A MATHEMATICAL MODEL FOR THE OPTIMAL CONTROL OF TRYPANOSOMIASIS IN A CATTLE POPULATION

by

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Declaration

Declaration by the Candidate

I declare that, except where explicit reference is made to the contribution of others, this thesis is the result of my own work and has not been submitted for any other degree at Maseno University or any other institution.

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Dedication

I dedicate this thesis to my sons, Cliff and Eddy

Abstract

Trypanosomiasis is a debilitating disease which is a major constraint to livestock production in sub-Saharan Africa. It leads to loss of productivity in animals and without treatment it is frequently fatal. The economic and social repercussions it causes in areas where it is endemic, makes its control a priority operation. In this study we formulate three models; a basic model to understand the transmission dynamics of the trypanosomiasis in a cattle population, a model with treatment to evaluate the role of treatment and a model to assess the impact of preventive and treatment control measures in a cattle population. The basic model and the model with treatment show that the global dynamics of the disease are completely determined by the threshold values: the basic reproduction number, R_0, and the effective reproduction number, R_{eff}, respectively. The parameters that have the greatest influence on R_0 are the rate at which the vectors bite the wild animal population and the vector survival rate which both increase endemicity of the disease while the vector death rate decreases disease prevalence. Treatment of a proportion of the infected cattle decreases disease prevalence. The proportion of cattle treated is an important parameter when treatment is used as an intervention strategy. We show that treating 0.5 - 0.75 of the infected cattle population is enough to eradicate the disease in the population. In the optimal control model, the existence of the optimal control is established, it is characterized using the *Maximum Principle* and solved numerically using a combination of forward and backward difference approximations. Numerical simulations and optimal analysis of the model show that the preventive and treatment control strategies help to reduce the number of infected cattle, however the net effect on disease prevalence when both strategies are used is greater than when they are used singly.

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Chapter 1

Introduction

1.1 Background to the study

African Animal Trypanosomiasis or *Nagana* is a highly prevalent parasitic vector-borne disease in sub-Saharan Africa [28]. It is a major impediment to livestock farming in sub-Saharan Africa and it limits the full potential of agricultural development in the thirty six (36) countries where it is endemic [67]. The disease has been under control by the reduction of sources of infection, the protection of cattle from infection and the control of vectors of transmission, yet in spite of this constant vigilance, it persists at an irreducible level with occasional outbreaks [87].

1.1.1 Trypanosomiasis: Cause and Transmission

Nagana is caused by a range of protozoan parasites of the genus trypanosoma [27]. The tsetse flies in the genus *Glossina* are the main biting insects that transmit the disease. The disease is an important constraint to livestock farming in tropical Africa [49], since it limits the potential of agriculture in areas where it is endemic. The epidemiology of trypanosomiasis involves at least four components, the tsetse fly, the trypanosome and more than one vertebrate species all operating within the physical environment. These components all differ in regard to their reservoir potential and level of susceptibility to the parasite species [65].

The tsetse flies are strictly blood feeders that live exclusively in tropical Africa [27]. They serve as both host and vector for the trypanosome parasites which they transmit during a meal of blood from an infected animal to a healthy one [14]. There are about thirty species or subspecies of tsetse fly each with distinct biological characteristics classified into three groups namely, *palpalis*, *morsitans* and *fusca*, that transmit the trypanosomes amongst various host species. However, only about 5% of them carry the trypanosomes that cause animal trypanosomiasis [88]. The three most notable species of trypanosomes responsible for the transmission of trypanosomiasis in cattle are *T. vivax*, *T. congolense* and *T. brucei*. Apart from only a small percentage of the tsetse flies carrying the trypanosome, the infection rates in the tsetse populations are equally low, ranging from about 5% for *T. vivax* and *T. congolense* to less than 1% for *T. brucei* [27].

Fly species differ in their susceptibility to trypanosomes, and their subsequent ability, if infected, to transmit trypanosomes [35]. The evolution of the disease also varies according to the trypanosome involved, the animal species and the breed infected [63]. Most bites from a tsetse fly are not dangerous and do not necessarily lead to the disease, however, livestock continually exposed to bites are at a higher risk of infection [27]. The susceptibility of cattle and the severity of any infection are highly variable and dependent on the breed, strain and nutritional status, degree of stress and age of the animals [63].

Wild animals, on the other hand, are an important source of food for the tsetse fly as well as being trypanosome carriers [27]. Specific tsetse fly species obtain much of their nourishment from a preferred small number of wild animal species such as the Warthog, Bush pig and the small Antelope, yet they are not rigidly dependent on the specific animals species; so that when the preferred host disappears it can feed on other species [74]. Animal trypanosomiasis infection, however, does not affect the health status of wild animals. In their study of monitored wild animals, Mattioli *et. al.*, [59], confirmed that wild animals are a reservoir of trypanosomes. The role the wild animals play in the epizootiology of animal trypanosomiasis varies according to the wild animal species, the tsetse fly species and the trypanosome involved and depends on the interactions between these three factors (the wild

animal species, the tsetse fly species and the trypanosome) in a given situation.

1.1.2 Trypanosomiasis: Social and Economic Impact

More than a third of the land area across Africa, approximately 8.7 million km^2, is infested with tsetse flies so that at least 46 million cattle are exposed to the risk of contracting trypanosomiasis [28]. The disease has a direct impact on the average number of livestock kept by farmers [10]. Since most of rural sub-Saharan Africa depends on agriculture for their livelihood, trypanosomiasis directly contributes to poverty, food insecurity and nutritional deficiencies in these areas [80]. In East Africa, the estimated annual cost of trypanosomiasis in terms of foregone meat and milk is around US$ 1.3 billion per year [48].

The disease leads to loss of productivity in animals and, without treatment is frequently fatal [27]. It directly affects livestock productivity by reducing calving rates by $1-12\%$ in trypanotolerant breeds and $11-12\%$ in susceptible breeds; increasing calf mortality by $0-10\%$ in tolerant breeds and $10-20\%$ for susceptible breeds and reducing milk offtake by $10-26\%$ in tolerant breeds [78]. Overall, the cattle population is reduced by $30-50\%$ because farmers keep their animals away from areas with a high tsetse challenge or trypanosomiasis risk [23].

Even more important in effect are the indirect impacts the disease has on settlement patterns, land use, draught power use, animal husbandry and farming [9]. The disease prevents the development of an integrated crop-livestock production system [23]. The risk of the disease in a tsetse-infested area means that tilling of the land is done by hand. This causes a reduction in agricultural productivity in comparison with a situation where healthy animals provide draught power. In fact, when trypanosomiasis prevalence exceeds 30%, it is virtually impossible to practise mixed farming [42]. Evidence from Ethiopia suggests that a team of oxen in a tsetse-infested area is only capable of cultivating 60% of the land that can be cultivated in a tsetse-free area [22].

The impact of animal trypanosomiasis is equally felt in Kenya, particularly in the agricultural and tourism sectors. Tsetse flies infest an area covering about 138,000 square kilometers,

approximately 23% of the country in area, yet in rural Kenya, 9 out of 10 people depend on livestock for their livelihood [64]. The problem is exacerbated by the fact that in the Kenyan economy, the sectors including agriculture, forestry, fishing and hunting impacted most by trypanosomiasis infection, earn 25.2% of her Gross Domestic Product (GDP) [4]. Since Kenya's major agricultural produce include livestock products, the prevalence of animal trypanosomiasis has dire consequences on the livelihood of the Kenyan population.

The effects of tsetse fly and trypanosomiasis infestation also glaringly affects the tourism industry in Kenya. This industry accounts for 21% of the total foreign exchange earnings and up to 12% of the Gross Domestic Product while wildlife contributes 70% of tourism earning [64]. The effect of trypanosomias in the sector is manifested in the unwillingness of tourists to visit tsetse fly infested areas, which are usually the natural habitat of wildlife [6]. This certainly contributes to loss in tourism earnings. To attain the tourism goals in Vision 2030, tsetse fly control and eradication is a priority operation.

1.1.3 Trypanosomiasis: Control Strategies

The considerable economic and social repercussions make the control of trypanosomiasis a priority operation for the development of a large part of the African continent and particularly the tsetse belts of Kenya. The options for controlling the disease include treating livestock with curative or prophylactic drugs, controlling tsetse populations using insecticide-impregnated traps/targets, insecticide-treated livestock or breeding trypanotolerant cattle [61]. Much is known about the biology and ecology of the vector, the transmission of the disease and a variety of control measures developed and demonstrated, yet trypanosomiasis is still a significant constraint on animal production, human health and agricultural livelihoods in many parts of Africa due to frequent re-infestation by immigrating flies [60].

The decline in the efficacy of tsetse control programmes in most tsetse infested areas has meant stock owners rely on drugs to cure or prevent trypanosomiasis [9]. It is possible to keep cattle alive on such drugs even in areas of high trypanosomiasis challenge though in the event of drug resistance, the trypanosomiasis problem will return [41]. The drugs have

no direct effect on the tsetse yet according to Jordan [44], the control of the the tsetse fly vector remains theoretically the most efficient and sustainable way of managing trypanasomiasis. Consequently, bait methods appear to be the remaining options for disease control for the individual stock owners. However, it is the relief from cattle disease rather than issues of tsetse fly control versus eradication, that interests stockholders in tsetse infested areas to become actively involved in tsetse and trypanosomiasis control [34], using treatment.

Apart from treatment, farmer based tsetse fly control also relies heavily on two bait systems. These are the traps/targets and the insecticide treated cattle [34]. The traps/targets are fabric sheets treated with insecticide while the insecticide treated cattle, who are either stationary or moving around the tsetse fly habitat, have insecticide applied on their body. Both methods rely on attracting the tsetse to the point source and killing or sterilizing them on contact. Both systems have the advantage of causing little direct damage to the environment and of being extremely effective if applied properly in the appropriate circumstances [50]. Unlike the other control methods the baits have the advantage of being relatively cheap and easy to apply [40].

Farmers therefore have to consider the costs and benefits of any choice of control strategy they settle for, which are not trivial decisions. The quantitative approach is likely to become prominent on making decisions on the appropriate method. In this approach, analytical models usually in the form of ordinary differential equations are used for researching the quantification of infectious processes [55]. Particular ones include population based models which integrate knowledge and data about an infectious disease. They include the natural history of the disease and transmission of the pathogen between individuals. Such models make it possible to better understand the disease and its population-level dynamics. They provide a useful tool for quantifying the spread of a potential epidemic and examine the effectiveness of control measures. They equally provide a practical procedure to evaluate the population level impact of interventions.

1.2 Statement of the Problem

Although a number of control measures exist that either target the trypanosome, the vector or the host, the disease persists at an irreducible level with occasional outbreaks [87]. The natural history of the disease and transmission of the pathogen between individuals indicates that dynamics of the disease is a function of various parameters. To effectively control Trypanosomiasis, there is need to establish which parameters are most sensitive to the dynamics of the disease in a cattle population. This would inform the appropriate control strategy and the rate at which it ought to be implemented. Furthermore, since the disease is prevalent in regions of the world which are not economically endowed, costs are crucial for the implementation of control strategies. The study therefore develops and analyzes a mathematical model for trypanosomiasis in a cattle population to establish the parameter that influences disease dynamics most. An optimal control problem is formulated whose objective is to minimize the number of infected cattle with minimum implementation cost.

1.3 Objective of the Study

The aim of this research is to develop a mathematical model for the transmission of African Animal Trypanosomiasis by the tsetse fly in a cattle population and analyse the effects of control measures on the dynamics of the disease. The specific objectives of this study are:

1. To analyze a basic model of the epizootiology of Trypanosomiasis in a cattle population and establish the threshold parameters that would help in the control or eradication of the disease.

2. To evaluate the role of treatment of the infected cattle on the dynamics of trypanosomiasis in a cattle population.

3. To determine cost effective control efforts for treatment of the infected cattle and prevention of the contacts between the cattle and the tsetse fly populations.

1.4 Significance of the Study

The formulation and analysis of a mathematical model for the transmission dynamics of tsetse transmitted animal trypanosomiasis is a learning paradigm to enhance knowledge of the parameters of interest necessary to control or completely eradicate the disease. The goal of the study is to use the analysis of ordinary differential equations to obtain the necessary threshold parameters for disease transmission dynamics and use optimal control theory for decision making to enable stock keepers improve livestock production in tsetse infested areas. The output of this study is a source material that the stock keepers can take up mentally and cause to be widely known by spreading the information to one another and managing the disease in a specified way.

1.5 Outline of the Study

Chapter 1 provides a basic framework for describing the transmission of African Animal Trypanosomiasis in cattle population. It discusses the cause of the disease, its social and economic impact and the control strategies available for the disease. The statement of the problem, the objectives and significance of the study are then stated.

A review of literature on the mathematical modeling of African Animal Trypanosomiasis is given in Chapter 2. Emphasis is on the control of the disease using treatment and vector control strategies. A review of studies done on optimal control theory is also provided.

In Chapter 3, a basic model for African Animal Trypanosomiasis in a cattle population is formulated and analyzed. The analysis is geared towards determining the parameter which has the greatest influence in the dynamics of the disease. Controlling that parameter would inform the appropriate control strategy.

Chapter 4 incorporates the treatment of a proportion of the infected cattle into the basic model introduced in Chapter 3. This is motivated by the fact that donors and many African governments have reduced their commitment to tsetse control, leaving operations to local communities and other inexperienced agencies [46]. Treatment of the cattle is considered since the decline in the efficacy of tsetse control programmes in most tsetse infested areas has meant stock owners rely on drugs to cure or prevent the disease [9]. Analysis of the model is done to evaluate the role of treatment of the infected cattle on the dynamics of African Animal Trypanosomiasis in a cattle population.

In Chapter 5, optimal control theory is applied to the model to study the impact of treatment and vector control on the dynamics of the disease in a cattle population. Vector control is considered in this case since though individual stock owners would resort to treatment of infected cattle as a control measure, it is documented that vector control, as a preventive strategy, does little damage to the environment and is very effective if applied properly in

appropriate circumstances [46, 34].

Finally in Chapter 6, a detailed discussion of the research findings and conclusion is provided reflecting on each of the study objectives. Recommendations and areas of further study are suggested.

Chapter 2

Literature Review

Mathematical models of infectious diseases have proven to be a valuable component for public health planning and responses, as well as an important application of population biology. A basic model may play a significant role in the development of a better understanding of the infectious disease and the various preventive strategies used against it [11]. A number of models for the spread of infectious diseases in populations have been analyzed mathematically and applied to specific diseases. These models provide conceptual results such as threshold values, the basic reproduction number, the contact number and replacement numbers to analyze the spread and control of the disease [38].

The emergence and re-emergence of vector-borne diseases has promoted interest in their mathematical modeling [89]. A number are the Ross-MacDonald type models which propose compartmental dynamics where the vector population is described by a system of susceptible and infected vectors (S-I model), while the dynamics of the host is described by a system of susceptible, infected and recovered or removed hosts (S-I-R model); usually the only mode of transmission is the vector [89]. Such models have also been developed for the transmission and control of African Animal trypanosomiasis. Optimal control theory has also been applied to vector-host models to study the impact of control strategies on the disease, though not for the trypanosomiasis disease model [8].

In this chapter a literature review of some of the studies on African Animal Trypanosomiasis

is presented. Studies developed to understand the dynamics and control of the disease are first presented followed by studies that have used optimal control theory to study the impact of control strategies on the spread of a disease.

2.1 Mathematical Models for the Transmission and Control of African Animal Trypanosomiasis

Regardless of the fact that animal trypanosomiasis has devastating effects on livestock production, data for the development of analytical models have only become available recently [58]. Though the simulation approach had been applied to animal trypanosomiasis Habtemariam *et. al.* [31] who modelled a single-parasite, single-vector, single-host species situation, one of the pioneering analytical compartmental model of the disease was developed by Milligan and Baker [63]. Their objective was to investigate the epizootiology of the disease and determine criteria for successful disease control by both mass and targeted chemotherapy and vector control.

Their model incorporated the heterogeneity in transmission due to tsetse fly feeding preferences because the disease involves several trypanosomes with varying transmission effects by a wide range of tsetse fly species [47, 63]. The difference in age in the vector population which present differences in susceptibility to infection was also incorporated. Since tsetse fly populations exhibit a range of seasonal behavior, from populations with large fluctuations with a peak in the late rainy season, to those which appear to be constant or to show only slight seasonality, their study included the seasonality in fly population which induced a similar effect in cattle parasitaemia.

The study established that the heterogeneity in transmission coupled with the variability of immunological characteristics of the vertebrate hosts account for the difference in prevalence of *T. vivax* and *T. congolense*. It also lead to an increase in the basic reproduction rate of the parasites and a corresponding decrease in vector population density threshold for disease

eradication or persistence. The long life-span of the vectors relative to the duration of the parasites developmental period lead to high infection rates in the vector and high values of R_0. As regards disease control, the efficacy of chemotherapeutic regimes depends on the relationship between the treatment rate and the duration of prophylaxis conferred by the drugs used. Their model's prediction of the effects of vector control were in broad agreement with published field data from Mtwapa Ranch, Tanzania. It indicated that with immigration of vectors, the disease is always endemic. A sensitivity analysis of the model parameters using Monte Carlo methods confirmed that the most important parameters are the vector biting rate, population density, and death rate, though the exact fly numbers become less critical when fly population densities are large, or when flies exhibit a strong feeding preference for wild animals.

In another study, Rogers [74] whose starting point was the basic Ross-Macdonald model for malaria as described by Aron and May [55], described an analytical model for African Trypanosomiasis that incorporated two vertebrate host, and one tsetse vector species with constant populations. The basic model incorporated most of the features of a vector-borne disease which makes it possible to assess the importance of each parameter in determining disease prevalence. It was modified to allow for incubation and immune periods in the two hosts and for variable efficiency of transmission of different trypanosome species from the vertebrates to the vectors and vice versa. Parameter values for African Trypanosomiasis were derived from literature and a typical West African village situation was considered with 300 humans, 50 domesticated animals and an average population of 5000 tsetse flies.

Equations were derived for equilibrium disease prevalence in all the species involved. An analysis of the model indicated that animal reservoir is crucial in determining not only the continued occurrence of the disease in humans, but its prevalence in the hosts as well. The study also examined the effect of changing average fly density on equilibrium disease prevalence and seasonal changes in fly numbers on disease incidence. In a seasonal situation changes in fly mortality rates affect both future population size and infection rate so that the peak disease incidence lags behind peak fly numbers. Most hosts are susceptible at the

time when tsetse fly numbers begin their annual increase. In relation to disease control the study concluded that the anti-tsetse measures were more certain of success.

In a later study, Hagrove *et al.* [32] generalized the Rogers [74] two-host model for Trypanosomiasis to one where a single species can feed off any finite number of vertebrate hosts. The study considered the situation typical of Eastern and Southern Africa, where *T. vivax*, *T. congolense* and *T. brucei rhodesiense* occur in livestock and wildlife and the last-named parasite also causes *Rhodesian* sleeping sickness in humans. The overall basic reproductive rate R_0 of the trypanosome species was calculated and the model used to compare the impact of drug- and insecticide-based interventions on R_0 with varying densities of cattle, humans and wild hosts.

The study established that intervention impact changes with the number of cattle treated and the proportion of the meals of blood tsetse take from cattle. R_0 was always reduced more by treating cattle with insecticides rather than by trypanocides. In situations where cattle provide the majority of bloodmeals for tsetse, their model suggests that the use of Insecticide Treated Cattle (ITC) should provide a potent tool for controlling, or even eliminating trypanosomiasis. In the absence of wild hosts, the model suggests that control of sleeping sickness ($R_0 < 1$) could be achieved by treating 65% of cattle with trypanocides or 20% with insecticide. However, the dynamics of transmission ensure that the requisite proportion favoring the use of ITC depends on the species of trypanosome involved. The presence of wild mammalian hosts leads to an increase in the coverage required and makes the control of *T. congolense* difficult.

Recently, Kajunguri [46] in his PhD dissertation formulated a mathematical model for transmission of *T. brucei rhodesiense*, the acute form of trypanosomiasis found in East Africa and Southern Africa, by tsetse vectors to a multi-host population and its control using insecticide-treated cattle. Two strategies were considered: whole-body and restricted application of insecticides to cattle. When considering three-hosts, that is cattle, humans and wildlife a sensitivity analysis of the basic reproduction number in the absence and presence of ITC

showed that it was more sensitive to the tsetse mortality rate. Numerical results showed that both strategies of insecticide-treated cattle decrease the incidence of *T. brucei rhodesiense* in humans and the tsetse density. Restricted application of insecticides to cattle was found to be a cheap, safe and farmer based strategy towards the control of *T. brucei rhodesiense* .

The above mentioned studies indicate that animal trypanosomiasis as an infectious disease involves the interaction between more than one host and the infectious agent which are varied. Further, the infection of one host provides a source of infection to the other hosts. This latter effect is inherently non-linear, generating epidemics that show complex patterns with time [62]. Consequently, as in Blayney *et. al.* [8], this study will use a dynamic model to study the disease. The host-vector interaction and the flow of populations between compartments will be described by a system of ordinary differential equations. The rates of infection in the cattle, vector and wild host population is a function of the average number of contacts, probability of infection upon contact, proportion of infectious vectors and hosts per unit time as in Roger [74].

Unlike Milligan and Baker [63], our interest is in a more strategic model which simplifies the system to its bare essentials and is useful for studying general disease dynamics and control [86]. We shall assume a single trypanosome is transmitted by a particular species of the tsetse fly in the cattle population. This is motivated by the fact that a further consequence of the unusual life history of tsetse is their tendency to have low genetic variability within a given population. This is partly a consequence of low dispersal rate, and partly due to the low reproductive rate, probably combined with selection for the most energetically-efficient individuals [47]. The tsetse fly have two feeding sources, the cattle and the wild animal, and the preferences in feeding are denoted by differences in transmission probabilities. The effect of the varied trypanosomes will hence be ignored.

Milligan and Baker [63] in their study considered the difference in age in the vector population which present differences in susceptibility to infection. Our study will assume that the age structure of the tsetse population is constant. This is a reasonable assumption where no

tsetse control efforts are in place, or when trypanosomiasis control consists simply of treating livestock with trypanocides that have no insecticidal effect [34]. Since some vectors do not effectively contribute to disease dynamics, they do not exist from the modeling point of view. We hence simplify the problem by dividing the vector population into the susceptible and infective vectors who directly affect disease dynamics.

The tsetse fly populations exhibit a range of seasonal behavior, from populations with large fluctuations with a peak in the late rainy season, to those which appear to be constant, or to show only slight seasonality [63]. Milligan and Baker [63] in their study included the seasonality in fly population which induces seasonality in cattle parasitaemia. It seems obvious to expect a rapid disease increase during the vector population maxima because the cattle receive more bites which increases the probability of disease transmission. Hence to model time in our study, we will concentrate on the dynamics of the disease during the peak periods.

In all the studies indicated above, the control of the disease is an intricate matter most probably due to devastating effects of the disease on animal production. There are three principal control strategies for tsetse-transmitted trypanosomiasis in a cattle population. These include the use of trypanocidal drugs (chemotherapy and chemoprophylaxis), tsetse control and the breeding of trypanotolerant cattle [27]. A number of studies have been carried out to combat vector-borne diseases and in most cases they focus is on vector control strategies which include bush-clearance (to eliminate tsetse resting sites), wild game culling (to reduce the parasite reservoirs and host availability for tsetse), and insecticidal spraying of tsetse resting sites [34]. These studies range from field and laboratory research [70] to mathematical models which are capable of predicting long term dynamics in the disease [7, 12]. In this study we consider an optimal control model with two controls, treatment and prevention.

2.2 The Application of Optimal Control Theory in Mathematical Disease Models

Optimal control theory is a powerful mathematical tool used to make decision involving complex dynamical systems [68]. For example in a cattle population susceptible to trypanosomiasis, we would use optimal control theory to determine the proportion of the infected cattle that should be treated and what rate of vector control is required to optimize control of the disease and at the same time minimize the cost of control. There have been a number of applications of optimal control theory on disease modeling [36, 2] and recently on vector-host models.

Blayney *et al.* [8] made one of the first attempts to implement optimal control theory in vector-host models. They considered an optimal control model with two controls, for treatment and prevention. The model was piecewise continuous on a finite interval since most vectors use favorable climatic conditions to flourish. The mathematical foundation of the control model and the derivation of optimal control pair of functions for the control system were given using Pontrayagin's Maximum Principle. The model was applied to study the effects of prevention and treatment controls on a malaria disease while keeping the implementation cost at a minimum. The results of their analytical and numerical techniques supported the hypothesis that among intervention techniques, preventive practices are very effective in reducing the incidence of infectious hosts and vectors.

To determine control programmes that effectively reduce the vector-borne disease in a community Ozair *et al.* [68], formulated an optimal control problem. The strategies they considered included personal protection by using preventive measures on the vector biting rate, treatment and spraying of insects using larvacides which reduce the vector population. A comparison between optimal control and no control indicated that the former has an effect of reducing the number of infected individuals. They established that an effective and optimal use of preventive measure in the population without the use of larvacide against the vector is not beneficial if total elimination of the disease is desirable in the community.

In yet another study, Lashari *et al.* [3] used optimal control to identify the best strategy of a vector-borne disease that would reduce infection and prevent vector-host as well as direct contacts by using three controls. The controls were a mosquito-reduction strategy, personal (human) protection and blood screening. They also applied the Pontryagins Maximum Principle, to perform the optimal analysis. Their results support the hypothesis that preventive practices are very effective in reducing the incidence of infectious hosts and vectors.

Since the trypanosomiasis disease persists at an irreducible level with occasional outbreaks in spite of the constant vigilance, our study will formulate an optimal control model and use it to derive optimal prevention and treatment strategies with minimal implementation cost.

Chapter 3

The Basic Model for Trypanosomiasis in a Cattle Population

3.1 Introduction

In this chapter, a basic model of trypanosomiasis in a cattle population is formulated. The model reduces the complicated epizootiology of trypanasomiasis in a cattle population to a mathematical model of several equations. The components of disease dynamics include the tsetse-fly vector which transmit the disease pathogens and the wild animal population which form an alternative feeding source for the tsetse fly and are a trypanosome reservoir.

The model is analyzed to gain insight into the epidemiological and dynamical features necessary for a better understanding of the dynamics of the disease in a population. Both analytic and numerical methods are applied to determine the epidemiological and demographic factors that influence the spread of the disease. The objective is to determine thresholds parameters that would control or eradicate the disease in a cattle population.

3.2 Derivation of the Model

Let $N_c(t)$, $N_v(t)$ and $N_w(t)$, represent the total populations of cattle, vectors and wild animals respectively at a given time t. We divide these populations into two compartments the

susceptibles $S_c(t)$, $S_v(t)$ and $S_w(t)$ that are at risk of being infected and the infectives denoted $I_c(t)$, $I_v(t)$ and $I_w(t)$ the number already infected and capable of transmitting infection to those at risk. Assuming the populations are closed, then

$$\begin{aligned} N_c(t) &= S_c(t) + I_c(t), \\ N_v(t) &= S_v(t) + I_v(t), \\ N_w(t) &= S_w(t) + I_w(t). \end{aligned} \tag{3.1}$$

For ease of presentation, throughout the document the number of individuals in the compartments at time t will be denoted as

$$\begin{aligned} N_c &= S_c + I_c, \\ N_v &= S_v + I_v, \\ N_w &= S_w + I_w. \end{aligned} \tag{3.2}$$

The model assumes that susceptible cattle, vector and wild animal populations are replenished mainly by birth at constant recruitment rates Λ_c, Λ_v and Λ_w respectively. They are decreased mainly by both forces of infection λ_c, λ_v and λ_w and natural death rates μ_c, μ_v and μ_w in the cattle, vector and animal populations respectively. The infective populations are replenished by the force of infection and decreased by the natural death rates in the populations. The infected cattle population are further decreased by disease-induced death at an average rate of κ.

Disease spreads in the cattle or in the wild animal population when an infected vector bites susceptible cattle or wild animals and they are infected. However, not all bites result in an infection. A transmission coefficient is used, as a measure of the likelihood that a contact between a susceptible and an infected will result in a new infection. The rate of infection is also a function of the tsetse fly survival rate. The longer the tsetse fly survives the larger the number of hosts it infects. It equally depends on the ratio of the infected to the whole population. Hence the rate of infection is jointly proportional to the biting rate, transmission coefficient, the vector survival rate and the ratio of the infected to the whole population.

The susceptible cattle acquire infection with trypanosomiasis following contacts with infected flies at an average rate $\lambda_c = \alpha_1 \tau_1 \varepsilon \frac{I_v}{N_c}$, where α_1 is the average biting rate of tsetse fly on the cattle, τ_1 is the transmission probability per bite per cow and ε the survival rate of a vector.

The susceptible wild animals and acquire infection with trypanosomiasis following contacts with infected flies at an average rate $\lambda_w = \alpha_2 \tau_4 \varepsilon \frac{I_v}{N_w}$, where α_2 is the average biting rate of tsetse fly on wild animals, τ_4 is the transmission probability per bite per wild animal. The wild animal populations are reservoirs of the trypanosomes and do not die from the disease.

Susceptible tsetse flies acquire infection with trypanosomiasis following contacts with cattle or wild animals infected with trypanosomiasis at an average rate of $\lambda_v = \alpha_1 \tau_2 \frac{I_c}{N_c} + \alpha_2 \tau_3 \frac{I_w}{N_w}$. τ_2 and τ_3 are the transmission probability for tsetse infection per bite per cow and wild animal respectively.

Assumptions

In view of the fact that the model under consideration monitors the dynamics of a disease in a cattle population it shall assume that all the state variables and parameters of the model are non-negative real values. The model equally assumes there is no vertical transmission of the disease and recruitment into the populations is by birth; hence all newborns into the populations are uninfected and they join the susceptible group. There is also no transmission of the disease by other biting flies. Though the tsetse populations exhibit a range of behavior which induces seasonality in cattle parasitaemia [63], the model will consider the period when maximum vector population is attained. Only a single trypanosome transmitted by a single species of the tsetse fly is assumed to cause infection. This is motivated by the low dispersal rate, low reproductive rate and selection for the most energetically efficient individuals which leads to a low genetic variability in a tsetse population [47].

