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KWAZULU-NATAL

Using epidemiological mathematical models to understand the transmission dynamics of bovine tuberculosis in buffalo and cattle populations

BY

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Submitted in fulfilment of the degree of Doctor of Philosophy at University of KwaZulu–Natal

This dissertation is submitted in fulfilment of the academic requirements for the degree of Doctor of Philosophy in Applied Mathematics to the School of Mathematics, Statistics and Computer Science; College of Agriculture, Engineering and Science, University of KwaZulu-Natal, Durban. .

As the candidate's supervisor, I have approved this dissertation for submission.

Signed: Dr. F. Chirove .....Signed: Prof. K. S. Govinder.....

Abstract

In South Africa, buffalo are the maintenance hosts of Mycobacterium bovis (*M. bovis*), a pathogen that causes bovine tuberculosis in wildlife and domesticated animals. To understand the transmission dynamics of *M. bovis*, mathematical epidemiological models are developed. The models address various questions about the transmission dynamics of bovine tuberculosis in both buffalo and cattle populations. The key questions addressed by the models are: can buffalo carriers fuel the re-occurance of bovine tuberculosis in buffalo population? Is the cross-infection transmission route responsible for the persistence of bovine tuberculosis in cattle population? Can the movement of buffalo from one patch to another be the reason for the spread of bovine tuberculosis in Kruger National Park? These questions are addressed in Chapters 2, 3 and 4 respectively. Both the mathematical and numerical analysis suggest that the infection parameters associated with buffalo carriers and cross-infection and movement parameters associated with the movement of susceptible and exposed buffalo from one patch to another are among the key drivers of bovine tuberculosis in buffalo and cattle populations. The findings have very vital implications for bovine tuberculosis control. If bovine tuberculosis is to be eliminated, there is need to develop tests that can detect buffalo carriers from buffalo population. This will accelerate the eradication of bovine tuberculosis (BTB) infection from the buffalo population. Measures need to be taken to prevent the mixing of cattle and buffalo populations at the interface and also restrict the movement of buffalo from one patch to another in Kruger National Park.

Declaration

I declare that the contents of this dissertation are original except where due reference has been made. It has not been submitted before for any degree to any other institution.

Patrick B. Phepa

Declaration 1 - Plagiarism

I, Patrick B. Phepa, declare that

1. The research reported in this thesis, except where otherwise indicated, is my original research.

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Contents

Chapter 1

Introduction

1.1 Background

Bovine tuberculosis (BTB) is a chronic and emaciating infectious disease, caused by *Mycobacterium bovis*, which affects domesticated and wild mammals [6]. *Mycobacterium bovis* forms part of the Mycobaterium tuberculosis complex. The Mycobacterium tuberculosis complex comprises tubercle bacilli of 8 distinct subgroups: *M. tubrculosis*, *M. bovis*, *M. africanum*, *M. canettii*, *M. caprae*, *M. pinnipedii*, *M. microti*, and *M. mungi*. Two other different branches of the M. tuberculosis complex phylogenetic tree exist, the *dassie* and *oryx bacilli*, which are causative agents of tuberculosis in the animal species after which they are named [8]. The BTB infection wrecks more havoc in the cattle industry in sub-Saharan countries, where diagnostic tests are not commonly used [16].

1.2 Epidemiology of bovine tuberculosis in Africa and other continents

Despite some success of control and eradication programs for BTB implemented in various countries which resulted in the drastic reduction of the new cases of BTB infection in certain

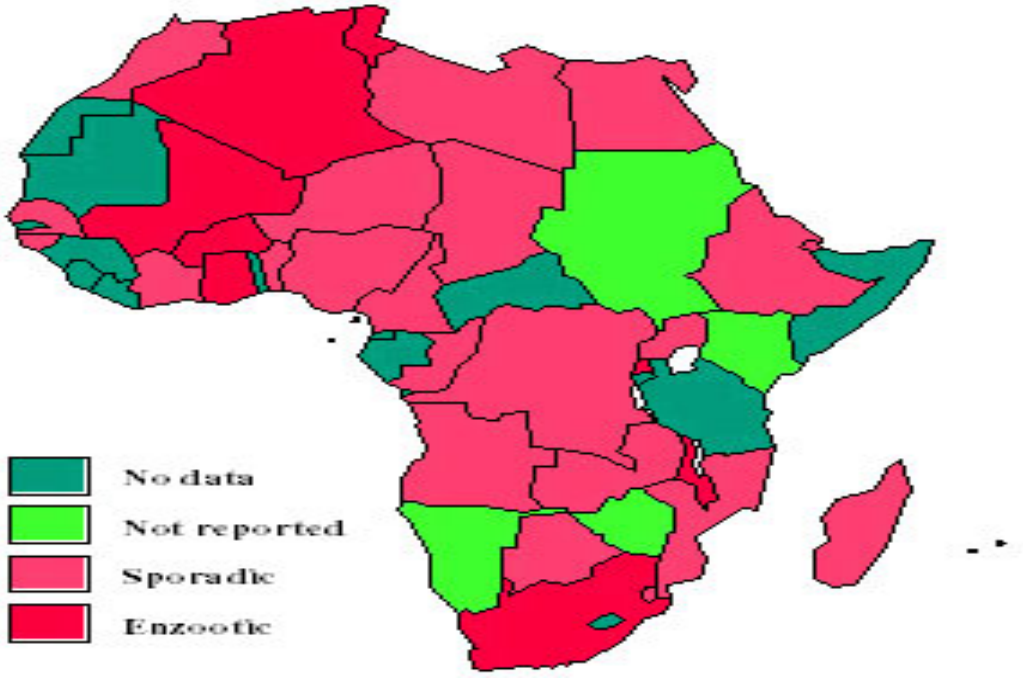

Figure 1.1: Bovine tuberculosis occurance, Africa [5].

regions, the infection is still prevalent in many parts of the world, particulary in Africa. One of the reasons for the lack of success is the high cost of sustainable testing procedures as well as logistic inputs and financial constraints [7, 17]. The prevalence data on bovine tuberculosis in developing countries are generally scarce but information on BTB occurrence is available. Of the 55 African countries, 25 reported sporadic occurrence of BTB infection; six reported enzootic disease, two were reported to have high prevalence, four did not report the disease and the remaining 18 countries did not have data. Only seven African countries used disease control measures and classified BTB as a notifiable disease [5]. This was attributed to the inadequate knowledge about BTB transmission dynamics and its impact in most African countries. Figure 1.1 shows the countries with reported occurrence of bovine tuberculosis.

In Asia, out of 36 nations, 16 reported sporadic occurrence of BTB, one classified the disease as enzootic, ten did not report cases on BTB and the remaining did not have data. Only seven countries used disease control measures and considered BTB as a notifiable disease.

Of the total Asian cattle and buffalo populations, 6% and less than 1%, respectively, are found in countries where bovine tuberculosis is notifiable and a test-and-slaughter policy is used. Of these populations 94% of the cattle and more than 99% of the buffalo are either only partly controlled for bovine tuberculosis or not controlled at all [5]. This poses a huge threat of the spill over of the BTB infection to human beings. Similar trends of the prevalence of the BTB infection in Latin America were also observed. Erratic occurrence of BTB infection was reported in 12 countries out of 34 countries. Enzootic was reported in seven countries and only one country described occurrence as high. The other two remaining countries did not have data for the disease [5]. (The data on the statistics of BTB in African and Asian countries was collected in the years of 1990 and 1995.)

It has been estimated that *M.bovis* accounts globally for 3.1% of all human TB cases (2.1% of all pulmonary and 9.4% of all extra-pulmonary TB cases). However the extent of *M. bovis* involvement in the global TB burden in Africa is still largely unknown. This is explained by the fact that in humans, TB due to *M. bovis* is indistinguishable from TB due to *M.tuberculosis* in terms of clinical signs, radiological and pathological features [19].

BTB infection also poses an economic threat to trade in animals and their products [9]. In South Africa, the average price for a disease-free buffalo in 2004 was almost ZAR150000, in 2008 was over ZAR160000, and in 2010 the price increased to over ZAR325000. In 2011 and 2012 the prices hit ZAR18 million and ZAR20 million per buffalo respectively. The advent of BTB infection risks the economic benefits realized from buffalo sales [11]. Subsequently, a great interest and commitment are devoted to studies that unravel the key drivers of the disease in buffalo and cattle.

1.3 Epidemiology of bovine tuberculosis in Kruger National Park

The area of Kruger National Park (KNP) in South Africa is 19488km^2. It is South Africa's largest wildlife refuge and a critical biodiversity resource. The Park holds up to 147 mammal

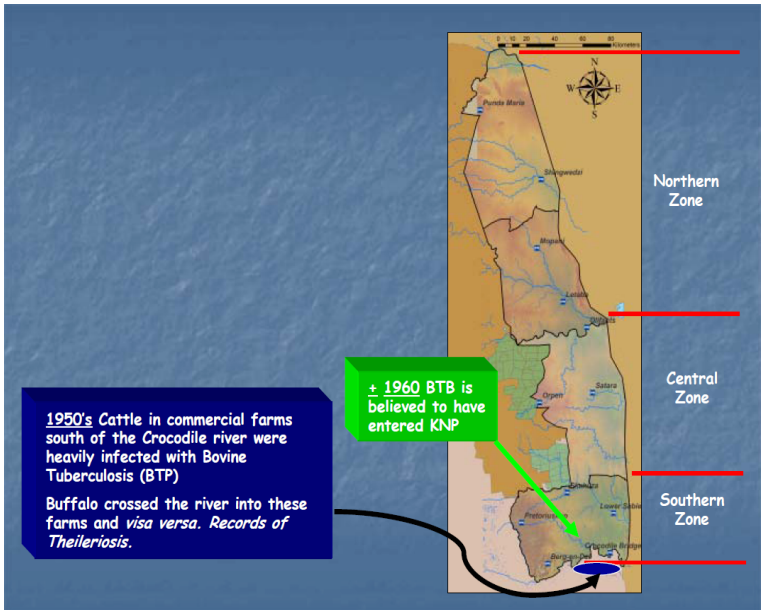

Figure 1.2: The map showing the spread of bovine tuberculosi in Kruger National Park [18]

species, including approximately 2700 African buffalo and 1700 lions. The park is bordered by Zimbabwe to the north and Mozambique to the east. The KNP stretches 320km from north to south and 65km from east to west. Several private game reserves have recently been combined to form Greater Kruger National Park Complex (GKNPC). The private game reserves are located on the western border of the park [14].

Bovine tuberculosis infection is said to be introduced in the park via co-grazing between cattle and buffalo in the far south of KNP near Crocodile Bridge prior to the 1960's (see Figure 1.2).

By the late 1980's, BTB infection was largely eliminated from the domestic animal populations surrounding KNP, but inside KNP it persisted undetected. The survey conducted in 1991/92 showed the bushfire like spread of BTB infection towards the north of the park. The southern part of the park was heavily infected with a prevalence of 27.1%. The central part of the park was moderately infected with a prevalence of 4.4% while 0% prevalence of the BTB infection was found in the northern part of the park. In the 1998 survey, the prevalence of the BTB infection in south, central and north of the park went up to 38.2%, 16% and 1.5% respectively [18]. The chronological events of the occurrence of BTB infection in all three regions of the

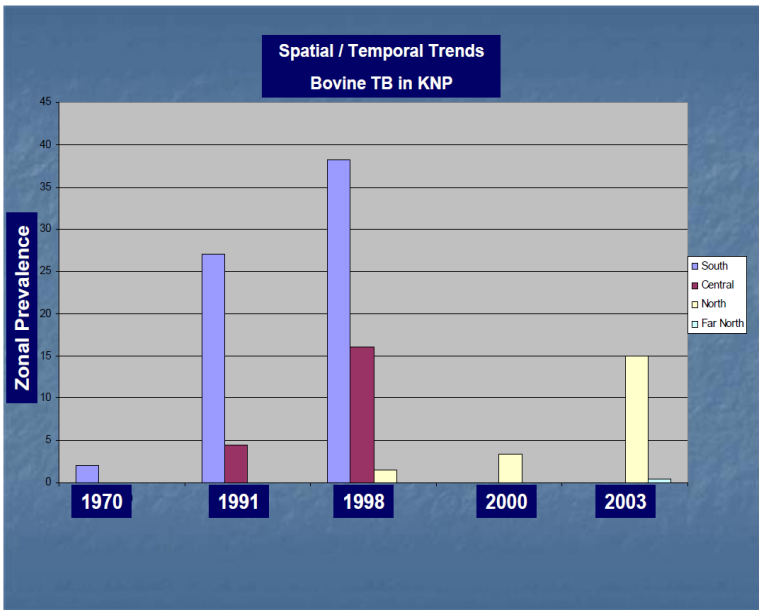

Figure 1.3: The map showing the spread trends of BTB infection in KNP from 1970 to 2003 [18]

park are depicted in Figure 1.3

The spreading trend of the BTB infection and its spill over effects have made scientists concerned. The ecotourism aspect of the park is also heavily affected due to a large of number of lions being infected. This is one of the reasons that has fueled more research activities of bovine tuberculosis in Kruger National Park to understand the transmission dynamics of the disease.

