_a(Y_{Izf} - Y_{lf})I_f \right. \right. \\ & \left. \left. -1 - \max \left\{ 0, \min \left(1, \frac{1}{Z_3 N_h} \vartheta_f \delta_f \left[I_w(Y_{lf} - Y_{Sh})S_h + I_w(Y_{lmf} - Y_{lm})I_m \right. \right. \right. \right. \right. \right. \\ & \left. \left. \left. + I_w(Y_{Izf} - Y_{Iz})I_z + I_w(Y_{lmz} - Y_{lm})I_{mz} + S_m(I_f + I_{mzf})Y_{lw} \right] \right\} \right) \right. \\ & \left. -S_m(I_z + I_{mz} + I_{zf} + \frac{\theta_f \delta_f I_w}{N_h})Y_{S_m} \right. \\ & \left. \frac{S_h}{N_h} \right. \end{aligned} \right| \end{aligned}$$

$$\begin{aligned} & \left| \begin{aligned} & 1 - \max \left\{ 0, \min \left(1, \frac{1}{Z_1 N_h} \vartheta_m \delta_m \left[-(\tau_z + \mu_h)I_z + \tau_m I_{mf} + \tau_f I_{zf} \right. \right. \right. \\ & \left. \left. \left. + I_p(Y_{Im} - Y_{Sh})S_h + I_p(Y_{lmf} - Y_{lf})I_f + I_p(Y_{lmz} - Y_{Iz})I_z \right] \right\} \right. \end{aligned} \right| \end{aligned}$$

[illegible]

$$\begin{aligned}
\frac{dI_w}{dt} = & \left(-\frac{1}{\mu_w I_w} - 1 - \max \left\{ 0, \min \left(1, \frac{1}{Z_3 N_h} \vartheta_f \delta_f \left[I_w (Y_{I_f} - Y_{S_h}) S_h + I_w (Y_{I_{mf}} - Y_{I_m}) I_m \right. \right. \right. \right. \\
& \left. \left. \left. + I_w (Y_{I_{zf}} - Y_{I_z}) I_z + I_w (Y_{I_{mzf}} - Y_{I_{mz}}) I_{mz} + S_m (I_f + I_{mzf}) Y_{I_w} - S_m (I_f + I_{mf} + I_{zf} \right. \right. \right. \\
& \left. \left. \left. + I_{mzf} \left(\theta_f \delta_f \right) \right) \right\} \right) \frac{N_h (I_f + I_{mzf})}{Y_{S_m}} S_m \\
\frac{dI_a}{dt} = & \left(-\frac{1}{\mu_{mla}} - 1 - \max \left\{ 0, \min \left(1, \frac{1}{Z_2 N_h} \vartheta_z \delta_z \left[I_a (Y_{I_z} - Y_{S_h}) S_h + I_a (Y_{I_{mz}} - Y_{I_m}) I_m \right. \right. \right. \right. \\
& \left. \left. \left. + I_a (Y_{I_{zf}} - Y_{I_f}) I_f + I_a (Y_{I_{mzf}} - Y_{I_{mf}}) I_{mf} + S_m (I_z + I_{mzf}) Y_{I_a} - S_m (I_z + I_{mz} + I_{zf} \right. \right. \right. \\
& \left. \left. \left. + I_{mzf} \left(\theta_z \delta_z (I - z + I_{mzf}) \right) \right) \right\} \right) \frac{N_h \theta_z \delta_z (I - z + I_{mzf})}{Y_{S_m}} S_m
\end{aligned}$$

The Systems (4.2) and (4.3) are computed numerically to derive the simulation graph for the optimal control problem. $\square$

4.2 Numerical Result on Optimal Control

The optimality System of the ordinary differential equations which consist of the state and adjoint equations was solved by the use of iterative method of the Runge Kutta fourth order scheme. The state and adjoint equations were solved using the backward in time and the initial guess for the controls simulated over time. This method is adapted so that the difference between the values of unknown at the previous iteration and that of the present iteration is negligibly small. The parameter values as described in Table 1 are used and the simulations of the model are done by using the initial conditions such that:

$$\begin{aligned}
S_h = 0.30, \quad I_m = 0.2, \quad I_f = 0.2, \quad I_z = 0.2, \quad I_z = 0.2, \quad I_{mz} = 0.2, \\
I_{mf} = 0.2, \quad I_{zf} = 0.2, \quad I_{mzf} = 0.2, \quad R_m = 0, \quad R_f = 0, \quad R_z = 0, \\
S_m = 0.4, \quad I_p = 0, \quad I_w = 0.1, \quad I_a = 0.1.
\end{aligned}$$

For the purpose of illustrating the optimal controls combined with the efforts that is required to minimize the number of infected humans and the vector

(mosquito) population as well as also minimizing the associated cost of the controls, the weight constant values in the objective function as shown in Equation (4.4) are chosen so that:

$$\begin{aligned} Z_1 = 1;5, \quad Z_2 = 45;5, \quad Z_3 = 10;5, \quad Z_4 = 15;10, \quad Z_5 = 25;10, \quad Z_6 &= \\ 10;10, \quad a_1 = 3;35, \quad a_2 = 7;15, \quad a_3 = 19;25, \quad a_4 = 15;25, \quad a_5 &= 18;05, \\ a_6 &= 20;28, \end{aligned}$$

and the parameter values used described in Table 1.

Table 1: Parameter value and their reference.

Parameter	Value	Reference(s)
Π_h	800	[Assumed]
τ_m	0.05	[Assumed]
Π_m	1000	(Blayneh et al., 2009) (Bonyah & Okosun, 2016)
η	0.05	[Assumed]
μ_h	0.00004	(Yang, 2000)
θ_z	0.40	(Andraud et al., 2012) (Gao et al., 2016)
μ_m	0.1429	(Makinde & Okosun, 2011)
δ_z	0.12	(Andraud et al., 2012)
θ_m	0.034	[Assumed]

τ_z	0.02	[Assumed]
δ_m	0.6502	(N. Chitnis et al., 2006)
θ_f	0.034	(Labadin et al., 2009)
δ_f	0.6502	(Labadin et al., 2009) (Bhunu & Mushayabasa, 2012)
τ_f	0.125	(Bhunu & Mushayabasa, 2012)

4.2.1 Insecticides Nets (u_1), Protective clothes (u_2), Insecticides Spray (u_3) and treatment (u_4) as control for Malaria

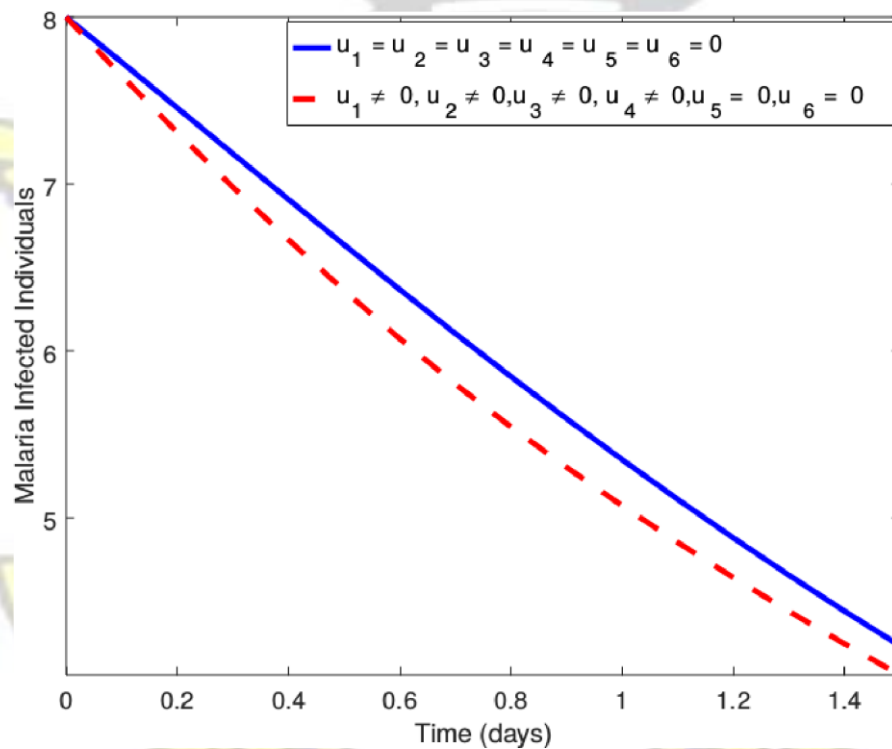


Figure 18: Simulations of the model showing the effect of protecting; spraying; insecticide net; and treatment only on malaria transmission.