Schematic Diagram

The compartmental model is represented as follows:

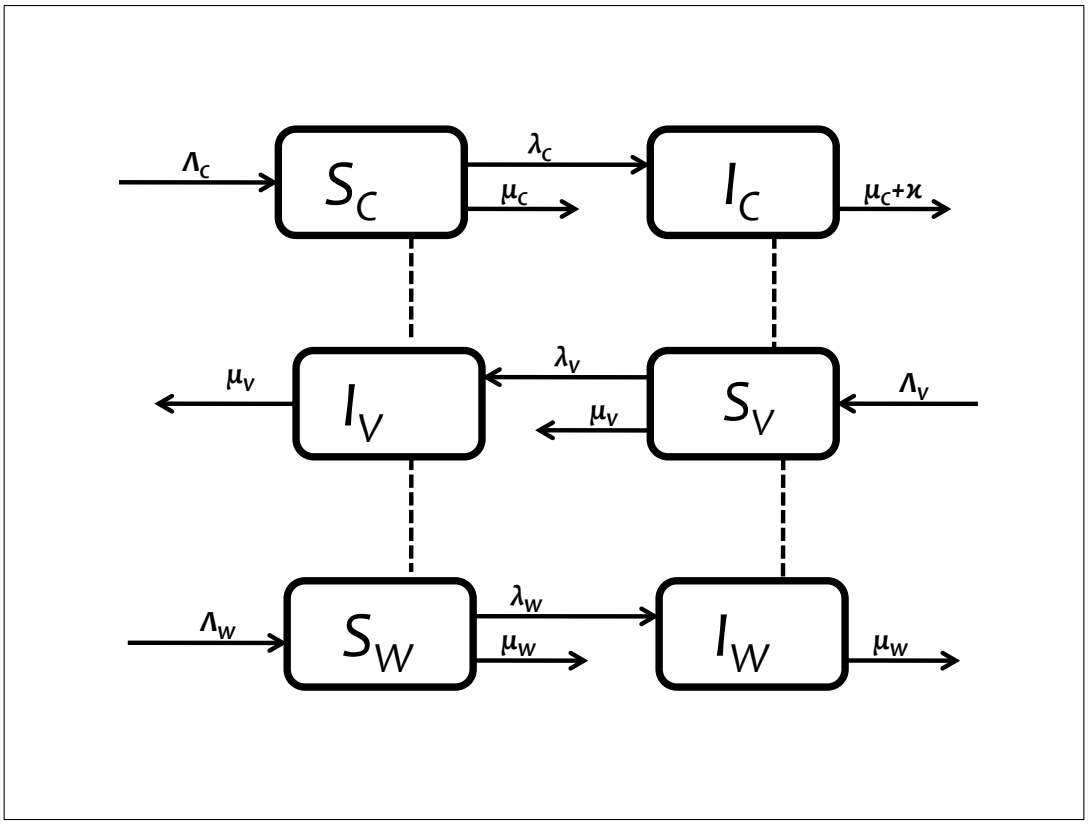

Figure 3.2.1: Compartmental model of trypanosomiasis in a cattle population

Model Equations

The mathematical equations modeling the description of our basic model are:

$$\begin{aligned}
\frac{dS_c}{dt} &= \Lambda_c - \left(\mu_c + \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}\right)S_c,\\
\frac{dI_c}{dt} &= \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}S_c - (\mu_c+\kappa)I_c,\\
\frac{dS_v}{dt} &= \Lambda_v - \left(\alpha_1\tau_2\frac{I_c}{N_c} + \alpha_2\tau_3\frac{I_w}{N_w} + \mu_v\right)S_v,\\
\frac{dI_v}{dt} &= \left(\alpha_1\tau_2\frac{I_c}{N_c} + \alpha_2\tau_3\frac{I_w}{N_w}\right)S_v - \mu_v I_v,\\
\frac{dS_w}{dt} &= \Lambda_w - \left(\alpha_2\tau_4\varepsilon\frac{I_v}{N_w} + \mu_w\right)S_w,\\
\frac{dI_w}{dt} &= \alpha_2\tau_4\varepsilon\frac{I_v}{N_w}S_w - \mu_w I_w.
\end{aligned} \tag{3.3}$$

with the corresponding populations changing at the rates

$$\begin{aligned}\frac{dN_c}{dt} &= \Lambda_c - \mu_c N_c - \kappa I_c,\\ \frac{dN_v}{dt} &= \Lambda_v - \mu_v N_v,\\ \frac{dN_w}{dt} &= \Lambda_w - \mu_w N_w.\end{aligned} \tag{3.4}$$

3.3 Properties of the Model

The System (3.3) describes cattle, vector and wild animal populations and therefore it is necessary to show that all populations totals at time t, S_c, I_c, S_v, I_v, S_w and I_w, are non-negative for all time ($t \geq 0$). In this section solutions of the System (3.3) with positive initial data are shown to remain positive for all time $t \geq 0$ and are bounded in a given region.

3.3.1 Positivity and Boundedness of Solutions

We define the set $\Omega = \{S_{c0}, I_{c0}, S_{v0}, I_{v0}, S_{w0}, I_{w0}\} \in R^6_+, 0 \leq N_c \leq \frac{\Lambda_c}{\mu_c}$, $0 \leq N_v \leq \frac{\Lambda_v}{\mu_v}$, $0 \leq N_w \leq \frac{\Lambda_w}{\mu_w}\}$ where N_c, N_v, N_w are as defined in Equation (3.2). We now show that the solution of System (3.3) with initial conditions in Ω remain in Ω for all $t \geq 0$. [That is, Ω is positively invariant with respect to the dynamics governed by Equation (3.3)].

Proof. From the first equation of System (3.3), since Λ_c is a positive constant and the ratio $\frac{I_v}{N_c}$ is taken as constant h because it is known that a vector takes a fixed number of blood meals per unit time independent of the population density in the host [21],

$$\begin{aligned}\frac{dS_c}{dt} &= \Lambda_c - \left(\mu_c + \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}\right)S_c,\\ \frac{dS_c}{dt} &\geq -(\mu_c + \alpha_1\tau_1\varepsilon h)S_c,\end{aligned}$$

implying

$$S_c \geq S_{c0}e^{-(\mu_c+\alpha_1\tau_1\varepsilon h)t} \geq 0.$$

Clearly, S_c is positive for all $t \geq 0$. Similarly, for the rest of the equations in System (3.3) with

$$\begin{aligned}
S_{v0} \geq 0, \ \frac{dS_v}{dt} &\geq -(\alpha_1\tau_2 c + \alpha_2\tau_3 w + \mu_v)S_v, \\
S_{w0} \geq 0, \ \frac{dS_w}{dt} &\geq -(\alpha_2\tau_4\varepsilon\rho + \mu_w)S_w, \\
I_{c0} \geq 0, \ \frac{dI_c}{dt} &\geq -(\mu_c + \kappa)I_c, \\
I_{v0} \geq 0, \ \frac{dI_v}{dt} &\geq -\mu_v I_v, \\
I_{w0} \geq 0, \ \frac{dI_w}{dt} &\geq -\mu_w I_w,
\end{aligned}$$

implying

$$\begin{aligned}
S_v(t) &\geq S_{v0}e^{-(\alpha_1\tau_2 c+\alpha_2\tau_3 w+\mu_v)t} > 0, \\
S_w(t) &\geq S_{w0}e^{-(\alpha_2\tau_4\varepsilon\rho+\mu_w)t} > 0, \\
I_c(t) &\geq I_{c0}e^{-(\mu_c+\kappa)t} > 0, \\
I_v(t) &\geq I_{v0}e^{-(\mu_v)} > 0, \\
I_w(t) &\geq I_{w0}e^{-(\mu_w)} > 0,
\end{aligned}$$

where $c = \dfrac{I_c}{N_c}$ and $w = \dfrac{I_w}{N_w}$ are proportions and $\rho = \dfrac{I_v}{N_w}$ a constant, indicates that the solution for the system remains positive for all $t \geq 0$. This result shows that solutions with initial values in Ω, remain non-negative for all $t \geq 0$. □

Since the model under consideration describes the dynamics of trypanosomiasis in a cattle population of varying size, it is assumed that, all the state variables and parameters of the model are non-negative $\forall t \geq 0$. In the absence of the disease, the first equation of Equation (3.4),

$$\frac{dN_c}{dt} \leq \Lambda_c - \mu_c N_c,$$

implying that

$$N_c \leq \frac{\Lambda_c}{\mu_c} - \left[\frac{\Lambda_c - \mu_c N_{c0}}{\mu_c}\right] e^{-\mu_c t}. \tag{3.5}$$

As $t \to \infty$ in Equation (3.5), $N_c \to \dfrac{\Lambda_c}{\mu_c}$ which implies that $0 \leq N_c \leq \dfrac{\Lambda_c}{\mu_c}$. Similarly from the second and third equations of Equation (3.4) we have $0 \leq N_v \leq \dfrac{\Lambda_v}{\mu_v}$ and $0 \leq N_w \leq \dfrac{\Lambda_w}{\mu_w}$ respectively.

Since $N_c = (S_c, I_c)$, $N_v = (S_v, I_v)$ and $N_w = (S_w, I_w)$, then the feasible solution set of System (3.3) enter and remain in the region:

$$\Omega = \left\{ (S_c, I_c, S_v, I_v, S_w, I_w) \in \mathbb{R}^6_+;\ 0 \leq N_c \leq \frac{\Lambda_c}{\mu_c},\ 0 \leq N_v \leq \frac{\Lambda_v}{\mu_v},\ 0 \leq N_w \leq \frac{\Lambda_w}{\mu_w} \right\}. \tag{3.6}$$

The above two results indicate that the System (3.3) is well posed epidemiologically and mathematically and it is consequently sufficient to study its dynamics in Ω. Therefore in the analysis of System (3.3), the state variables are restricted to those defined in Equation (3.6).

3.4 Analysis of the Model

3.4.1 Local Stability Analysis of the Disease Free Equilibrium, ε^o

The diseased classes in the cattle, vector (tsetse fly) and wild animal populations are I_c, I_v and I_w respectively. Setting the right hand side of System (3.3) to zero and solving for the state variables with $I_c = I_v = I_w = 0$, gives

$$\begin{aligned} S_c^o &= \frac{\Lambda_c}{\mu_c}, \\ S_v^o &= \frac{\Lambda_v}{\mu_v}, \\ S_w^o &= \frac{\Lambda_w}{\mu_w}. \end{aligned}$$

at disease free equilibrium. Hence the disease-free equilibrium point, is

$$\varepsilon^o = \left(\frac{\Lambda_c}{\mu_c},\ 0,\ \frac{\Lambda_v}{\mu_v},\ 0,\ \frac{\Lambda_w}{\mu_w},\ 0 \right). \tag{3.7}$$

In this subsection, the main result is to show that if $R_0 < 1$, the disease free equilibrium is asymptotically stable while when $R_0 > 1$ it is unstable. For this reason R_0, the basic

reproduction number needs to be determined. This is a statistic devised to measure an infections potential for spread in a defined population. Anderson and May [55], defined it as the "average" number of secondary infections produced when one infectious individual is introduced into a host population in which every host is susceptible.

R_0 for ε^o

To determine R_0, the "next generation" approach [19] is used, since we have a system in which there are multiple discrete types of infected individuals (cattle, tsetse flies, and wild animals). In this approach, R_0 is defined as the spectral density (dominant eigenvalue) of the "next generation operator". The operator is formed by distinguishing two disease states, infected and non-infected from the System (3.3). To distinguish new infections from all other changes in the population, the system equations are rearranged so that the first three equations correspond to the infected populations in the model. The System (3.3) is then written as:

$$\begin{aligned}
\frac{dI_c}{dt} &= \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}S_c - (\mu_c+\kappa)I_c,\\
\frac{dI_v}{dt} &= \left(\alpha_1\tau_2\frac{I_c}{N_c} + \alpha_2\tau_3\frac{I_w}{N_w}\right)S_v - \mu_v I_v,\\
\frac{dI_w}{dt} &= \alpha_2\tau_4\varepsilon\frac{I_v}{N_w}S_w - \mu_w I_w,\\
\frac{dS_c}{dt} &= \Lambda_c - \left(\mu_c + \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}\right)S_c,\\
\frac{dS_v}{dt} &= \Lambda_v - \left(\alpha_1\tau_2\frac{I_c}{N_c} + \alpha_2\tau_3\frac{I_w}{N_w} + \mu_v\right)S_v,\\
\frac{dS_w}{dt} &= \Lambda_w - \left(\alpha_2\tau_4\varepsilon\frac{I_v}{N_w} + \mu_w\right)S_w.
\end{aligned} \tag{3.8}$$

The next generation matrix (operator), FV^{-1}, is formed from matrices of the partial derivatives of $\mathcal{F}_i$ and $\mathcal{V}_i$ with respect to the infected classes computed at the disease-free equilibrium. $\mathcal{F}_i$ defines the appearance of new infections in compartment i, i being the I_c, I_v, I_w compartments. It includes only infections that are newly arising but does not include terms which describe the transfer of infectious individuals from one infected compartment to another. $\mathcal{V}_i = \mathcal{V}_i^- + \mathcal{V}_i^+$ where $\mathcal{V}_i^+$ is the rate of transfer of individuals into compartment i

by all other means other than disease while $\mathcal{V}_i^-$ is the rate of transfer of individuals out of compartment i.

From Equation (3.8), using the above description gives:

$$\mathcal{F}_i = \begin{pmatrix} \alpha_1\tau_1\varepsilon\dfrac{I_v}{N_c}S_c \\ \alpha_1\tau_2\dfrac{I_c}{N_c}S_v + \alpha_2\tau_3\dfrac{I_w}{N_w}S_v \\ \alpha_2\tau_4\varepsilon\dfrac{I_v}{N_w}S_w \end{pmatrix},$$

$$\mathcal{V}_i^- = \begin{pmatrix} (\mu_c+\kappa)I_c \\ \mu_v I_v \\ \mu_w I_w \end{pmatrix},$$

and

$$\mathcal{V}_i^+ = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}.$$

Hence

$$\mathcal{V}_i = \begin{pmatrix} (\mu_c+\kappa)I_c \\ \mu_v I_v \\ \mu_w I_w \end{pmatrix}.$$

The jacobian of $\mathcal{F}_i$ is given by

$$\mathbf{J}_{\mathcal{F}_i} = \begin{pmatrix} -\alpha_1\tau_1\varepsilon\dfrac{I_vS_c}{(S_c+I_c)^2} & \alpha_1\tau_1\varepsilon\dfrac{S_c}{S_c+I_c} & 0 \\ \alpha_1\tau_2\dfrac{S_v}{(S_c+I_c)} - \alpha_1\tau_2 I_c\dfrac{S_v}{(S_c+I_c)^2} & 0 & \alpha_2\tau_3\dfrac{S_v}{(S_w+I_w)} - \alpha_2\tau_3 I_w\dfrac{S_v}{(S_w+I_w)^2} \\ 0 & \alpha_2\tau_4\varepsilon\dfrac{S_w}{S_w+I_w} & -\alpha_2\tau_4\varepsilon I_v\dfrac{S_w}{(S_w+I_w)^2} \end{pmatrix},$$

At a disease free equilibrium, $I_c = I_v = I_w = 0$ and thus from Equation (3.1), $N_c = S_c, N_v = S_v, N_w = S_w$ which when used in $\mathcal{F}_i$ we obtain

$$F = \begin{pmatrix} 0 & \alpha_1\tau_1\varepsilon & 0 \\ \alpha_1\tau_2 h & 0 & \alpha_2\tau_3\rho \\ 0 & \alpha_2\tau_4\varepsilon & 0 \end{pmatrix},$$

with $h = \frac{N_v}{N_c}$ and $\rho = \frac{N_v}{N_w}$. The ratios h and ρ are taken as constant because it is known that a vector takes a fixed number of blood meals per unit time independent of the population density in the host [21]. Matrix F is the infection matrix.

Let (i, j) denote the entry in the i^{th} row and the j^{th} column of the matrix F. The entry at (i, j) represents the rate at which the infected individuals in compartment j produce new infections in the compartment i. The infected vectors produce new infections in the cattle population at the rate $\alpha_1\tau_1\varepsilon$ and in the wild animal population at the rate $\alpha_2\tau_4\varepsilon$, while the infected cattle and wild animal populations produce new infections in the vector population at the rate $\alpha_1\tau_2 h$ and $\alpha_2\tau_3\rho$ respectively.

The Jacobian of $\mathcal{V}_i$ at the disease-free equilibrium denoted by V is given by

$$V = \begin{pmatrix} (\mu_c + \kappa) & 0 & 0 \\ 0 & \mu_v & 0 \\ 0 & 0 & \mu_w \end{pmatrix}.$$

V is the transition matrix and the (i, j) entry is the rate individuals in stage j progress to stage i and its inverse given by

$$V^{-1} = \begin{pmatrix} \frac{1}{(\mu_c + \kappa)} & 0 & 0 \\ 0 & \frac{1}{\mu_v} & 0 \\ 0 & 0 & \frac{1}{\mu_w} \end{pmatrix},$$

The (i, j) entries in matrix V^{-1} is the expected time spent in compartment i by an individual initially in compartment j over the course of its infection. The average length of time an infected cow, vector and wild animal spends in the infected compartment during its lifetime assuming that the population remains near the disease-free equilibrium and barring infection is $\frac{1}{(\mu_c + \kappa)}$, $\frac{1}{\mu_v}$ and $\frac{1}{\mu_w}$ respectively. The next generation matrix or operator is hence given by

$$FV^{-1} = \begin{pmatrix} 0 & \frac{\alpha_1\tau_1\varepsilon}{\mu_v} & 0 \\ \frac{\alpha_1\tau_2 h}{(\mu_c+\kappa)} & 0 & \frac{\alpha_2\tau_3\rho}{\mu_w} \\ 0 & \frac{\alpha_2\tau_4\varepsilon}{\mu_v} & 0 \end{pmatrix}. \tag{3.9}$$

The (i, j) entry of FV^{-1} is the expected number of secondary infections produced in compartment i by an index case initially in the compartment j. The expected number of new infections in the infected vectors compartment, produced by the infected vectors originally introduced into the infected cattle and wild animal population is $\frac{\alpha_1\tau_1\varepsilon}{\mu_v}$ and $\frac{\alpha_2\tau_4\varepsilon}{\mu_v}$ respectively. Each infected wild animal produces $\frac{\alpha_2\tau_3\rho}{\mu_w}$ new infected vectors over its expected infectious period, and each infected vector produces $\frac{\alpha_2\tau_4\varepsilon}{\mu_v}$ new infected wild animals over its expected infectious period. Similarly each infected cow produces $\frac{\alpha_1\tau_2 h}{(\mu_c+\kappa)}$ new infected vectors over its expected infectious period and each infected vector produces $\frac{\alpha_1\tau_1\varepsilon}{\mu_v}$ new infected cows over its infectious period.

Hence, the basic reproduction number of System (3.3) R_0, defined as the spectral radius of the matrix FV^{-1}, is given by the dominant eigenvalue of FV^{-1} defined in Equation (3.9) as

$$R_0 = \sqrt{\frac{\alpha_2^2\tau_4\tau_3\varepsilon\rho}{\mu_v\mu_w} + \frac{\alpha_1^2\tau_2\tau_1\varepsilon h}{\mu_v(\mu_c+\kappa)}}. \tag{3.10}$$

The basic reproduction number calculated above is biologically meaningful because as expected, it is jointly proportional to the probability of infection per contact between a susceptible and an infectious individual, the average rate of contact between a susceptible and an infectious individual and the duration of infectiousness [43]. It is the product of the rate of production of new exposures and new infections.

As indicated by Chitnis *et. al.*[15], R_0 measures the initial disease transmission. It refers to the number of infections generated by the index case, i.e., generation zero [43].

Generations in epidemic models are the waves of secondary infections that flow from each

previous infection. The first generation of an epidemic is all the secondary infections that result from infectious contact with the index case, who is of generation zero. The number of new infections in cattle that one cow causes through their infectious period is R_0^2 and not R_0. This is because the definition of R_0 in Equation (3.10) based on the next generation approach [20], counts the number of infections from one generation to the next [15]. In this case, the number of new infections in the tsetse flies count as one generation. The square root in Equation (3.10) arises from the two "generations" required for an infected vector or host to "reproduce" itself.

Since the System (3.3) satisfies axioms (A1)-(A5) of the Theorem 2 in van den Driessche and Watmough [83], and since the R_0 calculated above is biologically meaningful, we have the following result:

Lemma 3.4.1. *The disease free equilibrium for System (3.3) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof. The Jacobian of System (3.3) calculated at the disease free equilibrium point Equation (3.7), $J(\varepsilon^o)$ is given by:

$$J(\varepsilon^o) = \begin{pmatrix} -\mu_c & 0 & 0 & -\alpha_1\tau_1\varepsilon & 0 & 0 \\ 0 & -(\mu_c+\kappa) & 0 & \alpha_1\tau_1\varepsilon & 0 & 0 \\ 0 & -\alpha_1\tau_2 h & -\mu_v & 0 & 0 & -\alpha_2\tau_3\rho \\ 0 & \alpha_1\tau_2 h & 0 & -\mu_v & 0 & \alpha_2\tau_3\rho \\ 0 & 0 & 0 & -\alpha_2\tau_4\varepsilon & -\mu_w & 0 \\ 0 & 0 & 0 & \alpha_2\tau_4\varepsilon & 0 & -\mu_w \end{pmatrix}. \tag{3.11}$$

The six dimensional matrix given by Equation (3.11) has at most six eigenvalues, three of which are $-\mu_c$, $-\mu_v$ and $-\mu_w$. To calculate the remaining eigenvalues, the rows and columns where $-\mu_c$, $-\mu_v$ and $-\mu_w$ lie are omitted to reduce the matrix to three dimensional given by:

$$\begin{pmatrix} -(\mu_c+\kappa) & \alpha_1\tau_1\varepsilon & 0 \\ \alpha_1\tau_2 h & -\mu_v & \alpha_2\tau_3\rho \\ 0 & \alpha_2\tau_4\varepsilon & -\mu_w \end{pmatrix}. \tag{3.12}$$

To show that the remaining eigenvalues are also negative, we require that the trace be negative and determinant positive. The trace of the matrix in Equation (3.12) is given by

$$-[(\mu_c+\kappa)+\mu_v+\mu_w],$$

and is negative while its determinant is given by

$$\det J(\varepsilon^o) = \alpha_2^2\tau_4\tau_3\varepsilon\rho(\mu_c+\kappa)+\alpha_1^2\tau_2\tau_1\varepsilon h\mu_w-(\mu_c+\kappa)\mu_v\mu_w,$$

A positive determinant implies

$$\alpha_2^2\tau_4\tau_3\varepsilon\rho(\mu_c+\kappa)+\alpha_1^2\tau_2\tau_1\varepsilon h\mu_w-(\mu_c+\kappa)\mu_v\mu_w>0$$

$$\alpha_2^2\tau_4\tau_3\varepsilon\rho(\mu_c+\kappa)+\alpha_1^2\tau_2\tau_1\varepsilon h\mu_w>(\mu_c+\kappa)\mu_v\mu_w$$

$$R_0^2>1$$

This implies $R_0>1$. The disease free equilibrium ε^o is locally asymptotically unstable. It is clear from the assumption that the disease is fatal without intervention that if the population is at disease free equilibrium, the introduction of infective cattle into the population would result in the disease being endemic in the cattle population. □

3.4.2 Global Stability Analysis of ε^o

To establish the global stability conditions for the disease-free equilibrium when $R_0<1$, the System (3.3) is written in the form as in [12],

$$\frac{dZ}{dt}=G(X,Z), \quad G(X,0)=0,$$
$$\frac{dX}{dt}=F(X,Z);$$

where $X\in\mathbb{R}^3$ denotes the number of uninfected individuals and $Z\in\mathbb{R}^3$ denotes the number of infected individuals.

Then the two conditions:

(i) For $\dfrac{dX}{dt} = F(X, 0), \quad X^*$ is globally asymptotically stable,

(ii) $G(X, Z) = AZ - \widehat{G}(X, Z), \quad \widehat{G}(X, Z) \geq 0$ for $(X, Z) \in \Omega$

where $A = D_Z G(X^*, 0)$ is an M-matrix (the off diagonal elements of A are non-negative) and Ω is the region as earlier defined, if met, also guarantee the global asymptotic stability of the disease free state [12]. If System (3.3) satisfies the above two conditions then the following theorem holds:

Theorem 3.4.1. *If $R_0 < 1$, then the disease-free equilibrium point is globally asymptotically stable on Ω.*

Proof. The proof begins by defining new variables and breaking System (3.3) into two: the susceptible and the infected sub-systems. With $Z = (I_c, I_v, I_w)$ and $X = (S_c, S_v, S_w)$, the System (3.3) can be written as:

$$\begin{aligned} \frac{dZ}{dt} &= G(X, Z), \quad G(X, 0) = 0, \\ \frac{dX}{dt} &= F(X, Z). \end{aligned} \tag{3.13}$$

where the two functions are given by:

$$\begin{aligned} G(X, Z) = \Bigg[& \alpha_1 \tau_1 \varepsilon \frac{I_v}{N_c} S_c - (\mu_c + \kappa) I_c; \quad (\alpha_1 \tau_2 \frac{I_c}{N_c} + \alpha_2 \tau_3 \frac{I_w}{N_w}) S_v - \mu_v I_v; \\ & \alpha_2 \tau_4 \varepsilon \frac{I_v}{N_w} S_w - \mu_w I_w \Bigg]^T, \end{aligned} \tag{3.14}$$

$$\begin{aligned} F(X, Z) = \Bigg[& \Lambda_c - (\mu_c + \alpha_1 \tau_1 \varepsilon \frac{I_v}{N_c}) S_c; \Lambda_v - (\alpha_1 \tau_2 \frac{I_c}{N_c} + \alpha_2 \tau_3 \frac{I_w}{N_w} + \mu_v) S_v; \\ & \Lambda_w - (\alpha_2 \tau_4 \varepsilon \frac{I_v}{N_w} + \mu_w) S_w \Bigg]^{\mathrm{T}}. \end{aligned}$$

From Equation (3.14) since $Z = (I_c, I_v, I_w)$ clearly $G(X, 0) = 0$. Consider the reduced system

$$\frac{dX}{dt} = F(X, 0)$$

$$\begin{aligned} \frac{dS_c}{dt} &= \Lambda_c - \mu_c S_c, \\ \frac{dS_v}{dt} &= \Lambda_v - \mu_v S_v, \\ \frac{dS_w}{dt} &= \Lambda_w - \mu_w S_w. \end{aligned} \tag{3.15}$$

Equating the equations in Equation (3.15) to 0 and solving for the state variables gives

$$\begin{aligned} \varepsilon^o &= (S_c^o, S_v^o, S_w^o) \\ &= \left(\frac{\Lambda_c}{\mu_c}, \frac{\Lambda_v}{\mu_v}, \frac{\Lambda_w}{\mu_w} \right) \end{aligned}$$

which provides the globally asymptotically stable equilibrium point for the reduced system $\frac{dX}{dt} = F(X, 0)$. Since the point is asymptotically stable and these asymptotic dynamics are independent of the initial conditions in Ω, then the convergence of the solutions of Equation (3.15) is global in Ω.

For the second condition, recall that $\varepsilon^o = (S_c^o, S_v^o, S_w^o) = \left(\frac{\Lambda_c}{\mu_c}, \frac{\Lambda_v}{\mu_v}, \frac{\Lambda_w}{\mu_w} \right)$ so that

$$G(\varepsilon^o, Z) = \begin{pmatrix} \alpha_1 \tau_1 \varepsilon I_v - (\mu_c + \kappa) I_c \\ \alpha_1 \tau_2 \dfrac{I_c}{N_c} \dfrac{\Lambda_v}{\mu_v} + \alpha_2 \tau_3 \dfrac{I_w}{N_w} \dfrac{\Lambda_v}{\mu_v} - \mu_v I_v \\ \alpha_2 \tau_4 \varepsilon I_v - \mu_w I_w \end{pmatrix},$$

and $G(X, Z) = AZ - \widehat{G}(X, Z)$ where $A = D_Z G(\varepsilon^o, 0)$. Hence

$$\begin{aligned} A &= D_Z G(\varepsilon^o, 0) \\ &= \begin{pmatrix} -(\mu_c + \kappa) & \alpha_1 \tau_1 \varepsilon & 0 \\ \alpha_1 \tau_2 \dfrac{\Lambda_v}{\mu_v N_c} & -\mu_v & \alpha_2 \tau_3 \dfrac{\Lambda_v}{\mu_v N_w} \\ 0 & \alpha_2 \tau_4 \varepsilon & -\mu_w \end{pmatrix} \end{aligned}$$

and

$$\widehat{G}(X,Z) = \begin{pmatrix} \widehat{G_1}(X,Z) \\ \widehat{G_2}(X,Z) \\ \widehat{G_3}(X,Z) \end{pmatrix} = \begin{pmatrix} \alpha_1\tau_1\varepsilon I_v(1-\frac{S_c}{N_c}) \\ \alpha_1\tau_2\frac{I_c}{N_c}\left(\frac{\Lambda_v}{\mu_v}-S_v\right)+\alpha_2\tau_3\frac{I_w}{N_w}\left(\frac{\Lambda_v}{\mu_v}-S_v\right) \\ \alpha_2\tau_4\varepsilon I_v\left(1-\frac{S_w}{N_w}\right) \end{pmatrix}.$$

$\widehat{G_1}(X,Z)$ and $\widehat{G_3}(X,Z)$ are both greater than 0 since $\frac{S_w}{N_w} < 1$ and $\frac{S_c}{N_c} <$. Equally since the vector population is bounded at $\frac{\Lambda_v}{\mu_v}$, the expression $\alpha_1\tau_2\frac{I_c}{N_c}\left(\frac{\Lambda_v}{\mu_v}-S_v\right)+\alpha_2\tau_3\frac{I_w}{N_w}\left(\frac{\Lambda_v}{\mu_v}-S_v\right)$ in $\widehat{G_2}(X,Z)$ is non-negative. Therefore since the disease-free equilibrium point is locally asymptotically stable for $R_0 < 1$, the global stability equilibrium follows from the theorem in [12]. □

3.4.3 The Endemic Equilibrium, ε^*

In this section a condition based on parameter values is derived such that when the condition holds, the endemic equilibrium exists, whereas when the condition is false, only the disease-free equilibrium exists. The existence of a unique endemic equilibrium point indicates that the disease has the ability to persist and invade the given cattle population and $R_0 > 1$ [37]. The existence of this condition, motivates the study of viable disease control strategies in the population.