The 1998 survey revealed that BTB infection spread at a speed of about 6km per year. The survey also indicated that buffalo less than 2 years old are mostly infected with BTB, which suggested a vertical transmission route as the main route of transmission in the young buffalo. The weakness of young buffalo immunity may enhance this transmission mode. Table 1.1 summarises the results of the survey.

Results from 1998 Survey

Zone	Animals sampled	Zonal prev.	% buffalo$\geq$ 9 yrs	Buffalo $\leq$ 2 yrs. % infected
South	206	38.5%	5.3%	30.3%
Central	206	19.7%	5.8%	17.2%
North	206	1.5%	15%	0.0%

Table 1.1: The table showing the age specific prevalence of BTB infection in buffalo [18]

1.4 Bovine tuberculosis in cattle population

Farmers are being denied of their only source of income when their herds of cattle are infected with *M. bovis*. Cattle die in large numbers when they are infected with *M. bovis*. The BTB infection is mainly a serious problem in countries where the control measures are inadequately or not applied at all [5]. Industrialised countries like England managed to reduce the negative effects of BTB infection in the cattle industry but their efforts are being thwarted by the existence of maintenance hosts like badgers [52]. The high prevalence of BTB infection is recorded at the wildlife-livestock interface. For instance, in Zambia a high prevalence of BTB infection in cattle is recorded at the Kafue basin, which interfaces with the rural areas [84]. In South Africa, more cases of BTB infection in cattle are recorded in areas that interface with Kruger National Park [18]. Considering the economic potential the cattle industry has in any country's economy, the priorities of most countries are tailored to research activities that aim to enhance the understanding of the transmission dynamics of BTB infection. This study will also explore the factors that promote the spread of the disease at the wildlife-livestock interface through mathematical models.

1.5 Biology of Mycobacterium bovis

The *M. bovis* is a slow-growing, acid-fast, gram-positive, rod-filamentous-shaped bacterium. It has a wide range of hosts and can infect all warm-blooded vertebrates, including humans. The *M. bovis* is an intracellular microbe of macrophages and does not multiply outside the

host except in cultured media [10]. The enviromental conditions dictate the survivability of *M. bovis* outside the host. In moist conditions, particularly those in which oxygen and organic matter are present, the pathogen survival time increases. A harsh environment decreases the survival time of the pathogen [15]. Some hosts of *M. bovis* have the ability to turn into a maintenance host, a host that is not harmed by the pathogen, but acts as a source of infection to other animals. Maintenance hosts include the possum in New Zealand, badgers in Ireland and Britain, Kudu in Zambia, cervids in United States and African buffalo in South Africa [3, 4]. It is the existence of maintenance hosts that has led to the failure of many intervention programs to eradicate bovine tuberculosis in developed countries. Other species have been identified as spill over hosts or dead end such as humans, coyotes and cats. In spill over hosts, infection in the population can not persist indefinitely unless there is re-infection from another species or a change in the population that enhances interspecies transmission [4].

Despite the long history of disease recognition, the disease dynamics of *M. bovis* are not well understood. The incubation period is not known for BTB infection. It ranges from days to several months or longer. Some animals appear in the course of infection to be asymptomatic, but the disease may progress rapidly in others. Progressive emaciation and weakness appear with stress or age. Respiratory signs include coughing, dyspnea, or exercise intolerance [17].

Transmission of *M. bovis* can occur via various transmission mechanisms. A single bacillus in a droplet may be sufficient to establish infection [15]. Aerosolization is thought to be the most infectious route of transmission, accounting for 80 to 90% of infections in cattle [13]. The gregarious behaviour of buffalo promotes this type of transmission mode. In Kruger National Park, lions become infected through eating infected buffalo (which is a maintenance host). Eating poorly cooked meat and drinking contaminated milk is another route that transmits infection to human [4].

1.6 Metapopulations

A metapopulation is a population of populations in which different subpopulations occupy spatially disconnected patches of habitat [12]. Initially, the metapopulation theory was par-

ticularly useful to wildlife biologists because most wildlife are fragmented or maintain some degree of patchiness. The idea of population persistence was achieved even in cases where local populations undergo extinction [12].

The concept of metapopulation was coined by Richard Levins in 1969. His model was based on a population in which individuals reproduce and die within local patches of the habitat, and their offspring disperse into other patches. The variable of interest was p, the fraction of occupied patches. The rate of change of p, $\frac{dp}{dt}$, determines whether p will increase, decrease or stay the same. The rate of change $\frac{dp}{dt}$ is given by the difference between colonization rate C and the extinction rate E. This is analogous to population growth rate as the difference between birth and death rates [12]. The governing equation of the assumed system is

$$\frac{dp}{dt} = C - E = cp(1-p) - ep.$$

In this model, the colonization rate depends on the number of occupied and unoccupied patches. This basic model was modified by various researchers as they tried to address problems in ecology. The metapopulation concept was applied to the study of infectious diseases by Julien Arino [2]. It was used in the field of mathematical epidemiology due: (i) The initial conditions of disease are often heterogeneous, with disease spreading geographically with time. For example, black death spread east to west and south to north along the trade routes of Europe between 1347 and 1350, and fox rabies spread west from Russian-Polish border in 1940 to reach France by 1968; (ii) The environment itself is heterogeneous both in a geographical sense and in a human sense with birth rates, death rates and health care facilities varying with location; (iii) Different species have travel rates, a factor that plays a huge role for diseases involving many species, for instance, the foot-and-mouth disease outbreak in the UK in 2001 and vector transmitted diseases; and (iv) For human diseases, social groupings and mixing patterns vary with geography and age. This is illustrated by comparing humans in a hospital setting with those in isolated communities in Canada's North and with children in schools [2].

To factor in the spatial variations in a model, two approaches may be used. The first approach uses continuous spatial models with continuous time that yield partial differential equations of reaction-diffusion type. The second approach uses discrete spatial models with continuous

time that yield systems of ordinary differential equations, which are metapopulation models involving movement of individuals between discrete spatial models [2]. The approach to be used in any modelling project depends on the questions to be addressed and the experience of the modeller.

1.7 Motivation

Despite the success in eradicating BTB infection in industrialized countries, the disease still remains a big challenge in Sub-Saharan countries. The reasons for the menace to continuously cause havoc in Sub-Saharan region are due to lack of awareness of the local authorities about the economic implications, the high cost of sustainable testing procedures as well as their logistic inputs and financial constraints, and the existence of maintenance hosts that act as the source of infections to other species [17]. In South Africa, BTB infection is endemic in Kruger National Park where significant research activities are being carried out. The benefits being yielded from the research activities are outweighed by the negative impact of the infection. The disease continues to spread and spill over to cattle in the areas closer to the park and other species in the park. The lion, one of the "Big Five" animals in the park is heavily infected; almost 90% of the lions are infected with *M. bovis* [1]. Worse still, the disease continues to spread northwards at a rapid rate, an observation, which is of great concern to policy makers and the park management structure. Additionally, BTB infection has a serious impact on the cattle industry which experiences massive death of cattle. This is expensive to both cattle owners and government. Cattle owners lose the source of income and government lose billions of money as it initiates programs that minimise the further spread of the disease. It is against this background that this project seeks to understand the transmission dynamics of the BTB infection via mathematical modelling. Mathematical models of different forms incorporating the environmental factors and movement factors are developed and analysed to help us to extract insights into the transmission dynamics of the disease. The knowledge gained will help policy makers to apply the correct intervention strategies to minimise the effects of the infection.

1.8 Objectives of the study

The aim of this research project is to formulate mathematical epidemiological models that can be used to study the dynamics of the bovine tuberculosis in both cattle and buffalo populations. The specific objectives of this study are

(i) To analyse the transmission dynamics of bovine tuberculosis so as to find the necessary conditions for the disease persistence.

(ii) To highlight the relative contribution of buffalo carriers and the environment in the disease transmission dynamics.

(iii) To evaluate the impact of cross-infection transmission route in the persistence of the BTB infection in cattle population.

(iv) To evaluate the role of movement of buffalo in the spread of bovine tuberculosis in buffalo population in the Kruger National Park.

1.9 Outline of this work

This work consists of three publications, two of which are under review while one is under revision. In Chapter 2, we provide a model for the transmission of bovine tuberculosis in buffalo only. Mathematical analysis and simulations of the model are given.

In Chapter 3, we give a model for the role of multi-transmission routes in the epidemiological of bovine tuberculosis in cattle and buffalo populations. Mathematical analysis in the presence of the cross-infection route is given. A numerical analysis of the model is also given.

In Chapter 4, we consider a metapopulation model for the role of movement of buffalo in the spread of bovine tuberculosis in Kruger National Park. Mathematical analysis and numerical simulations are both given.

In Chapter 5, we give a comprehensive conclusion of our findings.

1.10 Publications

This thesis is built around the following papers

Chapter 2

- Patrick B. Phepa, Faraimunashe Chirove and Keshlan S. Govinder (2015), Modelling of the transmission dynamics of bovine tuberculosis, *International Journal of Biomathematics*, (*Under review*).

Chapter 3

- Patrick B. Phepa, Faraimunashe Chirove and Keshlan S. Govinder (2015), Modelling the role of multi-transmission routes in the epidemiology of bovine tuberculosis in cattle and buffalo populations, *Journal of Mathematical Biosciences*, (*Under revision*).

Chapter 4

- Patrick B. Phepa, Faraimunashe Chirove and Keshlan S. Govinder (2015), Modelling the spatial heterogeneity of bovine tuberculosis in buffalo, *Journal of Applied mathematics and computation*, (*Under review*).

Chapter 2

Modelling the transmission dynamics of bovine tuberclosis in buffalo

Modelling the transmission dynamics of bovine tuberculosis in buffalo

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Abstract

Bovine TB infections has a significant impact on the growth of domestic and wildlife animals such as buffalo. The effects have an extended impact on the trade and products of these animals. As a result bovine tuberculosis (BTB) poses a zoonotic threat to the veterinary public health. We propose a mathematical model that studies the transmission dynamics of bovine TB in a buffalo population that seeks to enhance the understanding of BTB infection as a platform for the design of policies towards intervention. The basic reproduction number R_0 of the model was calculated to facilitate the qualitative analysis of the model. It was observed that if $R_0 < 1$, the solution converges to the disease free equilibrium and if $R_0 > 1$, the solution trajectories approach the endemic equilibrium point. Our results suggest that the evolution and the outcome of the disease is determined by horizontal transmission rates and the indirect transmission rate Γ. Higher values of these transmission rates result in higher levels of infected buffalo and carrier buffalo.