The strategy applied here is the use of insecticide treated nets (u_1), individuals protecting themselves from female *Aedes aegypti* mosquitoes through the wearing of long sleeves (u_2), individuals spraying (u_3) their environment to

increase the death rate of the Culex mosquito, providing treatment controls (u_4) are used to optimize the objective function. Thereby, setting abstaining from sexual intercourse and drug that lower microfilariae in the bloodstream to zero. It is observed in Figure 18 that due to the control strategies activated, the number of infected malaria individuals decreases from the blue line (which depicts without controls) to the red line.

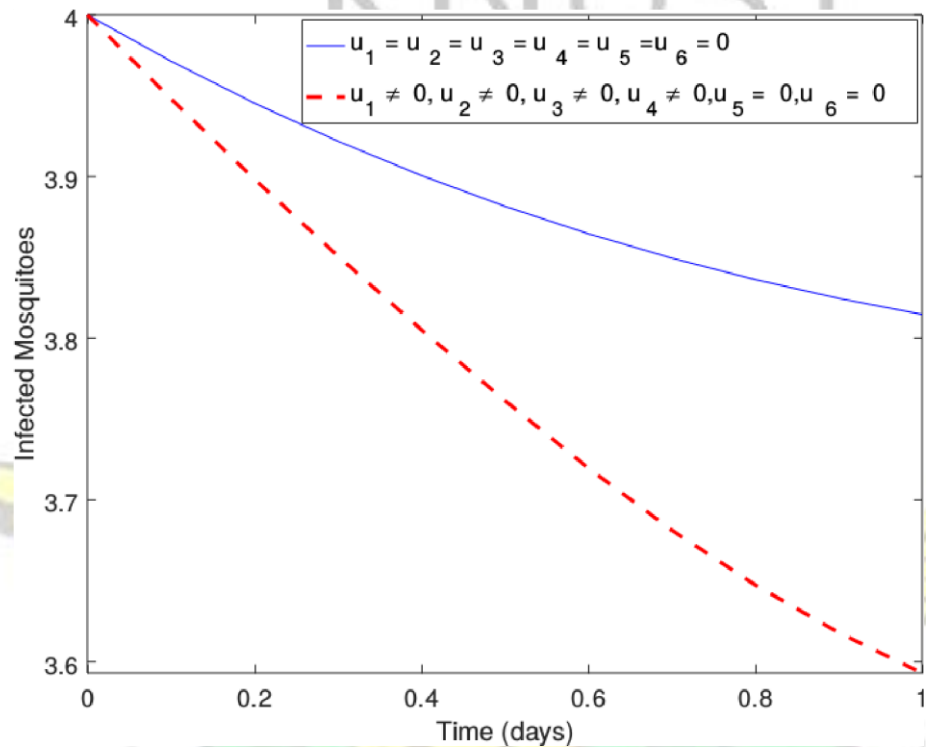


Figure 19: Simulations of the model showing the effect of protecting; spraying; insecticide net; and treatment only on the mosquito population.

Figure 19 depicts the behaviour of the mosquito population when the controls are applied and also when they are not applied. It is observe that when the strategy of using insecticide sprays and nets accompanied by protecting oneself are applied, the mosquito population that is capable of infecting an individual with malaria decreases while it increases when no control measure is applied indicated by the red and blue curve respectively.

4.2.2 Insecticide Spray (u_3) and Drug application (u_6) as control for Elephantiasis

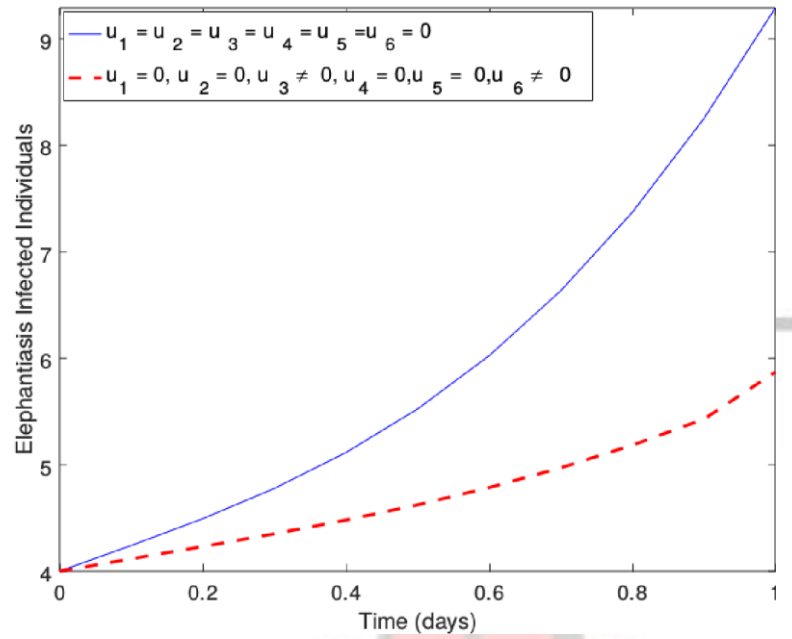


Figure 20: Simulations of the model showing the effect of insecticide spray and application of drug only on Elephantiasis transmission.

The strategy been applied in this section is to educate individuals in their application of insecticides (u_3) in order to help reduce the contact rate with the vector as well as providing drug to individuals (u_6) that will cause a reduction in the microfilariae population that lives in the bloodstream of elephantiasis infected individuals. By setting $u_1 = u_2 = u_4 = u_5 = 0$ to optimize the objective function, Figure 20 is attained. It is observed in Figure 20 that the introduction of the control strategies are effective in tacking the disease as it leads to a reduction in the population of individuals infected with elephantiasis.

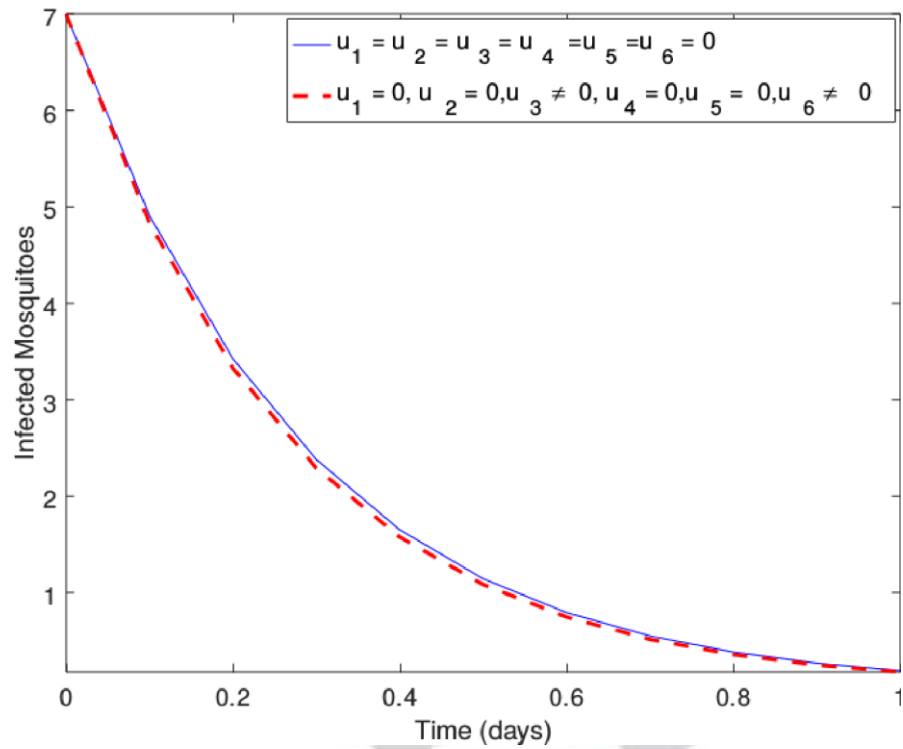


Figure 21: Simulations of the model showing the effect of insecticide spray and application of drug only on mosquito population.