Existence of an endemic equilibrium

Theorem 3.4.2. *The System (3.3) has a unique endemic equilibrium in Ω if $R_0 > 1$.*

Proof. Consider the steady state equations for I_c, I_v and I_w. From the second equation of System (3.3) we have

$$I_c = \frac{\alpha_1\tau_1\varepsilon I_v S_c}{(\mu_c+\kappa)N_c} \tag{3.16}$$

From the fourth equation of System (3.3) we get

$$I_v = \frac{\alpha_1\tau_2 I_c N_w S_v + \alpha_2\tau_3 I_w N_c S_v}{\mu_v N_c N_w} \tag{3.17}$$

From the sixth equation of System (3.3) we get

$$I_w = \frac{\alpha_2\tau_4\varepsilon I_v S_w}{\mu_w N_w} \tag{3.18}$$

Substituting for I_c from Equation (3.16) into Equation (3.17) we get

$$I_v = \frac{\alpha_1^2\tau_1\tau_2, I_v S_c N_w S_v + \alpha_2\tau_3(\mu_c+\kappa) I_w N_c^2 S_v}{\mu_v(\mu_c+\kappa) N_c^2 N_w} \tag{3.19}$$

and substituting for I_w from Equation (3.18) into Equation (3.19) we have

$$I_v = \left(\frac{\alpha_1^2\tau_2\tau_1\varepsilon h}{\mu_v(\mu_c+\kappa)} + \frac{\alpha_2^2\tau_4\tau_3\varepsilon\rho}{\mu_v\mu_w}\right) I_v \tag{3.20}$$

which is equivalently written as

$$I_v = R_0^2 I_v \tag{3.21}$$

where the ratios $h = \frac{S_v}{N_c}$ and $\rho = \frac{S_v}{N_w}$ are as defined earlier; $\frac{S_c}{N_c} = \frac{S_w}{N_w} = 1$ at the disease free steady state and R_0 is as defined in Equation (3.10). At the endemic equilibrium state, $I_v > 0$. We therefore solve Equation (3.21) for $I_v > 0$. Hence

$$\begin{aligned} R_0^2 I_v - I_v &> 0 \\ (R_0^2 - 1) I_v &> 0 \end{aligned}$$

This implies that either $I_v > 0$ or $R_0 > 1$.

This proves that a unique endemic equilibrium exists and is possible if $R_0 > 1$. □

3.4.4 Local Stability Analysis of ε^*

From the epidemiological point of view, the result in Theorem 3.4.2 means that the disease persists in the endemic state, which is of concern to the farmers. For that reason we need to analyze the stability of the endemic equilibrium, ε^*.

To analyze the stability of the equilibrium point ε^*, the Centre Manifold theorem as described in Theorem 4 of [12] is used. It states that if f is C^r (r times continuously differentiable)

then at every equilibrium point there is a unique C^r stable manifold, a unique C^r unstable manifold and a (not necessarily unique) C^{r-1} centre manifold [29]. As the stability of the equilibrium correlates with the stability of its manifolds, the existence of the centre manifold brings up the question of its dynamics. However, before stating our main result, we give the following theorem which will be useful in the subsequent section.

Theorem 3.4.3. *(Castillo and Song [13])*

Consider the general system of ordinary differential equations with a parameter ϕ:

$$\frac{dx}{dt} = f(x, \phi), f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n \quad \text{and} \quad f \in \mathbb{C}^2(\mathbb{R}^n \times \mathbb{R}). \tag{3.22}$$

Without loss of generality, it is assumed that 0 is an equilibrium for Equation (3.22) for all values of the parameter ϕ that is

$$f(0, \phi) \equiv 0 \quad \forall \phi,$$

and

A1 $A = D_x f(0,0) = \left(\dfrac{\partial f_i}{\partial x_i}(0,0)\right)$, *is the linearization of Equation (3.22) around the equilibrium 0 with ϕ evaluated at 0. Zero is a simple eigenvalue of A and all other eigenvalues of A have negative real parts;*

A2 *Matrix A has a nonnegative right eigenvector $\boldsymbol{w}$ and a left eigenvector $\boldsymbol{v}$ corresponding to the zero eigenvalue.*

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

$$\begin{aligned} a &= \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0), \\ b &= \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0). \end{aligned} \tag{3.23}$$

The local dynamics of Equation (3.22) around 0 are totally determined by the signs of a and b. Particularly, if $a > 0$ and $b > 0$, then a backward bifurcation occurs at $\phi = 0$, and if

i *$a > 0$, $b > 0$, when $\phi < 0$ with $\phi \ll 1$, 0 is locally asymptotically stable, and there exists a positive unstable equilibrium; when $0 < \phi \ll 1$, 0 is unstable and there exists a negative and locally asymptotically stable equilibrium;*

ii *$a < 0$, $b < 0$, when $\phi < 0$ with $\phi \ll 1$, 0 is unstable; when $0 < \phi \ll 1$, 0 is locally asymptotically stable and there exists a positive unstable equilibrium;*

iii *$a > 0$, $b < 0$, when $\phi < 0$ with $\phi \ll 1$, 0 is unstable, and there exists a locally asymptotically stable negative equilibrium; when $0 < \phi \ll 1$, 0 is stable and a positive unstable equilibrium appears;*

iv *$a < 0$, $b > 0$, when ϕ changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly, a negative unstable equilibrium becomes positive and locally asymptotically stable.*

To establish the local asymptotic stability of the endemic equilibrium ε^* we define $S_c = x_1$, $I_c = x_2$, $S_v = x_3$, $I_v = x_4$, $S_w = x_5$ and $I_w = x_6$. Using the vector notation $X = (x_1, x_2, x_3, x_4, x_5)^T$, System (3.3) can be written as:

$$\begin{aligned}
\frac{dx_1}{dt} = f_1 &= \Lambda_c - \left(\mu_c + \alpha_1\tau_1\varepsilon\frac{x_4}{x_1+x_2}\right)x_1,\\
\frac{dx_2}{dt} = f_2 &= \alpha_1\tau_1\varepsilon\frac{x_4}{x_1+x_2}x_1 - (\mu_c+\kappa)x_2,\\
\frac{dx_3}{dt} = f_3 &= \Lambda_v - \left(\alpha_1\tau_2\frac{x_2}{x_1+x_2} + \alpha_2\tau_3\frac{x_6}{x_5+x_6} + \mu_v\right)x_3,\\
\frac{dx_4}{dt} = f_4 &= \left(\alpha_1\tau_2\frac{x_2}{x_1+x_2} + \alpha_2\tau_3\frac{x_6}{x_5+x_6}\right)x_3 - \mu_v x_4,\\
\frac{dx_5}{dt} = f_5 &= \Lambda_w - \left(\alpha_2\tau_4\varepsilon\frac{x_4}{x_5+x_6} + \mu_w\right)x_5,\\
\frac{dx_6}{dt} = f_6 &= \alpha_2\tau_4\varepsilon\frac{x_4}{x_5+x_6}x_5 - \mu_w x_6.
\end{aligned} \tag{3.24}$$

The centre manifold theorem involves evaluating the Jacobian of Equation (3.24) at the disease-free equilibrium (ε^o) denoted by $J(\varepsilon^o)$ which is as given by Equation (3.11). Hence the reproduction number of Equation (3.24) is given as in Equation (3.10).

Since the tsetse fly bites both the wild animal and cattle populations though the rate at which they bite the wild animal population is higher [63]; then $\alpha_1 < \alpha_2$, (where α_1 is the

cattle biting rate and α_2, the wild animal biting rate) so that $\alpha_2 = \theta\alpha_1$, where $\theta > 1$ is the modification parameter which captures the increased transmissibility of animal trypanosomiasis when the vectors feed on the wild animal population. If we let $\alpha = \alpha_1$ and choose α to be the bifurcation parameter, the R_0 in Equation (3.10) is given thus:

$$R_0 = \alpha\sqrt{\frac{\theta^2\tau_4\tau_3\varepsilon\rho}{\mu_v\mu_w} + \frac{\tau_2\tau_1\varepsilon h}{\mu_v(\mu_c+\kappa)}}. \tag{3.25}$$

Solving for $\alpha = \alpha^*$ when $R_0 = 1$ gives

$$\alpha^* = \sqrt{\frac{\mu_v\mu_w(\mu_c+\kappa)}{\theta^2\tau_4\tau_3\varepsilon\rho(\mu_c+\kappa) + \tau_2\tau_1\varepsilon h\mu_w}}. \tag{3.26}$$

The linearized system of Equation (3.24) with $\alpha = \alpha^*$ chosen as a bifurcation parameter has a simple zero eigenvalue. Hence the Jacobian Equation (3.11) at $\alpha = \alpha^*$ has a right and left eigenvector $\mathbf{w}$ and $\mathbf{v}$ respectively.

Eigenvectors of $J(\varepsilon^o)$

The Jacobian of Equation (3.24) at $\alpha = \alpha^*$ has a right eigenvector (corresponding to the zero eigenvalue) given by $\mathbf{w} = (w_1, w_2, w_3, w_4, w_5, w_6)^T$, with

$$w_1 = \frac{\alpha^*\tau_1\varepsilon}{\mu_c}\eta w_4;\ w_2 = \frac{\alpha^*\tau_1\varepsilon}{(\mu_c+\kappa)}w_4;\ w_3 = \eta w_4;\ w_4 > 0;\ w_5 = -\frac{\theta\alpha^*\tau_4\varepsilon}{\mu_w}w_4;\ w_6 = \frac{\theta\alpha^*\tau_4\varepsilon}{\mu_w}w_4,$$

where $\eta = \dfrac{\alpha^{*2}\tau_2\tau_1\varepsilon h}{\mu_v(\mu_c+\kappa)} + \dfrac{\theta\alpha^{*2}\tau_4\tau_3\varepsilon\rho}{\mu_v\mu_w}$, and it has a left eigenvector (corresponding to the zero eigenvalue) given by $\mathbf{v} = (v_1, v_2, v_3, v_4, v_5, v_6)^T$, with

$$v_1 = 0; \quad v_2 = \frac{\alpha^*\tau_2 h}{(\mu_c+\kappa)}v_4; \quad v_3 = 0; \quad v_4 > 0; \quad v_5 = 0; \quad v_6 = \frac{\theta\alpha^*\tau_3\rho}{\mu_w}v_4.$$

For the Equation (3.24), the associated non-zero partial derivatives of $F = (f_1, f_2, f_3, f_4, f_5, f_6)$

as defined in Equation (3.24) at ε^o are given by

$$\begin{aligned}
\frac{\partial^2 f_2}{\partial x_2 \partial x_4} &= -c^* \alpha^* \tau_1 \varepsilon \mu_c, \\
\frac{\partial^2 f_4}{\partial x_1 \partial x_2} &= -c^* \alpha^* \tau_2 h \mu_c, \\
\frac{\partial^2 f_4}{\partial x_2^2} &= -c^* 2\alpha^* \tau_2 h \mu_c, \\
\frac{\partial^2 f_4}{\partial x_2 \partial x_3} &= c^* \alpha^* \tau_2 \mu_c, \\
\frac{\partial^2 f_4}{\partial x_3 \partial x_6} &= v^* \theta \alpha^* \tau_3 \mu_w, \\
\frac{\partial^2 f_4}{\partial x_5 \partial x_6} &= -v^* \theta \alpha^* \tau_3 \rho \mu_w, \\
\frac{\partial^2 f_4}{\partial x_6^2} &= -v^* 2\theta \alpha^* \tau_3 \rho \mu_w.
\end{aligned} \tag{3.27}$$

where $c^* = \dfrac{1}{\Lambda_c}$ and $v^* = \dfrac{1}{\Lambda_v}$.
From Equation (3.27), the parameter a as defined in Equation (3.23) is given by

$$a = -2\alpha^{*2} \left\{ M_1 M_4 + \eta(M_5 + c^* M_1 + M_1 M_3) \right\} v_4 w_4^2 \ < \ 0, \tag{3.28}$$

where $M_1 = \dfrac{\tau_2 \tau_1 \varepsilon h}{(\mu_c + \kappa)}$, $M_2 = v^* \theta^2 \tau_4 \tau_3 \varepsilon$, $M_3 = \dfrac{2\theta \alpha^* \tau_4 \varepsilon \rho}{\mu_w}$, $M_4 = 3c^* \alpha^* \tau_1 \varepsilon \mu_c$ and $M_5 = \dfrac{\alpha^* \tau_1}{(\mu_c + \kappa)}$.

To calculate b, the associated non-vanishing partial derivatives are:

$$\begin{aligned}
\frac{\partial^2 f_4}{\partial x_2 \partial \alpha} &= \tau_2 h, \\
\frac{\partial^2 f_4}{\partial x_6 \partial \alpha} &= \theta \tau_3 \rho,
\end{aligned}$$

so that

$$b = \left(\frac{\alpha \tau_2 \tau_1 \varepsilon h}{\mu_c + \kappa} + \frac{\theta^2 \alpha \tau_4 \tau_3 \varepsilon \rho}{\mu_w} \right) v_4 w_4 \ > \ 0. \tag{3.29}$$

From Equations (3.28) and (3.29), $a < 0$ and $b > 0$. Hence Lemma 3.4.2 follows.

Lemma 3.4.2. *The endemic equilibrium for System (3.3) exists and is locally asymptotically stable whenever $R_0 > 1$ as stated in [13] Theorem 4.1 (iv).*

The System (3.3) exhibits a supercritical bifurcation. This means that an exchange of stability between the disease-free and endemic steady states guarantees that the endemic steady state is locally asymptotically stable whenever $R_0 > 1$.

3.4.5 Global Stability Analysis of ε^*

The global stability of the endemic equilibrium of System (3.3) is established using the Lyapunov direct method.

Theorem 3.4.4. *Let $L(x,t)$ be a non-negative function with derivative $\dot{L}$ along the trajectories of the system. If $L(x,t)$ is a negative definite, then the origin of the system is globally uniformly asymptotically stable.*

Theorem 3.4.4 gives sufficient conditions for the global stability of a system. Though the search for a Lyapunov function establishing stability of an equilibrium point could be arduous, the Lyapunov function of the form $\widehat{L}(x_1, x_2, ..., x_n) = \sum_{i=1}^{n} c_i \left\{ x_i - x_i^* - x_i^* log \frac{x_1}{x_i^*} \right\}$ can be especially useful for host-vector models with any number of compartments [18].
From equating the equations of the system to zero, a unique endemic equilibrium $(S_c^*, I_c^*, S_v^*, I_v^*, S_w^*, I_w^*)$ exists and satisfies the following relations:

$$\begin{aligned}
\Lambda_c &= \mu_c S_c^* + \alpha_1 \tau_1 \varepsilon \frac{I_v^*}{N_c^*} S_c^*, \\
(\mu_c + \kappa) I_c^* &= \alpha_1 \tau_1 \varepsilon \frac{I_v^*}{N_c^*} S_v^*, \\
\Lambda_v &= \alpha_1 \tau_2 \frac{I_c^*}{N_c^*} S_v^* + \alpha_2 \tau_3 \frac{I_w^*}{N_w^*} S_v^* + \mu_v S_v^*, \\
\mu_v I_v^* &= \alpha_1 \tau_2 \frac{I_c^*}{N_c^*} S_v^* + \alpha_2 \tau_3 \frac{I_w^*}{N_w^*} S_v^*, \\
\Lambda_w &= \alpha_2 \tau_4 \varepsilon \frac{I_v^*}{N_w^*} S_w^* + \mu_w S_w^*, \\
\mu_w I_w^* &= \alpha_2 \tau_4 \varepsilon \frac{I_v^*}{N_w^*} S_w^*.
\end{aligned} \tag{3.30}$$

Theorem 3.4.5. *If $R_0 > 1$ then ε^* is globally asymptotically stable in Ω.*

Proof. The possible Lyapunov function

$L : (S_c, I_c, S_v, I_v, S_w, I_w) \in \Omega : S_c, I_c, S_v, I_v, S_w, I_w > 0 \to \mathbb{R}$ is defined by

$$\begin{aligned} L(S_c, I_c, S_v, I_v, S_w, I_w) = c_1 \left\{ S_c - S_c^* - S_c^* \log \frac{S_c}{S_c^*} \right\} + c_2 \left\{ I_c - I_c^* - I_c^* \log \frac{I_c}{I_c^*} \right\} + \\ c_3 \left\{ S_v - S_v^* - S_v^* \log \frac{S_v}{S_v^*} \right\} + c_4 \left\{ I_v - I_v^* - I_v^* \log \frac{I_v}{I_v^*} \right\} + \\ c_5 \left\{ S_w - S_w^* - S_w^* \log \frac{S_w}{S_w^*} \right\} + c_6 \left\{ I_w - I_w^* - I_w^* \log \frac{I_w}{I_w^*} \right\}, \end{aligned}$$

where

$$\begin{aligned} c_1 = c_2 &= \alpha_1 \tau_1 \varepsilon \frac{I_v^*}{N_c^*} S_c^*, \\ c_3 = c_4 &= \left\{ \alpha_1 \tau_2 \frac{I_c^*}{N_c^*} + \alpha_2 \tau_3 \frac{I_w^*}{N_w^*} \right\} S_v^*, \\ c_5 = c_6 &= \alpha_2 \tau_4 \varepsilon \frac{I_v^*}{N_w^*} S_w^*. \end{aligned}$$

This means L is C^1 in the interior of Ω, ε^* is the global minimum of L on Ω and $L(S_c^*, I_c^*, S_v^*, I_v^*, S_w^*, I_w^*) = 0$.

The derivative of L computed along the solutions of the System (3.3) is given by

$$\begin{aligned} \frac{dL}{dt} = &- \mu_c m^* \frac{S_c^*}{S_c} (S_c^* - S_c)^2 - m m^* S_c^{*2} \left(\frac{S_c}{S_c^*} \frac{I_c^*}{I_c} - 1 \right) - m^{*2} S_c^{*2} \left(\frac{S_c^*}{S_c} \right. \\ &\left. + \frac{I_c}{I_c^*} - 2 \right) - n^{*2} \frac{S_v^*}{I_v^*} \frac{S_v^*}{S_v} (S_v^* - S_v)^2 - n n^* S_v^{*2} \left(\frac{S_v}{S_v^*} \frac{I_v^*}{I_v} - 1 \right) - \\ &n^{*2} S_v^{*2} \left(\frac{S_v^*}{S_v} - 1 \right) - p^{*2} \frac{S_w^*}{S_w} \frac{S_w^*}{I_w^*} (S_w^* - S_w)^2 - p^{*2} S_w^{*2} \left(\frac{S_w^*}{S_w} \right. \\ &\left. + \frac{I_w}{I_w^*} - 2 \right) - p p^* S_w^{*2} \left(\frac{I_w^*}{I_w} \frac{S_w}{S_w^*} - 1 \right). \end{aligned} \tag{3.31}$$

where $m^* = \alpha_1 \tau_1 \varepsilon \frac{I_v^*}{N_c^*}$, $m = \alpha_1 \tau_1 \varepsilon \frac{I_v}{N_c}$, $n^* = \alpha_1 \tau_2 \frac{I_c^*}{N_c^*} + \alpha_2 \tau_3 \frac{I_w^*}{N_w^*}$, $n = \alpha_1 \tau_2 \frac{I_c}{N_c} + \alpha_2 \tau_3 \frac{I_w}{N_w}$, $p^* = \alpha_2 \tau_4 \varepsilon \frac{I_v^*}{N_w^*}$ and $p = \alpha_2 \tau_4 \varepsilon \frac{I_v}{N_w}$.

Since the arithmetic mean is greater than or equal to the geometric mean we have: $\frac{S_c}{S_c^*} \frac{I_c^*}{I_c} \geq 1$, $\frac{S_c^*}{S_c} + \frac{I_c}{I_c^*} \geq 2$, $\frac{S_v}{S_v^*} \frac{I_v^*}{I_v} \geq 1$, $\frac{S_v^*}{S_v} \geq 1$, $\frac{S_w^*}{S_w} + \frac{I_w}{I_w^*} \geq 2$, $\frac{I_w^*}{I_w} \frac{S_w}{S_w^*} \geq 1$, $\forall S_c, I_c, S_v, I_v, S_w, I_w \geq 0$, it implies $\dot{L} < 0$, hence $(S_c^*, I_c^*, S_v^*, I_v^*, S_w^*, I_w^*)$ is globally assymptotically stable.

Clearly from Equation (3.31), $\frac{dL}{dt} \leq 0$ always holds except at the steady state ε^*, the endemic equilibrium, of the System (3.3). Furthermore $\frac{dL}{dt} = 0$ if and only if $S_c = S_c^*$, $I_c = I_c^*$, $S_v = S_v^*$, $I_v = I_v^*$, $S_w = S_w^*$ and $I_w = I_w^*$. By LaSalle's invariant principle, ε^* is globally asymptotically stable in Ω. This completes the proof of Theorem 3.4.5. □

From the analysis of System (3.3), it is clear that the dynamics of trypanosomiasis in a cattle population is determined by R_0. However, since R_0 is a function of a number of disease and population parameters, a sensitivity analysis of these parameter value will aid decision making on which parameters to monitor in order to control the disease [39].

3.5 Sensitivity Analysis of R_0

It is generally agreed that the models are sensitive to input parameters in two distinct ways: one, the variability or uncertainty associated with a sensitive input parameter is propagated through the model resulting in a large contribution to the overall output variability, and two model results can be highly correlated with an input parameter so that small changes in the input values result in significant changes in the output [33]. Input parameters are either important or sensitive and [17] distinguishes them by referring to "important" parameters as those whose uncertainty contributes substantially to the uncertainty in assessment results and "sensitive" parameters as those who have significant influence on assessment results.

Whereas R_0 reports a single summary outcome, the expected number of secondary infections arising from a single individual during his or her entire infectious period in a population of susceptibles [37], the actual number of infected(s) will depend on the level of confidence or uncertainty in the various parameters that define R_0 [79]. These might involve the methodology used in constructing the disease model or could relate to the actual values that have been used to define R_0 since there are usually errors in data collection and presumed parameter values. For example, the cattle biting rate, α_1 may be too high in the disease model and one may wish to know the likely impact of using an alternative value of α_1. This means examining the sensitivity of R_0 to changes in the values of the parameters that define it.

Sensitivity analysis of R_0, allows the evaluation of its estimate to the uncertainty in estimating the values of each of its input parameters [77], however it can also be used to discover parameters that have a high impact on R_0 and should be targeted by intervention strategies [15]. The outcome of such analysis is a sensitivity index. It gives the ratio of the change of the output to change in input while other parameters remain constant [33]. These indices will indicate how influential each parameter is to disease transmission and prevalence and therefore should be targeted for disease control.

From Equation (3.10), the thirteen non-negative parameters that define R_0 are α_1, α_2, τ_1, τ_2, τ_3, τ_4, μ_c, μ_v, μ_w, κ, ε, $h = \dfrac{S_v}{N_w}$ and $\rho = \dfrac{S_v}{N_c}$. When an explicit algebraic equation describes the relationship between the independent variable and the dependent variable, the sensitivity index Υ_i for a particular independent variable can be calculated from the partial derivative of the dependent variable, i.e.

$$\Upsilon_{\alpha_1}^{R_0} = \frac{\partial R_0}{\partial \alpha_1} \frac{\alpha_1}{R_0},$$

where the quotient, $\dfrac{\alpha_1}{R_0}$, is introduced to normalize the index by removing the effects of units, [33].

The normalized sensitivity indices for the thirteen parameters are:

$$
\begin{aligned}
\Upsilon_{\alpha_2}^{R_0} &= \frac{\eta_1}{R_0^2\gamma_2}, \\
\Upsilon_{\alpha_1}^{R_0} &= \frac{\eta_2}{R_0^2\gamma_1}, \\
\Upsilon_{\tau_4}^{R_0} &= \frac{1}{2}\frac{\eta_1}{R_0^2\gamma_2}, \\
\Upsilon_{\tau_3}^{R_0} &= \frac{1}{2}\frac{\eta_1}{R_0^2\gamma_2}, \\
\Upsilon_{\tau_2}^{R_0} &= \frac{1}{2}\frac{\eta_2}{R_0^2\gamma_1}, \\
\Upsilon_{\tau_1}^{R_0} &= \frac{1}{2}\frac{\eta_2}{R_0^2\gamma_1}, \\
\Upsilon_{\varepsilon}^{R_0} &= \frac{1}{2}, \\
\Upsilon_{h}^{R_0} &= \frac{1}{2}\frac{\eta_2}{R_0^2\gamma_1}, \\
\Upsilon_{\rho}^{R_0} &= \frac{1}{2}\frac{\eta_1}{R_0^2\gamma_2}, \\
\Upsilon_{\mu_v}^{R_0} &= -\frac{1}{2}, \\
\Upsilon_{\mu_w}^{R_0} &= -\frac{1}{2}\frac{\eta_1}{R_0^2\gamma_2}, \\
\Upsilon_{\mu_c}^{R_0} &= -\frac{1}{2}\frac{\eta_2\mu_c}{R_0^2 m}, \\
\Upsilon_{\kappa}^{R_0} &= -\frac{1}{2}\frac{\eta_2\kappa}{R_0^2 m}.
\end{aligned}
\tag{3.32}
$$

where R_0 is as defined in Equation (3.10) and

$$
\begin{aligned}
\eta_1 &= \alpha_2^2\tau_4\tau_3\varepsilon\rho, \\
\eta_2 &= \alpha_1^2\tau_2\tau_1\varepsilon h, \\
\gamma_1 &= \mu_V(\mu_c + \kappa), \\
\gamma_2 &= \mu_v\mu_w, \\
m &= \mu_v(\mu_c + \kappa)^2.
\end{aligned}
$$

From Equation (3.32), all the sensitivity indices are positive except $\Upsilon_{\mu_v}^{R_0}$, $\Upsilon_{\mu_w}^{R_0}$, $\Upsilon_{\mu_c}^{R_0}$ and $\Upsilon_{\kappa}^{R_0}$. The natural death rate of the vectors, the natural death rate of the wild animals and the natural and disease-induced death rate in cattle that have the effect of reducing R_0. Further,

all are functions of the parameter values except $\Upsilon_{\varepsilon}^{R_0}$ and $\Upsilon_{\mu_v}^{R_0}$ and will change as the parameter values change. To determine how sensitive the parameters are, we will use parameter values from previous studies.

Table 3.1: Parameter values

Parameter	**Description**	**Value**	**Ref**
α_1	Probability of biting cattle	0.032	[63]
α_2	Probability of biting wild animals	0.97	[63]
μ_c	Natural mortality rate of cattle (inc. slaughter)$days^{-1}$	0.00055	[85]
μ_v	Natural mortality rate of vector $days^{-1}$	0.97	[74]
μ_w	Natural mortality rate of wild animals $days^{-1}$	0.0006	[63]
κ	Disease-induced death rate in cattle $days^{-1}$	0.006	[75]
τ_1	Transmission probability from vector to cattle	0.62	[74]
τ_2	Transmission probability from cattle to vector	0.7	[85]
τ_3	Transmission probability from wild animal to vector	0.05	[63]
τ_4	Transmission probability from vector to wild animal	0.2	[63]
ε	Survival rate of vector	0.5	*Estimated*
ρ	Ratio of susceptible vectors to cattle population	76	[63]
h	Ratio of susceptible vectors to wild animal population	76	[63]
Λ_c	Cattle recruitment rate	22.0	[85]
Λ_v	Tsetse recruitment rate	24.0	*Estimated*
Λ_w	Wild animal recruitment rate	27.5	*Estimated*

In Table 3.1, the probability of vectors biting cattle and wild animals assumes that the ratio of wild animals to cattle is 1. Using the parameter values in Table 3.1, the sensitivity indices are provided in Table 3.2.

Table 3.2: Sensitivity indices of parameter values in R_0

Parameter	**Sensitivity Index**
α_2	+0.99569
ε	+0.50000
μ_v	- 0.50000
τ_4	+0.49785
τ_3	+0.49785
ρ	+0.49785
μ_w	- 0.49785
α_1	+0.00431
τ_2	+0.00215
τ_1	+0.00215
h	+0.00215
κ	- 0.00197
μ_c	- 0.00018

3.5.1 Interpretation of Sensitivity Indicies

The sign of the sensitivity index indicates whether the parameter would increase (+) or decrease (−) the endemicity of the disease. Table 3.2, shows that when the parameters α_2, ε, τ_4, τ_3, ρ, α_1, τ_2, τ_1 and h are increased keeping other parameters constant, they increase the value of R_0; The parameters μ_w, μ_v, μ_c and κ decrease the value of R_0 when they are increased keeping the other parameters constant.

The magnitude of the sensitivity index indicates the influence the parameter has on R_0. The greater the magnitude the greater the influence. The parameter with the highest influence on R_0 is the rate at which the vectors bite the wild animal population α_2. Other important parameters include the vector survival rate ε, the vector death rate μ_v and the transmission probabilities in the vector and wild animal populations, τ_4 and τ_3. The least sensitive parameters are the disease-induced death rate in the cattle population κ, the natural death

rate of the wild animal population μ_w and the natural death rate of the vector population, μ_v. It is also important to note that the sensitivity indices of R_0 with respect to ε, the vector survival rate and μ_v, the natural death rate of the vector are constant. They do not depend on parameter values.

3.5.2 Discussion on Sensitivity Analysis of R_0

From the analysis in Section 3.5.1 , the rate at which the vectors bite the wild animal population has the greatest influence on the dynamics of the disease. The fact that the wild animal population is tolerant and provides a reservoir to the trypanosome, accelerates the disease in a cattle population. In the Mtwapa case study [63], sensitivity analysis of the model was done using Monte-Carlo methods to enable an assessment of the relative importance of the parameters to be made. Their results emphasized the need for studies of the wild animal reservoir to be carried out alongside entomological studies in order to control the disease. The survival rate of the vector also contributes a great deal to the disease in a cattle population. The indices show that the death rate of the vectors has the highest effect of decreasing R_0. Hence efforts should be made to increase the efficacy of controlling the tsetse flies in the physical environment.