Keywords: Bovine tuberculosis, Buffalo, Mycobacterium bovis, Kruger National park, Modelling, Sensitivity analysis

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1. Introduction

Bovine tuberculosis (BTB), an airborne, chronic bacterial disease, caused by *Mycobacterium bovis* (*M. bovis*), is one of the most significant zoonotic infections worldwide [1]. The significance of tuberculosis in wild animals specifically has been acknowledged recently. Many wild animals, once infected, demonstrated the potential to act as reservoirs of the disease for both domestic cattle and other important wildlife species [2, 3]. The brushtail Possum in New Zealand, European badger (*meles meles*) in United Kingdom and Ireland, Bison (*Bison bison*) in North America, African buffalo (*Syncerus Caffer*) in Africa, Kafue Lechwe (*kobus leche*) in Zambia and White-tailed deer (*Odocoileus Virginiarus*) in Michigan can all act as maintenance hosts for bovine tuberculosis, allowing the persistence of the infection in wildlife and enabling the horizontal transmission of the pathogen between species [1, 4, 5, 6].

The modes of transmission that promote the spread of BTB infection to wildlife, livestock and human beings are: aerosol transmission that occurs through inhaling the air droplets that contain *M. bovis*, vertical or pseudovertical transmission which occurs when *M. bovis* is passed on to not yet born offspring or through milk suckling from an infected mother and consuming inadequately cooked infected meat [7], or indirect transmission that occurs through grazing the pastures contaminated with *M. bovis*. Most buffalo contract BTB infection through aerosol transmission. Vertical and psuedovertical transmission are rare modes of transmission of BTB infection in buffalo. Some carnivores such as lions acquire BTB infection through the ingestion of infected buffalo. BTB infection is also transmitted to human beings through eating poorly cooked infected meat and drinking unpasteurised milk, especially in rural areas [6, 8, 9, 10, 11]. Wildlife species may also become infected through indirect transmission by grazing the contaminated pasture. Irrespective of the type of the route of transmission, it takes either months or years for clinical signs of BTB infection to appear [1, 4, 5, 6] . The propagation of *M. bovis* within the animal is considered to be a relatively slow process in ruminants and large carnivores, with the most infected animals being asymptomatic until disseminated lesions develop during the late stages of infection [3].

The BTB infection in buffalo progresses as follows: initial exposure of susceptible buffalo to *M. bovis* leads to the exposed stage, the stage in which

the infected animal is not infectious but has *M. bovis*. This is followed by the infective stage where an infected animal sheds off the *M. bovis* and spreads the infection to other animals. The infective stage is followed by the chronic or carrier stage. In the chronic stage, an infected animal still harbours and spreads the pathogen but at a reduced rate. Note that both the latter stages are asymptomatic. A few studies on BTB infection have been carried out so far worldwide (Africa included). The studies are inadequate due to lack of awareness of the local authorities about the economic implications, the high cost of sustainable testing procedures as well as logistic inputs and financial constraints [3, 16]. BTB infection studies conducted in South Africa, particularly in Kruger National Park (KNP), showed that BTB infection was introduced in KNP from domestic cattle between 1950 and 1960. The presence of the disease was detected in 1990 [17]. It was established that BTB infection was increasing in prevalence in the southern parts of KNP while spreading northwards. This put the whole park at risk of being completely infected. The studies further showed that more than 90% of lions in KNP were infected with BTB infection [18]. The scenario in KNP prompted further studies to enhance the understanding of the epidemiology of BTB infection in KNP. A number of clinical and statistical studies have been carried out on both animal and human tuberculosis in Africa. Studies in South Africa showed that social contact prompted the fast transmission of BTB infection from one animal to another [3, 19]. Transmission of BTB infection from one animal to another was increased when animals from different herds were put into one grazing area where some animals were infected [20]. The mixing of infectious animals with non-infectious animals was the most prominent mode of transmission of BTB infection among buffalo herds in KNP [19].

Mathematical models carried out to understand the BTB infection in buffalo are rare. A model assessing vaccination as a control strategy in an ongoing epidemic of bovine tuberculosis was developed in [6]. The results showed that vaccination alone can not completely control bovine tuberculosis and that it should be combined with other control measures in order to eradicate BTB infection. Related models were developed to understand BTB infection in other animal species [21, 22, 23]. The models developed so far do not consider the carrier sub-class as a confounding factor influencing the dynamics of BTB infection in buffalo. The models did not factor in the effects of indirect transmission of BTB infection as one of the modes of transmission that links

the species under study and the environment as well as other species.

Our study seeks to develop a mathematical model that can be used to understand and analyse the transmission dynamics and control of bovine tuberculosis in buffaloes. We seek to answer the following question: *Do the buffalo carriers influence the persistence of BTB infection in buffalo population?* In section 2 we formulate the mathematical model incorporating the carrier buffalo in the compartmental structure and indirect BTB transmission as additional modes of infection. Section 3 deals with the model analysis. In sections 4 and 5, we shall carry out simulations and present sensitivity analysis results respectively. The discussion and conclusion of results are presented in section 6.

2. Mathematical model

In this section, we present a continuous mathematical epidemiological model for the transmission and evolution of bovine tuberculosis in the buffalo population. We are guided by the information on the natural history of BTB infection to arrive at basic assumptions on the model formulation as it is indicated in [24, 25, 26, 27]. The total population, $N(t)$, is divided into four sub-populations: susceptible buffalo population, $B_s(t)$, that is free from *M. bovis* but at risk of infection, exposed buffalo population, $B_e(t)$, with *M. bovis* but not yet infectious, infected buffalo population, $B_i(t)$, having *M. bovis*, do not show show signs and are infectious and carrier buffalo population, $B_c(t)$, having *M. bovis* do not show signs of infection but infect the susceptible buffalo at a reduced rate compared to the infectious buffalo. Susceptible buffalo are recruited through a constant natural birthrate π. The susceptible buffalo leaves the class either through a constant death rate d or through infection from infectious buffalo, carrier buffalo and external environment with a force of infection defined in equation via

$$\lambda = \frac{\beta B_i + \gamma \beta B_c}{N}. \tag{1}$$

The effective contact rate of susceptible buffalo and infectious buffalo occurs at constant rate β while that of carrier buffalo occur at a rate $\gamma\beta$, $0 \leq \gamma < 1$. When the susceptible buffalo contracts *M. bovis*, they progress as a source to the exposed buffalo population. The natural death rate d is the same for all classes. The exposed buffalo leave their class either through natural death

rate or when they develop clinical symptoms and begin to shed *M. bovis* at a constant rate α into the infectious buffalo class $B_i(t)$. The infectious buffalo leave their class through natural death, through death induced by BTB infection at a rate ϵ and through progression to the carrier buffalo class at a constant rate θ. The progression to carrier buffalo occurs when the infectious buffalo heal from the lesions so that their infectiousness is reduced but they continue to shed *M. bovis*. The carrier buffalo can die naturally or die due to BTB infection at a rate ϵ.

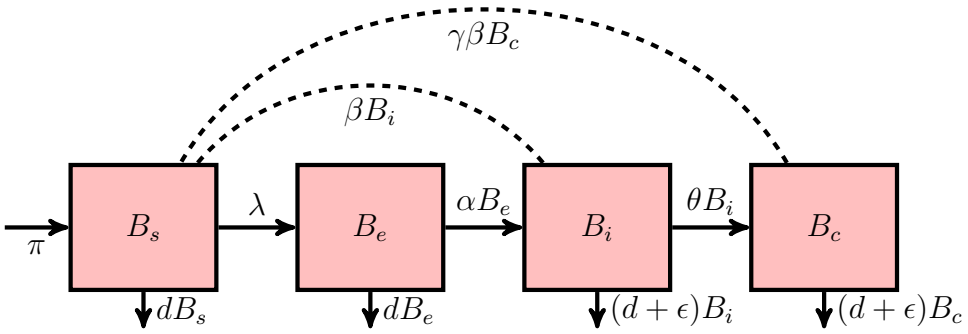

Figure 1: The flow diagram for bovine tuberculosis infection in buffalo population as defined in system 3. The dashed lines represent the transmission routes.

$$N(t) = B_s(t) + B_e(t) + B_i(t) + B_c(t). \tag{2}$$

We illustrate the conceptual model in Figure 1. It is translated into a mathematical model consisting of the following non-linear ordinary differential

equations

$$\begin{aligned}
\frac{dB_s}{dt} &= \pi - \lambda B_s - dB_s \\
\frac{dB_e}{dt} &= \lambda B_s - (\alpha + d)B_e, \\
\frac{dB_i}{dt} &= \alpha B_e - (\theta + d + \epsilon)B_i \\
\frac{dB_c}{dt} &= \theta B_i - (d + \epsilon)B_c.
\end{aligned} \tag{3}$$

3. Model analysis

In this section, we prove the positivity and boundedness of the model (3) to establish the well posedness of our model. We also determine the existence of equilibrium points and their stability to gain insights into the prognosis of the BTB infection in the buffalo population. We shall calculate the basic reproduction number R_0, an epidemiological quantity that gives insight on the processes that are key drivers of BTB infection. The reproduction number is defined as the average number of buffalo secondary infections generated by one infectious buffalo during its entire infectious period in a wholly susceptible buffalo population.

3.1. Feasible region

Since model (3) tracks the buffalo population, we assume that all the state variables and parameters of model (3) are positive for time $t \geq 0$. The bovine tuberculosis transmission model (3) will then be analysed in a suitable feasible region given by

$$\Omega = \left\{ (B_s, B_e, B_i, B_c) \in \Re_+^4 | 0 \leq N(t) \leq \frac{\pi}{d} \right\}.$$

We show that the region Ω is positively invariant. For model (3) to be epidemiologically useful, it is important to show that all its state variables are non-negative for all time. In other words, solutions of model (3) with positive initial data remain positive for all time $t \geq 0$.

Let $B_s \geq 0, B_e \geq 0, B_i \geq 0, B_c \geq 0, \forall t \geq 0$. From the first equation of model (3) we have

$$\frac{dB_s}{dt} = \pi - (d + \lambda)B_s,$$

which can be solved to obtain

$$\begin{aligned} B_s(t) &= B_s(0)exp\left[-\left(dt + \int_0^t \lambda(s)ds\right)\right] + exp\left[-\left(dt + \int_0^t \lambda(s)ds\right)\right] \\ &\left(\int_0^t \pi exp\left[dt + \int_0^s \lambda(w)dw\right]ds\right) \geq 0, \forall t \geq 0. \end{aligned}$$

From the second equation of model (3) we have

$$\frac{dB_e}{dt} + (d + \alpha)B_e = \lambda(t)B_s,$$

with solution

$$B_e(t) = e^{-(d+\alpha)t}\int_0^t \lambda(s)e^{(d+\alpha)s}B_s(s)ds + B_e(0)e^{-(d+\alpha)t} \geq 0.$$

Using the same techniques we also show that $B_i(t) \geq 0$ and $B_c(t) \geq 0$. Thus all the solutions of model (3) are non-negative in Ω.

We now show that all feasible solutions are bounded in a proper subset of Ω. Adding all the equations in model (3) gives

$$\begin{aligned} \dot{N} &= \pi - dN(t) - \epsilon(B_i + B_c), \\ &\leq \pi - dN(t). \end{aligned}$$

Solving the inequality gives

$$0 \leq N(t) \leq \frac{\pi}{d} + \left(N(0) - \frac{\pi}{d}\right)e^{-dt},$$

where $N(0)$ represents the initial value of $N(t)$. Thus, as $t \to \infty$, $0 \leq N(t) \leq \frac{\pi}{d}$. Therefore, all solutions of model (3) enter the region from the boundary of Ω. This means that all possible solutions of model (3) will enter the region Ω and stay inside Ω. Hence the region Ω, of biological interest, is positively-invariant under the flow induced by model (3).