In Figure 21 a proportional decrease in the behaviour of the mosquito population is observed when the controls are applied. It can be seen that even when we consider the strategy of using insecticide sprays only, since drug application cannot be administered on the vector, the mosquito population that is capable of infecting an individual with elephantiasis decreases while it increases when no control measure is applied indicated by the red and blue curve respectively.

4.2.3 Protection (u_2); Insecticide Spray (u_3) and Condom use (u_5) as control for Zika Virus

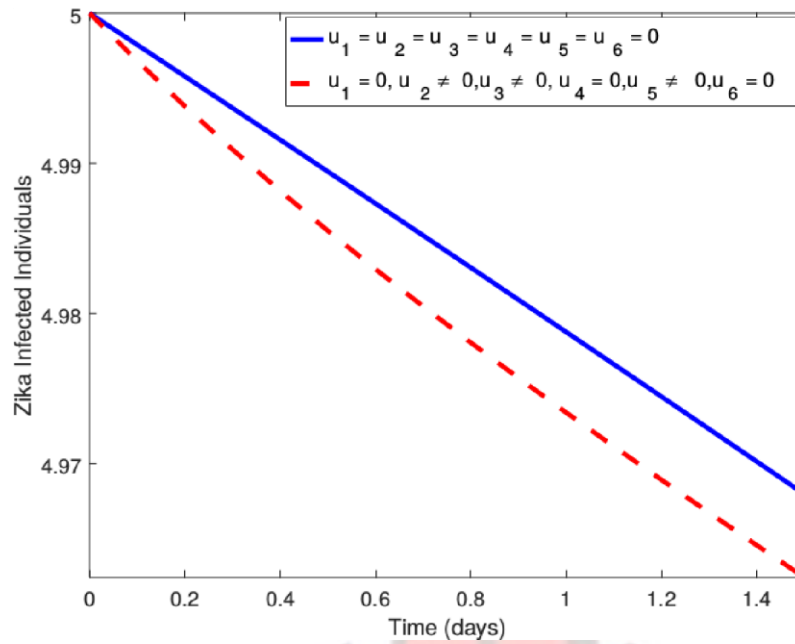


Figure 22: Simulations of the model showing the effect of protecting; insecticides spray and condom use on Zika Virus transmission.

In this strategy, preventive measures that will help individuals from protecting themselves from female *Aedes aegypti* mosquito biting by wearing long sleeves (u_2) especially during the day, educating individuals to use insecticides spray to help reduce the contact with *Culex* mosquito (u_3) and also using condoms during sexual intercourse (u_5) since the mode of Zika transmission has also been observed to be via sexual while setting $u_1 = u_4 = u_6 = 0$ are used to optimize the objective function. In Figure 22, it is observed that due to the introduction of the control strategies, the number of infected humans reduces as not without the control strategies (in blue).

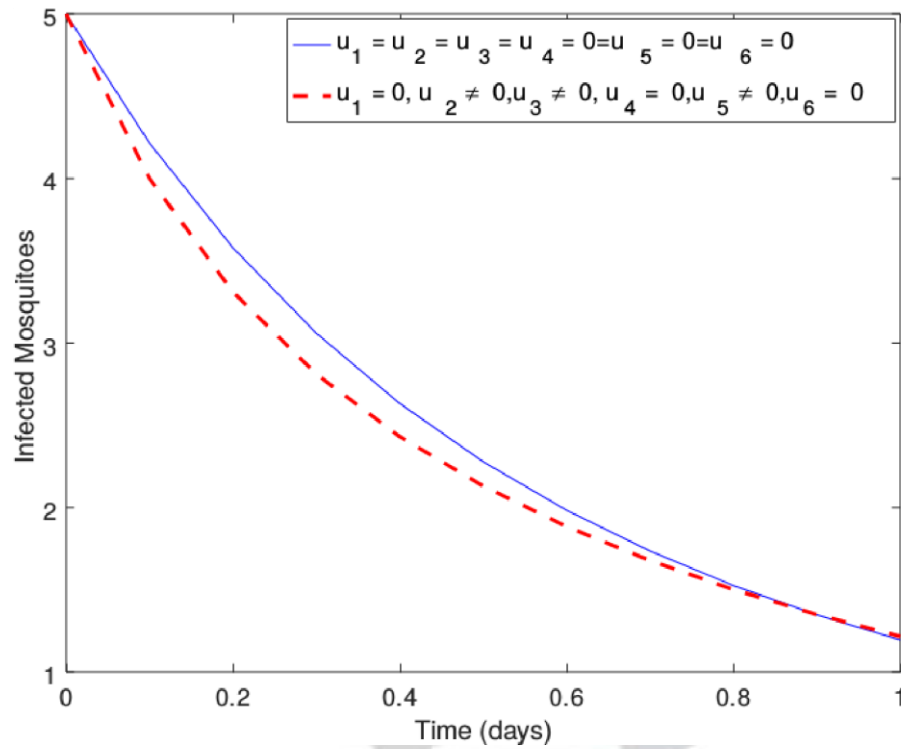


Figure 23: Simulations of the model showing the effect of protecting; insecticides spray and condom use on the mosquito population.

Figure 23 also depicts the behaviour of the mosquito population that causes Zika virus when the controls are applied and also when they are not applied. It is observe that when the strategy of using insecticide sprays is considered, there is a proportional decrease in the mosquito population that is capable of infecting an individual with zika virus while it increases slightly when no control measure is applied indicated by the red and blue curve respectively.

4.2.4 Insecticide Nets (u_1); Protection (u_2); Insecticides Spray (u_3); Treatment (u_4) and Condom use (u_5) as Control for Co-infected Malaria and Zika virus

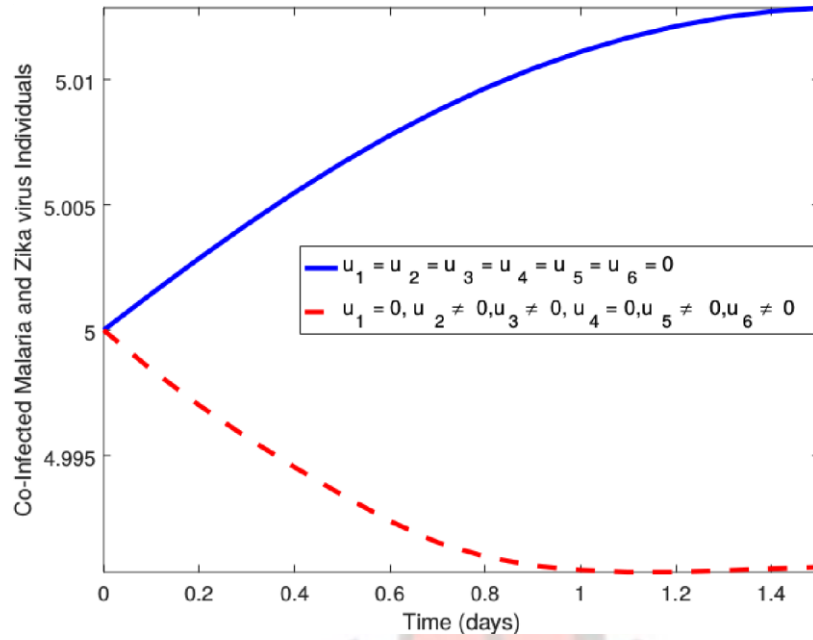


Figure 24: Simulations of the model showing the effect of insecticide nets; protection; insecticides spray; treatment and condom use on co-infected Malaria and Zika Virus transmission.

With the successful implementation of the use of insecticides treated nets (u_1), individual protecting themselves from female *Aedes aegypti* mosquitoes through the wearing of long sleeves (u_2), individual applying insecticides (u_3) to increase the death rate of the *Culex* mosquito in order to reduce its contact rate with humans as well as providing treatment controls (u_4) to curtail the transmission of malaria and also using condoms during sexual intercourse (u_5) that helps to reduce the transmission of Zika virus, these controls were activated simultaneously to ascertain its effect on an individual having been infected by both malaria and Zika. It was observed that the combined strategies of $u_1 = u_2 = u_3 = u_4 = u_5 = 0$ while $u_6 \neq 0$ worked as it led to a reduction in the population of individuals who are co-infected Malaria and Zika virus.