In a cattle population where the disease is endemic, concern would be on the parameters that the farmer has the ability to control in order to reduce R_0. Considering the parameters related to the cattle population, the biting rate of the cattle population is the most sensitive parameter. R_0 would be reduced by reducing the cattle biting rate; the transmission probability from infective vector to cattle population ; transmission probability from infective cattle to susceptible vectors and the proportion susceptible vectors to the cattle population in that order. In essence, the analysis suggests reducing the contact between the vector and the cattle populations.

3.6 Numerical Simulations and Discussion

The analytical results of the study are illustrated by carrying out numerical simulations of System (3.3) using the parameter values given in Table 3.1. The parameters were obtained from literature while the parameters which were not available in literature were estimated. The model is simulated using ODE solvers coded in Matlab programming language. The initial values of the population compartments are $S_{c0} = 5000$, $I_{c0} = 10$, $S_{v0} = 100$, $I_{v0} = 10$, $S_{w0} = 300$ and $I_{w0} = 10$. Numerical simulations of the disease states are shown. The state dynamics are also shown for varying values of the most sensitive disease parameters.

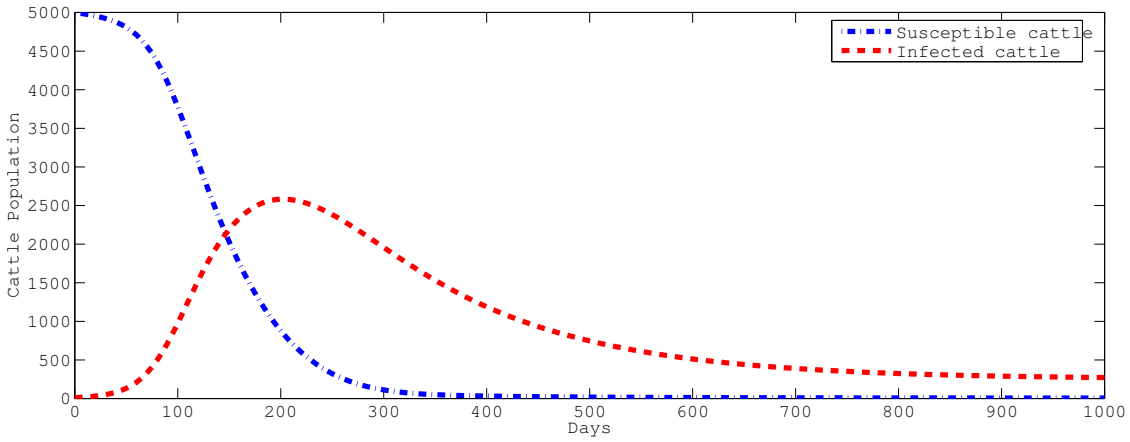

Figure 3.6.2: Population dynamics of the cattle population

Figure 3.6.2 shows the susceptible and the infected cattle populations over a span of 1000 days. The results show a sharp decrease in the number of susceptible individuals corresponding to an increase in the infected population during the initial stages of the epidemic before settling to a steady state which is either disease-free or endemic. The susceptible population is steadily reduced due to continuous infection and the infection population steadily reduced due fatality of the disease.

Figure 3.6.3 depicts the typical trajectories for the trypanosomiasis epidemic in a cattle population in the $S - I$ plane. It illustrates the invariance property of the model. The System

(3.3) simulated for varying initial conditions indicate the model solutions converge to the endemic state. These results further confirm the global stability results established earlier.

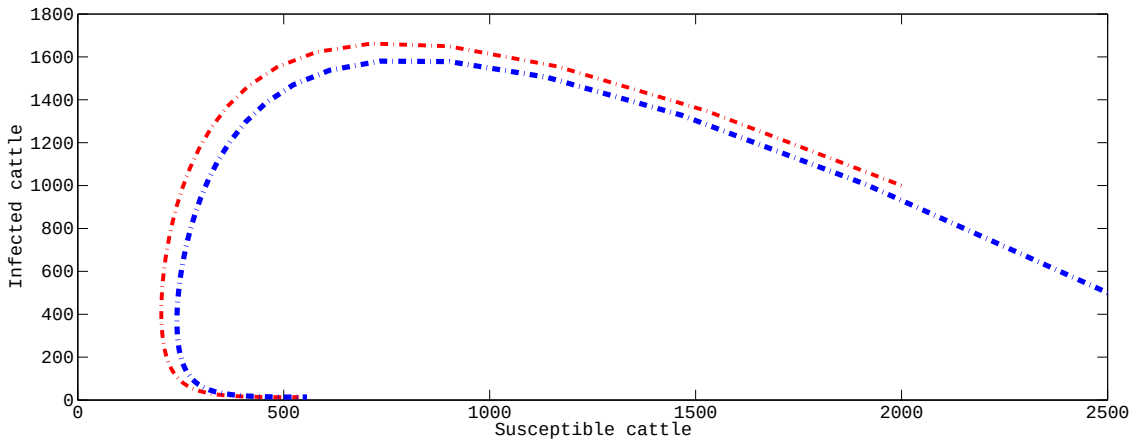

Figure 3.6.3: Phase portrait of the dynamics of the susceptible and infected cattle populations.

The analysis of System (3.3) indicated that disease prevalence in a cattle population is determined by the basic reproduction number R_0, which is a function of various parameters. Our analytical results showed that the parameter with the greatest influence on R_0 is the rate at which the vectors bite the wild animal population, α_2. Figure 3.6.4 shows the trypanosomiasis model simulated with varying values of α_2 to see their effect on the infected cattle population. Indeed with a higher wild animal biting rate, the infected populations rises steeply to its maximum value faster than when there is a lower wild animal biting rate.

In the cattle population the parameter which has the greatest influence on R_0 is the rate at which the vectors bite the cattle population. Varying the cattle population biting rate α_1 shows more varied differences in the population of the infected cattle as shown in Figure 3.6.5. The population of infected cattle also rises much higher due to the vector biting rate on the cattle. The simulations indicate that to control the disease in a cattle population, one would decrease the rate at which the vector bite the wild animal and the cattle populations.

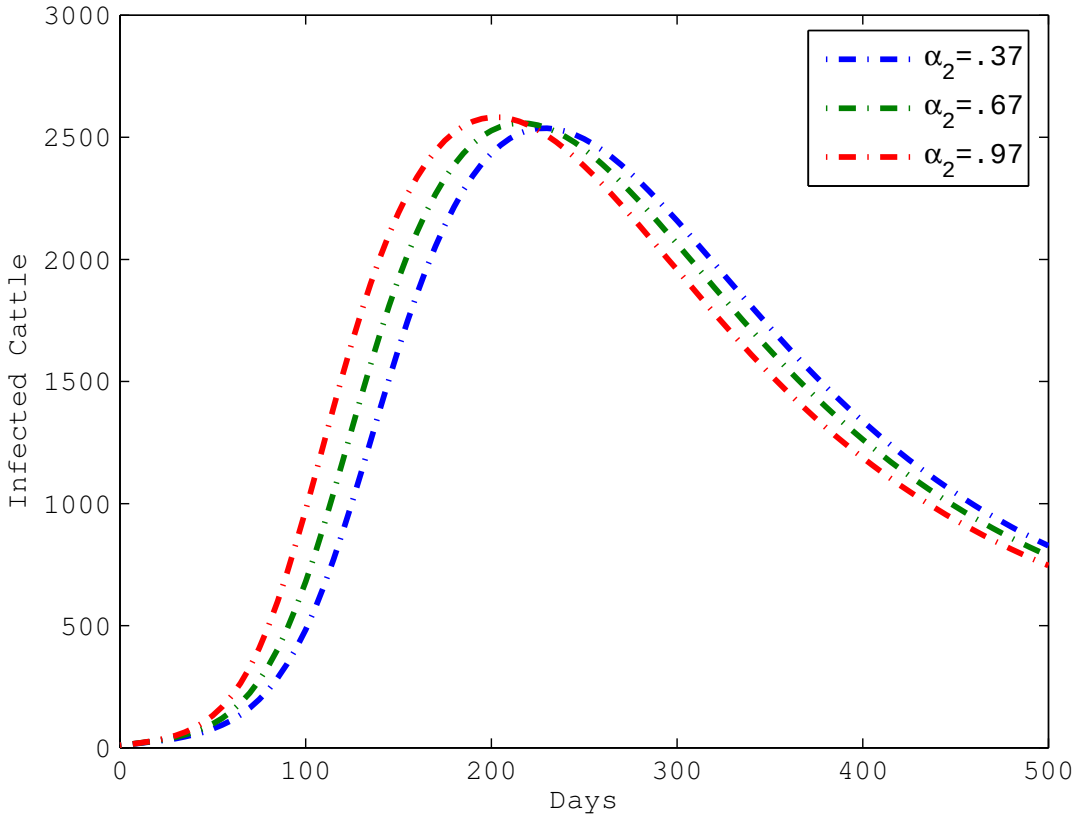

Figure 3.6.4: Infected cattle population at various vector wild animal biting rate

In the vector population, the parameter that has the greatest influence on R_0 is the vector survival rate, ϵ. Its sensitivity index is positive implying that if it is increased, it increases the endemicity of the disease. Indeed one of the major factors that contribute to the complexity of trypanosomiasis is the fact that the trypanosomes are transmitted cyclically by tsetse, of which there are some 36 species and subspecies, each adapted to different climatic and ecological conditions [65]. The cyclical transmission of infection represents the most important problem because, once the tsetse fly becomes infected, it remains infective for a long period [27]. The longer the vector survives the more cattle one would expect it to infect.

Figure 3.6.6 shows the infected cattle population at various levels of $\varepsilon = 0.3, 0.5 \quad and \quad 0.97$. At $\varepsilon = 0.97$, 3000 heads of cattle are infected in 100 days whereas at $\varepsilon = 0.3$, approximately

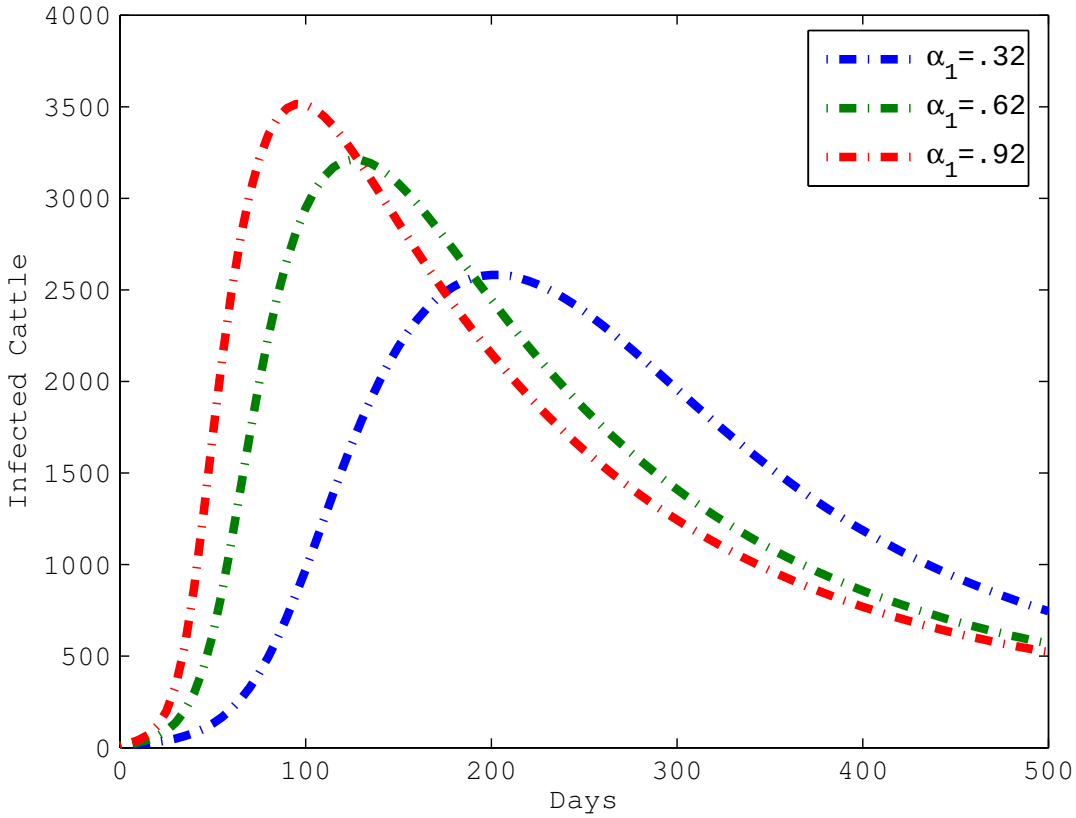

Figure 3.6.5: Infected cattle population at various vector cattle biting rate

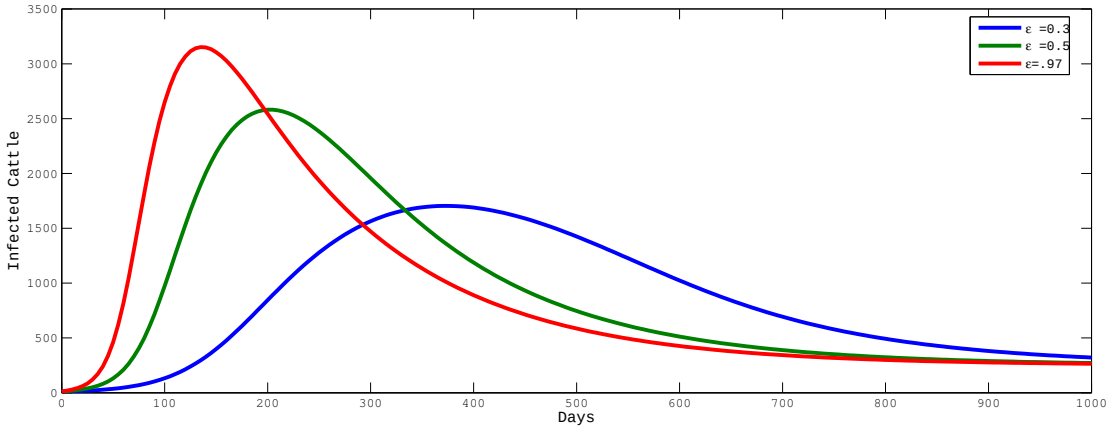

Figure 3.6.6: Infected cattle population at various vector survival rates

1500 heads of cattle are infected in about 400 days. The figure also shows that the infected cattle stabilize in the long run. The vector survival rate should therefore be one of the parameters one would target to control trypanosomiasis in a cattle population.

3.7 Summary

In this chapter a mathematical model for trypanosomiasis, a vector transmitted disease in a cattle population with fatality has been proposed and analyzed. The dynamics of the disease is further influenced by the wild animal population, which is an alternative feeding source for the vector. Using the theory of differential equations an invariant set in which the solutions of the model are biologically meaningful, Ω, was derived. Boundedness of solutions was also proved. Analysis of the model equilibria showed that, there exist two possible steady states, namely the disease-free point and the endemic equilibrium point and that the dynamics of the disease in a cattle population is completely determined by the basic reproduction number, R_0, which is the average number of secondary cases generated by a primary case.

Further analysis showed that the disease can invade into the susceptible cattle population and a unique endemic state exists when $R_0 > 1$, whereas the disease dies out when $R_0 < 1$. When $R_0 < 1$ the disease-free equilibrium is globally asymptotically stable and the infection could be cleared from the cattle population. However when $R_0 > 1$, a unique endemic equilibrium exists which is globally stable in the feasible region, Ω. This implies that the disease is present in the population and will become endemic. The proof is based on the second Lyapunov method with Lyapunov functions obtained by known functions in literature. R_0 is therefore an important threshold in the dynamics of the disease. The devastating nature of the disease, both economically and socially motivates the control of the disease, which from the analysis suggests reducing R_0, a function of disease parameters, to less than 1.

From Equation (3.10), R_0 is a function of various parameters which define the dynamics of the disease. These parameters obviously have varying influence on R_0, hence a sensitivity analysis of the parameters that define R_0 was carried out to evaluate or assess the influence

of each parameter on the magnitude of R_0. The analysis indicates that the parameters with the highest influence on R_0 are the rate at which the vectors bite the wild animal population, the survival rate of the vectors and the transmission probability from infective wild animal to susceptible vector. The wild animal population clearly has a great influence on the disease dynamics in the cattle population. Since they are tolerant to and provide a reservoir to the trypanosome, they accelerate the disease in a cattle population. Just as in [63], this study suggests a close monitoring of the disease dynamics in the wild animal population to suggest methods of disease control in the cattle population.

From the sensitivity indices provided in Table 3.2, the survival rate of the vector contributes a great deal to the disease in a cattle population while the death rate of the vectors has the highest effect of decreasing R_0. This indicates that to control the disease efforts should be made to increase the efficacy of controlling the tsetse flies in the physical environment.

Considering the parameters related to the cattle population, the biting rate of the cattle population is the most sensitive parameter. Other important parameters are the transmission probability from infective vector to cattle population and the proportion susceptible vectors to the cattle population. In essence the analysis suggests that control strategies that reduce the contact between the vector and the cattle population would be a way of eradicating the disease in a cattle population. Reducing the transmission probability from infective vector to the cattle population would mean the cattle become more tolerant of the trypanosomes and hence suggests breeding trypanotolerant cattle in areas where the disease is endemic.

The particular values of the sensitivity indices of the reproduction number, R_0, to the different parameters depend on the parameter values in the previous studies and on the assumptions on which the System (3.3) is made. To effectively guide policy, the model and parameter values would need to be tested against recent data from trypanosomiasis-endemic regions. The current analysis however remains an important step in simplifying the study of the general Trypanosomiasis disease dynamics in a given cattle population. In the next chapter, treatment as an intervention strategy will be incorporated into the basic trypanosomiasis

model.

Chapter 4

The Trypanosomiasis Model with Treatment Intervention

4.1 Introduction

This chapter considers a model for treatment of trypanosomiasis in a cattle population. It investigates the impact of treatment in mitigating against the spread of the disease in a cattle population. Treatment is administered to a proportion of the infected cattle. Analytical and numerical methods are both applied to determine the effect of treating different proportions of the infected cattle. The aim is to evaluate the role of treatment on the dynamics of the disease.

A treatment model is hence formulated and its basic properties necessary to state the proofs of stability are established. The effective reproductive number R_{eff} which determines the dynamical behavior of the disease is computed; the existence and stability of the equilibrium points are also established. The steady state solutions and their corresponding stability are characterized in terms of the effective reproduction number, a threshold parameter that determines the outcome or behavior of the epidemic. Numerical simulations of the model are presented and a discussion of the results is then given.

4.2 Model Framework

The basic trypanosomiasis model provided in Chapter 3, is extended by including treatment of the infected cattle as an intervention strategy. This will facilitate the mathematical analysis of the effect of treatment on the dynamics of the disease. A variant of the basic model is created by not making the assumption of a closed vector population. This is because in reality vector control programs are frequently blighted by reinvasion since barriers can rarely be made completely effective permanently, due to density dependent immigration into control areas [73].

The total vector population therefore changes through migration and the balance between births and deaths. A simple regulating migratory mechanism as in Artzrouni and Gouteux [56] is assumed, so that density-dependent immigration (or emigration) takes place when the total vector population N_v is below (or above) a biologically determined threshold value V. During a time interval dt, the net growth of the vector population due to migration is of the form $k(V - N_v)$, $k \geq 0$. The parameter k measures the magnitude of the migratory flows or expresses the force of this density-dependent migratory process. V is the critical value of the total vector population below which there is in-migration and above which there is out-migration. Thus when N_v is larger than V, there are $-k(V - N_v)$ flies that leave the area per unit of time; when N_v is smaller than V there are $k(V - N_v)$ flies that enter the area [5].

Since the epidemiology of trypanosomiasis is characterized by periods of quiescence and flare-up, reflecting intermittent vector control measures to reduce transmission [81, 63] and that during an epidemic the overwhelming majority of flies remain uninfected [44], we assume that migrations occur in the susceptible compartment. This implies only healthy flies migrate [56]. The wild animal population, as in the basic model System (3.3) play the role of an alternative food source for the tsetse fly and also as a reservoir for the trypanosomes.

As a control measure treatment is an important method to decrease the spread of diseases

as documented in studies such as [26]. The treatment of trypanosomiasis in cattle can be targeted or selective treatment where only those animals showing symptoms are treated. Here the rate of treatment is assumed to be proportional to the number of infectives. Alternatively it could be mass-treatment where treatment is done at a certain rate, such that the treatment rate is constant [63]. The suitable choice on the treatment strategy clearly depends on the resources available and the number of infectives.

For the effective use of resources, a farmer needs to determine a suitable capacity for the treatment of the disease. This is because for a treatment rate of infective cattle assumed to be proportional to the number of the infectives, the resources should be quite large. If the capacity of treatment is too large, the farmer pays for unnecessary cost while if it is too small, the farmer runs the risk of an outbreak of the disease [27]. Treatment is included in the model as a linear transfer between the infected and removed compartments in the cattle population. Treatment of a proportion of the infected cattle population is denoted γI_c and it is assumed there is no incidence of drug resistance.

The total cattle population then further includes a class of those who are removed, R_c because their risk of transmitting the parasite becomes negligible. The removed cattle population re-enter the susceptible population when they are cured or they die in the removed compartment and are replaced through births in the susceptible compartment, which is mathematically equivalent to a recovery [56]

Treatment of the infected cattle reduces the mortality due to disease of the infected cattle. If the duration of the prophylactic effect of the drug is longer than the duration in which treated the cattle get re-infected, the removed cattle will become susceptible again at the rate ω. It also reduces the trypanosome reservoirs and hence reduces the rate of infection of the vectors from infected cattle by $\zeta < 1$. We assume that when a cow gets into the treatment class, death cannot occur due to the disease.

4.2.1 Model Equations

The equations describing the above description are given as follows:

$$\begin{aligned}
\frac{dS_c}{dt} &= \Lambda_c - \left\{\mu_c + \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}\right\}S_c + \omega R_c,\\
\frac{dI_c}{dt} &= \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}S_c - (\mu_c+\kappa)I_c - \gamma I_c,\\
\frac{dR_c}{dt} &= \gamma I_c - (\mu_c+\omega)R_c,\\
\frac{dS_v}{dt} &= \Lambda_v + k(V-N_v) - \left\{\mu_v + (1-\zeta)\alpha_1\tau_2\frac{I_c}{N_c} + \alpha_2\tau_3\frac{I_w}{N_w}\right\}S_v,\\
\frac{dI_v}{dt} &= \left\{(1-\zeta)\alpha_1\tau_2\frac{I_c}{N_c} + \alpha_2\tau_3\frac{I_w}{N_w}\right\}S_v - \mu_v I_v,\\
\frac{dS_w}{dt} &= \Lambda_w - \left\{\alpha_2\tau_4\varepsilon\frac{I_v}{N_w} + \mu_w\right\}S_w,\\
\frac{dI_w}{dt} &= \alpha_2\tau_4\varepsilon\frac{I_v}{N_w}S_w - \mu_w I_w,
\end{aligned} \tag{4.1}$$

with initial conditions

$$S_{c0}\geq 0,\ I_{c0}\geq 0,\ R_{c0}\geq 0,\ S_{v0}\geq 0,\ I_{v0}\geq 0,\ S_{w0}\geq 0,\ I_{w0}\geq 0, \tag{4.2}$$

which together with

$$\begin{aligned}
N_c(t) &= S_c(t) + I_c(t) + R_c(t),\\
N_v(t) &= S_v(t) + I_v(t),\\
N_w(t) &= S_w(t) + I_w(t),
\end{aligned} \tag{4.3}$$

(which we will write as

$$\begin{aligned}
N_c &= S_c + I_c + R_c,\\
N_v &= S_v + I_v,\\
N_w &= S_w + I_w,
\end{aligned} \tag{4.4}$$

for ease of presentation), implies that the corresponding populations are changing at the rates:

$$\begin{aligned}
\frac{dN_c}{dt} &= \Lambda_c - \mu_c N_c - \kappa I_c,\\
\frac{dN_v}{dt} &= \Lambda_v + k(V-N_v) - \mu_v N_v,\\
\frac{dN_w}{dt} &= \Lambda_w - \mu_w N_w.
\end{aligned} \tag{4.5}$$

4.2.2 Properties of the Model

Positivity and boundedness of solutions

Proposition 4.2.1. *The region*

$$\Omega = \left\{ S_c, I_c, R_c, S_v, I_v, S_w, I_w \in \mathbb{R}^7_+ : N_c \leq \frac{\Lambda_c}{\mu_c}, N_v \leq \frac{\Lambda_v + kV}{k + \mu_v}, N_w \leq \frac{\Lambda_w}{\mu_w} \right\}, \tag{4.6}$$

is positively invariant and attracting for System (4.1).

Proof. Consider the following vector in $\mathbb{R}^3$

$$N = \{N_c, N_v, N_w\} = \{S_c + I_c + R_c,\ S_v + I_v,\ S_w + I_w\}.$$

Its time derivative satisfies

$$\begin{aligned} \frac{dN}{dt} &= \left\{ \frac{dN_c}{dt}, \frac{dN_v}{dt}, \frac{dN_w}{dt} \right\}, \\ \frac{dN}{dt} &= \{\dot{S}_c + \dot{I}_c + \dot{R}_c, \dot{S}_v + \dot{I}_v, \dot{S}_w + \dot{I}_w\}, \\ \frac{dN}{dt} &= \{\Lambda_c - \kappa I_c - \mu_c N_c,\ \Lambda_v + k(V - N_v) - \mu_v N_v,\ \Lambda_w - \mu_w N_w\}. \end{aligned} \tag{4.7}$$

This implies

$$\begin{aligned} \frac{dN_c}{dt} &= \Lambda_c - \kappa I_c - \mu_c N_c \leq 0, \text{for } N_c \geq \frac{\Lambda_c}{\mu_c}, \\ \frac{dN_v}{dt} &= \Lambda_v + kV - (k + \mu_v) N_v \leq 0, \text{for } N_v \geq \frac{\Lambda_v + kV}{k + \mu_v}, \\ \frac{dN_w}{dt} &= \Lambda_w - \mu_w N_w \leq 0, \text{for } N_w \geq \frac{\Lambda_w}{\mu_w}. \end{aligned} \tag{4.8}$$

It follows that $\frac{dN}{dt} \leq 0$ which implies that Ω is a positively invariant set. Furthermore if we solve Equation (4.8) we get

$$0 \leq \{N_c, N_v, N_w\} \leq \left\{ \frac{\Lambda_c}{\mu_c} + N_{c0} e^{-\mu_c t}, \frac{\Lambda_v + kV}{k + \mu_v} + N_{v0} e^{-(k+\mu_v)t}, \frac{\Lambda_w}{\mu_w} + N_{w0} e^{-\mu_w t} \right\},$$

where N_{c0}, N_{v0} and N_{w0} are respectively the initial conditions of N_c, N_v and N_w. Therefore as $t \to \infty$, $0 \leq \{N_c, N_v, N_w\} \leq \left\{ \frac{\Lambda_c}{\mu_c}, \frac{\Lambda_v + kV}{k + \mu_v}, \frac{\Lambda_w}{\mu_w} \right\}$ and this implies Ω is an attractive set. Hence the proof. □

System (4.1) is well-posed epidemiologically and mathematically; it is sufficient to study the dynamics of this system in Ω as defined in Equation (4.6).

4.3 Equilibria: Existence and Stability

4.3.1 Non-dimensionalisation of the Model

Differential equations that show up in modeling *real world situations* usually have many variables in them. Often one can reduce the number of variables in a problem by choosing the right units for the various quantities in the problem. Since the System (4.1) is written in terms of the population totals in each of the compartments, these equations can be written in terms of the proportion of individuals in each of the population compartments. This is done by scaling the sub-populations for N_c, N_v and N_w using the following set of new variables:

$$s_c = \frac{S_c}{N_c}, i_c = \frac{I_c}{N_c}, r_c = \frac{R_c}{N_c}, s_v = \frac{S_v}{N_v}, i_v = \frac{I_v}{N_v}, s_w = \frac{S_w}{N_w}, i_w = \frac{I_w}{N_w}. \tag{4.9}$$

The ratio of the total vector population to the total cattle population and total wild animal populations respectively, are denoted by:

$$\begin{aligned} h &= \frac{N_v}{N_c}, \\ \rho &= \frac{N_v}{N_w}. \end{aligned} \tag{4.10}$$

The ratios in Equation (4.10) are considered constant since even though the vector population is open, migration into the vector population is density-dependent.