3.2. Equilibrium points

In this section we investigate the existence of equilibria of model (3). Solving the right hand side of the model by equating it to zero, we obtain the following biologically relevant equilibria:

3.2.1. Disease-free equilibrium point and its stability

The disease-free equilibrium of model system (3) is given by

$$E_0 = \left(\frac{\pi}{d}, 0, 0, 0\right).$$

The stability of E_0 is governed by the basic reproduction number. We shall use the next generation operator [28, 30] to establish the stability of E_0. Using the notation in [30] for model (3), the matrix of new infections $\mathbf{F}$ into compartments and the matrix of transfer terms $\mathbf{V}$ in and out of compartments are given

$$F = \begin{pmatrix} 0 & \frac{\beta\pi}{d} & \frac{\gamma\beta\pi}{d} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \qquad V = \begin{pmatrix} d+\alpha & 0 & 0 \\ -\alpha & \theta+\epsilon+d & 0 \\ 0 & -\theta & \epsilon+d \end{pmatrix} \tag{4}$$

so that

$$V^{-1} = \begin{pmatrix} \frac{1}{d+\alpha} & 0 & 0 \\ \frac{\alpha(d+\epsilon)}{(d+\alpha)(d+\epsilon)(d+\epsilon+\theta)} & \frac{1}{\theta+\epsilon+d} & 0 \\ \frac{\alpha\theta}{(d+\alpha)(d+\epsilon)(d+\epsilon+\theta)} & \frac{\theta(d+\alpha)}{(d+\alpha)(d+\epsilon)(d+\epsilon+\theta)} & \frac{1}{\epsilon+d} \end{pmatrix}.$$

Following [28], the basic reproduction number of model (3) is

$$R_0 = \rho(FV^{-1})$$

where ρ represents the spectral radius of the matrix FV^{-1}. R_0 is BTB infection basic reproduction number given by

$$R_0 = \frac{\pi}{d}\left(\frac{\beta\alpha}{(d+\alpha)(d+\epsilon+\theta)} + \frac{\alpha\theta\gamma\beta}{(d+\alpha)(d+\epsilon)(d+\epsilon+\theta)}\right)$$

The first term of R_0 represents the contribution of infected buffalo and the second term represents the contribution of buffalo carriers. The stability of E_0 is stated in the following theorem:

Theorem 1. *The disease-free equilibrium E_0 of model (3) is locally asymptotically stable whenever $R_0 < 1$ and unstable otherwise.*

Proof. The approach used to find R_0 guarantees the local stability of disease-free equilibrium E_0. For stability of E_0, we need to show that all the eigenvalues of the Jacobian matrix of model (3) evaluated at E_0 are negative or have negative real parts. It is sufficient to consider the stability of the matrix $F - V$ [28]:

$$F - V = \begin{pmatrix} -(d+e) & \frac{\beta\pi}{d} & \frac{\gamma\beta\pi}{d} \\ \alpha & -(\theta+\epsilon+d) & 0 \\ 0 & \theta & -(\epsilon+d) \end{pmatrix}.$$

The eigenvalues of $F - V$ are solutions to the characteristic equation

$$\lambda^3 + G_1\lambda^2 + G_2\lambda + G_3 = 0,$$

where

$$G_1 = (3d + \alpha + \theta + 2\epsilon)$$

$$G_2 = ((d+\alpha)(d+\epsilon) + (d+\alpha)(\theta+\epsilon+d) + (\theta+\epsilon+d)(\epsilon+d) - \frac{\beta\pi\alpha}{d})$$

$$G_3 = (\epsilon+d)(d+\alpha)(\theta+\epsilon+d)(1-R_0).$$

The Routh-Hurwitz Stability Criterion is used to establish that eigenvalues are either negative or have negative real parts.

So $G_2G_1 - G_3 = B_1 + B_2 + B_3 + B_4(B_5(1-R_0) + \alpha\theta\gamma\beta\frac{\pi}{d}) > 0,$

where

$$
\begin{aligned}
B_1 &= (\epsilon + d)^2(d + \alpha) + (\epsilon + d)(d + \alpha)^2, \\
B_2 &= 2(\epsilon + d)(d + \alpha)(d + \theta + \epsilon) + (d + \alpha)^2(d + \theta + \epsilon)^2, \\
B_3 &= (d + \theta + \epsilon)^2(\epsilon + d) + \alpha\beta\frac{\pi}{d}\gamma\theta \\
B_4 &= \frac{(d + \theta + \epsilon + d + \epsilon)}{(\epsilon + d)}, \\
B_5 &= (d + \alpha)(d + \theta + \epsilon).
\end{aligned}
$$

Since all the Routh-Hurwitz conditions are satisfied when $R_0 < 1$, then all the eigenvalues are negative. Thus the disease free equilibrium point is locally asymptotically stable when $R_0 < 1$. □

To guarantee the global asymptotic stability of the disease-free state, we rewrite the model (3) in the form

$$
\begin{cases}
\frac{dX}{dt} &= F(X, Z), \\
\frac{dY}{dt} &= G(X, Z), \quad G(X, \mathbf{0}) = 0,
\end{cases}
$$

where $X = B_s$ and $Y = (B_e, B_i, B_c)^T$ with $X \in \Re_+$ denoting the number of susceptible buffalo and $Y \in \Re_+^3$ denoting the number of infected buffalo.

The disease-free equilibrium is now denoted by $E_0 = (X_0, \mathbf{0})$ where $X_0 = \frac{\pi}{d}$ and $\mathbf{0}$ is a zero vector. The following conditions $\mathbf{H_1}$ and $\mathbf{H_2}$ should be satisfied to guarantee global asymptotic stability:

- $\mathbf{H_1}$: For $\frac{dX}{dt} = F(X_0, \mathbf{0})$, X_0 is globally asymptotically stable.
- $\mathbf{H_2}$: $G(X, Z) = AY - \tilde{G}(X, Y)$, $\tilde{G}(X, Y) \geq 0$ for $(X, Y) \in \Omega$, where $A = D_Y(G(X_0, \mathbf{0}))$ is an M-matrix. If model (3) satisfies the conditions $\mathbf{H_1}$ and $\mathbf{H_2}$, then the following result holds.

Theorem 2. *The disease-free equilibrium point $E_0 = (X_0, \mathbf{0})$ is a globally asymptotically stable equilibrium of the system (3) provided that $R_0 < 1$ and the assumptions $\mathbf{H_1}$ and $\mathbf{H_2}$ are satisfied.*

Proof. Consider

$$
F(X, 0) = \pi - dB_s, \quad G(X, Y) = AY - \tilde{G}(X, Y)
$$

where

$$A = \begin{pmatrix} -(d+\alpha) & \frac{\beta\pi}{d} & \frac{\gamma\beta\pi}{d} \\ \alpha & -(\theta+\epsilon+d) & 0 \\ 0 & \theta & -(\epsilon+d) \end{pmatrix},$$

and

$$\tilde{G}(X,Y) = \begin{pmatrix} \lambda N(1-\frac{B_s}{N}) \\ 0 \\ 0 \end{pmatrix}.$$

The first condition $\mathbf{H_1}$ is satisfied when X is a globally asymptotically stable equilibrium point of the equation

$$\frac{dB_s}{dt} = \pi - dB_s. \tag{5}$$

Solving (5) we obtain

$$B_s(t) = \frac{\pi}{d} - B_s(t)e^{-dt},$$

Taking limits as $t \to \infty$ we obtain,

$$\lim_{t\to\infty} B_s(t) = X_0.$$

This suggests that independent of the initial conditions the solution of the equation (5) converges to X_0. Thus, X_0 is a globally asymptotically equilibrium point of (5). To prove condition $\mathbf{H_2}$, we observe that $\tilde{G}(X,Y) \geq 0$, so this completes the proof of both conditions. □

The significance of Theorem (2) is that BTB infection can be eradicated completely from the buffalo population in the long run whenever $R_0 < 1$.

3.2.2. Endemic equilibrium point

The coordinates of the endemic equilibrium point $E_1^* = (B_s^*, B_e^*, B_i^*, B_c^*)$ of model (3) are obtained in terms of the force of infection, using the approach in [29] as follows

$$\begin{aligned} \pi - \lambda^* B_s^* - dB_s^* &= 0, & (6)\\ \lambda^* B_s^* - (\alpha+d)B_e^* &= 0, & (7)\\ \alpha B_e^* - (\theta+d+\epsilon)B_i^* &= 0, & (8)\\ \theta B_i^* - (d+\epsilon)B_c^* &= 0. & (9) \end{aligned}$$

From equation (5) we have

$$B_s^* = \frac{\pi}{\lambda^* + d}. \tag{10}$$

Substituting equation (9) into equation (6) we obtain

$$B_e^* = \frac{\pi\lambda^*}{(\lambda^* + d)(\alpha + d)}. \tag{11}$$

Substituting equation (11) into equation (7) we find that

$$B_i^* = \frac{\alpha\pi\lambda^*}{(\theta + d + \epsilon)(\lambda^* + d)(\alpha + d)}. \tag{12}$$

Substituting equation (12) into equation (8) we obtain

$$B_c^* = \frac{\alpha\pi\lambda^*}{(\theta + d + \epsilon)(\lambda^* + d)(\alpha + d)(d + \epsilon)}. \tag{13}$$

Our force of infection at the equilibrium point is

$$\lambda^* = \frac{\beta(B_i^* + \gamma B_c^*)}{N^*}, \tag{14}$$

where

$$N^* = \frac{\pi(\theta + d + \epsilon)(d + \epsilon)(\alpha + d) + \lambda^*\pi((\theta + d + \epsilon)(d + \epsilon) + Q}{(\theta + d + \epsilon)(\alpha + d)(d + \epsilon)(\lambda^* + d)}. \tag{15}$$

where

$$Q = \alpha\lambda^*\pi(d + \epsilon) + \alpha\lambda^*\pi$$

If (12), (13) and (15) are substituted into (14), we obtain the equation in terms of λ^*:

$$\lambda^*(D_1\lambda^* + D_2) = 0, \tag{16}$$

where

$$D_2 = 1 - R_0, \quad D_1 = \frac{(\theta + d + \epsilon)(d + \epsilon) + \alpha((d + \epsilon) + 1)}{(\theta + d + \epsilon)(d + \epsilon)(\alpha + d)}.$$

The roots of equation (16) are $\lambda_1^* = 0$ and $\lambda_2^* = \frac{R_0 - 1}{D_1}$. $\lambda_1^* = 0$ corresponds to the disease free equilibrium point and λ_2^* is therefore the root that corresponds to the endemic equilibrium point provided $R_0 > 1$. We summarize the existence results as follows:

Theorem 3. *The BTB endemic equilibrium point E_1^* exists and is unique whenever $R_0 > 1$.*

Theorem 4. *The unique endemic equilibrium E_1 is locally asymptotically stable for $R_0 > 1$.*

Proof. To determine the local stability of the equilibrium point E_1, we use the center manifold theory by making the following change of variables: $B_s = x_1, B_e = x_2, B_i = x_3$ and $B_c = x_4$. Let $X = (x_1, x_2, x_3, x_4)^\top$ where $\top$ denotes the transpose of a matrix. Model (3) can be written in the form $\frac{dX}{dt} = g = (g_1, g_2, g_3, g_4)^\top$, so that

$$\begin{aligned}
\frac{dx_1}{dt} &= g_1 = \pi - \frac{(\beta x_3 + \gamma\beta x_4)}{x_1 + x_2 + x_3 + x_4} x_1 - dx_1, \\
\frac{dx_2}{dt} &= g_2 = \frac{(\beta x_3 + \gamma\beta x_4)}{x_1 + x_2 + x_3 + x_4} x_1 - (\alpha + d)x_2, \\
\frac{dx_3}{dt} &= g_3 = \alpha x_2 - (\theta + d + \epsilon)x_3, \\
\frac{dx_4}{dt} &= g_4 = \theta x_3 - (d + \epsilon)x_4.
\end{aligned} \tag{17}$$

Choosing β as a bifurcation parameter and noting that $R_0 = 1$ gives the bifurcation point, we obtain

$$\beta = \beta^* = \frac{d(d+\alpha)(d+\epsilon)(d+\epsilon+\theta)}{\pi\alpha(d+\epsilon+\gamma\theta)}.$$