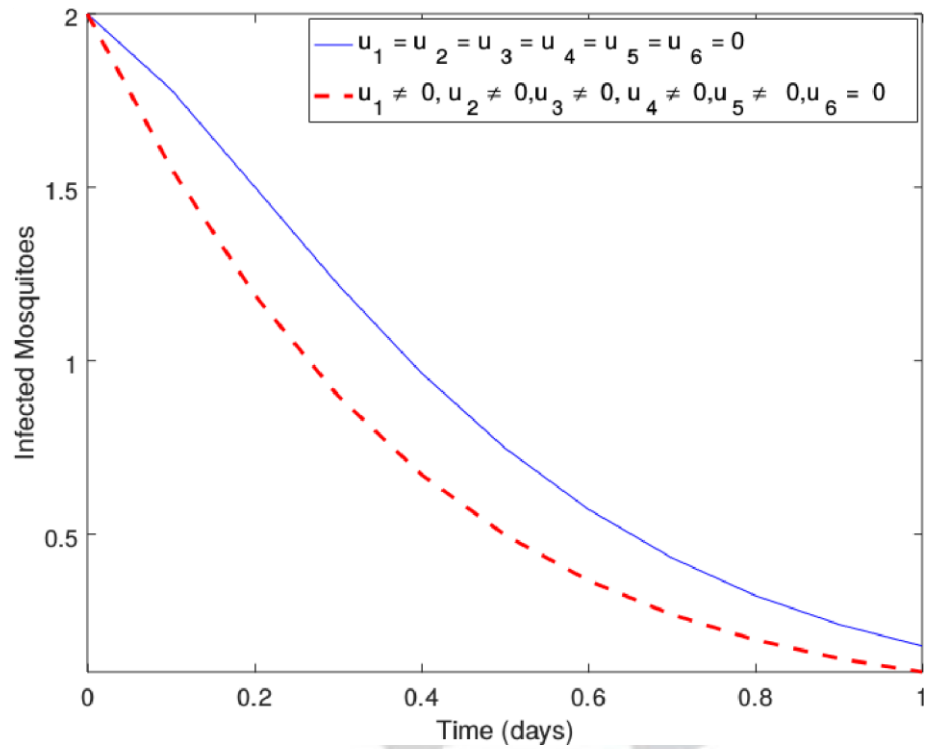


Figure 25: Simulations of the model showing the effect of insecticide nets; protection; insecticides spray; treatment and condom use on mosquito population.

The mosquito populations that cause an individual to be co-infected with both Malaria and Zika virus is observed to proportionally decrease when the control measures as insecticides sprays and nets are applied. This can be seen in Figure 25 with the blue curve depicting the nature of when no control measures are applied and the red curve showing the application of the controls.

4.2.5 Insecticide Nets (u_1); Protection (u_2); Insecticide spray (u_3); Treatment (u_4) and Drug application (u_6) as control for Co-Infected Malaria and Elephantiasis

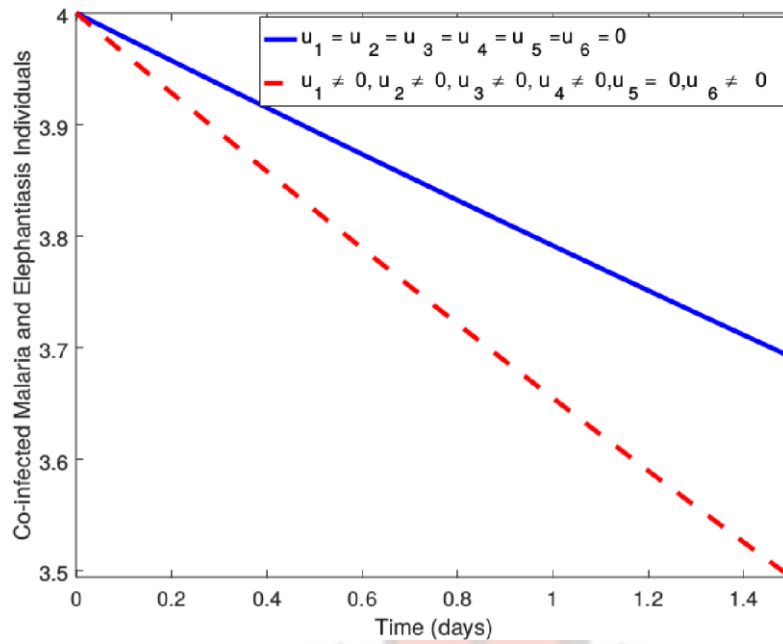


Figure 26: Simulations of the model showing the effect of insecticide nets; protection; insecticides spray; treatment and drug application on co-infected Malaria and Elephantiasis transmission.

Figure 26 shows the outcome obtained when the control strategies of setting $u_1 = u_2 = u_3 = u_4 = u_6 = 0$ while $u_5 = 0$ is activated led to a reduction in the number of individuals co-infected with malaria and elephantiasis. Furthermore, with the inclusion of insecticide sprays as part of the controls, the infected mosquito population that causes an individual to be co-infected with Malaria and Elephantiasis is seen to proportionally decrease as shown in Figure 27. The application of controls are shown by the red curve while without the controls are shown by the blue curve.

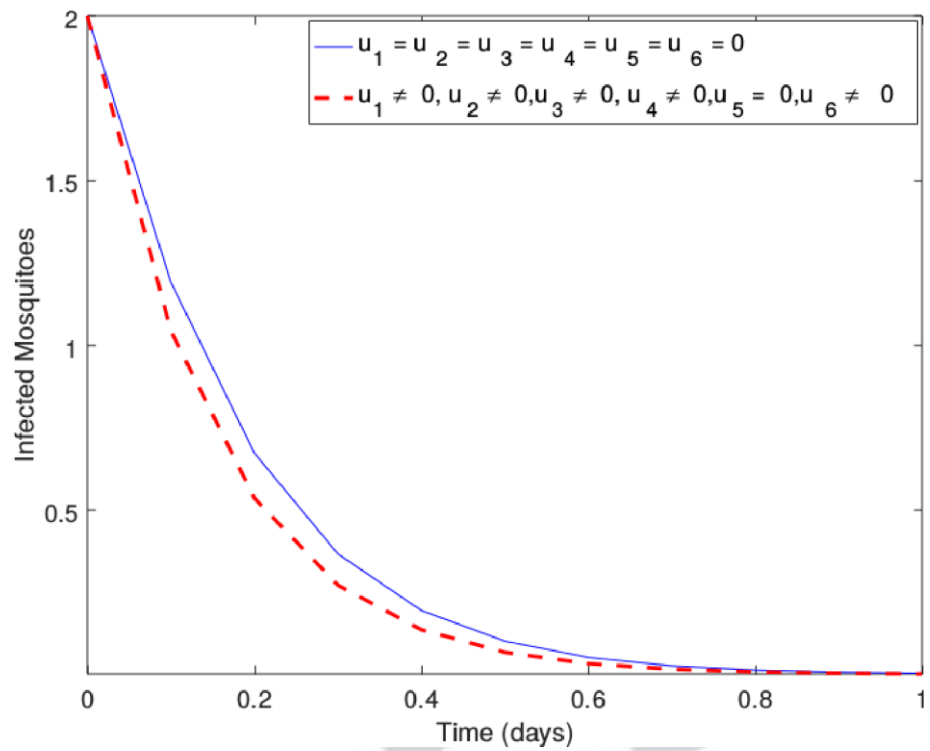


Figure 27: Simulations of the model showing the effect of insecticide nets; protection; insecticides spray; treatment and drug application on mosquito population.