The equations in System (4.1) are written in terms of the new set of variables defined in Equation (4.9). From the first equation of Equation (4.9) we have

$$\begin{aligned} s_c &= \frac{S_c}{N_c}, \\ \frac{ds_c}{dt} &= \frac{1}{N_c}\left\{\frac{dS_c}{dt} - \frac{S_c}{N_c}\frac{dN_c}{dt}\right\}, \\ \frac{ds_c}{dt} &= \frac{\Lambda_c}{N_c} + \left\{\kappa i_c - \frac{\Lambda_c}{N_c} - \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}\right\}s_c + \omega r_c. \end{aligned}$$

Similarly, writing the populations in terms of the proportions and differentiating with respect to time t, the rest of the equations of System (4.1) satisfy the following system of differential equations:

$$\begin{aligned}
\frac{ds_c}{dt} &= \frac{\Lambda_c}{N_c} + \left\{\kappa i_c - \frac{\Lambda_c}{N_c} - \alpha_1\tau_1\varepsilon h i_v\right\} s_c + \omega r_c,\\
\frac{di_c}{dt} &= \alpha_1\tau_1\varepsilon h i_v s_c - \left\{\frac{\Lambda_c}{N_c} + (1-i_c)\kappa\right\} i_c - \gamma i_c,\\
\frac{dr_c}{dt} &= \gamma i_c - \left\{\frac{\Lambda_c}{N_c} + \omega - \kappa i_c\right\} r_c,\\
\frac{ds_v}{dt} &= \left\{\frac{\Lambda_v}{N_v} - k\left\{1 - \frac{V}{N_v}\right\}\right\} i_v - \left\{(1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w\right\} s_v,\\
\frac{di_v}{dt} &= \left\{(1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w\right\} s_v - \left\{\frac{\Lambda_v}{N_v} - k\left\{1 - \frac{V}{N_v}\right\}\right\} i_v,\\
\frac{ds_w}{dt} &= (1-s_w)\frac{\Lambda_w}{N_w} - \alpha_2\tau_4\varepsilon\rho i_v s_w,\\
\frac{di_w}{dt} &= \alpha_2\tau_4\varepsilon\rho i_v s_w - \frac{\Lambda_w}{N_w} i_w,
\end{aligned} \tag{4.11}$$

with

$$\begin{aligned}
s_c + i_c + r_c &= 1,\\
s_v + i_v &= 1,\\
s_w + i_w &= 1,\\
\frac{dN_c(t)}{dt} &= \left\{\frac{\Lambda_c}{N_c} - \mu_c - \kappa i_c\right\} N_c,\\
\frac{dN_v(t)}{dt} &= \left\{\frac{\Lambda_v}{N_v} + \frac{k(V-N_v)}{N_v} - \mu_v\right\} N_v,\\
\frac{dN_w dt}{dt} &= \left\{\frac{\Lambda_w}{N_w} - \mu_w\right\} N_w.
\end{aligned} \tag{4.12}$$

We simplify System (4.1) and reduce it to four-dimension by eliminating r_c, s_v and s_w since $r_c = (1 - s_c - i_c)$, $s_v = (1 - i_v)$ and $s_w = (1 - i_w)$ respectively in Ω as defined in Equation (4.6). The reduced system is thus given by:

$$
\begin{aligned}
\frac{ds_c}{dt} &= \frac{\Lambda_c}{N_c} + \left\{\kappa i_c - \frac{\Lambda_c}{N_c} - \alpha_1\tau_1\varepsilon h i_v\right\} s_c + \omega(1 - s_c - i_c),\\
\frac{di_c}{dt} &= \alpha_1\tau_1\varepsilon h i_v s_c - \left\{\frac{\Lambda_c}{N_c} + (1 - i_c)\kappa\right\} i_c - \gamma i_c,\\
\frac{di_v}{dt} &= ((1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w)(1 - i_v) - \left\{\frac{\Lambda_v}{N_v} - k\left\{1 - \frac{V}{N_v}\right\}\right\} i_v,\\
\frac{di_w}{dt} &= \alpha_2\tau_4\varepsilon\rho i_v(1 - i_w) - \frac{\Lambda_w}{N_w} i_w.
\end{aligned}
\tag{4.13}
$$

Since the equations of the System (4.13) written in terms of proportions still depends on the total cattle, vector and wild animal population, from Equation (4.12) at steady state, we substitute for $\frac{\Lambda_c}{N_c} = \mu_c + \kappa i_c$, $\frac{\Lambda_v}{N_v} = \mu_v - \frac{1}{N_v}k(V - N_v)$ implying $\frac{1}{N_v}\{\Lambda_v + k(V - N_v)\} = \mu_v$ and $\frac{\Lambda_w}{N_w} = \mu_w$ giving the following system:

$$
\begin{aligned}
\frac{ds_c}{dt} &= \mu_c + \kappa i_c - (\alpha_1\tau_1\varepsilon h i_v + \mu_c) s_c + \omega(1 - s_c - i_c),\\
\frac{di_c}{dt} &= \alpha_1\tau_1\varepsilon h i_v s_c - (\mu_c + \kappa + \gamma) i_c,\\
\frac{di_v}{dt} &= ((1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w)(1 - i_v) - \mu_v i_v,\\
\frac{di_w}{dt} &= \alpha_2\tau_4\varepsilon\rho i_v(1 - i_w) - \mu_w i_w.
\end{aligned}
\tag{4.14}
$$

In the subsequent analysis of System (4.1), the non-dimensionalized and reduced System (4.14) is used. System (4.14) is qualitatively analyzed to provide some preliminary results concerned with the threshold values for the existence of the endemic equilibrium. We begin by observing that System (4.14) admits a disease-free equilibrium point.

4.3.2 The Disease Free Equilibrium, ε^{o1}

The disease free equilibrium, ε^{o1}, of System (4.14) is given by

$$
\varepsilon^{o1} = (1, 0, 0, 0). \tag{4.15}
$$

4.3.3 The Effective Reproduction Number, R_{eff}

In this section we determine the threshold parameter that governs the spread of a disease called the effective basic reproduction number, R_{eff}. The effective basic reproduction number measures the average number of new infections generated by a typical infectious individual in a community when an intervention strategy is in place. Mathematically, it is the spectral radius of the next generation matrix [83]. The next generation approach as discussed in Chapter 3: Section 3.4.2, is used to compute the effective basic reproduction number.

To decompose System (4.14), the equations are rewritten starting with the infective classes to obtain:

$$\begin{aligned}
\frac{di_c}{dt} &= \alpha_1\tau_1\varepsilon h i_v s_c - (\mu_c + \kappa + \gamma)i_c,\\
\frac{di_v}{dt} &= ((1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w)(1-i_v) - \mu_v i_v,\\
\frac{di_w}{dt} &= \alpha_2\tau_4\varepsilon\rho i_v(1-i_w) - \mu_w i_w,\\
\frac{ds_c}{dt} &= \mu_c + \kappa i_c - (\alpha_1\tau_1\varepsilon h i_v + \mu_c)s_c + \omega(1-s_c-i_c).
\end{aligned} \tag{4.16}$$

From Equation (4.16), $\mathcal{F}_i$ and $\mathcal{V}_i$ are defined as

$$\mathcal{F}_i := \begin{pmatrix} \alpha_1\tau_1\varepsilon h i_v s_c \\ (1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w \\ \alpha_2\tau_4\varepsilon\rho i_v \end{pmatrix}, \tag{4.17}$$

and

$$\mathcal{V}_i := \begin{pmatrix} (\mu_c + \kappa + \gamma)i_c \\ ((1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w + \mu_v)i_v \\ (\alpha_2\tau_4\varepsilon\rho i_v + \mu_w)i_w \end{pmatrix}. \tag{4.18}$$

The partial derivatives of $\mathcal{F}_i$ and $\mathcal{V}_i$ with respect to $i = (i_c, i_v, i_w)$ are

$$D_i\mathcal{F}_i = \begin{pmatrix} 0 & \alpha_1\tau_1\varepsilon h s_c & 0 \\ (1-\zeta)\alpha_1\tau_2 & 0 & \alpha_2\tau_3 \\ 0 & \alpha_2\tau_4\varepsilon\rho & 0 \end{pmatrix}, \tag{4.19}$$

and

$$D_i\mathcal{V}_i = \begin{pmatrix} \mu_c+\kappa+\gamma & 0 & 0 \\ (1-\zeta)\alpha_1\tau_2 i_v & (1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w + \mu_v & \alpha_2\tau_3 i_v \\ 0 & \alpha_2\tau_4\varepsilon\rho i_w & \alpha_2\tau_4\varepsilon\rho i_w + \mu_w \end{pmatrix}, \tag{4.20}$$

where at disease-free equilibrium, the matrices become

$$F := D_i\mathcal{F}_i(0,\varepsilon^{o1}) \begin{pmatrix} 0 & \alpha_1\tau_1\varepsilon h & 0 \\ (1-\zeta)\alpha_1\tau_2 & 0 & \alpha_2\tau_3 \\ 0 & \alpha_2\tau_4\varepsilon\rho & 0 \end{pmatrix}, \tag{4.21}$$

and

$$V := D_i\mathcal{V}_i(0,\varepsilon^{o1}) \begin{pmatrix} \mu_c+\kappa+\gamma & 0 & 0 \\ 0 & \mu_v & 0 \\ 0 & 0 & \mu_w \end{pmatrix}. \tag{4.22}$$

Taking the inverse of V gives

$$V^{-1} = \begin{pmatrix} \dfrac{1}{\mu_c+\kappa+\gamma} & 0 & 0 \\ 0 & \dfrac{1}{\mu_v} & 0 \\ 0 & 0 & \dfrac{1}{\mu_w} \end{pmatrix}. \tag{4.23}$$

Computing FV^{-1} gives

$$FV^{-1} = \begin{pmatrix} 0 & \dfrac{\alpha_1\tau_1\varepsilon h}{\mu_v} & 0 \\ \dfrac{(1-\zeta)\alpha_1\tau_2}{\mu_c+\kappa+\gamma} & 0 & \dfrac{\alpha_2\tau_3}{\mu_w} \\ 0 & \dfrac{\alpha_2\tau_4\varepsilon\rho}{\mu_v} & 0 \end{pmatrix}. \tag{4.24}$$

The eigenvalues of FV^{-1} are

$$\begin{aligned} \lambda_1 &= 0, \\ \lambda_2 &= -\sqrt{\frac{\alpha_2^2\tau_4\tau_3\varepsilon\rho}{\mu_v\mu_w} + \frac{(1-\zeta)\alpha_1^2\tau_2\tau_1\varepsilon h}{\mu_v(\mu_c+\kappa+\gamma)}}, \\ \lambda_3 &= \sqrt{\frac{\alpha_2^2\tau_4\tau_3\varepsilon\rho}{\mu_v\mu_w} + \frac{(1-\zeta)\alpha_1^2\tau_2\tau_1\varepsilon h}{\mu_v(\mu_c+\kappa+\gamma)}}. \end{aligned}$$

The spectral radius (dominant eigenvalue) of the Equation (4.24) is λ_3 hence $R_{eff} = \lambda_3$.

The effective reproduction number is a function of γ and ζ. As expected, treatment and the rate of infection in the cattle population have an effect on the dynamics of the disease. Though vector control programs are frequently blighted by reinvasion in control areas, R_{eff} is not a function of the migratory flows. This is probably due to the assumption that only susceptible flies migrate into the population. A variant of the model would be to consider the option of infected vectors also migrating into the population.

4.3.4 Analysis of R_{eff}

In this section we study the effect of treatment on the generation of secondary cases in the presence of intervention. R_{eff} can be expressed as

$$R_{eff} = \sqrt{R_{0wT}^2 + R_{0cT}^2}, \tag{4.25}$$

where

$$R_{0wT}^2 = \frac{\alpha_2^2 \tau_4 \tau_3 \varepsilon \rho}{\mu_v \mu_w},$$
$$R_{0cT}^2 = \frac{(1-\zeta)\alpha_1^2 \tau_2 \tau_1 \varepsilon h}{\mu_v(\mu_c + \kappa + \gamma)},$$

are threshold quantities in the population under intervention and are defined as:

1. R_{0wT}, the reproduction number when the host population are wild animals and they are all susceptible.

2. R_{0cT}, the reproduction number when the host population are cattle and they are all susceptible.

Similarly, the basic reproduction number R_0 as defined in Equation (3.10) can also be expressed as

$$R_0 = \sqrt{R_{0w}^2 + R_{0c}^2}, \tag{4.26}$$

where

$$R_{0w}^2 = \frac{\alpha_2^2 \tau_4 \tau_3 \varepsilon \rho}{\mu_v \mu_w},$$
$$R_{0c}^2 = \frac{\alpha_1^2 \tau_2 \tau_1 \varepsilon h}{\mu_v(\mu_c + \kappa)},$$

are threshold quantities in the population with no intervention and are defined as:

1. R_{0w}, the reproduction number when the host population are wild animals and they are all susceptible.

2. R_{0c}, the reproduction number when the host population are cattle and they are all susceptible.

Equations (4.25) and (4.26) both indicate that the overall contributors to trypanosomiasis in a cattle population are disease transmission in a susceptible cattle population and in a susceptible wild animal population. It is also clear that the treatment of infected cattle as a control strategy does not have an effect on the disease dynamics in the wild animal population since $R_{0wT} = R_{0w}$. Treatment of the infected cattle population on the other hand reduces disease transmission in a susceptible cattle population since $R_{0cT} < R_{0c}$. This indicates that treatment of the infected cattle has the effect of reducing the number of new infections in the population that one cow produces in its infectious period since

$$\begin{aligned} R_{eff}^2 &= \frac{\alpha_2^2 \tau_4 \tau_3 \varepsilon \rho}{\mu_v \mu_w} + \frac{(1-\zeta)\alpha_1^2 \tau_2 \tau_1 \varepsilon h}{\mu_v(\mu_c + \kappa + \gamma)}, \\ R_{eff}^2 &= \frac{\alpha_2^2 \tau_4 \tau_3 \varepsilon \rho}{\mu_v \mu_w} + (1-\zeta)\left\{\frac{\alpha_1^2 \tau_2 \tau_1 \varepsilon h}{\mu_v(\mu_c + \kappa) + \mu_v \gamma}\right\}, \\ R_{eff}^2 &< R_0^2, \end{aligned}$$

because $(1-\zeta)$ is a proportion.

In the absence of treatment, that is $(\gamma = 0, \zeta = 0)$, R_{eff} is reduced to

$$R_{eff} = \sqrt{R_{0w}^2 + R_{0c}^2} = R_0,$$

and if $R_0 > 1$, the epidemic will develop, but if $R_0 < 1$ it will die out. In the extreme case if $\gamma = \infty$, all infected cattle have access to treatment, $R_{0cT} = 0$. This implies that the

epidemic will be fully controlled in the cattle population as this leads to no other infections. However, the disease remains endemic in the wild animal population.

It follows that if $R_{eff} < 1 < R_0$ then treatment has a positive impact and reduces the spread of the disease in the cattle population. While if $1 < R_{eff} < R_0$ then the epidemic develops in the population prompting intervention strategies. It is clear that merely ensuring that the basic reproduction number R_0 is less than unity in an infected cattle population under treatment would not ensure the disease is getting eradicated in the population. All the same, in a cattle population with treatment as an intervention strategy, R_{eff} will be less than R_0 if $\gamma > 0$ and $(1 - \zeta) < \gamma$.

Since with treatment $R_{eff} < R_0$ yet there is no reduction of disease transmission in the wild animal population, the effective reproduction number R_{eff} could further be reduced by using an intervention strategy that would instead control the vector biting rate in the wild animal population. This motivates a combination of multiple control strategies, such as treatment and vector control in the cattle population.

4.4 Asymptotic Stability Analysis

In this section we study the local and global stability properties of System (4.14).

4.4.1 Local Stability of ε^{o1}

Theorem 4.4.1. *If $R_{eff} < 1$, then the disease-free equilibrium ε^{o1} is locally asymptotically stable.*

Proof. We study the local stability of the trivial equilibrium point ε^{o1}. The Jacobian matrix

J of System (4.14) is given by

$$\mathbf{J} = \begin{pmatrix} -\alpha_1\tau_1\varepsilon h i_v - \mu_c - \omega & \kappa - \omega & -\alpha_1\tau_1\varepsilon h s_c & 0 \\ \alpha_1\tau_1\varepsilon h i_v & -\mu_c - \kappa - \gamma & \alpha_1\tau_1\varepsilon h s_c & 0 \\ 0 & (1-\zeta)\alpha_1\tau_2(1-i_v) & -(1-\zeta)\alpha_1\tau_2 i_c - \alpha_2\tau_3 i_w - \mu_v & \alpha_2\tau_3(1-i_v) \\ 0 & 0 & \alpha_2\tau_4\varepsilon\rho(1-i_w) & -\alpha_2\tau_4\varepsilon\rho i_v - \mu_w \end{pmatrix}.$$

Then, the local stability of ε^{o1} is governed by the eigenvalues of the Jacobian matrix, at disease-free equilibrium and is given by:

$$J_{\varepsilon^{o1}} = \begin{pmatrix} -(\mu_c + \omega) & \kappa - \omega & -\alpha_1\tau_1\varepsilon h & 0 \\ 0 & -(\mu_c + \kappa + \gamma) & \alpha_1\tau_1\varepsilon h & 0 \\ 0 & (1-\zeta)\alpha_1\tau_2 & -\mu_v & \alpha_2\tau_3 \\ 0 & 0 & \alpha_2\tau_4\varepsilon\rho & -\mu_w \end{pmatrix}. \tag{4.27}$$

One of the eigenvalues of Equation (4.27) is $-(\mu_c + \omega)$. The other eigenvalues are got by reducing the matrix to three dimensional by eliminating the row and column where $-(\mu_c+\omega)$ lies to find the matrix:

$$J^{'} = \begin{pmatrix} -(\mu_c + \kappa + \gamma) & \alpha_1\tau_1\varepsilon h & 0 \\ (1-\zeta)\alpha_1\tau_2 & -\mu_v & \alpha_2\tau_3 \\ 0 & \alpha_2\tau_4\varepsilon\rho & -\mu_w \end{pmatrix}. \tag{4.28}$$

The characteristic polynomial of $J^{'}$ is given by:

$$\lambda^3 + A_1\lambda^2 + A_2\lambda + A_3 = 0, \tag{4.29}$$

where

$$A_1 = (\mu_w + \mu_v + \mu_c + \kappa + \gamma) > 0.$$

$$A_2 = -\alpha_2^2\tau_4\tau_3\varepsilon\rho - (1-\zeta)\alpha_1^2\tau_2\tau_1\varepsilon h + \mu_w\mu_v + \mu_v(\mu_c + \kappa + \gamma) + \mu_w(\mu_c + \kappa + \gamma).$$

$A_2 > 0$ if

$$\alpha_2^2\tau_4\tau_3\varepsilon\rho + (1-\zeta)\alpha_1^2\tau_2\tau_1\varepsilon h < \mu_w\mu_v + \mu_v(\mu_c + \kappa + \gamma) + \mu_w(\mu_c + \kappa + \gamma).$$

For $R_{eff}^2 < 1 \Rightarrow R_{eff} < 1$,

$$\alpha_2^2\tau_4\tau_3\varepsilon\rho < \mu_v\mu_w,$$

$$(1-\zeta)\alpha_1^2\tau_2\tau_1\varepsilon h < \mu_v(\mu_c + \kappa + \gamma). \tag{4.30}$$

Adding the inequalities in Equation (4.30) gives

$$\begin{aligned}\alpha_2^2\tau_4\tau_3\varepsilon\rho + (1-\zeta)\alpha_1^2\tau_2\tau_1\varepsilon h &< \mu_w\mu_v + \mu_v(\mu_c+\kappa+\gamma),\\ &< \mu_w\mu_v + \mu_v(\mu_c+\kappa+\gamma) + \mu_w(\mu_c+\kappa+\gamma).\end{aligned}$$

Hence $A_2 > 0$ when $R_{eff} < 1$.

$$\begin{aligned}A_3 &= -\alpha_2^2\tau_4\tau_3\varepsilon\rho(\mu_c+\kappa+\gamma) - (1-\zeta)\alpha_1^2\tau_2\tau_1\varepsilon h\mu_w + \mu_v\mu_w(\mu_c+\kappa+\gamma),\\ &= \mu_v\mu_w(\mu_c+\kappa+\gamma)(1-R_{eff}^2).\end{aligned}$$

$A_3 > 0$ when $R_{eff} < 1$.

The three eigenvalues of Equation (4.29) have negative real part if and only if the coefficients are positive, and this occurs if and only if $R_{eff} < 1$. Therefore ε^{o1} is locally asymptotically stable for $R_{eff} < 1$. For $R_{eff} > 1$, the equilibrium ε^{o1} becomes an unstable hyperbolic point. This proves Theorem 4.4.1. □

4.4.2 Global Stability of ε^{o1}

Lemma 4.4.1. *The disease free equilibrium ε^{o1} of System (4.14) is globally asymptotically stable if $R_{eff} < 1$ and unstable if $R_{eff} > 1$.*

Proof. The proof is based on using a Comparison Theorem [69]. The equations of the infected compartments in System (4.14) can be written as:

$$\begin{bmatrix} i_c' \\ i_v' \\ i_w' \end{bmatrix} = [F-V]\begin{bmatrix} i_c \\ i_v \\ i_w \end{bmatrix} - \begin{bmatrix} (1-s_c)\alpha_1\tau_1\varepsilon h i_v \\ ((1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w)i_v \\ (\alpha_2\tau_4\varepsilon\rho i_v)i_w \end{bmatrix},$$

where F and V are as defined in Equations (4.21) and (4.22) respectively. Since $s_c, i_v, i_w \leq 1$, (for all $t \geq 0$) in Ω, it follows that

$$\begin{bmatrix} i_c' \\ i_v' \\ i_w' \end{bmatrix} \leq [F-V]\begin{bmatrix} i_c \\ i_v \\ i_w \end{bmatrix}. \tag{4.31}$$

Using the fact that the eigenvalues of the matrix $F - V$ all have negative real parts, it follows that the linearized differential inequality Equation (4.31) is stable whenever $R_{eff} < 1$. Consequently, $\{i_c, i_v, i_w\} \to \{0, 0, 0\}$ as $t \to \infty$. Thus by Comparison Theorem [69] $\{i_c, i_v, i_w\} \to \{0, 0, 0\}$ and evaluating Equation (4.14) at $i_c = i_v = i_w = 0$ gives $s_c \to s_{c0}$ for $R_{eff} < 1$. Hence, the disease-free equilibrium is globally asymptotically stable for $R_{eff} < 1$. □

4.4.3 The Endemic Equilibrium, ε^{*1}

Let $\varepsilon^{*1} = (s_c^*, i_c^*, i_v^*, i_w^*)$ represent any arbitrary endemic equilibrium of System (4.14). Solving the equations in System (4.14) at steady state gives

$$\begin{aligned} s_c^* &= \frac{(\mu_c + \omega)(\mu_c + \kappa + \gamma)}{\alpha_1\tau_1\varepsilon h(\mu_c + \gamma + \omega)i_v^* + (\mu_c + \omega)(\mu_c + \kappa + \gamma)}, \\ i_c^* &= \frac{\alpha_1\tau_1\varepsilon h(\mu_c + \omega)i_v^*}{\alpha_1\tau_1\varepsilon h(\mu_c + \gamma + \omega)i_v^* + (\mu_c + \omega)(\mu_c + \kappa + \gamma)}, \\ i_w^* &= \frac{\alpha_2\tau_4\varepsilon\rho i_v^*}{\alpha_2\tau_4\varepsilon\rho i_v^* + \mu_w}. \end{aligned} \tag{4.32}$$

Let

$$\begin{aligned} a &= (\mu_c + \omega)(\mu_c + \kappa + \gamma), \\ b &= (\mu_c + \gamma + \omega), \\ c &= \alpha_1\tau_1\varepsilon h, \\ n &= \alpha_2\tau_4\varepsilon\rho, \\ m &= (\mu_c + \omega), \\ k &= \mu_w. \end{aligned}$$

Then the steady states in terms of i_v^* can be written as

$$\begin{aligned} s_c^* &= \frac{a}{bci_v^* + a}, \\ i_c^* &= \frac{cmi_v^*}{cbi_v^* + a}, \\ i_w^* &= \frac{ni_v^*}{ni_v^* + k}. \end{aligned}$$

Substituting s_c^*, i_c^*, and i_w^* into the third equation of System (4.14) gives

$$Ai_v^{*3} + Bi_v^{*2} + Ci_v^* = 0. \tag{4.33}$$

where

$$\begin{aligned} A &= -[(1-\zeta)\alpha_1\tau_2 cmn + \alpha_2\tau_3 ncb + cbn\mu_v], \\ B &= (1-\zeta)\alpha_1\tau_2 cm(n-k) + \alpha_2\tau_3 n(cb-a) - (cbk+an)\mu_v, \\ C &= (1-\zeta)\alpha_1\tau_2 cmk + \alpha_2\tau_3 na - ak\mu_v. \end{aligned} \tag{4.34}$$

From Equation (4.34), C can be written in terms of R_{eff} as:

$$C = (\mu_c + \omega)[\mu_v\mu_w(\mu_c + \kappa + \gamma)(R_{eff}^2 - 1)]. \tag{4.35}$$

The solutions of Equation (4.33) are

$$\begin{aligned} i_v^* &= 0, \\ Ai_v^{*2} + Bi_v^* + C &= 0. \end{aligned} \tag{4.36}$$

The form of the solution of the quadratic equation in Equation (4.36) is given by the discriminant of the equation

$$\Delta = B^2 - 4AC.$$

The equation $Ai_v^{*2} + Bi_v^* + C = 0$ corresponds to a situation when the disease persists or is endemic in the population. Since the coefficient A is always negative, then depending on the signs of B and C there are three scenarios we need to consider.

1. For $C > 0$ then $B^2 - 4AC > 0$, Equation (4.36) has one positive and one negative real equilibria, regardless of the sign of B.

2. For $C < 0$, $B > 0$ and $B^2 - 4AC > 0$, Equation (4.36) has two positive real equilibria (two positive roots). In this case there is a possibility of backward bifurcation occurring.

3. For $C = 0$ and $B < 0$ then Equation (4.36) has a unique endemic equilibrium point (one positive root) and there is no possibility of backward bifurcation.

From Equation (4.35), it is clear that C is positive if $R_{eff} < 1$ and it is negative if $R_{eff} > 1$. From this model and discussion we state the following result.

In the trypanosomiasis model with treatment in a cattle population:

1. One endemic equilibrium exists if $C > 0$ then $B^2 - 4AC > 0$ implying $R_{eff} > 1$,
2. One unique endemic equilibrium exists if $C = 0$ and $B < 0$ or if $B^2 - 4AC = 0$,
3. Two endemic equilibrium exist if $C < 0$, $B > 0$ and $B^2 - 4AC > 0$.

Hence we can state a theorem necessary for the existence of the endemic equilibrium point ε^{*1}.

Theorem 4.4.2. *A unique endemic equilibrium exists if and only if* $R_{eff} > 1$.

4.4.4 Global Stability of ε^{*1}

The global stability of the endemic equilibrium ε^{*1} is analyzed using the following constructed Lyapunov function by [51].

Theorem 4.4.3. *If* $R_{eff} > 1$ *the endemic equilibrium* ε^{*1} *of System* (4.14) *is globally asymptotically stable.*

Let

$$L(s_c^*, i_c^*, i_v^*, i_w^*) = \left\{ s_c - s_c^* - s_c^* \log \frac{s_c^*}{s_c} \right\} + \left\{ i_c - i_c^* - i_c^* \log \frac{i_c^*}{i_c} \right\} + \left\{ i_v - i_v^* - i_v^* \log \frac{i_v^*}{i_v} \right\} + \left\{ i_w - i_w^* - i_w^* \log \frac{i_w^*}{i_w} \right\}$$

be the Lyapunov function, $L : D \subset \mathbb{R}^n \to \mathbb{R}$ satisfying $L(0) = 0$ and $L(x) \geq 0$ for all $x \in D \backslash \{0\}$. Calculating the derivative of L along the solution of System (4.14) we have

$P - Q$ where

$$
\begin{aligned}
P = {} & \mu_c + \omega + \kappa i_c + \omega i_c^* + \kappa \frac{i_c^* s_c^*}{s_c} + \omega \frac{i_c s_c^*}{s_c} + \alpha_1\tau_1\varepsilon h i_v s_c + \alpha_1\tau_1\varepsilon h i_v^* s_c^* + \alpha_1\tau_1\varepsilon h \frac{i_v s_c^* i_c^*}{i_c} \\
& + \alpha_1\tau_1\varepsilon h \frac{i_v^* s_c i_c^*}{i_c} + (1-\zeta)\alpha_1\tau_2 i_c + \alpha_2\tau_3 i_w + (1-\zeta)\alpha_1\tau_2 \frac{i_c^* i_v^*}{i_v} + \alpha_2\tau_3 \frac{i_w^* i_v^*}{i_v} \\
& + \alpha_2\tau_4\varepsilon\rho i_v + \alpha_2\tau_4\varepsilon\rho \frac{i_v^* i_w^*}{i_w} + \alpha_1\tau_1\varepsilon h i_v^* s_c + 2\alpha_1\tau_1\varepsilon h i_v s_c^* + 2\mu_c s_c^* + 2\omega s_c^* + \alpha_1\tau_1\varepsilon h \frac{i_v^* s_c^{*2}}{s_c} \\
& + 2\mu_c i_c^* + 2\kappa i_c^* + 2\gamma i_c^* + (1-\zeta)\alpha_1\tau_2 i_c^* i_v + \alpha_2\tau_3 i_w^* i_v + 2(1-\zeta)\alpha_1\tau_2 i_c i_v^* + 2\alpha_2\tau_3 i_w i_v^* \\
& + 2\mu_v i_v^* + (1-\zeta)\alpha_1\tau_2 \frac{i_c^* i_v^{*2}}{i_v} + \alpha_2\tau_3 \frac{i_w^* i_v^{*2}}{i_v} + \alpha_2\tau_4\varepsilon\rho i_v^* i_w + 2\alpha_2\tau_4\varepsilon\rho i_v i_w^* + 2\mu_w i_w^* \\
& + \alpha_2\tau_4\varepsilon\rho \frac{i_v^* i_w^{*2}}{i_w}.
\end{aligned}
$$

and

$$
\begin{aligned}
Q = {} & \kappa i_c^* + \omega i_c + \frac{\mu_c s_c^*}{s_c} + \frac{\omega s_c^*}{s_c} + \kappa \frac{i_c s_c^*}{s_c} + \omega \frac{i_c^* s_c^*}{s_c} + \alpha_1\tau_1\varepsilon h i_v s_c^* + \alpha_1\tau_1\varepsilon h i_v^* s_c + \alpha_1\tau_1\varepsilon h \frac{i_v s_c i_c^*}{i_c} \\
& + \alpha_1\tau_1\varepsilon h \frac{i_v^* s_c^* i_c^*}{i_c} + (1-\zeta)\alpha_1\tau_2 i_c^* + \alpha_2\tau_3 i_w^* + (1-\zeta)\alpha_1\tau_2 \frac{i_c i_v^*}{i_v} + \alpha_2\tau_3 \frac{i_w i_v^*}{i_v} + \alpha_2\tau_4\varepsilon\rho i_v^* \\
& + \alpha_2\tau_4\varepsilon\rho \frac{i_v i_w^*}{i_w} + \alpha_1\tau_1\varepsilon h i_v s_c + \mu_c s_c + \omega s_c + 2\alpha_1\tau_1\varepsilon h i_v^* s_c^* + \alpha_1\tau_1\varepsilon h \frac{i_v s_c^{*2}}{s_c} + \mu_c \frac{s_c^{*2}}{s_c} \\
& + \omega \frac{s_c^{*2}}{s_c} + \mu_c i_c + \kappa i_c + \gamma i_c + \mu_c \frac{i_c^{*2}}{i_c} + \kappa \frac{i_c^{*2}}{i_c} + \gamma \frac{i_c^{*2}}{i_c} + (1-\zeta)\alpha_1\tau_2 i_c i_v + \alpha_2\tau_3 i_w i_v + \mu_v i_v \\
& + 2(1-\zeta)\alpha_1\tau_2 i_c^* i_v^* + 2\alpha_2\tau_3 i_w^* i_v^* + (1-\zeta)\alpha_1\tau_2 \frac{i_c i_v^{*2}}{i_v} + \alpha_2\tau_3 \frac{i_w i_v^{*2}}{i_v} + \mu_v \frac{i_v^{*2}}{i_v} \\
& + \alpha_2\tau_4\varepsilon\rho i_v i_w + \mu_w i_w + 2\alpha_2\tau_4\varepsilon\rho i_v^* i_w^* + \alpha_2\tau_4\varepsilon\rho \frac{i_v^* i_w^{*2}}{i_w} + \mu_w \frac{i_w^{*2}}{i_w}.
\end{aligned}
$$

Therefore if $P = Q$ then $\dfrac{dL}{dt} = 0$; it is also clear that $\dfrac{dL}{dt} = 0$ if and only if $s_c = s_c^*$; $i_c = i_c^*$; $i_v = i_v^*$; $i_w = i_w^*$.