Substituting $\beta = \beta^*$ into the Jacobian matrix of (17) we obtain the following eigenvalues:

$$\lambda_1 = 0, \quad \lambda_2 = -(d+\alpha), \quad \lambda_{3,4} = -\frac{d_1}{2} \pm \sqrt{\left(\frac{d_1}{2}\right)^2 - d_0}$$

where

$$\begin{aligned}
d_0 &= k_1k_2 + k_1k_3 + k_2k_3 - \frac{\alpha\beta^*\pi}{d} \\
d_1 &= k_1 + k_2 + k_2,
\end{aligned}$$

and

$$k_1 = d + \alpha, \quad k_2 = \theta + \epsilon + d, \quad k_3 = d + \epsilon.$$

Clearly zero is a simple eigenvalue and thus the center manifold theory can be used to analyse the dynamics of the system of equations (17) near $\beta = \beta^*$. The Jacobian matrix of (17) evaluated at E_0 using $\beta = \beta^*$ has a right eigenvector associated with the zero eigenvalue given by

$$w = [w_1, w_2, w_3, w_4]^\top,$$

where

$$w_1 = -\frac{\beta\pi\alpha}{d(\theta + d + \epsilon)}\left(1 + \frac{\gamma\theta}{d + \epsilon}\right), \quad w_2 = 1, \quad w_3 = \frac{\alpha}{\theta + d + \epsilon}, \quad w_4 = \frac{\theta\alpha}{d + \epsilon}.$$

The left eigenvector of $J(E_0)$ associated with the zero eigenvalue at $\beta = \beta^*$ is given by

$$v = [v_1, v_2, v_3, v_4]^\top,$$

where

$$v_1 = 0, \quad v_2 = \frac{\alpha}{\alpha + d}, \quad v_3 = 1, \quad v_4 = \frac{\gamma\beta\pi\alpha}{d(\alpha + d)(d + \epsilon)}.$$

To calculate **a** we use the following non-vanishing partial derivatives of g

$$\frac{\partial^2 g_2}{\partial x_2 \partial x_3} = \frac{-\pi\beta}{d}, \quad \frac{\partial^2 g_2}{\partial x_2 \partial x_4} = \frac{-\beta\gamma\pi}{d},$$

so that

$$a = \sum_{i,j,k=1}^{4} v_k w_i w_j \frac{\partial^2 g_k}{\partial x_i \partial x_j}(0,0) \quad = \quad -2v_2\left(\frac{\pi}{d} w_1 w_3 + \frac{\gamma\pi}{d} w_1 w_4\right) < 0.$$

We proceed to compute the bifurcation coefficient **a** and **b** as follows: The expression for **b** is obtained from the following non-vanishing partial derivatives of g

$$\frac{\partial^2 g_2}{\partial x_3 \partial \beta^*} = \frac{\pi}{d}, \quad \frac{\partial^2 g_2}{\partial x_4 \partial \beta^*} = \frac{\gamma\pi}{d},$$

so that

$$b = \sum_{i,k=1}^{4} v_k w_i \frac{\partial^2 g_k}{\partial x_i \partial \beta^*}(0,0) \quad = \quad v_2\left(\frac{\pi}{d} w_3 + \frac{\gamma\pi}{d} w_4\right) > 0.$$

Thus, $a < 0$ and $b > 0$. □

Model (3) exhibits a transcritical bifurcation which is a supercritical bifurcation. In a supercritical bifurcation scenario, the exchange of stability between the uninfected and infected equilibrium points guarantees that the infected equilibrium point is locally asymptotically stable whenever $R_0 > 1$. This means on one hand when $R_0 > 1$, BTB infection persists in the buffalo population. On the other hand, if the condition on R_0 is reversed to $R_0 < 1$, then the disease free equilibrium point is the only equilibrium point in existence [25]. Hence, according to the model prediction, it is possible to eradicate BTB infection in buffalo population by introducing and maintaining favourable conditions.

3.2.3. Analysis of R_0

As earlier stated, the basic reproduction number measures the average number of new infections generated by a single infected buffalo in a completely susceptible buffalo population. We can re-write R_0 as

$$R_0 = R_{0i} + R_{0c} \tag{18}$$

where

$$R_{0i} = \frac{\pi\alpha\beta}{d(d+\alpha)(d+\epsilon+\theta)},$$
$$R_{0c} = \frac{\gamma\beta\pi\alpha\theta}{d(d+\alpha)(d+\epsilon)(d+\epsilon+\theta)},$$

R_{0i} defines the reproduction number due to infective buffalo and R_{0c} is the reproduction number due to carrier buffalo. The terms in (18) can be explained as follows: $\frac{1}{d+\alpha}$, $\frac{1}{\theta+d+\epsilon}$, $\frac{1}{d+\epsilon}$ are the average times an individual spends in exposed class B_e, infected class B_i and the carrier class B_c respectively. The term $\frac{\alpha}{\alpha+d}$ is the probability that an individual progresses to an infective class from the exposed class, while the term $\frac{\theta}{d+\epsilon+\theta}$ is the probability that an individual progresses to a carrier class from an infective class. The terms $\frac{\beta\pi}{d}\left(\frac{\alpha}{d+\alpha}\right)\left(\frac{1}{d+\epsilon+\theta}\right)$ and $\frac{\gamma\beta\pi}{d}\left(\frac{\alpha}{d+\alpha}\right)\left(\frac{1}{d+\epsilon+\theta}\right)\left(\frac{1}{d+\epsilon}\right)$ can be explained as the secondary infections caused by infective and carrier buffalo respectively. The conditions $R_0 < 1$ and $R_0 > 1$ can be interpreted as in Table (1) in relation with the status of the equilibrium point indicated in

Table 1: Table of R_0 scenarios

Case	R_{0i}	R_{0c}	R_0	Region
(i)	> 1	> 1	> 1	E
(ii)	> 1	< 1	> 1	D
iii)	< 1	> 1	> 1	C
iv)	< 1	< 1	> 1	B
v)	< 1	< 1	< 1	A

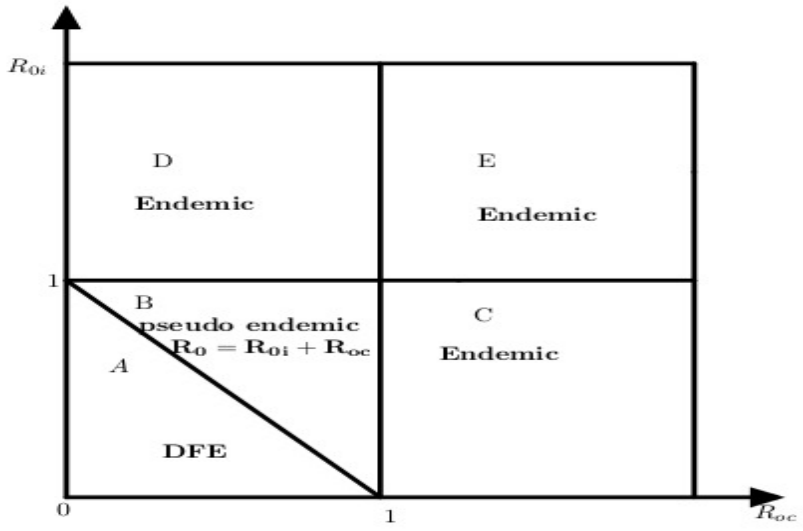

Figure 2: The figure showing four possible scenarios for bovine tuberculosis stages.

Figure (2).

In region A, the BTB infection dies out without any intervention. The pseudo endemic equilibrium point exists in region B where BTB infection is sustained by the combined effort from both infected and carrier buffalo. Region C represents an endemic equilibrium region where BTB infection is being driven by carrier buffalo only. Region D represents an endemic equilibrium point where the infection is being driven by infected buffalo only. Region E represents an endemic equilibrium point where the infection is driven by both infected buffalo and carrier buffalo. The pseudoendemic equilibrium point is in the interface of the rest of the equilibria. Thus to move from one equilib-

rium point to another, the system always passes through the pseudoendemic equilibrium. The implication regarding the endemic equilibrium status is that once the buffalo population is in equilibria C, D and E, reversing the system to disease free status will call for persistence efforts towards achieving this goal. This means highly accurate control measures need to be implemented to be completely sure that the system has achieved the disease-free status.

4. Numerical simulations

We present a detailed account on how the parameters used in the model are estimated. We then use the parameters to carry out numerical simulations that will enhance further understanding of the model predictions. For some parameters, we shall perform sensitivity analysis to assess their influence on the outputs of the model.

4.1. Parameter estimation

All parameter values used in the numerical simulations are given in Table 4 together with their sources. Some parameters are taken as they appear in the literature while other parameter values are determined based on the explanation given in the literature. Those with no known values from literature are determined by the conditions subjected to them in the model formulation. The values used in the simulations are indicated on the legends of the graphs. The values of β and α are obtained from [6]. The reduction factor for the infective rate of the carrier buffalo, γ, is determined based on the fact that it lies between 0 and 1. The parameter ϵ is determined based on the fact that it takes a long time for an infected buffalo to die from the infection and research shows that bovine tuberculosis increases mortality by approximately 10% [3, 4, 20]. The parameter π is estimated from the estimates given in the literature, for instance in [31] and ranges from 252 to 1200. The parameter d is estimated using the life expectancy of a buffalo which ranges between 20 and 29 years and so the death rate ranges between $\frac{1}{29}$ and $\frac{1}{20}$ [31]. The transfer rate, θ, is also assumed as there is no literature that gives the estimate of the rate the infected buffalo class move to carrier buffalo class. The estimated initial conditions we use are $B_s(0) = 24052$, $B_e(0) = 948$, $B_i(0) = 100$ and $B_c(0) = 50$ [20, 31].

5. Sensitivity Analysis

The sensitivity analysis of parameters used in our simulation was done using the method of Latin Hypercube Sampling with partial rank correlation coefficient index (PRCC). PRCC's falls between -1 and 1, with an absolute value of PRCC close to 1 indicating the parameter has a strong impact on the model output. Furthermore, PRCC provides a measure of the relative influence of these parameters on the targeted model output [33]. We test the effects of all the input parameters used in our model on the output variables. Of particular interest is the influence of the parameters on the infected buffalo and carrier buffalo which are the problematic variables towards the progression of BTB infection. The PRCC's are calculated at one year as well as at fifteen years. The choice of the first point is influenced by the fact that within a year, BTB infection is in its incubation period. The second point is selected to compare the long term impact of the parameters over time. The results in Table 2 suggest that β and Γ are some of the dominant parameters that drive the BTB infection. The relative importance of some parameters increases or decreases in the course of infection. For instance, the relative importance towards the evolution of BTB infection of π increases to 1 from 0.998. The relative significance of α, the transition rate from exposed class to infectious class increases to -0.7 from -0.5. This suggests that the effect of parameters π and α increases in the course of infection. Table 2 gives detailed account of the evolution of parameters from the initial stages of the infection (1 year) up to the very late of the infection (15 years).

Sensitivity analysis done on carrier buffalo sub-population aimed to identify the parameters that impact on the carrier buffalo. The parameters, π, β and Γ also emerged as some of the parameters that play crucial role in the epidemiology of carrier buffalo. The relative importance of other parameters towards the dynamics of carrier buffalo either increases or decreases. For instance, the relative importance of π increases to 0.91 from 0.84. The parameter, θ, shifted its relative importance from negative to positive. Table 3 has the details of the relative importance of model parameters from the initial stages (1 year) to the late stages of the infection (15 years).