4.2.6 Protection (u_2); Insecticide Spray (u_3); Condom use (u_5); and

Drug application (u_6)

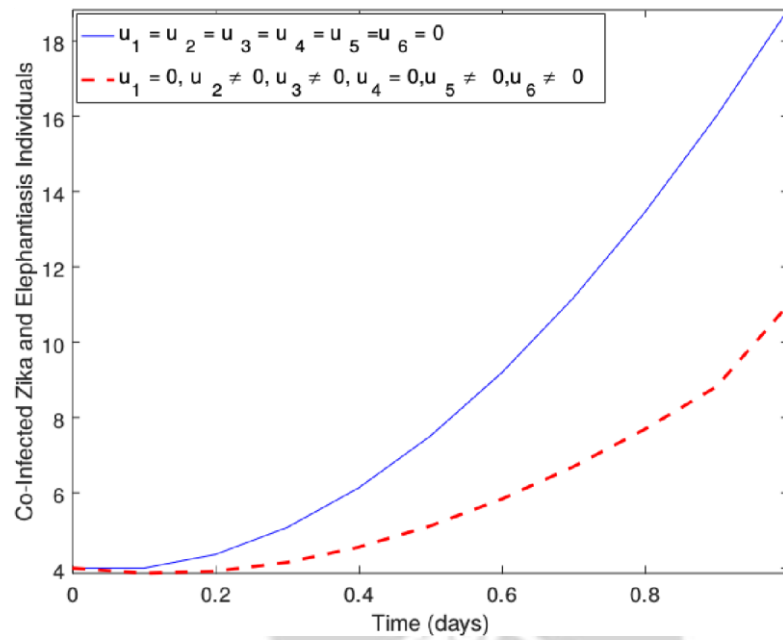


Figure 28: Simulations of the model showing the effect of protection; insecticides spray; condom use and drug application on co-infected Zika virus and Elephantiasis transmission.

In a similar manner, the combined control strategies activated by $u_2 = u_3 = u_5 = u_6 \neq 0$ while $u_1 = u_4 = 0$ showed that by applying those controls in the population there is a reduction in the number of individuals co-infected with Zika and elephantiasis as depicted in Figure 28. However, it is observed that there is no change in the mosquito population that causes an individual to be co-infected with Zika and Elephantiasis indicating that insecticide spray alone cannot help to eradicate the vector population. This can be seen in Figure 29 with the red curve showing the application of the controls and the blue curve showing the effect of not applying the controls.

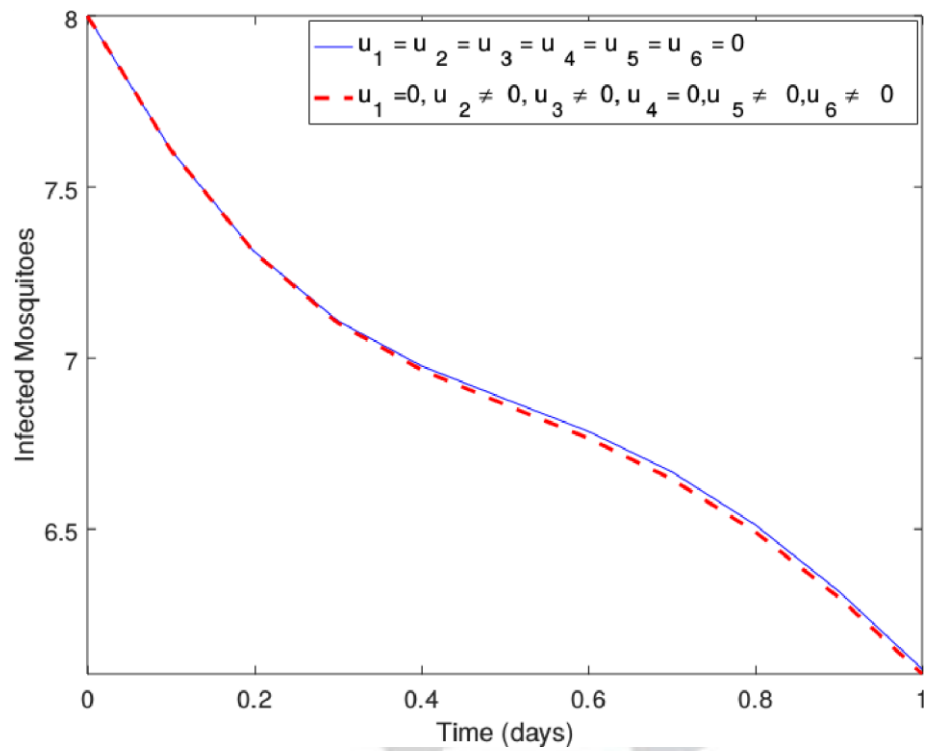


Figure 29: Simulations of the model showing the effect of protection; insecticides spray; condom use and drug application on mosquito population.



4.2.7 Insecticide Nets (u_1); Protection (u_2); Insecticide Spray (u_3); Treatment (u_4); Condom use (u_5) and Drug application (u_6) as control for Multi-Infection

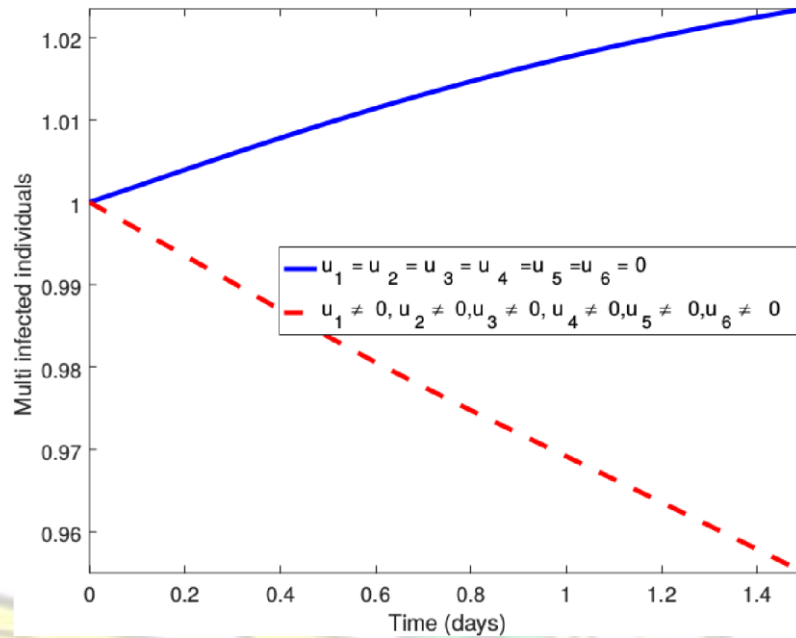


Figure 30: Simulations of the model showing the effect of insecticide nets; protection; insecticides spray; treatment; condom use and drug application on multi infected (Malaria-Zika Virus-Elephantiasis) transmission.

Figure 30 shows the strategy of using all six controls $u_1; u_2; u_3; u_4; u_5$ and u_6 to optimize the objective function. It was observed that the control strategies resulted in a decrease in the number of individuals that has been infected with the Malaria, Zika and Elephantiasis. Likewise the application of the controls causes the mosquito population to decrease as shown in Figure 31.