Hence the largest compact invariant set in $\left\{(s_c^*, i_c^*, r_c^*, s_v^*, i_v^*, s_w^*, i_w^*) \in \Omega : \dfrac{dL}{dt} = 0\right\}$ is the singleton ε^{*1} where ε^{*1} is the endemic equilibrium of System (4.14). By LaSalle's invariant principle, it implies that ε^{*1} is globally asymptotically stable in Ω if $P < Q$.

4.5 Sensitivity Analysis and Numerical Simulations

4.5.1 Numerical Sensitivity Analysis

The normalized forward sensitivity index of a variable, u, that depends differentiably on a parameter, p, is defined as:

$$\Upsilon_p^u = \frac{\partial u}{\partial p} \times \frac{p}{u}.$$

Using the explicit formula for R_{eff}, we derive an analytical expression for the sensitivity of R_{eff} for each of the parameters. For example the sensitivity index of R_{eff} with respect to ε is

$$\Upsilon_{\varepsilon}^{R_{eff}} = \frac{\partial R_{eff}}{\partial \varepsilon} \times \frac{\varepsilon}{R_{eff}} = \frac{1}{2}$$

The other indices were calculated in the same way and are tabulated in Table 4.1.

Table 4.1: Numerical values of sensitivity indices of R_{eff}

Parameter	**Sensitivity index**
α_2	$+9.9996 \times 10^{-1}$
τ_4	$+9.9996 \times 10^{-1}$
ε	$+5.0000 \times 10^{-1}$
μ_v	-5.0000×10^{-1}
ρ	$+4.9998 \times 10^{-1}$
μ_w	-4.9998×10^{-1}
τ_3	-4.9998×10^{-1}
α_1	$+3.9000 \times 10^{-5}$
h	$+2.0000 \times 10^{-5}$
τ_1	$+2.0000 \times 10^{-5}$
τ_2	$+2.0000 \times 10^{-5}$
γ	-2.0000×10^{-5}
ζ	-2.0000×10^{-6}
κ	-2.0000×10^{-7}
μ_c	-2.0000×10^{-8}

The parameters in Table 4.1 are ordered from the most sensitive to the least and their sensitivity indices are determined using parameter values provided in Table 3.1 with $\zeta = 0.4$ ($Estimated$) and $\gamma = 0.65$ [32].

Table 4.1 shows that the magnitude of the sensitivity index indicates the influence the parameter has on R_{eff}; the greater it is, the greater the influence it has on R_{eff}; for example in the parameters α_2, τ_4, ε, ρ, α_1, h, τ_1 and τ_2. Table 4.1 also shows that the parameters which have the greatest influence on R_{eff} are related to the dynamics of the disease in the wild animal and the vector populations. These include α_2, τ_4, μ_w and τ_3 in the wild animal population; and τ_2, ε, μ_v and ρ in the vector population.

This gives an indication that to further intervene against the disease in a cattle population we should consider intervention strategies that reduce the influence of the disease in the wild animal population and to some extent in the vector population. Since the disease is transmitted by the vector, likely intervention measures would be those that reduce the contact between the vectors and both the wild animal and the cattle populations. They would they reduce the probability of transmission of the disease causing pathogen.

4.5.2 Numerical Simulations

In this section, we illustrate the analytical results of the study by carrying out simulations of the model given by System (4.1) using the set of estimated parameter values given in Table 4.2

Table 4.2: Parameter values for trypanosomiasis model with treatment

Parameter	**Value**	**Reference**
α_1	0.032	[63]
α_2	0.97	[63]
μ_c	0.00055	[85]
μ_v	0.97	[74]
μ_w	0.0006	[63]
κ	0.006	[75]
τ_1	0.62	[74]
τ_2	0.7	[85]
τ_3	0.05	[63]
τ_4	0.2	[63]
ε	0.5	*Estimated*
ρ	1	[63]
h	1	[63]
γ	0.65	[32]
ζ	0.4 - 0.6	*Estimated*
ω	0.002	*Estimated*
Λ_c	22.0	[85]
Λ_v	24.0	*Estimated*
Λ_w	27.5	*Estimated*

The model given by System (4.1) is simulated using ODE solvers coded in Matlab programming language for varying proportions of the infected cattle treated; $\gamma \in 0.1, 0.5, 0.75, 0.9$ with initial values $S_{c0} = 2000$, $I_{c0} = 1000$, $R_{c0} = 0$, $S_{v0} = 10000$, $I_{v0} = 8000$, $S_{w0} = 3000$ and $I_{w0} = 2000$.

The simulation results are depicted in Figure 4.5.1. (a) shows the model with $\gamma = 0.1$, (b) with $\gamma = 0.5$, (c) with $\gamma = 0.75$ and (d) with $\gamma = 0.9$.

The infected cattle population drops steadily except when the proportion of treated cattle is

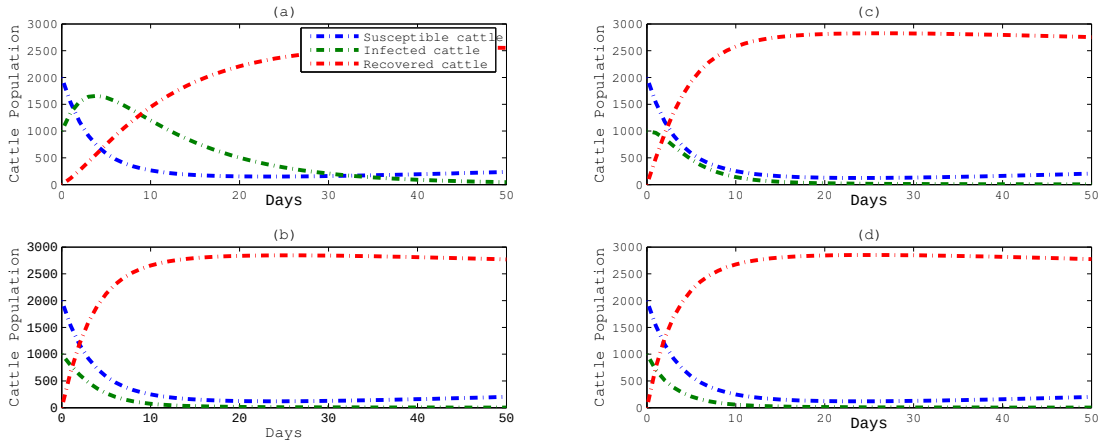

Figure 4.5.1: Dynamics of the Susceptible, Infected and Recovered cattle population under treatment intervention

as low as $\gamma = 0.1$. Increasing the proportion of cattle treated reduces the susceptible cattle population and increases the population of recovered cattle; though when the proportion of infected cattle treated is as low as $\gamma = 0.1$ the recovered population does not increase as fast. It also has the effect of decreasing the severity of the epidemic as seen by the decrease in the peaks and time lags between peaks as γ increases as depicted in Figure 4.5.2.

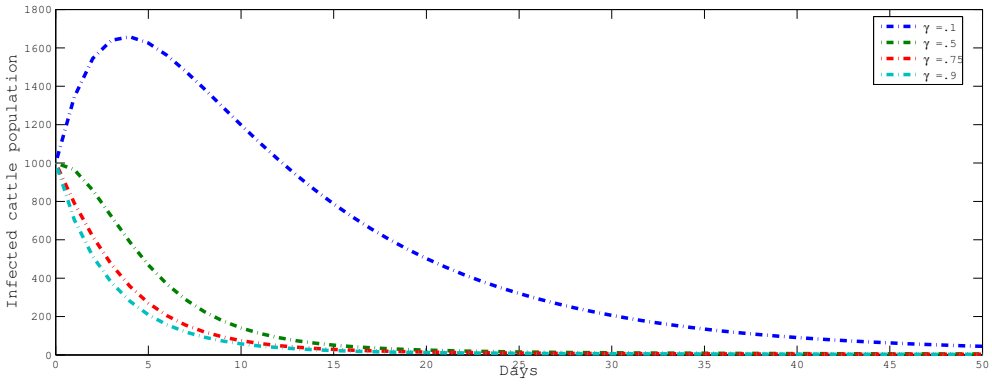

Figure 4.5.2: Infected cattle population at various proportions of treatment

Since treatment of the infected cattle is at a cost, it is of interest to the individual stock owner that they need not treat all the infected cattle to curb the disease in their cattle

population. Figure 4.5.2 indicates that approximately the same effect is got by treating 75% and 90% of the infected cattle population.

Figure 4.5.3 confirms the global stability results of Equation (4.1) shown analytically.

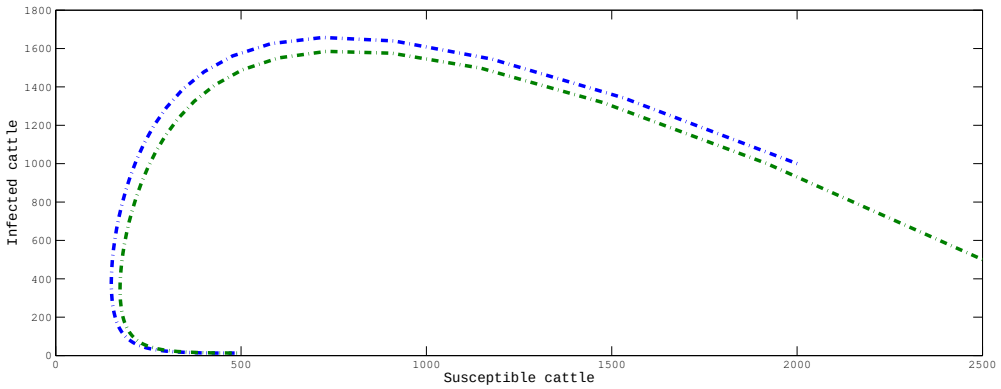

Figure 4.5.3: Global stability of equilibrium points of model under treatment intervention

We further calculate the reproduction numbers to assess the degree of transmission as well as determine the effect of treatment on disease transmission. Table 4.3 shows the reproduction number for various levels of γ.

Table 4.3: Reproduction numbers for various levels of γ

γ	R_{eff}	R_{0cT}	R_{0wT}
0.1	16.1680	0.2042	16.1667
0.5	16.1669	0.0937	16.1667
0.75	16.1668	0.0766	16.1667
0.9	16.1668	0.0700	16.1667

The effect of treatment is not so evident on the R_{eff} since treatment has no effect on disease transmission in the wild animal population. In the cattle population it is evident that as the proportion of infected cattle treated increases, the reproduction number in the cattle population decreases. From Table 4.3, it is clear that increasing the proportion of infected cattle treated would not eradicate the disease in the population unless a second intervention

strategy in put in place to reduce the effect of disease transmission in the wild animal population on the disease dynamics in the cattle population.

The most influential parameter on R_{eff} in the wild animal population is the vector biting rate on the wild animal population α_2. Reducing α_2 to 0.5 from the documented 0.97 reduces R_{eff} to 8.333 on average for the proportion of infected cattle treated shown in Table 4.3. Since the tsetse fly have the wild animal population as an alternative feeding source, an intervention strategy that reduces the contact between the cattle and the tsetse fly would control the disease further in the cattle population.

Of interest in treatment as an intervention strategy is the proportion of infected cattle which would be treated to eradicated the disease in a cattle population. Figure 4.5.4 shows the recovered cattle population at treatment of various proportions of infected cattle. As the

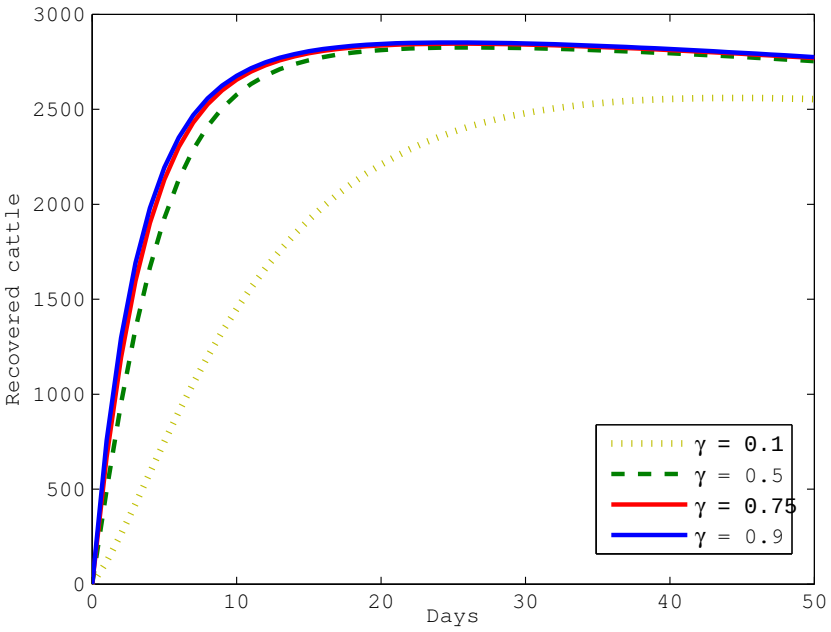

Figure 4.5.4: Recovered cattle population at treatment of various proportions of infected cattle

treatment rate increases the number of recovered cattle increases faster as shown by the

varying peaks of the curves in Figure 4.5.4. For treatment proportions between 0.75 and 0.9, the difference in the number of recovered cattle is not marked. Treating 0.9 of the infected cattle does not seem to be an improvement of treating 0.75 of them. Indeed in [32] it was established that in the absence of the wild animal population the disease could be controlled by treating 65% of the cattle with trypanocides and 20% with insecticides. The whole infected cattle need not be treated to control the disease. Since costs are involved in controlling the disease, the study suggests establishing what proportion of the cattle should be treated to optimize control and equally minimize costs.

4.6 Summary

In this Chapter, the trypanosomiasis model with treatment intervention in cattle population was formulated and analyzed. Since individual stock owners in tsetse-invested areas in Africa use trypanocidal drugs to mitigate against the disease, the objective was to evaluate the role of treatment of the infected cattle on the dynamics of the disease. The model assumes farmers treated a proportion of the infected cattle and there is no incidence of drug resistance. The model also includes immigration of vectors into the population though it is assumed that only susceptible vectors immigrate.

An invariant set in which the solutions of the model are biologically meaningful was derived and the boundedness of the solutions also proved. A threshold parameter that governs the spread of the disease, the effective reproduction rate R_{eff} was derived. R_{eff} is a function of the rate of treatment γ and ζ the rate at which the treatment intervention reduces infection in the cattle population. R_{eff}, however is not a function of the migratory flow of the susceptible vectors.

Analysis of the model showed that there exist two possible solutions, the disease-free and the endemic equilibrium point. The disease-free point is both locally and globally stable implying that, small perturbations and fluctuations on the disease state will result in clearance of the epidemic if $R_{eff} < 1$ and a unique endemic equilibrium exists if $R_{eff} > 1$.

R_{eff} indicates that the overall contributors to the disease are disease transmission in a susceptible cattle population and in a susceptible wild animal population. Treatment of a proportion of the infected cattle reduces infection in the cattle population though it has not effect on the disease dynamics in the wild animal population. In fact treating $0.5-0.75$ of the infected would adequately control the disease in the absence of the wild animal population.

Since treatment has no effect on the wild animal population, yet disease dynamics in the cattle is affected by the wild animals, an additional control strategy which reduces the contact between the cattle and the tsetse fly is necessary. The next chapter explores the effect of both treatment and preventive strategies on the disease dynamics. Since disease control involves costs it will establish optimal control strategies at minimized costs.

Chapter 5

Optimal Control of Trypanosomiasis in a Cattle Population

5.1 Introduction

In this Chapter, time dependent treatment and preventive efforts are considered in the basic model for trypanosomiasis in a cattle population provided in Chapter 3. Optimal control theory is applied to establish cost effective control efforts for treatment of the cattle and prevention of cattle - tsetse fly contact. The aim is to establish analytically the existence of optimal control and then investigate numerically the effects of the control strategies on the dynamics of the disease in a cattle population.

The preventive control involves treating cattle with insecticides that kill the tsetse vectors without having any direct effect on the trypanosomes. Studies have shown that the use of insecticide treated cattle provides one of the cheapest and most effective methods of controlling the disease, [32] since it reduces host-vector contacts. The treatment control on the other hand involves injecting trypanocides into the infected cattle that kill the parasites but leave the tsetse flies unharmed. It is documented that small-scale livestock owners, regard their own involvement in vector control programs as economically non viable and prefer, to spend money only on treating seriously ill cattle, in particular those that are most valuable to them, [45].

Despite superficial similarities, prevention and treatment are profoundly different in their effects and desirability for different levels of disease prevalence. While optimal prevention directly targets susceptible cattle and thus disease incidence it will tend to push prevalence towards intermediate levels that is towards an interior steady state. Optimal treatment on the other hand directly targets infected cattle and thus disease prevalence and will tend to push prevalence towards the extremes, that is, towards corner steady states with either very high or very low infection levels, [72].

In this chapter, the basic trypanosomiasis model System (3.3) is extended to include preventive and treatment strategies. The model is analyzed as an optimal control problem. The effect of the optimal control strategies is investigated numerically and results discussed and summarized.

5.2 Model Framework

The basic epidemic model for trypanosomiasis in a cattle population, System (3.3), is extended to assess the impact of control measures prevention and treatment. The cattle population therefore further includes an extra compartment of treated cattle, T_c, generated by a proportion φ of the infected cattle and depleted by a natural death rate μ_c. The treated cattle recover and become susceptible to the disease at the rate r. The interaction of the cattle, vector and wild animal populations is therefore described using a system of seven differential equations given by:

$$
\begin{aligned}
\frac{dS_c}{dt} &= \Lambda_c - \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}S_c - \mu_c S_c + rT_c,\\
\frac{dI_c}{dt} &= \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}S_c - (\varphi + \mu_c + \kappa)I_c,\\
\frac{dT_c}{dt} &= \varphi I_c - (r + \mu_c)T_c,\\
\frac{dS_v}{dt} &= \Lambda_v - \left(\alpha_1\tau_2\frac{I_c}{N_c} + \alpha_2\tau_3\frac{I_w}{N_w} + \mu_v\right)S_v,\\
\frac{dI_v}{dt} &= \left(\alpha_1\tau_2\frac{I_c}{N_c} + \alpha_2\tau_3\frac{I_w}{N_w}\right)S_v - \mu_v I_v,\\
\frac{dS_w}{dt} &= \Lambda_w - (\alpha_2\tau_4\varepsilon\frac{I_v}{N_w} + \mu_w)S_w,\\
\frac{dI_w}{dt} &= \alpha_2\tau_4\varepsilon\frac{I_v}{N_w}S_w - \mu_w I_w.
\end{aligned}
\tag{5.1}
$$

with initial conditions

$$
S_c(0) \geq 0,\ I_c(0) \geq 0,\ T_c(0) \geq 0,\ S_v(0) \geq 0,\ I_v(0) \geq 0,\ S_w(0) \geq 0,\ I_w(0) \geq 0. \tag{5.2}
$$

5.2.1 Model Properties

The recruitment rates $\Lambda_c \geq 0$, $\Lambda_v \geq 0$ and $\Lambda_w \geq 0$ are assumed to be constant and remain bounded with upper bounds c_o, v_o and w_o respectively. This is because density dependent factors such as competition for resources contribute to the bounded recruitment rates. The natural death rates μ_c, μ_v and μ_w are also assumed to be constant.

From the first three equations of Equation (5.1)

$$
\begin{aligned}
\frac{dN_c}{dt} &= \Lambda_c - \mu_c N_c - \kappa I_c,\\
\frac{dN_c}{dt} &\leq \Lambda_c - \mu_c N_c,\\
\frac{dN_c}{dt} &\leq c_o - \mu_c N_c.
\end{aligned}
\tag{5.3}
$$

It follows that $N_c \leq \frac{c_o}{\mu_c}$ for initial value $N_c(0)$. Similarly, if $\Lambda_v \leq v_o$ and $\Lambda_w \leq w_o$ we have $N_v \leq \frac{v_o}{\mu_v}$ for initial value $N_v(0)$ and $N_w \leq \frac{w_o}{\mu_w}$ for initial value $N_w(0)$. Based on the above discussion, we define a set Ω as

$$
\Omega = \left\{(N_c, N_v, N_w) \in \mathbb{R}^6_+, 0 \leq N_c \leq \frac{c_o}{\mu_c}, 0 \leq N_v \leq \frac{v_o}{\mu_v}, 0 \leq N_w \leq \frac{w_o}{\mu_w}\right\}. \tag{5.4}
$$

The state variables are hence restricted to the set defined in Equation (5.4).

5.2.2 Invariant Region

Theorem 5.2.1. Ω *is positively invariant under System* (5.1).

Proof. Consider the cattle population and let $C_1 = -(\alpha_1\tau_1\varepsilon\frac{I_v}{N_c} + \mu_c)$, $C_2 = -(\varphi + \mu_c + \kappa)$ and $C_3 = -(r + \mu_c)$. Clearly $\frac{dS_c}{dt} \geq C_1S_c$ for $S_c(0) \geq 0$, $\frac{dI_c}{dt} \geq C_2I_c$ for $I_c(0) \geq 0$ and $\frac{dT_c}{dt} \geq C_3T_c$ for $T_c(0) \geq 0$.

Similarly for the vector population putting $V_1 = -(\alpha_1\tau_2\frac{I_c}{N_c} + \alpha_2\tau_3\frac{I_w}{N_w} + \mu_v)$ and $V_2 = -\mu_v$ it is clear that $\frac{dS_v}{dt} \geq V_1S_v$ for $S_v(0) \geq 0$ and $\frac{dI_v}{dt} \geq V_2S_c$ for $I_v(0) \geq 0$.

For the wild animal population, putting $W_1 = -(\alpha_2\tau_4\varepsilon\frac{I_v}{N_w} + \mu_w)$ and $W_2 = -\mu_w$, $\frac{dS_w}{dt} \geq W_1S_v$ for $S_w(0) \geq 0$ and $\frac{dI_w}{dt} \geq W_2I_w$ for $I_w(0) \geq 0$. This means that solutions with initial values in Ω remain non-negative for all $t \geq 0$.

Since $N_c = (S_c + I_c + T_c)$, $N_v = (S_v + I_v)$ and $N_w = (S_w + I_w)$, from Equation (5.3), it follows that $N_c \leq \frac{c_o}{\mu_c}$, $N_v \leq \frac{v_o}{\mu_v}$ and $N_w \leq \frac{w_o}{\mu_w}$. Therefore, Ω is positively invariant under System (5.1). □

5.3 The Optimal Control Problem

Optimal Control Theory is an approach to dynamic optimization that uses the control variables to optimize the functional. Once the optimal path or value of the control variables is found, the solution to the state variables, or the optimal paths for the state variables are derived.

The objective in optimal control problems is to determine a function that minimizes a specified functional termed the *the performance measure*. A functional J is a rule of correspondence that assigns to each function $\mathbf{x}$ in a certain class Ω, the domain of the functional, a unique real number, the range of the functional. If $\mathbf{x}$ and $\mathbf{x} + \delta\mathbf{x}$ are functions for which the

functional J is defined, then the increment of J denoted by ΔJ is

$$\Delta J \triangleq J(\mathbf{x} + \delta\mathbf{x}) - J(\mathbf{x}). \tag{5.5}$$

Equation (5.5) would be written as $\Delta J(\mathbf{x}, \delta\mathbf{x})$ to emphasize that the incremental depends on the function $\mathbf{x}$ and $\delta\mathbf{x}$. The variable $\delta\mathbf{x}$ is called the variation of the function $\mathbf{x}$. The variation of a functional plays the same role in determining extreme values of functionals as the differential does in finding maxima and minima of functions.

In this study, the problem is to minimize the infected cattle population and maximize the proportion of cattle who get treated in order to control or even eradicate the disease. The control functions $u_1(t)$ and $u_2(t)$ represent time dependent efforts of prevention and treatment respectively practiced on a time interval $[0, T]$, [8].

The associated force of infection in the cattle population is reduced by a factor of $(1 - u_1(t))$, $0 \leq u_1(t) \leq 1$. If $u_1(t) = 1$ the prevention effort is 100% effective while if $u_1(t) = 0$, we find the model for trypanosomiasis in a cattle population without the preventive control effort. The proportion of treated cattle φ is proportional to $u_2(t)$, $0 \leq u_2(t) \leq 1$ where $0 \leq \varphi \leq 1$ is constant and represents the proportion of effective treatment since we assume there is no natural recovery from trypanosomiasis in a cattle population. If $u_2(t) = 1$ then a proportion φ of the infected cattle get treated whereas when $u_2(t) = 0$ there is no treatment of the infected cattle.

The interaction of the cattle, vector and wild animal populations and the control functions give the following system of differential equations:

$$
\begin{aligned}
\frac{dS_c}{dt} &= \Lambda_c - \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}(1-u_1(t))S_c - \mu_c S_c + rT_c,\\
\frac{dI_c}{dt} &= \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}(1-u_1(t))S_c - (\varphi u_2(t) + \mu_c + \kappa)I_c,\\
\frac{dT_c}{dt} &= \varphi u_2(t)I_c - (r+\mu_c)T_c,\\
\frac{dS_v}{dt} &= \Lambda_v - \left(\alpha_1\tau_2\frac{I_c}{N_c}(1-u_1(t)) + \alpha_2\tau_3\frac{I_w}{N_w} + \mu_v\right)S_v,\\
\frac{dI_v}{dt} &= \left(\alpha_1\tau_2\frac{I_c}{N_c}(1-u_1(t)) + \alpha_2\tau_3\frac{I_w}{N_w}\right)S_v - \mu_v I_v,\\
\frac{dS_w}{dt} &= \Lambda_w - (\alpha_2\tau_4\varepsilon\frac{I_v}{N_w} + \mu_w)S_w,\\
\frac{dI_w}{dt} &= \alpha_2\tau_4\varepsilon\frac{I_v}{N_w}S_w - \mu_w I_w.
\end{aligned}
\tag{5.6}
$$

subject to the initial conditions given by Equation (5.2). Equation (5.6) is the control system which is the basic ingredient of an optimal control problem.

The main objective of this optimal control problem is to minimize the number of cattle that become infected, I_c, and the cost of implementing the control by using possible minimal control variable u_i for $i = 1, 2$. The cost associated with the first control, u_1, could come from the cost of the insecticide, insecticide sprays, educating people on how to apply the insecticide and for personal protection during application. Similarly, the cost associated with the second control, u_2, could come from cost of drug, costs associated with surveillance, follow-up of drug management and fighting the emergence of drug-resistant strains, [8]. These costs are assumed to be non-linear and are proportional to the square of the corresponding control function.

Together with the mathematical model described in Equation (5.6), the second basic ingredient is the objective functional for the control problem. The objective functional consists of a function of the final state and a cost function that is integrated over time. It associates a cost with each possible behavior. Our problem is to minimize the objective functional

$$
J(u_1, u_2) = \int_0^T AI_c(t) + \frac{B_1}{2}u_1^2(t) + \frac{B_2}{2}u_2^2(t)dt \tag{5.7}
$$

subject to the state system given by Equation (5.6).

In the objective functional, A represents the weight constants of infected cattle population while B_1 and B_2 are weight constants for prevention and treatment respectively. The terms $\frac{1}{2}B_1u_1^2$ and $\frac{1}{2}B_2u_2^2$ describe the costs associated with prevention of vector-host contacts and treatment respectively, which form the running cost.

Our aim is to determine an optimal control pair u_1^* and u_2^* such that

$$J(u_1^*, u_2^*) = min\{J(u_1, u_2)|(u_1, u_2) \in \mathcal{U}\}. \tag{5.8}$$

subject to Equation (5.2) and the control set

$$\mathcal{U} = \{(u_1, u_2) \mid u_i(t) \text{ is piecewise continuous on } [0, T] : 0 \leq u_i(t) \leq 1, i = 1, 2\}.$$

The basic framework of the problem is to prove the existence of an optimal control and then characterize it through the optimality system.

5.3.1 Existence of an Optimal Control

The existence of the optimal control is of crucial importance, since it does not make much sense to seek a solution if it does not exist. A type of controllability is assumed that the control pair u_1 and u_2 drives the state of the system from the initial condition to a target set otherwise, the problem is ill-posed. Since we will be working not only with the control set $\mathcal{U}$ but with the set of all points reachable from the initial value using controls that take values in $\mathcal{U}$, the problem becomes well posed when the set is compact (bounded and closed) and convex [53].

For the control System (5.6), subject to the initial conditions in Equation (5.2) and for bounded Lebesgue measurable controls and non-negative initial conditions, non-negative bounded solutions to the state system exist [54]. For the existence of our control problem, we state and prove the following theorem.