	PRCC: 1 year		PRCC: 15 years
Parameter	PRCC Index	Parameter	PRCC Index
π	0.998	π	1
β	0.6	β	0.6
γ	0.7	γ	0.46
d	0.1	d	0.087
θ	0.081	θ	0.084
ϵ	-0.7	ϵ	-0.7
α	-0.5	α	-0.7

Table 2: PRCC indices at two different time points on infected buffalo

	PRCC: 1 year		PRCC: 15 years
Parameter	PRCC Index	Parameter	PRCC Index
π	0.84	π	0.91
β	0.07	β	0.07
γ	-0.087	γ	-0.1
d	-0.8	d	-0.8
θ	-0.012	θ	0.01
ϵ	-0.1	ϵ	-0.067
α	-0.089	α	-0.1

Table 3: PRCC indices at two different time points on carrier buffalo

5.1. Simulations

We present numerical simulations of model (3) to explore the overall impact of various transmission mechanisms of bovine tuberculosis in the buffalo population. The transmission mechanisms due to contaminated environment and those due to effective contacts between susceptible, infected and carrier buffalo are explored. This is necessary to determine the control strategies of BTB infection since we need to know which processes cause the greatest damage towards the progression of BTB in the buffalo population. Using parameter values in Table 4, we firstly explore the role of environmental transmission mode in the epidemiology of BTB infection which is achieved by increasing parameter Γ while keeping the horizontal and carrier transmission rates low. Secondly, we investigate the effects of horizontal transmission represented by β in the evolution of BTB infection by varying parameter β when Γ and γ are kept low. Thirdly, we explore the effect of carrier buffalo in the evolution

Table 4: Table of parameter values used in the model

Name	Range	Units	Reference
π	[252, 1200]	$year^{-1}$	[31]
α	[0.03, 0.08]	$year^{-1}$	[6]
β	[0.01, 0.053]	$year^{-1}$	[6]
ϵ	[0.1, 0.53]	$year^{-1}$	[3, 32]
d	$[\frac{1}{29}, \frac{1}{20}]$	$year^{-1}$	[31]
θ	[0.01, 0.05]	$year^{-1}$	estimated
γ	[0, 1]	$year^{-1}$	see section (2)

of BTB infection in the cases of high and low β and Γ. Lastly, we carry out sensitivity analysis to determine the influential parameter values that drive BTB infection in the buffalo population.

Figure 3 explores the scenario of varying the horizontal transmission rate in the epidemiology of bovine tuberculosis in buffalo population. The results show that horizontal transmission does not only have a negative effect on buffalo population, but it also promotes the persistence of the infection. Thus the endemic levels of infected and carrier buffalo when $R_0 > 1$ are high compared to endemic levels when the environmental transmission rate is considered. From the veterinary public health point of view, this scenario is a threat to the survival of buffalo since BTB infection can easily spill over to other species, a situation that puts the whole park at risk of being completely invaded.

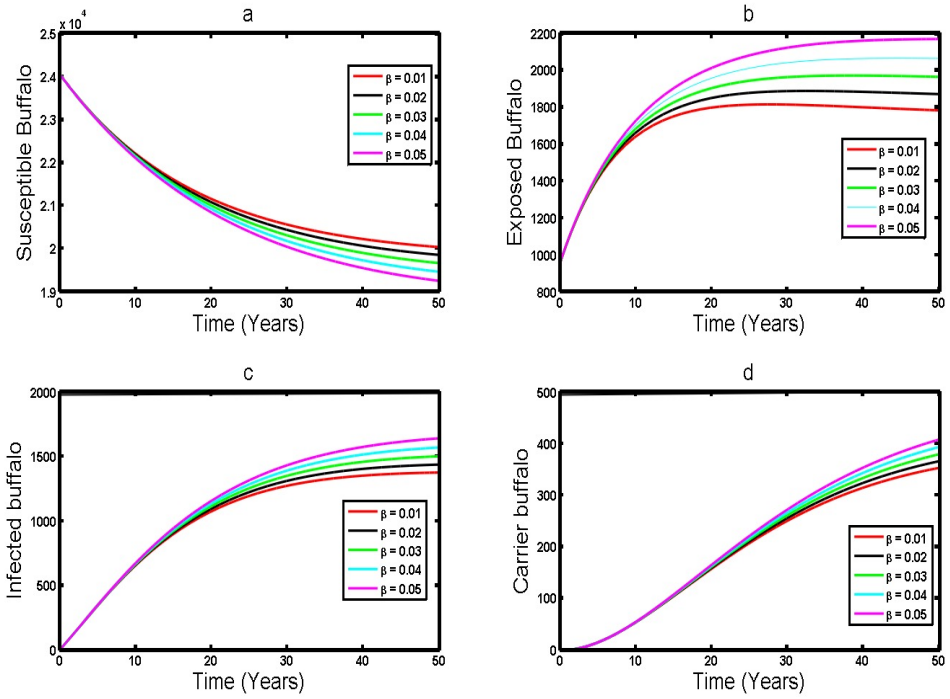

Figure 3: Graph showing the effects of increasing the horizontal transmission rate of BTB infection. $\pi = 1200, \epsilon = 0.2, \alpha = 0.07, d = 0.05, \theta = 0.02, \Gamma = 0.001, \gamma = 0.01$

6. Discussion

The mathematical model presented in this paper captures the effects of various transmission routes of bovine tuberculosis such as indirect transmission mechanism and horizontal transmission mechanism initiated by infected and carrier buffalo. We ensured that the model was both biologically and mathematically tractable. The basic reproduction number R_0 was calculated and used to determine the global dynamics and the outcome of the disease and if the threshold parameter $R_0 < 1$, the solution trajectories converge to the disease free equilibrium. On the other hand, if $R_0 > 1$, the solution converges to the endemic equilibrium point. The center manifold theory was used to prove the local stability of endemic equilibrium point. We used numerical simulations as baselines to illustrate the different scenarios from the model analysis. Sensitivity analysis was also conducted using Latin Hypercube Sampling method to determine the model parameters that drive the

transmission dynamics of BTB infection. Most baseline values for our parameters were taken from indicated sources and for some which were not available in literature we resorted to estimation guided by the underlying biological scenarios from literature. The simulations allowed us to observe the effect of the parameters on the transmission dynamics of bovine tuberculosis in buffalo population.

Using the parameter values used in the simulations, the estimated value of R_0 is 7.8, the value that shows the endemicity of BTB infection in buffalo population. To control the disease, the control measures that target at reducing the horizantal transmission rate and at promoting the screening activities should be adopted. For instance, a 50% decrease in horizontal transmission rate, causes R_0 to reduce to 3.9. A 50% decrease in the transition rate α, results in a drop of only 0.79. A significant drop of 5.4 in R_0 is observed when the combined efforts are employed, thus control measures that reduce the β and α simultaneously. The analysis shows that integrated efforts are required from all stakeholders to reduce $R_0 < 1$.

Numerical simulations also suggest the social behaviour of buffalo, a feature captured in β, promotes the persistence of BTB infection in buffalo population. The result is illustrated by the trajectory solutions of $B_s(t), B_e(t), B_i(t)$ and B_c in Figure 3. The observation further confirms the fact that BTB infection can only be eliminated if the transmission routes are well understood and can be accurately measured. The greatest challenge is that these different transmission routes cannot be quantified exactly so that any intervention strategy is most likely to depend on estimates especially in large parks. If there are only buffalo carriers in the ecosystem, BTB infection is not sustained in the ecosystem. This becomes possible if we assume that the environment is not heavily contaminated and very little activities that promote horizontal transmission, which practically is not feasible. Ecologically this means that the transmission through carriers remains a serious problem that requires considerable attention from all players involved in BTB infection.

Further, through sensitivity analysis, our results show that if all three modes of transmission are promoted, BTB infection can spread rapidly in buffalo population as evidenced by the significant effects of parameters β and γ in Table 2. This can cause direct economic loss plus secondary losses, for example due to an accelerating death of lions, which attract many tourists in

Kruger National Park. Sensitivity analysis also revealed that β is of the parameters that drives the transmission dynamics of BTB infection. This knowledge can be used by policy makers to come up with holistic control measures to control the BTB infection. However, to effectively guide public policy and public health decision making, the model and parameter values would need to be tested against data from bovine tuberculosis field sites. The current analysis, however, remains an important first step in comparing the effectiveness of different control strategies.

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Chapter 3

Modelling the role of multi-transmission routes in the epidemiology of bovine tuberculosis in cattle and buffalo populations

Modelling the role of multi-transmission routes in the epidemiology of bovine tuberculosis in cattle and buffalo populations.

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Abstract

A mathematical model that describes the transmission dynamics of bovine tuberculosis (BTB) in both buffalo and cattle populations is proposed. The model incorporates cross-infection and contaminated environment transmission routes. A full analysis of the model is undertaken. The reproduction number of the entire model is comprised of cross-infection and contaminated parameters. This underscores the importance of including both cross-infection and contaminated environment transmission routes. Crucially our simulations suggest that the disease has a more devastating effect on cattle populations than on buffalo populations when all transmission routes are involved. This has important implications for agriculture and tourism.

Keywords: Cattle, Cross-infection, Buffalo, Environment, Mathematical modelling, Mycobacterium bovis

1. Introduction

Bovine tuberculosis (BTB) results from infection by mycobacterium bovis (*M. bovis*), a Gram positive, acid-fast bacterium in the mycobacterium tuberculosis complex of the family mycobacteriaceae [2]. BTB is a chronic bacterial disease

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that affects all species of mammals including buffalo, cattle and humans [1, 2]. It is spread through inhaling contaminated aerosol droplets, drinking unpasteurised milk, eating poorly cooked meat, scavenging infected animals, grazing on contaminated pasture and also through vertical transmission (from an infected female animal to a newly born animal) [3, 4, 13, 14, 15, 16, 17]. BTB infection can be dormant for years and reactivate later in the lifespan of an animal due to stress or old age [2, 3, 14, 18].

It has been estimated that *M. bovis* accounts globally for 3.1% of all human tuberculosis cases (2.1% of all pulmonary and 9.4% of all extra-pulmonary tuberculosis cases). However, the extent of *M. bovis* involvement in the global tuberculosis burden in Africa is still largely unknown. This can be partly explained by the fact that in humans, tuberculosis due to *M. bovis* is indistinguishable from that due to *M. tuberculosis* in terms of clinical signs, radiological and pathological features. In addition, various laboratories in sub-Saharan Africa do not have the capacity to differentiate *M. bovis* from *M. tuberculosis* [23]. The paucity of information on BTB infection in Africa [5] with the exception of South Africa where a substantial research in BTB infection has been carried [14], has led to a poor understanding of its transmission dynamics in animals and humans. This work aims to enhance the understanding of the transmission dynamics of BTB infection through mathematical models.

Mathematical modelling has become an important tool in analysing the epidemiological characteristics of infectious diseases and can provide insight into useful control measures [24]. Various models have been formulated to explore various aspects of BTB infection. A non-linear transmission model consisting of susceptible and infected possum populations was developed [25]. The model was used to explain bovine tuberculosis dynamics in a heterogeneous possum population, taking into account the patchy distribution of the infection. A deterministic/stochastic model was developed to explore the factors that drive the spread of BTB infection in possum population and social contact was found to promote the spread of BTB infection [6]. A spatial stochastic model was developed in [26] to assess fertility control as a means of controlling bovine tuberculosis in badgers. The results showed that fertility control alone cannot completely eradicate BTB infection from badger populations.

Apart from using mathematical models to understand the transmission dynamics of BTB infection in wildlife, epidemiological models were also used in livestock. A model comprised of seven sub-populations was formulated to enhance the understanding of the transmission dynamics in cattle [4]. One of the main results of

the model was that imported infected cattle were responsible for the persistence of BTB infection in cattle population. A discrete mathematical model was developed in [14] to assess vaccination as a control strategy in an ongoing epidemic of bovine tuberculosis in African buffalo. The model established that BTB infection can be completely wiped out if various strategies are used in combination. The concept of cross-infection of BTB between buffalo and cattle populations was not considered in any of the models formulated so far. This is in contrast to other zoonotic diseases like brucellosis disease that is transmitted from sheep to people [27]. The inclusion of cross-infection transmission route in the model was necessitated by the observation that BTB infection prevalence was higher in cattle and buffalo populations, in areas at the interface with wildlife than those that are not at the interface [7]. This suggested that cross-infection route may play a role in the epidemiology of BTB infections in both populations. It is at the interface where cattle/buffalo interactions are experienced [13].