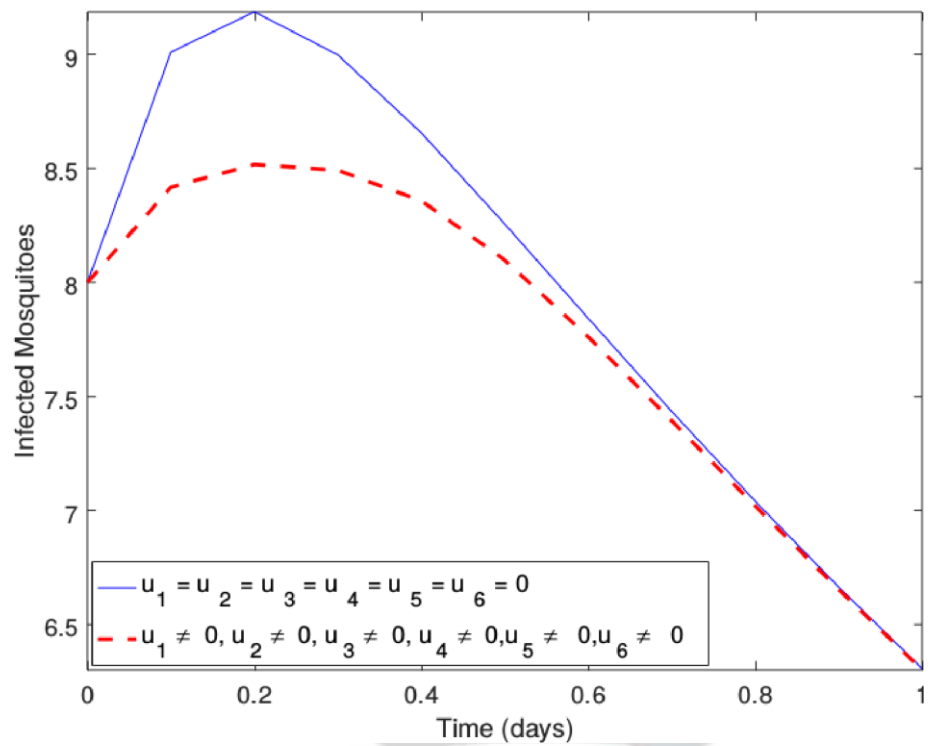
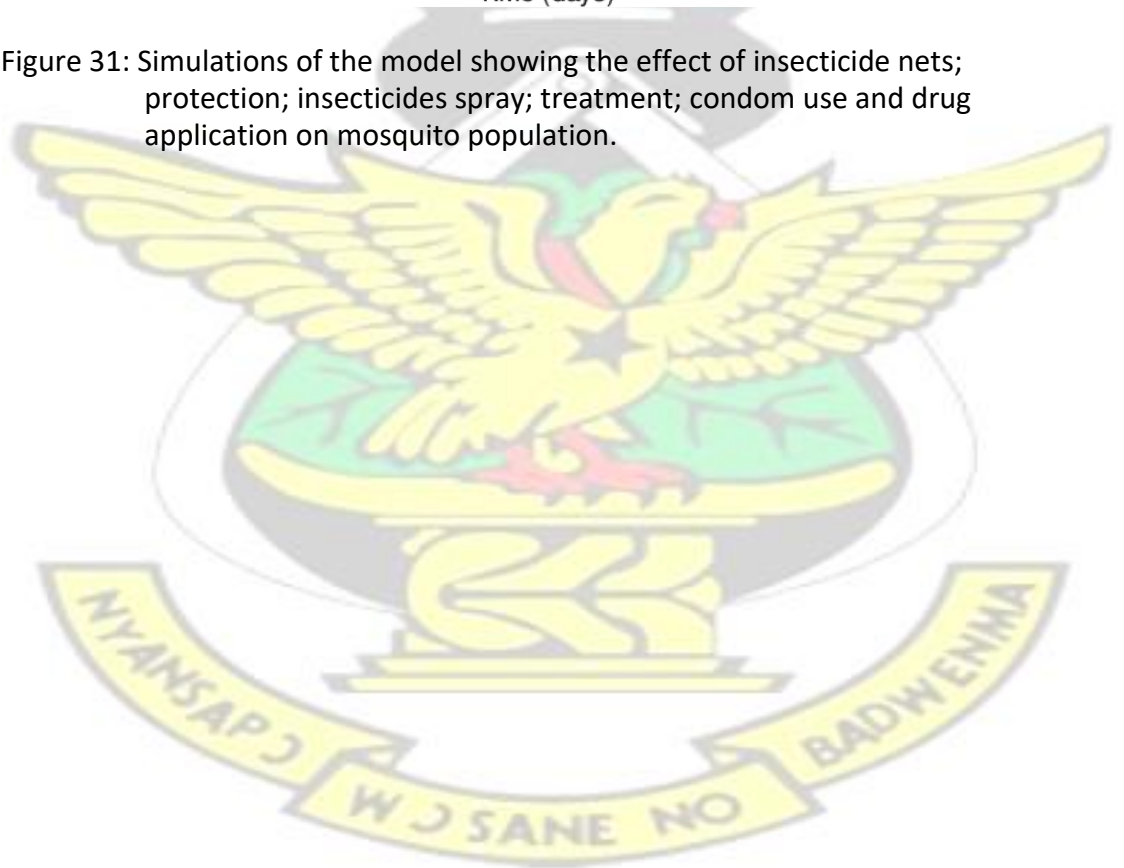


Figure 31: Simulations of the model showing the effect of insecticide nets; protection; insecticides spray; treatment; condom use and drug application on mosquito population.



CHAPTER FIVE

CONCLUSIONS AND RECOMMENDATIONS

The multi-infections disease (Malaria, Elephantiasis and Zika virus) is a novelty that this study seeks to contribute to existing knowledge. This work became necessary as a result of arboviruses patients who have been often misdiagnosed as malaria patients due to their similarities in clinical presentation by the health officials in some parts of Africa and other parts of the world where infectious disease can concurrently exist in the malaria endemic regions.

The study introduced multi-infections model which was mathematically formulated to study the transmission dynamics of Malaria, Zika virus and Elephantiasis diseases in the mosquitoes endemic region so as to be able to apply it to other parts of the world that may experience multi-infection in future. The basic reproduction numbers R_0 were derived from multi-infections and the submodels. Stability analysis on multi-infections and various sub-models were also performed to determine both disease free and endemic equilibrium. Investigation of the existence and stability of equilibria for multi-infections, co-infections and the single infections were proved. The model was found to have a global stable disease free equilibrium of $R_0 < 1$ and global stable endemic equilibrium of $R_0 > 1$. The model was also found to exhibit backward bifurcation, so that $R_0 < 1$ was not sufficient enough to eradicate the disease from the population. There is the need to lower R_0 below a certain threshold for effective disease control. Sensitivity analysis was performed to determine parameters that have high influence on the basic reproduction number. Figure 5 tracked the changes in the population of individuals infected with malaria. It was observed that the infected human population with malaria will increase if the probability of transmission of infection from a mosquito with parasite infection to a susceptible human given that a contact between the two occurs.

It also increases as well as if there is also an increase in the number of bites of humans per Anopheles mosquito per unit time. With parameter values shown in Table 3 and also using the following values for the state variables; $S_h = 0.30$, $I_m = 0.2$, $I_f = 0.2$, $I_z = 0.2$, $I_{mz} = 0.2$, $I_{mf} = 0.2$, $I_{zf} = 0.2$, $I_{mfz} = 0.2$, $R_m = 0$, $R_f = 0$, $R_z = 0$, $S_m = 0.40$, $I_p = 0.1$, $I_w = 0.1$, $I_a = 0.1$, we observe that when we set the values for both θ_m and δ_m to 0.1 the graph settles at the disease free equilibrium shown by the magenta colour and this is due to the small probability of transmission as well as the low occurrence of bites of humans by anopheles mosquito. But if the values of θ_m and δ_m is increased to 0.3, 0.5, 0.7, and 0.9, the infected human population with malaria also increase as respectively shown by the black, green, red and blue line in the graph. Therefore, for an increase in probability of transmission and the number of bites of humans by anopheles mosquito there will be a corresponding increase in the number of individuals infected with malaria.

For the given parameter values shown in Table 3 and using the values for the state variables shown in the explanation of Figure 4 and also varying the values for θ_m , θ_z , δ_m and δ_z we determine their effect on the co-infected malaria and Zika compartment. It was noticed that if the probability of transmission of both θ_m and θ_z are high and relate positively with also a high number of bites of humans by mosquito (that is a corresponding high values of θ_m and θ_z) then the probability of one being infected with both disease is very high. Figure 5 tracks this as no assertion, it was observed that when we set $\theta_m = \theta_z = \delta_m = \delta_z = 0.1$ respectively the magenta line, the level of transmission is not effective and the individuals in the co-infected population tends to zero. However, the number of individuals in the co-infected population increases when the values are increased to 0.3, 0.5, 0.7 and 0.9 shown by their respective colours black, green, red and blue. In the case of the multi-infected compartment, it was observed that the value of the state variable (I_{mzf}) has more effect on the compartment

compared to the major transmission parameters that has to do with the multi-infected differential equation (θ_m , θ_f , θ_z , δ_m , δ_f and δ_z) as shown in Figure 7a and 7b respectively.