Theorem 5.3.1. *There exists an optimal control* $u^* = \{u_1^*, u_2^*\} \in \mathcal{U}$ *such that*

$$J(u^*) = min\{J(u_1, u_2), \mathcal{U} \in (u_1, u_2)\}.$$

subject to Equation (5.6) *with the initial condition Equation* (5.2).

Proof. To prove the existence of an optimal control, we use the result in [52], and the fact that the control and state variables are non-negative values. In this minimizing problem, the necessary convexity of the objective functional in u_1, u_2 are satisfied. The set of control variables $(u_1, u_2) \in \mathcal{U}$ is also convex and closed by definition. The optimal system is bounded which determines the compactness needed for the existence of the optimal control and the integrand in the objective functional Equation (5.7)

$$AI_c(t) + \frac{1}{2}B_1u_1^2(t) + \frac{1}{2}B_2u_2^2(t)$$

is convex on the control set $\mathcal{U}$. In any case, the result follows directly from Equation (5.8). □

5.3.2 Characterization of the Optimal Control

Having established the existence of the optimal control , an optimality system is presented using a result from Lewis and Syrmos, the *Maximum Principle*, [52]. In order to find an optimal solution, we first formulate the Lagrangian as a Hamiltonian function denoted as H,

$$H = AI_c(t) + \frac{B_1}{2}u_1^2(t) + \frac{B_2}{2}u_2^2(t) + \Sigma_{i=1}^{7}\lambda_i g_i. \tag{5.9}$$

where $\lambda_i(t)$ are the Lagrange multipliers also referred to as the adjoint variables or as the costate variables.

The *Maximum Principle* states that if $(\mathbf{x}^*, \mathbf{u}^*)$ is an optimal solution for an optimal control problem, then there exists a non-trivial vector function $\lambda = (\lambda_1, \lambda_2, \ldots, \lambda_n)$ which satisfies the following necessary conditions:

$$\dot{x} = \frac{\partial H}{\partial \lambda}, \tag{5.10}$$

$$\dot{\lambda} = -\frac{\partial H}{\partial x}, \tag{5.11}$$

$$\frac{\partial H}{\partial u} = 0, \tag{5.12}$$

$$\lambda(T) = 0. \tag{5.13}$$

Equation (5.10) provides the equation of motion of x, the state variables. Although it is a mere restatement of the relationship between the state and control variable, the equation of motion of λ, Equation (5.11), is set such that $\dot{\lambda}$ equates with the negative derivative of the Hamiltonian function. Equation (5.12) gives the differential equation for the control variable which requires that u maximizes the Hamiltonian while Equation (5.13) explains the tranversality condition. The tranversality condition provides the terminal conditions for each state variable i.e. it describes what must be satisfied at the end of the time horizon, in this case

$$\lambda_i(T) = 0 \quad for \quad i = 1, 2, \ldots, 7$$

The Equations (5.10) and (5.11) together are said to comprise a Hamiltonian differential system.

The function u^* that minimizes the functional $\mathbf{J}$, Equation (5.7), is called an optimal control, the corresponding state x^* is called the optimal state, and the pair (x^*, u^*) is called the optimal trajectory.

The optimal solution

The necessary conditions are then applied to the Hamiltonian, H in Equation (5.9). Since the integrand of the functional is differentiable, we write the first order condition with respect to u as:

$$\frac{\partial H}{\partial u_1} = B_1 u_1 + (\lambda_1 - \lambda_2)\alpha_1\tau_1\varepsilon\frac{I_v}{N_c}S_c + (\lambda_4 - \lambda_5)\alpha_1\tau_2\frac{I_c}{N_c}S_v = 0, \tag{5.14}$$

$$\frac{\partial H}{\partial u_2} = (\lambda_3 - \lambda_2)\varphi I_c + B_2 u_2 = 0. \tag{5.15}$$

Solving for the optimal control u_1^* and u_2^* gives

$$\begin{aligned} u_1^* &= \frac{1}{B_1}\left[(\lambda_2 - \lambda_1)\alpha_1\tau_1\varepsilon\frac{I_v}{N_c}S_c + (\lambda_5 - \lambda_4)\alpha_1\tau_2\frac{I_c}{N_c}S_v\right], \\ u_2^* &= \frac{1}{B_2}\left[\lambda_2 - \lambda_3\right]\varphi I_c. \end{aligned} \tag{5.16}$$

Imposing the bounds $0 \leq u_1 \leq 1$ and $0 \leq u_2 \leq 1$ on the control gives

$$\begin{aligned} u_1^* &= min\left\{max\left\{0, \frac{1}{B_1}\left[(\lambda_2-\lambda_1)\alpha_1\tau_1\varepsilon\frac{I_v}{N_c}S_c + (\lambda_5-\lambda_4)\alpha_1\tau_2\frac{I_c}{N_c}S_v\right]\right\}, 1\right\} \\ u_2^* &= min\left\{max\left\{0, \frac{1}{B_2}\left[\lambda_2-\lambda_3\right]\varphi I_c\right\}, 1\right\}. \end{aligned} \tag{5.17}$$

Equation (5.17) provides the characterization of the optimal control.
Next we solve for the optimal value of the costate variable λ using $\dot{\lambda} = -\frac{\partial H}{\partial x}$ where x are the state variables S_c, I_c, T_c, S_v, I_v, S_w and I_w. This implies

$$\begin{aligned} \dot{\lambda_1} &= (\lambda_2-\lambda_1)\left\{\alpha_1\tau_1\varepsilon\frac{I_v}{N_c^2}S_c - \alpha_1\tau_1\varepsilon\frac{I_v}{N_c}\right\}(1-u_1(t)) + \lambda_1\mu_c \\ &\quad + (\lambda_5-\lambda_4)\alpha_1\tau_2\frac{I_c}{N_c^2}S_v(1-u_1(t)), \\ \dot{\lambda_2} &= -A + \lambda_2(\mu_c+\kappa) + (\lambda_2-\lambda_3)\varphi u_2(t) + (\lambda_4-\lambda_5)\left\{\frac{\alpha_1\tau_2}{N_c} - \alpha_1\tau_2\frac{I_c}{N_c^2}\right\}S_v(1-u_1(t)) \\ &\quad + (\lambda_2-\lambda_1)\alpha_1\tau_1\varepsilon\frac{I_v}{N_c^2}S_c(1-u_1(t)), \\ \dot{\lambda_3} &= (\lambda_3-\lambda_1)r + \lambda_3\mu_c + (\lambda_2-\lambda_1)\alpha_1\tau_1\varepsilon\frac{I_v}{N_c^2}S_c(1-u_1(t)) \\ &\quad + (\lambda_5-\lambda_4)\alpha_1\tau_2\frac{I_c}{N_c^2}S_v(1-u_1(t)), \\ \dot{\lambda_4} &= (\lambda_4-\lambda_5)\left(\alpha_1\tau_2\frac{I_c}{N_c}(1-u_1(t)) + \alpha_2\tau_3\frac{I_w}{N_w}\right) + \lambda_4\mu_v, \\ \dot{\lambda_5} &= (\lambda_1-\lambda_2)\alpha_1\tau_1\varepsilon\frac{S_c}{N_c}(1-u_1(t)) + \lambda_5\mu_v + (\lambda_6-\lambda_7)\alpha_2\tau_4\varepsilon\frac{S_w}{N_w}, \\ \dot{\lambda_6} &= (\lambda_7-\lambda_6)\left\{\alpha_2\tau_4\varepsilon\frac{I_v}{N_w^2}S_w - \alpha_2\tau_4\varepsilon\frac{I_v}{N_w}\right\} + \lambda_6\mu_w + (\lambda_5-\lambda_4)\alpha_2\tau_3\frac{I_w}{N_w^2}S_v, \\ \dot{\lambda_7} &= (\lambda_4-\lambda_5)\left\{\frac{\alpha_2\tau_3}{N_w} - \alpha_2\tau_3\frac{I_w}{N_w^2}\right\}S_v + (\lambda_7-\lambda_6)\alpha_2\tau_4\varepsilon\frac{I_v}{N_w^2}S_w + \lambda_7\mu_w, \end{aligned} \tag{5.18}$$

If we let S_c^*, I_c^*, T_c^*, S_v^*, I_v^*, S_w^* and I_w^* be the optimal state solutions with associated control variables (u_1^*, u_2^*) for the optimal control problem and using the characterization of the optimal control, we have the following optimality system:

$$
\begin{aligned}
S_c^* &= \Lambda_c - \alpha_1\tau_1\varepsilon\frac{I_v^*}{N_c^*}S_c^*(1-u_1^*) - \mu_c S_c^* + rT_c^*,\\
I_c^* &= \alpha_1\tau_1\varepsilon\frac{I_v^*}{N_c^*}S_c^*(1-u_1^*) - (\varphi u_2^* + \mu_c + \kappa)I_c^*,\\
T_c^* &= \varphi u_2^* I_c^* - (r+\mu_c)T_c^*,\\
S_v^* &= \Lambda_v - \left\{\alpha_1\tau_2\frac{I_c^*}{N_c^*}(1-u_1^*) + \alpha_2\tau_3\frac{I_w^*}{N_w^*} + \mu_v\right\}S_v^*,\\
I_v^* &= \left\{\alpha_1\tau_2\frac{I_c^*}{N_c^*}(1-u_1^*) + \alpha_2\tau_3\frac{I_w^*}{N_w^*}\right\}S_v^* - \mu_v I_v^*,\\
S_w^* &= \Lambda_w - \left\{\alpha_2\tau_4\varepsilon\frac{I_v^*}{N_w^*} + \mu_w\right\}S_w^*,\\
I_w^* &= \alpha_2\tau_4\varepsilon\frac{I_v^*}{N_w^*}S_w^* - \mu_w I_w^*,\\
\dot{\lambda_1} &= (\lambda_2-\lambda_1)\left\{\alpha_1\tau_1\varepsilon\frac{I_v^*}{N_c^{*2}}S_c^* - \alpha_1\tau_1\varepsilon\frac{I_v^*}{N_c^*}\right\}(1-u_1^*) + \lambda_1\mu_c\\
&\quad + (\lambda_5-\lambda_4)\alpha_1\tau_2\frac{I_c^*}{N_c^{*2}}S_v^*(1-u_1^*),\\
\dot{\lambda_2} &= -A + \lambda_2(\mu_c+\kappa) + (\lambda_2-\lambda_3)\varphi u_2^* + (\lambda_4-\lambda_5)\left\{\frac{\alpha_1\tau_2}{N_c^*} - \alpha_1\tau_2\frac{I_c^*}{N_c^{*2}}\right\}S_v^*(1-u_1^*)\\
&\quad + (\lambda_2-\lambda_1)\left\{\alpha_1\tau_1\varepsilon\frac{I_v^*}{N_c^{*2}}S_c^*(1-u_1^*)\right\},\\
\dot{\lambda_3} &= (\lambda_3-\lambda_1)r + \lambda_3\mu_c + (\lambda_2-\lambda_1)\alpha_1\tau_1\varepsilon\frac{I_v^*}{N_c^{*2}}S_c^*(1-u_1^*)\\
&\quad + (\lambda_5-\lambda_4)\alpha_1\tau_2\frac{I_c^*}{N_c^{*2}}S_v^*(1-u_1^*),\\
\dot{\lambda_4} &= (\lambda_4-\lambda_5)\left\{\alpha_1\tau_2\frac{I_c^*}{N_c^*}(1-u_1^*) + \alpha_2\tau_3\frac{I_w^*}{N_w^*}\right\} + \lambda_4\mu_v,\\
\dot{\lambda_5} &= (\lambda_1-\lambda_2)\alpha_1\tau_1\varepsilon\frac{S_c^*}{N_c^*}(1-u_1^*) + (\lambda_6-\lambda_7)\alpha_2\tau_4\varepsilon\frac{S_w^*}{N_w^*} + \lambda_5\mu_v,\\
\dot{\lambda_6} &= (\lambda_7-\lambda_6)\left\{\alpha_2\tau_4\varepsilon\frac{I_v^*}{N_w^{*2}}S_w^* - \alpha_2\tau_4\varepsilon\frac{I_v^*}{N_w^*}\right\} + \lambda_6\mu_w + (\lambda_5-\lambda_4)\alpha_2\tau_3\frac{I_w^*}{N_w^{*2}}S_v^*,\\
\dot{\lambda_7} &= (\lambda_4-\lambda_5)\left\{\frac{\alpha_2\tau_3}{N_w^*} - \alpha_2\tau_3\frac{I_w^*}{N_w^{*2}}\right\}S_v^* + (\lambda_7-\lambda_6)\alpha_2\tau_4\varepsilon\frac{I_v^*}{N_w^{*2}}S_w^* + \lambda_7\mu_w,
\end{aligned}
\tag{5.19}
$$

with $\lambda_1(T) = 0$, $\lambda_2(T) = 0$, $\lambda_3(T) = 0$, $\lambda_4(T) = 0$, $\lambda_5(T) = 0$, $\lambda_6(T) = 0$, $\lambda_7(T) = 0$, $S_c(0) = S_{c0}$, $I_c(0) = I_{c0}$, $T_c(0) = T_{c0}$, $S_v(0) = S_{v0}$, $I_v(0) = I_{v0}$, $S_w(0) = S_{w0}$ and $I_w(0) = I_{w0}$.

The optimal control is found by solving the optimality system, which consists of the state System (5.6), the adjoint System (5.18), boundary conditions Equation (5.2), the transversality conditions Equation (5.13) and the characterization of the optimal control Equation (5.17). Further, since the second derivative of the Lagrangian with respect to u_1 and u_2 respectively are positive, the optimal problem is minimum at controls u_1^* and u_2^*.

5.4 Numerical Results and Discussion

In this section we use an iterative method to find the numerical solution of our control problem. The numerical algorithm presented is a semi-implicit finite difference method. The interval $[t_0, T]$ is discretized at the points $t_i = t_0 + ih$ $(i = 0, 1, \ldots, \ldots n)$, where h is the time step such that $t_n = T$.

The state variables $S_c(t)$, $I_c(t)$, $T_c(t)$, $S_v(t)$, $I_v(t)$, $S_w(t)$, $I_w(t)$, the adjoint variables $\lambda_1(t)$, $\lambda_2(t)$, $\lambda_3(t)$, $\lambda_4(t)$, $\lambda_5(t)$, $\lambda_6(t)$, $\lambda_7(t)$ and the controls $u_1(t)$, $u_2(t)$ are then defined in terms of the nodal points S_c^i, I_c^i, T_c^i, S_v^i, I_v^i, S_w^i, I_w^i, λ_1^i, λ_2^i, λ_3^i, λ_4^i, λ_5^i, λ_6^i, λ_7^i, u_1^i and u_2^i. A combination of forward and backward difference approximation is used as follows.

The Method developed by [30] and presented in [36] is given as:

$$
\begin{aligned}
\frac{S_c^{i+1} - S_c^i}{h} &= \Lambda_c - \alpha_1\tau_1\varepsilon\frac{I_v^i}{S_c^{i+1} + I_c^i + T_c^i}S_c^{i+1}(1 - u_1^i) - \mu_c S_c^{i+1} + rT_c^i,\\
\frac{I_c^{i+1} - I_c^i}{h} &= \alpha_1\tau_1\varepsilon\frac{I_v^i}{S_c^{i+1} + I_c^{i+1} + T_c^i}S_c^{i+1}(1 - u_1^i) - (\varphi u_2^i + \mu_c + \kappa)I_c^{i+1},\\
\frac{T_c^{i+1} - T_c^i}{h} &= \varphi u_2^i I_c^{i+1} - (r + \mu_c)T_c^{i+1},\\
\frac{S_v^{i+1} - S_v^i}{h} &= \Lambda_v - \left\{\alpha_1\tau_2\frac{I_c^{i+1}}{S_c^{i+1} + I_c^{i+1} + T_c^{i+1}}(1 - u_1^i) + \alpha_2\tau_3\frac{I_w^i}{S_w^i + I_w^i} + \mu_v\right\}S_v^{i+1},\\
\frac{I_v^{i+1} - I_v^i}{h} &= \left\{\alpha_1\tau_2\frac{I_c^{i+1}}{S_c^{i+1} + I_c^{i+1} + T_c^{i+1}}(1 - u_1^i) + \alpha_2\tau_3\frac{I_w^i}{S_w^i + I_w^i}\right\}S_v^{i+1} - \mu_v I_v^{i+1},\\
\frac{S_w^{i+1} - S_w^i}{h} &= \Lambda_w - \left\{\alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{S_w^{i+1} + I_w^i} + \mu_w\right\}S_w^{i+1},\\
\frac{I_w^{i+1} - I_w^i}{h} &= \alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{S_w^{i+1} + I_w^{i+1}} - \mu_w I_w^{i+1}.
\end{aligned}
$$

Using a similar technique, the time derivatives of the adjoint variables are approximated by their first order backward difference and the appropriated scheme is used as follows:

$$\begin{aligned}
\frac{\lambda_1^{n-i}-\lambda_1^{n-i-1}}{h} &= (\lambda_2^{n-i}-\lambda_1^{n-i-1})\left\{\alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1^2}}S_c^{i+1}-\alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1}}\right\}(1-u_1^i)\\
&\quad+\lambda_1^{n-i-1}\mu_c+(\lambda_5^{n-i}-\lambda_4^{n-i})\alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1^2}}S_v^{i+1}(1-u_1^i),\\
\frac{\lambda_2^{n-i}-\lambda_2^{n-i-1}}{h} &= -A+\lambda_2^{n-i-1}(\mu_c+\kappa)+(\lambda_2^{n-i-1}-\lambda_3^{n-i})\varphi u_2^i+(\lambda_4^{n-i}\\
&\quad-\lambda_5^{n-i})\left\{\frac{\alpha_1\tau_2}{N_c^{i+1}}-\alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1^2}}\right\}S_v^{i+1}(1-u_1^i)\\
&\quad+(\lambda_2^{n-i-1}-\lambda_1^{n-i-1})\alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1^2}}S_c^{i+1}(1-u_1^i),\\
\frac{\lambda_3^{n-i}-\lambda_3^{n-i-1}}{h} &= (\lambda_3^{n-i-1}-\lambda_1^{n-i-1})r+\lambda_3^{n-i-1}\mu_c\\
&\quad+(\lambda_2^{n-i-1}-\lambda_1^{n-i-1})\alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1^2}}S_c^{i+1}(1-u_1^i)\\
&\quad+(\lambda_5^{n-i}-\lambda_4^{n-i})\alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1^2}}S_v^{i+1}(1-u_1^i),\\
\frac{\lambda_4^{n-i}-\lambda_4^{n-i-1}}{h} &= (\lambda_4^{n-i-1}-\lambda_5^{n-i})\left\{\alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1}}(1-u_1^i)+\alpha_2\tau_3\frac{I_w^{i+1}}{N_w^{i+1}}\right\}+\lambda_4^{n-i-1}\mu_v,\\
\frac{\lambda_5^{n-i}-\lambda_5^{n-i-1}}{h} &= (\lambda_1^{n-i-1}-\lambda_2^{n-i-1})\alpha_1\tau_1\varepsilon\frac{S_c^{i+1}}{N_c^{i+1}}(1-u_1^i)+(\lambda_6^{n-i}-\lambda_7^{n-i})\alpha_2\tau_4\varepsilon\frac{S_w^{i+1}}{N_w^{i+1}}\\
&\quad+\lambda_5^{n-i-1}\mu_v,\\
\frac{\lambda_6^{n-i}-\lambda_6^{n-i-1}}{h} &= (\lambda_7^{n-i}-\lambda_6^{n-i-1})\left\{\alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{N_w^{i+1^2}}S_w^{i+1}-\alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{N_w^{i+1}}\right\}\\
&\quad+\lambda_6^{n-i-1}\mu_w+(\lambda_5^{n-i-1}-\lambda_4^{n-i-1})\alpha_2\tau_3\frac{I_w^{i+1}}{N_w^{i+1^2}}S_v^{i+1},\\
\frac{\lambda_7^{n-i}-\lambda_7^{n-i-1}}{h} &= (\lambda_4^{n-i-1}-\lambda_5^{n-i-1})\left\{\frac{\alpha_2\tau_3}{N_w^{i+1}}-\alpha_2\tau_3\frac{I_w^{i+1}}{N_w^{i+1^2}}\right\}S_v^{i+1}\\
&\quad+(\lambda_7^{n-i-1}-\lambda_6^{n-i-1})\alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{N_w^{i+1^2}}S_w^{i+1}+\lambda_7^{n-i-1}\mu_w.
\end{aligned}$$

The algorithm describing the approximation method for obtaining the optimal control is as follows:

Algorithm

step 1:

$S_c(0)=S_{c0},\ I_c(0)=I_{c0},\ T_c(0)=T_{c0},\ S_v(0)=S_{v0},\ I_v(0)=I_{v0},\ S_w(0)=S_{w0},\ I_w(0)=I_{w0},$

$\lambda_i(T) = 0$ $(i = 1, 2, \ldots, 7)$, $u_1(0) = u_2(0) = 0$.

step 2:

for $i = 1, \ldots, n-1$, do:

$$
\begin{aligned}
S_c^{i+1} &= \frac{1}{2}\frac{1}{h\mu_c + 1}\{\Lambda_c h + S_c^i - I_c^i - T_c^i - h\mu_c(I_c^i + T_c^i) + rhT_c^i \\
&+ [\Lambda_c^2 h^2 + 2\Lambda_c h^2(\mu_c I_c^i - \alpha_1\tau_1\varepsilon I_v^i(1-u_1^i) + (r+\mu_c)T_c^i) \\
&+ 2\Lambda_c h(S_c^i + I_c^i + T_c^i) + S_c^{i^2} + I_c^{i^2} + T_c^{i^2} + 2(S_c^i I_c^i + S_c^i T_c^i + I_c^i T_c^i) \\
&+ 2\alpha_1\tau_1\varepsilon h I_v^i(1-u_1^i)(h\mu_c(I_c^i + T_c^i) + rhT_c^i + S_c^i + I_c^i + T_c^i) + (\mu_c^2 h^2 + 2\mu_c h)(I_c^{i^2} + T_c^{i^2}) \\
&+ \alpha_1^2\tau_1^2\varepsilon^2 h^2 I_v^{i^2}(1-u_1^i)^2 + 2h(\mu_c + r)S_c^i T_c^i + 2\mu_c h I_c^i(S_c^i + 2T_c^i) \\
&+ r^2 h^2 T_c^{i^2} + 2rhT_c^i(1 + h\mu_c)(I_c^i + T_c^i) + 2h^2\mu_c^2 I_c^i T_c^i]^{\frac{1}{2}}\}, \\
I_c^{i+1} &= \frac{1}{2}\frac{1}{h(\varphi u_2^i + \mu_c + \kappa) + 1}\{I_c^i - T_c^i - S_c^{i+1} - h(\varphi u_2^i + \mu_c + \kappa)(T_c^i + S_c^{i+1}) \\
&+ [S_c^{i+1^2} + I_c^{i^2} + T_c^{i^2} + 4\alpha_1\tau_1\varepsilon h I_v^i S_c^{i+1}(1-u_1^i)(1 + h(\varphi u_2^i + \mu_c + \kappa)) \\
&+ 2hI_c^i(\varphi u_2^i + \mu_c + \kappa)(S_c^{i+1} + T_c^i) + h^2(\varphi u_2^i + \mu_c + \kappa)^2(S_c^{i+1^2} + T_c^{i^2}) \\
&+ 2(I_c^i T_c^i + S_c^{i+1} I_c^i + S_c^{i+1} T_c^i) + 2h(\varphi u_2^i + \mu_c + \kappa)(S_c^{i+1} + T_c^i)^2 \\
&+ 2h^2(\varphi u_2^i + \mu_c + \kappa)^2 S_c^{i+1} T_c^i]^{\frac{1}{2}}\}, \\
T_c^{i+1} &= \frac{h\varphi u_2^i I_c^{i+1} + T_c^i}{h(r + \mu_c) + 1}, \\
S_v^{i+1} &= \frac{h\Lambda_v + S_v^i}{h\left\{\alpha_1\tau_2\frac{I_c^{i+1}}{S_c^{i+1} + I_c^{i+1} + T_c^{i+1}}(1-u_1^i) + \alpha_2\tau_3\frac{I_w^i}{S_w^i + I_w^i} + \mu_v\right\} + 1}, \\
I_v^{i+1} &= \frac{1}{h\mu_v + 1}\left\{h\left\{\alpha_1\tau_2\frac{I_c^{i+1}}{S_c^{i+1} + I_c^{i+1} + T_c^{i+1}}(1-u_1^i) + \alpha_2\tau_3\frac{I_w^i}{S_w^i + I_w^i}\right\}S_v^{i+1} + I_v^i\right\}, \\
S_w^{i+1} &= \frac{1}{2}\frac{1}{h\mu_w + 1}\{\Lambda_w h + S_w^i - I_w^i - \alpha_2\tau_4\varepsilon h I_v^{i+1} - h\mu_w I_w^i + [\Lambda_w^2 h^2 + 2h\Lambda_w(S_w^i + I_w^i) \\
&+ 2h^2\Lambda_w(\mu_w I_w^i - \alpha_2\tau_4\varepsilon I_v^{i+1}) - 2\alpha_2\tau_4\varepsilon h(S_w^i - I_w^i)I_v^{i+1} + (S_w^i + I_w^i)^2 + 2h\mu_w I_w^i(S_w^i + I_w^i) \\
&+ h^2\mu_w^2 I_w^{i^2} + \alpha_2^2\tau_4^2\varepsilon^2 h^2 I_v^{i+1} + 2h^2\alpha_2\tau_4\varepsilon\mu_w I_v^{i+1} I_w^i]^{\frac{1}{2}}\}, \\
I_w^{i+1} &= \frac{1}{2}\frac{1}{h\mu_w + 1}\{I_w^i - (h\mu_w + 1)S_w^{i+1} + [(S_w^{i+1} + I_w^i)^2 + 4\alpha_2\tau_4\varepsilon h(h\mu_w + 1)I_v^{i+1} \\
&+ 2h\mu_w S_w^{i+1}(S_w^{i+1} + I_w^i) + h^2\mu_w^2 S_w^{i+1^2}]^{\frac{1}{2}}\},
\end{aligned}
$$

$$\lambda_1^{n-i-1} = \frac{1}{h[\{\alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1^2}}S_c^{i+1} - \alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1}}\}(1-u_1^i)-\mu_c]-1}\{h[\lambda_2^{n-i}\{\alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1^2}}S_c^{i+1}$$
$$- \alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1}}\}(1-u_1^i) + (\lambda_5^{n-i}-\lambda_4^{n-i})\alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1^2}}S_v^{i+1}(1-u_1^i)] - \lambda_1^{n-i}\},$$

$$\lambda_2^{n-i-1} = \frac{1}{h(\varphi u_2^i + \alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1^2}}S_c^{i+1}(1-u_1^i) + (\mu_c+\kappa)) + 1}[\lambda_2^{n-i}$$
$$+ h(\lambda_3^{n-i}\varphi u_2^i + \lambda_1^{n-i-1}\alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1^2}}S_c^{i+1}(1-u_1^i) + A - (\lambda_4^{n-i}$$
$$- \lambda_5^{n-i})\left\{\frac{\alpha_1\tau_2}{N_c^{i+1}} - \alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1^2}}\right\}S_v^{i+1}(1-u_1^i))],$$

$$\lambda_3^{n-i-1} = \frac{1}{h(\mu_c+r)+1}[\lambda_3^{n-i} + h(r\lambda_1^{n-i-1} - (\lambda_2^{n-i-1}-\lambda_1^{n-i-1})\alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1^2}}S_c^{i+1}(1-u_1^i)$$
$$- (\lambda_5^{n-i}-\lambda_4^{n-i})\alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1^2}}S_v^{i+1}(1-u_1^i))],$$

$$\lambda_4^{n-i-1} = \frac{1}{h(\left\{\alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1}}(1-u_1^i) + \alpha_2\tau_3\frac{I_w^{i+1}}{N_w^{i+1}} + \mu_v\right\}) + 1}[\lambda_4^{n-i}$$
$$+ \lambda_5^{n-i}h(\alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1}}(1-u_1^i) + \alpha_2\tau_3\frac{I_w^{i+1}}{N_w^{i+1}})],$$

$$\lambda_5^{n-i-1} = \frac{1}{h\mu_v+1}[\lambda_5^{n-i} - h((\lambda_1^{n-i-1}-\lambda_2^{n-i-1})\alpha_1\tau_1\varepsilon\frac{S_c^{i+1}}{N_c^{i+1}}(1-u_1^i)$$
$$+ (\lambda_6^{n-i}-\lambda_7^{n-i})\alpha_2\tau_4\varepsilon\frac{S_w^{i+1}}{N_w^{i+1}})],$$

$$\lambda_6^{n-i-1} = \frac{1}{h(\{\alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{N_w^{i+1^2}}S_w^{i+1} - \alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{N_w^{i+1}}\} - \mu_w) - 1}[\lambda_7^{n-i}h(\{\alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{N_w^{i+1^2}}S_w^{i+1}$$
$$- \alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{N_w^{i+1}}\}) + (\lambda_5^{n-i-1}-\lambda_4^{n-i-1})\alpha_2\tau_3 h\frac{I_w^{i+1}}{N_w^{i+1^2}}S_v^{i+1} - \lambda_6^{n-i}],$$

$$\lambda_7^{n-i-1} = \frac{1}{h(\alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{N_w^{i+1^2}}S_w^{i+1} + \mu_w) + 1}[h(\lambda_6^{n-i-1}\alpha_2\tau_4\varepsilon\frac{I_v^{i+1}}{N_w^{i+1^2}}S_w^{i+1}$$
$$- (\lambda_4^{n-i-1}-\lambda_5^{n-i-1})\left\{\frac{\alpha_2\tau_3}{N_w^{i+1}} - \alpha_2\tau_3\frac{I_w^{i+1}}{N_w^{i+1^2}}\right\}S_v^{i+1})$$
$$+ \lambda_7^{n-i}],$$

$$B_1^{i+1} = \frac{1}{B_1}[(\lambda_2^{n-i-1}-\lambda_1^{n-i-1})\alpha_1\tau_1\varepsilon\frac{I_v^{i+1}}{N_c^{i+1}}S_c^{i+1} + (\lambda_5^{n-i-1}-\lambda_4^{n-i-1})\alpha_1\tau_2\frac{I_c^{i+1}}{N_c^{i+1}}S_v^{i+1}],$$

$$B_2^{i+1} = \frac{1}{B_2}(\lambda_2^{n-i-1}-\lambda_3^{n-i-1})\varphi I_c^{i+1},$$

$$u_1^{i+1} = min\{max\{0, B_1^{i+1}\}, 1\},$$

$$u_2^{i+1} = min\{max\{0, B_2^{i+1}\}, 1\}.$$

end for

step 3:

for $i = 1, \ldots, n-1$, write $S_c^*(t_i) = S_c^i$, $I_c^*(t_i) = I_c^i$, $T_c^*(t_i) = T_c^i$, $S_v^*(t_i) = S_v^i$, $I_v^*(t_i) = I_v^i$, $S_w^*(t_i) = S_w^i$, $I_w^*(t_i) = I_w^i$, $u_1^*(t_i) = u_1^i$, $u_2^*(t_i) = u_2^i$.

end for

To simulate the model, parameter values available were taken from [63, 85, 74, 75] while the rest were estimated. The values are $\alpha_1 = 0.032$, $\alpha_2 = 0.97$, $\mu_c = 0.00055$, $\mu_v = 0.97$, $\mu_w = 0.0006$, $\kappa = 0.006$, $\tau_1 = 0.62$, $\tau_2 = 0.7$, $\tau_3 = 0.05$, $\tau_4 = 0.2$, $\varepsilon = 0.5$, $h = \frac{I_v}{N_c}$, $\rho = \frac{I_v}{N_w}$, $r = 0.014$, $\varphi = 0.5 - 0.75$, $\Lambda_c = \mu_c N_c$, $\Lambda_v = 24$, $\Lambda_w = 27.5$; with initial values $S_{c0} = 2000$, $I_{c0} = 1000$, $T_{c0} = 0$, $S_{v0} = 10000$, $I_{v0} = 8000$, $S_{w0} = 3000$ and $I_{w0} = 2000$. Weight constant values $A = 1$ and $B_1 = B_2 = 50$ are chosen to balance the host populations and control functions because their magnitudes are on different scales. The model is simulated both with and without control using ODE solvers coded in MATLAB programming language.