We will build a model that will characterise the epidemiological features of BTB infection transmission mechanisms involving buffalo and cattle populations. The model will address the following questions:

- *Does the shedding off of M. bovis in the environment promote the persistence of the infection in cattle and buffalo populations?*
- *Is cross- infection of BTB infection from buffalo responsible for higher prevalence of the infection in cattle?*

2. Mathematical model

In this section, we introduce a continuous mathematical epidemiological model for the transmission and evolution of bovine tuberculosis in both buffalo and cattle populations. Guided by the information on the natural history of BTB infection in both cattle and buffalo population to determine, the basic plausible assumptions for the model formulation are determined [28, 29, 30]. A population size of cattle, $N_c(t)$, which is time varying, is partitioned into three classes consisting of cattle that are susceptible to the disease, $C_s(t)$, exposed cattle that have *M. bovis* but are not infectious, $C_e(t)$, and infectious cattle that spread the disease to both cattle and buffalo, $C_i(t)$. The buffalo population of size, $N_b(t)$, which is also time varying, is compartmentalised into buffalo that are susceptible to disease, $B_s(t)$, exposed and non-infectious buffalo, $B_e(t)$, and infectious buffalo that spread the disease to both buffalo and cattle, $B_i(t)$. Due to the nature of BTB infection, a recovery class is not considered because it is assumed that an

animal does not recover from infection [9]. A variable, V, is used to denote the quantity of infectious *M. bovis* in the enviroment, which is shed off at a rate σ by the infected buffalo and cattle through the activities of urination and excretion of feces. We assume that *M. bovis* in the environment decays at the rate θ. The maximum carrying capacity of *M. bovis* in the environment is represented by K. We assume that a susceptible cow progresses to the exposed class, $C_e(t)$, through either an effective contact with the infected cattle at a constant rate β_c, an effective contact with the infected buffalo at a rate β_{cb} or through contact with the contaminated environment at a rate ψ_c. The exposed cow progresses to the infectious class at a rate ϕ_c. The natural and disease induced death rates of the cattle are μ_c and ϵ_c respectively. The recruitment rate of cattle to a susceptible class is π_1. We also assume that a susceptible buffalo progresses to the exposed buffalo class, $B_e(t)$, through either an effective contact with the infected buffalo at the rate β_b, an effective contact with the infected cattle at a rate β_{bc} or through contact with the contaminated environment at rate ψ_b. The exposed buffalo population progresses to the infected class, $B_i(t)$, at the rate ϕ_b. The recruitment rate π_2 of susceptible buffalo is assumed to be constant. The natural and disease induced death rates of buffalo are μ_b and ϵ_b respectively. It is further assumed that the infection rate from cattle to cattle β_c is greater than the infection rate from infected buffalo to susceptible cattle population β_{cb}. The same assumption also holds in buffalo population, thus $\beta_b > \beta_{bc}$ [10]. Homogeneous mixing is assumed, thus all susceptible cattle have the same likelihood to be infected and also susceptible buffalo have the same chance of being infected. The force of infection for cattle is given by

$$\lambda_c = \frac{\beta_c C_i}{N_c} + \frac{\beta_{cb} B_i}{N_b} + \frac{\psi V}{K}, \tag{1}$$

and the force of infection for buffalo is defined by

$$\lambda_b = \frac{\beta_b B_i}{N_b} + \frac{\beta_{bc} C_i}{N_c} + \frac{\psi V}{K}. \tag{2}$$

The possible interactions among and between cattle and buffalo are illustrated in Figure 1.

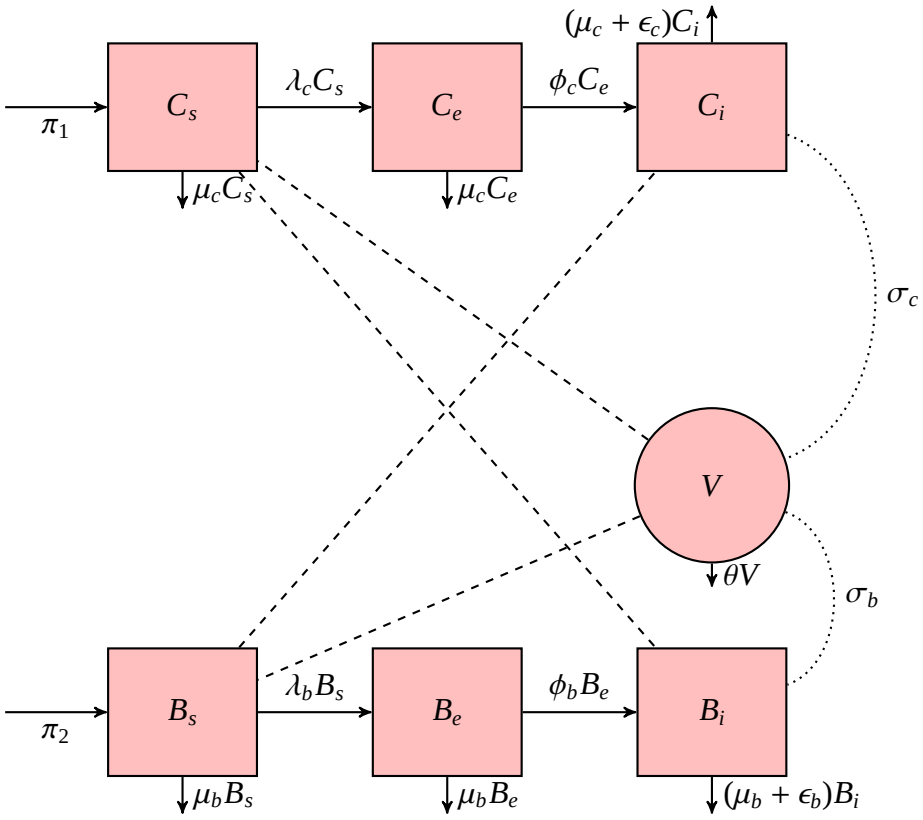

Figure 1: The flowchart of the transmission dynamics of bovine tuberculosis in buffalo and cattle population. The dashed lines represent the transmission routes. The dotted lines represent the shedding off of *M. bovis* in the environment.

The compartmental model in Figure 1 is thus represented by the following of

non-linear system of ordinary differential equations ,

$$\begin{aligned}
\frac{dC_s}{dt} &= \pi_1 - \lambda_c C_s - \mu_c C_s, \\
\frac{dC_e}{dt} &= \lambda_c C_s - \phi_c C_e - \mu_c C_e, \\
\frac{dC_i}{dt} &= \phi_c C_e - (\mu_c + \epsilon_c) C_i, \\
\frac{dV}{dt} &= \sigma_c C_i + \sigma_b B_i - \theta V, \\
\frac{dB_s}{dt} &= \pi_2 - \lambda_b B_s - \mu_b B_s, \\
\frac{dB_e}{dt} &= \lambda_b B_s - \phi_b B_e - \mu_b B_e, \\
\frac{dB_i}{dt} &= \phi_b B_e - (\mu_b + \epsilon_b) B_i.
\end{aligned} \tag{3}$$

where $N_c(t) = C_s(t) + C_e(t) + C_i(t)$ and $N_b(t) = B_s(t) + B_e(t) + B_i(t)$ with

$$\begin{aligned}
\frac{dN_b}{dt} &= \pi_2 - \mu_b N_b - \epsilon_b B_i, \\
\frac{dN_c}{dt} &= \pi_1 - \mu_c N_c - \epsilon_c C_i.
\end{aligned}$$

We introduce the following dimensionless parameters:
$\tau = \mu_c t,\ B_c = \frac{\beta_c}{\mu_c}, \Psi_c = \frac{\psi_c}{\mu_c}, \Psi_b = \frac{\psi_b}{\mu_c},\ B_b = \frac{\beta_b}{\mu_c},\ B_{cb} = \frac{\beta_{cb}}{\mu_c},\ B_{bc} = \frac{\beta_{bc}}{\mu_c}, \Sigma_c = \frac{\sigma_c}{\mu_c}, \Sigma_b = \frac{\sigma_b}{\mu_c}, \Theta = \frac{\theta}{\mu_c}, \Phi_c = \frac{\phi_c}{\mu_c}, \Phi_b = \frac{\phi_b}{\mu_c},\ E_c = \frac{\epsilon_c}{\mu_c},\ M_b = \frac{\mu_b}{\mu_c},\ E_b = \frac{\epsilon_b}{\mu_c}.$

The dimensionless variables then are

$x_1 = \frac{C_s}{N_c}, x_2 = \frac{C_e}{N_c}, x_3 = \frac{C_i}{N_c}, x_4 = \frac{V}{K}, x_5 = \frac{B_s}{N_b}, x_6 = \frac{B_e}{N_b}, x_7 = \frac{B_i}{N_b}, \Pi_1 = \frac{\pi_1}{N_c \mu_c}, \Pi_2 = \frac{\pi_2}{N_b \mu_c}.$

The forces of infection become

$$\Lambda_c = B_c x_3 + B_{cb} x_7 + \Psi_c x_4, \quad \Lambda_b = B_b x_7 + B_{bc} x_3 + \Psi_b x_4.$$

Now our system (3) becomes

$$\begin{aligned}
\frac{dx_1}{d\tau} &= \Pi_1 - \Lambda_c x_1 - x_1, \\
\frac{dx_2}{d\tau} &= \Lambda_c x_1 - \Phi_c x_2 - x_2, \\
\frac{dx_3}{d\tau} &= \Phi_c x_2 - (1 + E_c) x_3, \\
\frac{dx_4}{d\tau} &= \Sigma_c x_3 + \Sigma_b x_7 - \Theta x_4, \\
\frac{dx_5}{d\tau} &= \Pi_2 - \Lambda_b x_5 - M_b x_5, \\
\frac{dx_6}{d\tau} &= \Lambda_b x_5 - \Phi_b x_6 - M_b x_6, \\
\frac{dx_7}{d\tau} &= \Phi_b x_6 - (M_b + E_b) x_7.
\end{aligned} \tag{4}$$

We now proceed to analyse the transformed nonlinear system (4) as the dynamics of system (4) are qualitatively equivalent to the dynamics of the system (3).

3. Cattle sub-population model

By setting $B_{cb} = B_{bc} = \Psi_b = \Sigma_b = 0$, we obtain the following cattle sub-population model:

$$\begin{aligned}
\frac{dx_1}{d\tau} &= \Pi_1 - \Lambda_c x_1 - x_1, \\
\frac{dx_2}{d\tau} &= \Lambda_c x_1 - \Phi_c x_2 - x_2, \\
\frac{dx_3}{d\tau} &= \Phi_c x_2 - (1 + E_c) x_3, \\
\frac{dx_4}{d\tau} &= \Sigma_c x_3 - \Theta x_4.
\end{aligned} \tag{5}$$

This sub-model describes the transmission dynamics of bovine tuberculosis in cattle only. The sub-model also takes into account the role of contaminated pasture in the evolution of bovine tuberculosis in the cattle population.

3.1. Feasible region

Since sub-model (5) monitors the cattle population, we assume that all state variables and parameters are positive for time $\tau > 0$. The bovine tuberculosis transmission sub-model will then be analysed in a suitable feasible region given by

$$\Omega_1 = \left\{(x_1, x_2, x_3, x_4) \in \Re_+^4 | x_1 \geq 0, x_2 \geq 0, x_3 \geq 0, x_4 \geq 0, N_c \leq \Pi_1, x_4 \leq \frac{\Sigma_c}{\Theta}\right\}.$$

We show that the region Ω_1 is positively invariant. For sub-model (5) to be epidemiologically useful, it is important to show that all its state variables are non-negative for all time.