From Figure 7a, it is observed that when you set the value of the state variable of the multi-infected compartment (I_{mzf}) to 70, the disease settles at the endemic state and this increases when the value is further increased from 70 to 90, 110, 130 and 150 as represented by the respective magenta, black, green, red and blue line. However, in Figure 7b, it is observed that no matter how much you increase the corresponding values for the transmission parameters for the various disease (that is malaria, elephantiasis and Zika) indicated by (θ_m , θ_f and θ_z) from 0.1, 0.3, 0.5, 0.7 and 0.9 corresponding number of bites per together with an increase in their unit time (θ_m , θ_f and δ_z) also from 0.1, 0.3, 0.5, 0.7 and 0.9 shown by the magenta, black, green, red and line respectively, the graph tends to zero.

The optimal control policies were incorporated in a transmission dynamics model of SIR type to derive the optimal level of the system. In order to obtain the optimal control strategies for the multi-infections (Malaria, Zika-virus and Elephantiasis) model, the control functions: insecticides treated nets (ITNs) individual protecting themselves from female *Aedes aegypti* mosquitoes through the wearing of long sleeves, individual applying insecticides to increase the death rate of the *Culex* mosquito in order to reduce its contact rate with humans as well as providing treatment controls to curtail the transmission of malaria and also using condoms during sexual intercourse that helps to reduce the transmission of Zika virus. This was done through simulation.

5.0.8 Findings

A mathematical model on multi-infections (malaria-zika-elephantiasis) where susceptible human can simultaneously be infected through the same vector

but different species has been demonstrated as a novelty that has been contributed to the existing knowledge and literature.

Investigation from the mathematical model and analysis performed showed that the model exhibited some form of bifurcation; a backward bifurcation phenomena and as a result requires additional measures in order to control the disease .

By the implementation of the control measures introduced and discussed, it was seen that;

- The application of insecticides spray and the drugs are effective in the control of elephantiasis.
- The application of protecting oneself, insecticides spray, insecticides nets and treatment are effective in controlling malaria.
- The application of condoms, insecticides sprays and protecting oneself are effective in controlling Zika virus.
- Combining the controls also help to control the co-infected and multi diseases.

5.0.9 Limitations and Recommendations

One of the limitations as far as this thesis was concerned was lack of adequate data for multi-infections disease (Malaria, Elephantiasis and Zika). This is because for an individual having multi-infections such as the thesis topic is uncommon in our part of the world .The conclusion drawn from the study are limited to only the area considered in the research since the vector that cause the transmission of elephantiasis is geographically dependent. It is recommended that further studies are focused on variables whose conclusions could be extended beyond the scope.

The following recommendations are made with respect to the outcome of the

thesis;

- The application of fractional optimal control can be considered.
- The model can also be extended by including the effects of environment such as the impact of climatic change on the spread of multi-infections disease (Malaria, Elephantiasis and Zika). Here, environmental factors such as rainfall and humidity affect some parameters in the model including biting rate of the mosquitoes and incubation period.



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APPENDICES



APPENDIX A

Code for Sensitivity Graph for R_f

```
#!/usr/bin/python
#Codes for tornado plot import
matplotlib.pyplot as plt import numpy as
np from scipy import integrate import
pylab as plt from matplotlib import
rc,rcParams
# Sensitivity graphs objects = (r'$\Pi_h$', '$\Pi_m$',
'$\mu_h$',
'$\mu_m$', r'$\vartheta_f$', '$\delta_f$', r'$\tau_f$') y_pos =
np.arange(len(objects)) performance = [-0.4363, 0.4848,
0.4880, -0.8337, 0.9987, 0.9987, -0.4363] barlist = plt.bar(y_pos, performance,
align='center', alpha = 1) barlist[0].set_color('black') barlist[1].set_color('black')
barlist[2].set_color('black') barlist[3].set_color('black') barlist[4].set_color('b')
barlist[5].set_color('b') barlist[6].set_color('b') #barlist[7].set_color('b')
plt.xticks(y_pos, objects, fontsize=14, weight = 'bold')
plt.xlabel('', fontsize = 17, weight = 'bold')
fig=plt.gcf() fig.subplots_adjust(bottom=0.1)
plt.ylabel('Index', fontsize=17, weight='bold')
plt.title('Sensitivity Index Profile for
$R_{f}$', fontsize = 17, weight = 'bold') plt.show()
```

APPENDIX B

Code for Sensitivity graph for $R_{\{mz\}}$

```
#!/usr/bin/python
```

```
#Codes for tornado plot import
```

```
matplotlib.pyplot as plt import numpy as
```

```
np from scipy import integrate import
```

```
pylab as plt from matplotlib import
```

```
rc,rcParams
```

```
# Sensitivity graphs objects = (r'$\Pi_h$', '$\Pi_m$',
```

```
'$\mu_h$',
```

```
'$\mu_m$', r'$\vartheta_m$', '$\delta_m$', r'$\tau_m$', '$\eta$') y_pos =
```

```
np.arange(len(objects)) performance = [-0.4655, 0.4857, 0.4857,
```

```
-0.9107, 0.9974, 0.9974,-0.4655,-0.2428] barlist = plt.bar(y_pos, performance,
```

```
align='center', alpha = 1) barlist[0].set_color('black') barlist[1].set_color('black')
```

```
barlist[2].set_color('black') barlist[3].set_color('black')
```

```
barlist[4].set_color('b') barlist[5].set_color('b')
```

```
barlist[6].set_color('b') barlist[7].set_color('b') plt.xticks(y_pos,
```

```
objects, fontsize=14,weight = 'bold') plt.xlabel("", fontsize = 17,
```

```
weight = 'bold') fig=plt.gcf() fig.subplots_adjust(bottom=0.1)
```

```
plt.ylabel('Index', fontsize=17, weight='bold') plt.title('Sensitivity
```

```
Index Profile for
```

```
 $R_{\{mz\}}$ , fontsize = 17, weight = 'bold') plt.show()
```

APPENDIX C

```
#!/usr/bin/python #Codes for tornado plot
import matplotlib.pyplot as plt import
numpy as np from scipy import integrate
import pylab as plt from matplotlib import
rc,rcParams
# Sensitivity graphs objects = (r'$\Pi_h$',
r'$\vartheta_z$',
r'$\delta_z$', r'$\tau_z$', r'$\Pi_m$', r'$\mu_h$', r'$\mu_m$') y_pos =
np.arange(len(objects)) performance = [-0.4350, 1.0012, 0.10012,
-0.4350, 0.4887, 0.4887, 0.8337]
barlist = plt.bar(y_pos, performance,
align='center', alpha = 1)
barlist[0].set_color('black')
barlist[1].set_color('black')
barlist[2].set_color('black')
barlist[3].set_color('black') barlist[4].set_color('b')
barlist[5].set_color('b') barlist[6].set_color('b')
#barlist[7].set_color('b') plt.xticks(y_pos, objects,
fontsize=14, weight = 'bold') plt.xlabel("", fontsize
= 17, weight = 'bold') fig=plt.gcf()
fig.subplots_adjust(bottom=0.1) plt.ylabel('Index',
fontsize=17, weight='bold') plt.title('Sensitivity
Index Profile for
$R_{zv}$', fontsize = 17, weight = 'bold') plt.show()
```