Figure 5.5.1 shows the model without control, Figure 5.5.2 the model with the preventive control u_1 only, Figure 5.5.3 the model with the treatment control u_2 only and Figure 5.5.4 with both the preventive control u_1 and the treatment control u_2. The red lines represent the model without control and the blue lines the model with control. In the figures, the plots a, b, c, d, e, f and g are for the susceptible cattle, the infected cattle, the treated cattle, the susceptible vector, the infected vector, the susceptible wild animal and the infected wild animal populations respectively. The last two plots, (h) and (i) are the control profiles for u_1 and u_2 respectively.

5.4.1 Use of Preventive Measures $(u_1 \neq 0)$ only

With this strategy, only the preventive control u_1 on the vector biting rate is used to optimize the objective function J, while the control u_2 on treating a proportion of the infected cattle population is set to zero. Figure 5.5.2(a) shows that the susceptible cattle population stays constant at 2000 while Figure 5.5.2(b) indicates that the infected cattle reduce steadily from the initial value of 1000 to 0. Figures 5.5.2(d) and 5.5.2(e) show that the preventive

control has no marked effect on the vector population, however in the susceptible wild animal population, Figure 5.5.2(f), there are no marked differences in the initial time period but the population does not drop as low as without control. Not as many susceptible wild animals get infected as when there is no preventive control.

5.4.2 Use of Treatment ($u_2 \neq 0$) only

With this strategy, only the treatment control u_2 on the infected cattle population is used to optimize the objective function J, while the preventive control u_1 on the vector biting rate is set to zero. Figure 5.5.3 shows that the treatment control does not have much effect on the vector and wild animal populations. Under treatment control, the susceptible cattle population drops from 2000 and then progressively rises to way above 2500 as shown in Figure 5.5.3(a). The infected cattle population drops gradually from 1000 to 200 as is shown in Figure 5.5.3(b). The treated cattle population rises steadily to a maximum of slightly above 400 and drops gradually to 0 as shown in Figure 5.5.3(c).

5.4.3 Use of both Preventive Measures ($u_1 \neq 0$) and Treatment ($u_2 \neq 0$)

With this strategy, the control u_1 and the control u_2 are all used to optimize the objective function J. In Figures 5.5.4(b) and 5.5.4(g), it is observed that the control strategies resulted in a decrease in the number of infected cattle I_c, and infected wild animal population I_w . An increase is observed in the susceptible cattle S_c and the susceptible wild animal S_w populations in the strategy with control. The treated cattle population increase steadily to a maximum of 300 which is lower than when treatment alone is used to control the disease and drops gradually to 0 as shown in Figure 5.5.4(c).

The numerical simulations show that the preventive and treatment control strategies help to reduce the number of infected cattle. The preventive control does it more significantly, as says the proverb: prevention is better than cure. When both strategies are used infection in the alternative host, the wild animal population, is also reduced. However, both strategies

do not have an effect on the tsetse population.

5.5 Summary

In this chapter, optimal control theory is used to study the effect of a preventive control to reduce tsetse fly-cattle contacts and a treatment control to reduce the infected cattle in a cattle population. Pontryagins Maximum Principle is used to characterize the optimal control and the optimality system which minimizes both the number of infected cattle and the cost of applying the controls is derived and solved numerically.

From the numerical analysis, it may be hypothesized that the most effective way to lower the incidence rate and prevalence level of trypanosomiasis in a cattle population is to use a preventive control strategy that reduces contact between the tsetse fly and the cattle population. However, this does not have much effect on the wild animal population whose presence have considerable effect on the dynamics of the disease. When both treatment and prevention strategies are in place, there is an effect in the wild animal population. The susceptible wild animal population is increased while the infected wild animals decrease. The net effect on disease dynamics when both strategies are used is greater that when they are used singly.

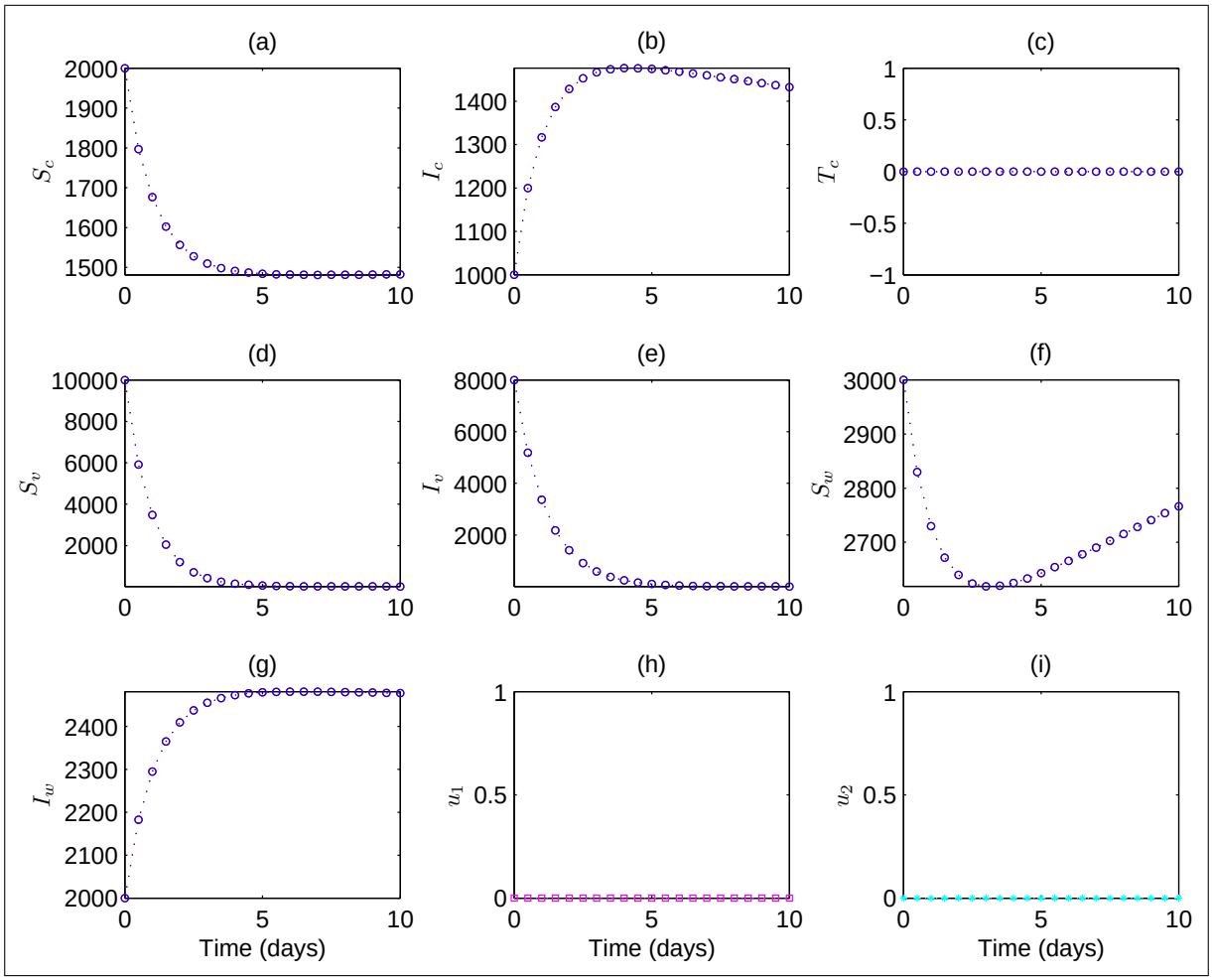

Figure 5.5.1: The cattle, vector and wild animal populations without control

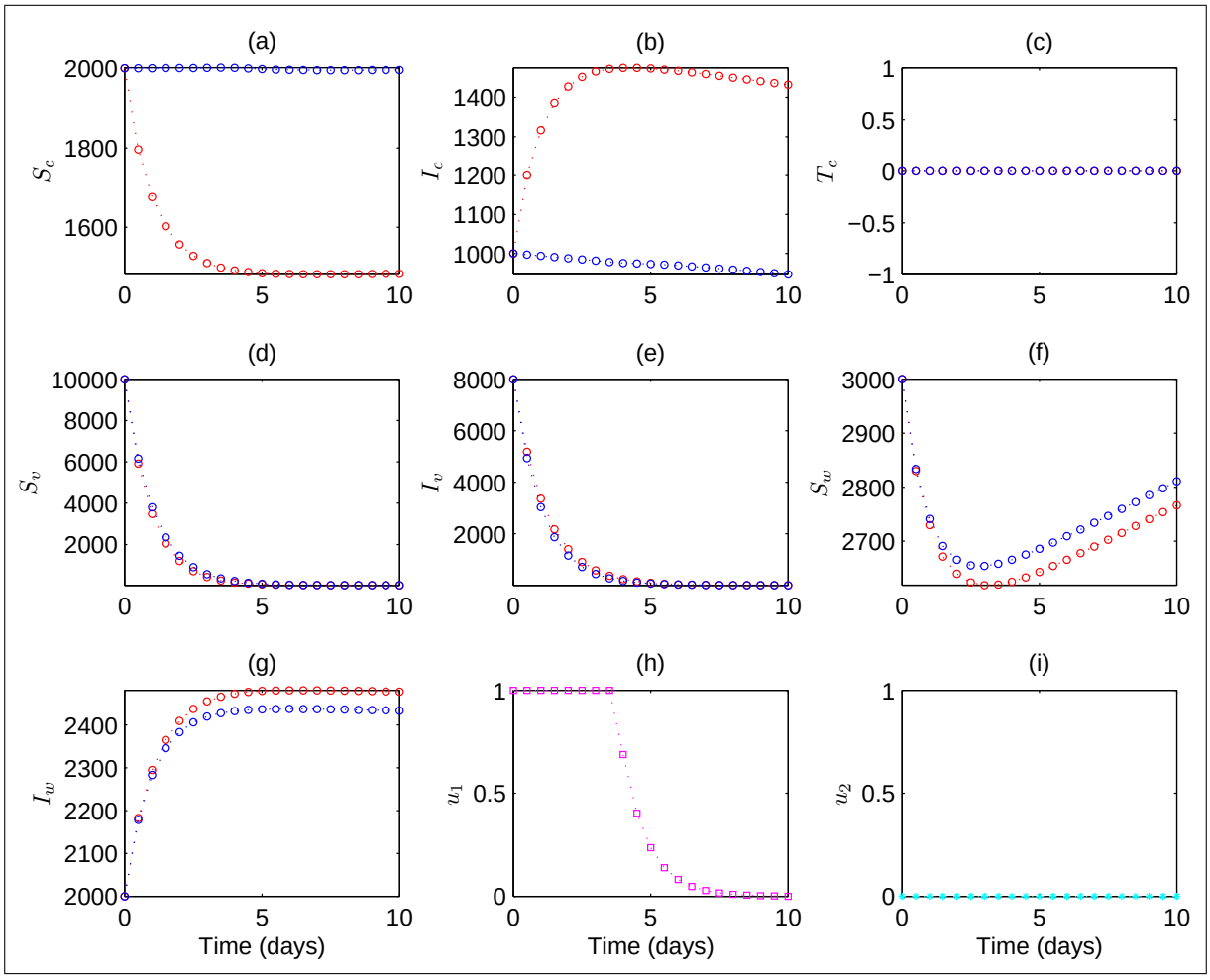

Figure 5.5.2: The cattle, vector and wild animal populations with preventive control

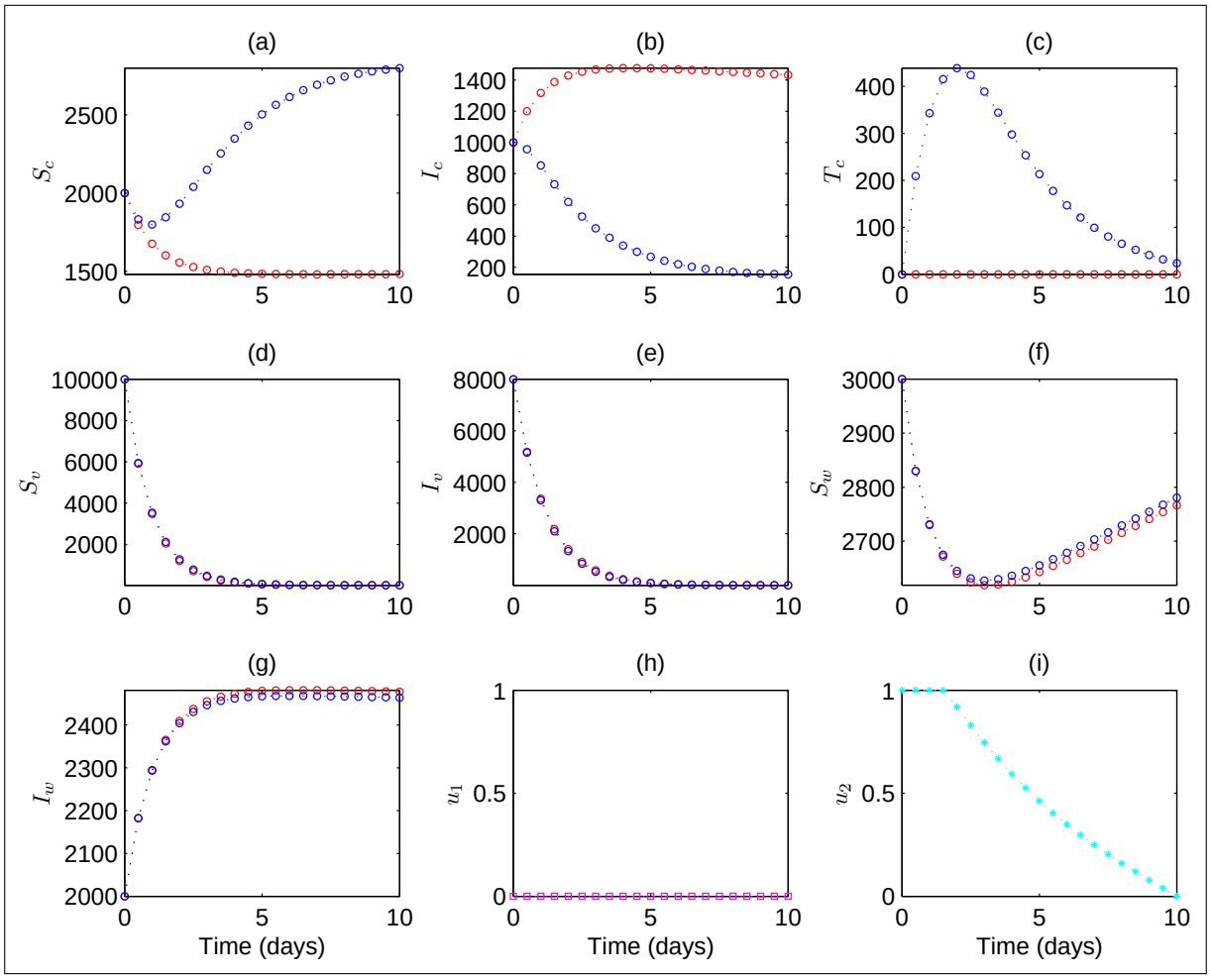

Figure 5.5.3: The cattle, vector and wild animal populations with treatment control

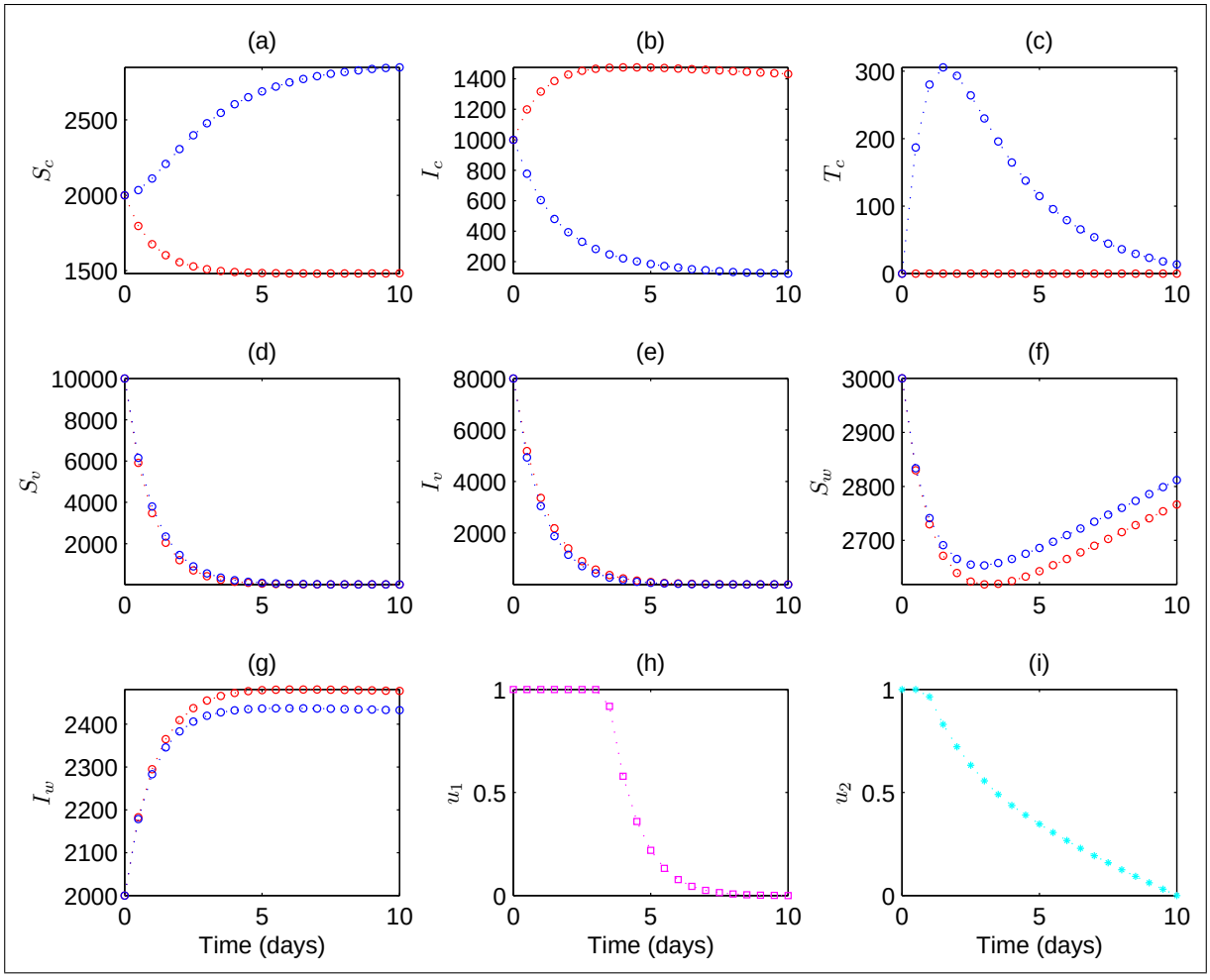

Figure 5.5.4: The cattle, vector and wild animal populations with both preventive and treatment control

Chapter 6

Discussion, Conclusion, Recommendation and Future work

6.1 Discussion

In this study a deterministic population based model for trypanosomiasis in a cattle population was formulated and analyzed. The dynamics of the disease involve trypanosomes, the pathogen, tsetse flies, the vectors of transmission, the cattle population where the disease is fatal if there is no intervention and the wild animal population who act as reservoirs for the disease pathogens. Although the disease is complex and involves several trypanosomes and different fly species each with varied transmission effects, the model assumes only a single trypanosome transmitted by a single species of the tsetse fly causes infection in this population. The tsetse populations are known to exhibit a range of behavior which induces seasonality in cattle parasitaemia [63], however the model considers just the period when maximum vector population is attained. The model developed is strategic and is used to study general disease dynamics and control.

In Chapter 3 a basic model was formulated with the aim of establishing the threshold parameters which would control or eradicate the disease in a cattle population. The model is well posed and exists in a feasible region where the disease-free and endemic equilibrium points are obtained and their stability investigated. The model has a locally and globally

asymptotically stable disease-free equilibrium when $R_0 < 1$; and it has a unique and globally asymptotically endemic equilibrium when $R_0 > 1$. The Centre Manifold Theorem is used to show that the model exhibits a supercritical bifurcation. This means that exchange of stability between the disease-free and endemic states guarantees that the endemic steady state is locally asymptotically stable whenever $R_0 > 1$. It is clear that the dynamics of the disease in the population is determined by the basic reproduction number.

Since R_0 is an important parameter in the dynamics of the disease and yet it is a function of various disease parameters, a sensitivity analysis of R_0 is carried out. This is used to establish the most important or most influential parameter that should be targeted by intervention strategies for disease control. To determine how sensitive the parameters are, parameter values from previous studies were used. The analysis indicated that the important parameters are the rate at which the vectors bite the wild animals, the survival rate of the vectors and the transmission probability from infective wild animal to susceptible vector. Just as in [63] this study suggests a close monitoring of the disease dynamics in the wild animal population to inform methods of disease control in the cattle population.

In the cattle population, the most sensitive parameter is the rate at which the vectors bite the cattle population, the transmission probability from infective vector to cattle population and the proportion of susceptible vectors to the cattle population. Generally the vector biting rate is an important parameter in the dynamics of the disease. The analysis suggests that an effective control strategy would be one that reduces the contact between the cattle and the vector populations. This means that effective control strategies should generally target the vector. However, for individual stock owners the use of trypanocides is the main strategy that they use throughout tsetse-infested Africa to control Trypanosomiasis [9]. In Chapter 4 the basic model is extended to include treatment of a proportion of the infected cattle.

The model is formulated to include a simple regulating migratory mechanism as in [56] since control measures in tsetse-infected regions are frequently blighted by immigration of tsetse

flies [63]. An assumption made is that only susceptible flies migrate into the vector population. The effect of treatment on the dynamics of the cattle is investigated by considering treatment of a proportion of the infected cattle population. The model has a disease-free equilibrium which is locally and globally asymptotically stable whenever its associated effective reproduction number R_{eff} is less than unity. It shows that this model has a unique endemic equilibrium under certain conditions which is globally asymptotically stable when the effective reproduction number R_{eff} exceeds unity.

An analysis of R_{eff} which measures the average number of new infections when an intervention strategy is in place indicates $R_{eff} < R_0$ if $\gamma > 0$ and $(1 - \zeta) < \gamma$, where γ is the proportion of infected cattle treated and ζ denotes the reduction in the rate of infection of the vectors from infected cattle. This means that in a cattle population with intervention against the disease, it is not enough to ensure $R_0 < 1$ since this will not indicate the disease is being eradicated in the population. Instead this would create a possibility of backward bifurcation in the disease model. This means the disease would still be endemic in the population though $R_0 < 1$. Further still, if $R_{eff} < 1 < R_0$ then treatment has a positive impact and reduces the spread of the disease in the cattle population. While if $1 < R_{eff} < R_0$ then the epidemic develops in the population prompting intervention strategies.

Notably, treatment as an intervention strategy has no effect in the disease dynamics in the wild animal population. Though $R_{eff} < R_0$ there is no reduction of disease transmission in the wild animal population, R_{0wT}. Eradicating the disease in the cattle population is hence complicated by the existence of the wild animal population which constitute the omnipresent reservoirs of the disease, [27]. This must have motivated the control strategy used in West and Central Africa in the early days of destroying the wild animals in order to eliminate both the reservoir and the parasite but of course which had more disadvantages than advantages. Instead a combination of multiple intervention strategies particularly to ensure that the vectors who are in contact with the wild animal population do not get into contact with the cattle population would suffice.

A sensitivity analysis of R_{eff} indicates that treatment of a proportion of the infected cattle population reduces the endemicity of the disease. Indeed by the time you have treated a proportion of $0.5 - 0.75$, the effect would be similar to treating all the infected cattle. Such information would be beneficial to farmers who have to consider the costs and benefits of any choice of control strategy they settle for. Treating all infected cattle, though would seem the best option for trypanosomiasis disease control, is really not necessary. The extra cost incurred could instead be used to fund a second intervention strategy.

Since the model with treatment established that treating a proportion of the cattle was not enough to eliminate the disease, in Chapter 5 the model is modified to conduct a systematic analysis of different interventions within a single disease model. It determines cost effective strategies for combating the spread of trypanosomiasis in a cattle population. By the application of Pontryagin's Maximum Principle, an optimal analysis of the model was performed considering two controls, one for lowering disease incidence (the rate of new infections) using a costly preventive effort and the other for lowering disease prevalence (number of infected cattle) using a costly treatment effort. The number of infected cattle was minimized using the two controls.

The dynamics of the model have been investigated by a numerical method based on optimal control to identify the best strategy. From the numerical simulations it is clear that both controls reduce the number of infected cattle, however only the preventive control has the effect of reducing the number of infected wild animals. This is equivalent to reducing the endemicity of the disease in the wild animal population. Coupled with treatment which reduces endemicity of the disease in the cattle population, $R_{c0T} < R_{0T}$, the net effect will be a reduction in R_{eff}.

6.2 Conclusion

Trypanosomiasis in a cattle population has such devastating effects both socially and economically in the communities where it is endemic. The study of its disease dynamics are

usually geared towards being able to control the disease. The disease dynamics in populations without and with control strategies are determined by the threshold values R_0 and R_{eff} respectively. However, these threshold values are functions of both disease and population parameters some of which are more influential than others. The influential parameters give guidance on the control strategies that would reduce disease prevalence.

When there are no control strategies in the population, the parameters that are of greatest influence are the wild animal vector biting rate, the survival rate of the vector which both increase the endemicity of the disease while the vector death rate reduces the endemicity of the disease. Obviously, without the vector of transmission the disease would die out in the population. The wild animal vector biting rate α_2 and the vector survival rate, ε both suggest control strategies that reduce contact between the cattle and the vector population.

In the cattle population, the vector biting rate is the most influential parameter and it increase disease prevalence whereas in the vector population the vector survival rate is most influential so that the longer the vector remains alive the more hosts it is able to infect. These two parameters also indicate the disease would be reduced in the cattle population by vector control strategies. It follows that the most effective way to lower the incidence rate and prevalence level of trypanosomiasis in a cattle population is to use a preventive control strategy that reduces contact between the tsetse fly and the cattle population. The preventive control strategy reduces endemicity of the disease in the wild animal population since the control reduces the rate of infection in the vector population.

Treatment of a proportion of the infected cattle reduces disease prevalence in the cattle population. However, it has no effect on the wild animal population who constitute a trypanosome reservoir. It is also not necessary to treat all the infected cattle but any proportion between 0.5 to 0.75 to control the disease in a cattle population. This suggests that a small proportion of infected cattle can exist in the cattle population and disease does not grow into an epidemic. Though the preventive effort reduces the number of infected cattle faster, the net effect on disease dynamics when both strategies, preventive and treatment are used,

is greater that when they are used singly.

6.3 Recommendation

From the study it is clear that if the farmers use the preventive procedures diligently, then the spread of the disease can be controlled even for relatively low proportion of treated cattle. However, they would have to ensure that the cattle do not get in contact with the infected vector population. It is necessary that farmers are educated on the use of traps, targets and treating cattle with insecticides which are some of the available preventive strategies. These education programs must reach the community at all social levels, especially in lower classes, to increase the awareness about the disease and the protection techniques so that the spread of the disease can be controlled. Treating a proportion of the infected cattle would mean they do not reach a level that the disease becomes endemic in the cattle population. This would be achieved by ensuring that the farmers are able to diagnose the disease in cattle effectively in order to treat them on time.

6.4 Future Work

Trypanosomiasis in a cattle population is a debilitating disease whose social and economic impact are immense and negative. Considering effective control strategies would still be a necessary area of research. From the analysis of our strategic model, it is clear that both intervention strategies singly and combined do not have an effect on the vector population. Incidentally, the vector, is an important component in the dynamics of trypanosomiasis in a cattle population since it transmits the pathogen that causes the disease. The effect of control strategies that reduce both the susceptible and infected vectors need to be considered.

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