APPENDIX D

Code for Endemic Graph library(deSolve)

```
tbimmune.Model = function(t, x, params){
with(as.list(c(x, params)),{ pi_h = 0.000215; pim = 0.07;
muh = 0.00004; mum = 0.1429; varthetam =
0.034; deltam = 0.3; taum = 0.05; eta = 0.05; varthetaz =
0.034; deltaz = 0.3; tauz = 0.02; varthetaf = 0.034; deltaf =
0.3; tauf = 0.125; alpham = varthetam*deltam*Ip alphaf =
varthetaf*If*Iw alphaz = varthetaz*deltaz*Ia lambdap =
varthetam*deltam*(Im+Imz+Imzf)*Sm lambdaw =
varthetaf*deltaf*(If+Imf+Izf+Imzf)*Sm lambdaa =
varthetaz*deltaz*(Iz+Imz+Izf+Imzf)*Sm dS_h = pi_h +
phi*Rm + psi*Rf - alpham*S_h -muh*S_h - alphaz*S_h-
alphaf*S_h dIm = alpham*S_h - taum*Im-(muh+ eta)*Im +
tauf*Imf - alphaf*Im + tauz*Imz - alphaz*Im dIf =
alphaf*S_h - muh*If -alpham*If
+taum*Imf - tauf*If +tauz*Izf - alphaz*If dIz =
alphaz*S_h - tauz*Iz - alpham*Iz + taum*Imz +
tauf*Izf - alphaf*Iz - muh*Iz dImz = alphaz*Im -
tauz*Imz - (muh + eta)
*Imz + tauf*Imzf - alphaf*Imz + alpham*Iz taum*Imz dImf
= alphaf*Im - tauf*Imf - (muh+eta)*Imf + tauz*Imzf -
alphaz*Imf + alpham*If - taum*Imf dIzf = alphaz*If -
tauf*Izf - muh*Izf + taum*Imzf - alpham*Izf + alphaf*Iz
tauz*Izf dImzf = alpham*Izf - taum*Imzf -
(muh+eta)*Imzf - tauf*Imzf +alphaf*Imz + alphaz*Imf - tauz*Imzf dRm =
taum*Im - (muh + phi)*Rm
```

```

dRz = tauz*Iz - muh*Rz dRf = tauf*If - (muh + psi)*Rf
dSm = pim - mum*Sm - lambdap*Sm - lambdaw*Sm
- lambdaa*Sm dIp = lambdap*Sm - mum*Ip dIw =
lambdaw*Sm - mum*Iw dIa = lambdaa*Sm -mum*Ia
list(c(dS_h,dIm, dIf, dIz, dImz,dImf, dIzf, dImzf, dRm,
dRz, dRf, dSm, dIp, dIw, dIa)))
}

```

```

params <-c(pi_h =0.000215 , pim = 0.07, muh =
0.00044, mum = 0.034, phi = 0.05, psi = 0.02)

```

```

times <- seq(0, 100, 0.1)

```

```

x_init = c(S_h = 0.30, Im = 0.2, If = 0.2, Iz = 0.2, Imz =
0.2, Imf =0.2, Izf = 0.2,
Imzf = 0.2, Rm = 0, Rz = 0, Rf = 0,
Sm = 0.40, Ip = 0.1, Iw = 0.1, Ia = 0.1)

```

```

out = as.data.frame(ode(y = x_init, times, tbimmune.Model, parms =
params, maxsteps = 10000))

```

```

plot(times, out[,8], type= "l", col='blue', lwd =3, ylab='Infected', xlab='Time
(Days)', ylim = c(0,1)) lines(times, out[,3], col = 'green', lty = 3,lwd = 3)
grid(lwd=2)

```

```
# In drawing the individual plots for the state variables I only change the
numbers in the out[, 'number'] a = c("Susceptible Human Pop",
"Infected H/Malaria Pop.", "Infected H/Elephantiasis Pop",
"Infected H/Zika Pop", "Co-inf Mal/Zika", "Co-Inf-Mal/Zika",
"Co-Inf-Mal/Ele", "Co-Inf-Zika/Ele",
"Multi-Inf-Mal/Zika/Ele",
"Recovered H/Mal", "Recovered H/Ele", "Recovered H/Zika",
"Susceptible malaria Pop",
"Infected P", "Infected W", "Infected A") for(i in
2:14){ plot(times, out[,i] , type= "l", col='blue', lwd =3,
ylab= a[i-1], xlab='Time (Days)') grid(lwd=2)
}
```



APPENDIX E

Code for Individual Graph library(deSolve)

```
tbimmune.Model = function(t, x, params){
  with(as.list(c(x, params)),{ alpham =
    varthetam*deltam*Ip alphaf = varthetaf*If*Iw
    alphaz = varthetaz*deltaz*Ia
    lambdap = varthetam*deltam*(Im+Imz+Imzf)*Sm lambdaw =
    varthetaf*deltaf*(If+Imf+Izf+Imzf)*Sm lambdaa =
    varthetaz*deltaz*(Iz+Imz+Izf+Imzf)*Sm dS_h = pi_h + phi*Rm
    + psi*Rf -
    alpham*S_h-muh*S_h - alphaz*S_h-alphaf*S_h dIm =
    alpham*S_h - taum*Im-(muh+ eta)*Im
    + tauf*Imf - alphaf*Im + tauz*Imz
    alphaz*Im dIf = alphaf*S_h - muh*If -
    alpham*If
    +taum*Imf - tauf*If +tauz*Izf - alphaz*If dIz =
    alphaz*S_h - tauz*Iz - alpham*Iz
    + taum*Imz + tauf*Izf - alphaf*Iz
    - muh*Iz dImz = alphaz*Im -
    tauz*Imz -
    (muh + eta)*Imz + tauf*Imzf - alphaf*Imz + alpham*Iz
    - taum*Imz dImf = alphaf*Im - tauf*Imf -
    (muh+eta)*Imf
    + tauz*Imzf - alphaz*Imf + alpham*If taum*Imf
    dIzf = alphaz*If - tauf*Izf - muh*Izf
```

```

+ taum*Imzf - alpham*Izf + alphaf*Iz tauz*Izf
dImzf = alpham*Izf - taum*Imzf -
(muh+eta)*Imzf - tauf*Imzf +alphaf*Imz +
alphaz*Imf - tauz*Imzf dRm = taum*Im - (muh +
phi)*Rm dRz = tauz*Iz - muh*Rz dRf = tauf*If - (muh
+ psi)*Rf dSm = pim - mum*Sm - lambdap*Sm
lambdaw*Sm - lambdaa*Sm dlp = lambdap*Sm -
mum*lp dlw = lambdaw*Sm - mum*Iw dla =
lambdaa*Sm -mum*Ia list(c(dS_h,dIm, dIf, dIz,
dImz,dImf, dIzf, dImzf, dRm, dRz, dRf, dSm, dlp, dlw,
dla))))
} params<-c(pi_h = 0.000215, pim = 0.07, #pi_h = 800; pim =
1000; muh = 0.00004, mum = 0.1429, varthetam = 0.3045,
deltam = 0.9, taum = 0.05,eta = 0.05, varthetaz = 0.1, deltaz =
0.9, tauz = 0.02,phi = 0.05, varthetaf = 0.5, deltaf = 0.7, tauf =
0.125, psi = 0.02)

#params <-c(pi_h , pim = 1000, muh = 0.00044, mum =
0.034, varthetam = 0.0005, phi = 0.05,# psi = 0.02)

times <- seq(0, 100, 0.1)

x_init = c(S_h = 0.3, Im = 0, If = 70,
Iz = 0, Imz = 0, Imf = 0, Izf = 0,
Imzf = 0.1, Rm = 0, Rz = 0, Rf = 0,
Sm = 0.40,lp = 0.1, lw = 0.1, Ia = 0.1)
#x_init = c(S_h = 5000, Im = 100, If = 10,

```

```

lz = 20, lmz = 0, lmf = 0, lzf = 0,
lmzf = 10, Rm = 0, Rz = 0, Rf = 0,
Sm = 200,
# lp = 0, lw = 0, la = 0)
out = as.data.frame(ode(y = x_init, times, tbimmune.Model, parms =
  params, maxsteps
    = 10000))

```

```

plot(times, out[,8] , type= 'l' , col='blue', lwd =1,
ylab='Multi Infected Human Population.', xlab='Time
(Days)') lines(times, out[,8], col = 'red', lty = 1, lwd = 1)
lines(times, out[,8], col = 'green', lty = 1,lwd = 1)
lines(times, out[,8], col = 'black', lty = 1,lwd = 1)
lines(times, out[,8], col = 'magenta', lty = 1,lwd = 1)
grid(lwd=1) legend("topleft",
c(expression(vartheta_m
  = delta_m = 0.9), expression(vartheta_m
  = delta_m = 0.7), expression(vartheta_m =
delta_m =
0.5),expression(vartheta_m = delta_m = 0.3),
expression(vartheta_m = delta_m = 0.1)), col =
c("blue", "red","green","black"),
  pch = c('l', NA), lty = c(1,2), lwd=2)

```