Let $x_1 \geq 0, x_2 \geq 0, x_3 \geq 0, x_4 \geq 0, \forall \tau \geq 0$. From the first equation of sub-model (5) we have

$$\frac{dx_1}{d\tau} = \Pi_1 - (1 + \Lambda_c)x_1,$$

which can be solved to obtain

$$\begin{aligned} x_1(\tau) &= x_1(0)exp\left[-\left(\tau + \int_0^\tau \Lambda_c(s)ds\right)\right] + exp\left[-\left(\tau + \int_0^\tau \Lambda_c(s)ds\right)\right] \\ &\left(\int_0^\tau \Pi_1 exp\left[\tau + \int_0^\tau \Lambda_c(w)dw\right]ds\right) \geq 0, \forall \tau \geq 0. \end{aligned}$$

Similarly

$$\begin{aligned} x_2(\tau) &= e^{-(1+\Phi_c)\tau}\int_0^\tau \Lambda_c(s)e^{(1+\Phi_c)s}x_1(s)ds + x_2(0)e^{-(1+\Phi_c)\tau} \geq 0. \\ x_3(\tau) &= x_3(0)e^{-(1+\ Ec)\tau}, \\ x_4(\tau) &= x_4(0)e^{-\Theta\tau} \geq 0. \end{aligned}$$

Thus all the solutions of sub-model (5) are non-negative in Ω_1.

We now show that all feasible solutions are bounded in a proper subset of Ω_1. Adding all the equations in sub-model (5) gives

$$\begin{aligned} \dot{N}_c &= \Pi_1 - N_c(\tau) - E_c x_3, \\ &\leq \Pi_1 - N_c(\tau), \end{aligned}$$

where $N_c(\tau) = x_1 + x_2 + x_3$.

Solving the inequality gives

$$0 \leq N_c(\tau) \leq \Pi_1 + (N_c(0) - \Pi_1)\, e^{-\tau},$$

where $N_c(0)$ represents the initial value of $N_c(t)$. Thus, as $\tau \to \infty$, $0 \leq N_c(\tau) \leq \Pi_1$. Note that also $\frac{dx_4}{d\tau} = \Sigma_c x_3 - \Theta x_4 \leq \Sigma_c - \Theta x_4$. We can thus easily obtain $0 \leq x_4 \leq \dfrac{\Sigma_c}{\Theta}$. Therefore, all solutions of sub-model (5) enter the region from the boundary of Ω_1. This means that all possible solutions of sub-model (5) will enter the region Ω_1 and stay inside Ω_1. Hence the region Ω_1, of biological interest, is positively-invariant under the flow induced by sub-model (5).

3.2. Equilibrium points

In this section we investigate the existence of equilibria of sub-model (5). Solving the right hand side of the sub-model by equating it to zero, we obtain the disease free equilibrium given by

$$E_{0c} = (\Pi_1, 0, 0, 0)\,.$$

The stability of E_{0c} is governed by the basic reproduction number which is obtained by the next generation operator [31, 32].

The basic reproduction number of model (5) is hence given by

$$R_{0c} = \frac{\Pi_1\, B_c \Phi_c}{(\,E_c + 1)(1 + \Phi_c)} + \frac{\Psi_c \Pi_1 \Sigma_c \Phi_c}{\Theta(\,E_c + 1)(1 + \Phi_c)}.$$

Our R_{0c} captures parameters from the two transmission routes that drive the infection in cattle population and it is defined as the expected number of secondary infections generated due to the interactions between susceptible cattle and infective cattle and contaminated environment. The first term of R_{0c} represents the infection due to the interaction between susceptible cattle and infected cattle. The infection due to the interaction of susceptible cattle and the environment is represented by the second term of R_{0c}.

To test the parameters that significantly affect the transmission dynamics of BTB in cattle, sensitivity analysis on R_{0c} was carried out through differentiating R_{0c}

with respect to parameters of the model. The following results were obtained

$$\frac{\partial R_{0c}}{\partial \Psi_c} = \frac{\Pi_1 \Sigma_c \Phi_c}{\Theta(\ E_c + 1)(1 + \Phi_c)},$$
$$\frac{\partial R_{0c}}{\partial \Sigma_c} = \frac{\Pi_1 \Psi_c \Phi_c}{\Theta(\ E_c + 1)(1 + \Phi_c)},$$
$$\frac{\partial R_{0c}}{\partial \Theta} = -\frac{\Psi_c \Pi_1 \Sigma_c \Phi}{\Theta^2(\ E_c + 1)(1 + \Phi_c)}.$$

The sensitivity analysis on R_{0c} shows that Ψ_c and Σ_c contributes towards the epidemiology of bovine tuberculosis in cattle community. Thus the risk measure of the outbreak of BTB is increased when the infective rate due to contaminated environment and the shedding rate of infectious mycobacterium bovis into the environment increase. However, any increase in the decaying rate of the infectious unit in the environment leads to a decrease in R_{0c}. From the policy maker perspective, this implies that the controlling measures applied should focus on reducing environment infective rate and *M. bovis* shedding off rate and increasing the decaying rate of *M. bovis* in the environment in order to reduce bovine tuberculosis in cattle population.

The stability of E_{0c} is stated in the following theorem:

Theorem 1. *If $R_{0c} < 1$, the disease-free equilibrium E_{0c} of the sub-model (5) is locally asymptotically stable, and is unstable if $R_{0c} > 1$.*

Proof. For stability of E_{0c}, we need to show that all the eigenvalues of the Jacobian matrix of model (5) evaluated at E_{0c} are negative or have negative real parts. It is sufficient to consider the stability of the matrix $F - V$, where F is a matrix that contains transmission terms that describe the production of new infections and V is the matrix that contains the transition terms that describe changes in the state variables [31] whose eigenvalues of $F - V$ are solutions to the characteristic equation

$$\lambda^3 + A\lambda^2 + B\lambda + C = 0$$

where

$A = \Theta + \ E_c + 2 + \Phi_c$, $B = \Theta^2(2 + \ E_c\Phi_c) + \Phi_c\Pi_1\Sigma_c\Psi_c + \frac{1}{\Theta(1+\ E_c)(\Phi_c+1)}(1 - R_{0c})$,
$C = \frac{1}{\Theta(1+\ E_c)(\Phi_c+1)}(1 - R_{0c})$.

The Routh-Hurwitz Stability Criterion is used to establish that eigenvalues are

either negative or have negative real parts. It can be observed that $A > 0$ and $C > 0$ when $R_{0c} < 1$. It can also be established that

$$BA - C = Q + \Theta^2(2 + E_c + \Phi_c) + \Phi_c\Pi_1\Sigma_c\Psi_c > 0$$

where

$$Q = (1 + \Theta + E_c + \Phi_c)\left[(J + \frac{1}{\Theta(1 + E_c)(\Phi_c + 1)}(1 - R_{0c})\right]$$

where $J = \Theta^2(2 + E_c\Phi_c) + \Phi_c\Pi_1\Sigma_c\Psi_c$. When $R_{0c} < 1$, then all the eigenvalues are negative or have negative real parts. If $R_{0c} > 1$, it is easy to see that $A > 0$, $C < 0$, and despite the sign of B we have, using Descarte's rule of signs, there is only one positive eigenvalue. This makes E_{0c} a saddle point and therefore unstable. Thus the disease free equilibrium point E_{0c} is locally asymptotically stable when $R_{0c} < 1$ and unstable when $R_{0c} > 1$. □

3.2.1. The endemic equilibrium and its stability

Here, we study the existence and stability of the endemic equilibrium point. By straightforward computation, if $R_{0c} > 1$, then the cattle sub-model (5) has a unique endemic equilibrium given by $E_c^* = (x_1^*, x_2^*, x_3^*, x_4^*)$ in Ω_1 with

$$x_1^* = \frac{\Theta\Pi_1(\Theta B_c + \Psi_c\Sigma_c)}{(R_{0c} - 1)(\Theta B_c + \Psi_c\Sigma_c) + \Theta(\Theta B_c + \Psi_c\Sigma_c)},$$

$$x_2^* = \frac{(1 + E_c)\Sigma_c(R_{0c} - 1)}{\Phi_c(\Theta B_c + \Psi_c\Sigma_c)}, \quad x_3^* = \frac{(R_{0c} - 1)}{\Theta B_c + \Psi_c\Sigma_c},$$

$$x_4^* = \frac{\Sigma_c(R_{0c} - 1)}{\Theta B_c + \Psi_c\Sigma_c}.$$

Theorem 2. *If $R_{0c} > 1$, the endemic equilibrium E_c^* of the model (5) is locally asymptotically stable in Ω_2.*

Proof. In order to explore the local stability of the endemic equilibrium point E_c, we evaluate the Jacobian $J(x_1^*, x_2^*, x_3^*, x_4^*)$ at the endemic equilibrium point and we get

$$J(E_c^*) = \begin{pmatrix} -B_c x_3^* - \Psi_c x_4^* - 1 & 0 & -B_c x_1^* & -\Psi_c x_1^* \\ B_c x_3^* + \Psi_c x_4^* & -(1 + \Phi_c) & B_c x_1^* & \Psi_c x_1^* \\ 0 & \Phi_c & -(1 + E_c) & 0 \\ 0 & 0 & \Sigma_c & -\Theta \end{pmatrix}.$$

The eigenvalues of $J(E_c)$ are calculated using $Det(J(E_c - \lambda I_4)) = 0$

$$Det\begin{pmatrix} -A_1 & 0 & -A_2 & -A_3 \\ A_4 & -A_5 & A_2 & A_3 \\ 0 & \Phi_c & -A_6) & 0 \\ 0 & 0 & \Sigma_c & -A_7 \end{pmatrix} = 0.$$

where

$A_1 = B_c x_3^* + \Psi_c x_4^* + 1 + \lambda; \quad A_4 = B_c x_3^* + \Psi_c x_4^*; \quad A_2 = B_c x_1^*; \quad A_3 = \Psi_c x_1^*$
$A_5 = 1 + \Phi_c + \lambda; \quad A_6 = 1 + E_c + \lambda; \quad A_7 = \Theta + \lambda$

The first two eigenvalues of the Jacobian matrix are $\lambda_1 = -\left(B_c x_3^* + \Psi_c x_4^* + 1\right)$ and $\lambda_2 = -(1 + \Phi_c)$ The other eigenvalues are obtained from

$$\lambda^2 + b_1\lambda + b_2 = 0,$$

where

$$b_1 = \Theta + n + \Sigma_c c_3; \quad b_2 = \Sigma_c \Phi_c A_3(\, B_c x_3^* + \Psi_c x_4^*),$$

The eigenvalues $\lambda_{3,4}$ are both negative due to the existence of x_3^*, x_4^* and x_1^* when $R_{0c} > 1$. This implies that all four eigenvalues of our Jacobian matrix are negative, which proves the local stability of endemic equilibrium point E_c. □

4. Buffalo sub-population

By setting $B_{bc} = B_{cb} = \Sigma_c = \Psi_c = 0$, we obtain the following buffalo sub-population model:

$$\begin{aligned} \frac{dx_5}{d\tau} &= \Pi_2 - \Lambda_b x_5 - M_b x_5, \\ \frac{dx_6}{d\tau} &= \Lambda_b x_5 - \Phi_b x_6 - M_b x_6, \\ \frac{dx_7}{d\tau} &= \Phi_b x_6 - (\, M_b + E_b) x_7, \\ \frac{dx_4}{d\tau} &= \Sigma_b x_7 - \Theta x_4, \end{aligned} \tag{6}$$

which describes the transmission dynamics of bovine tuberculosis in buffalo only. The sub-model also takes into account the role of contaminated pasture in the spread of bovine tuberculosis in the buffalo population.

4.1. Feasible region

Since the sub-model (6) tracks the buffalo population we assume that all state variables and parameters are positive for all $\tau > 0$. The bovine tuberculosis transmission sub-model will then be analysed in a suitable feasible region given by

$$\Omega_2 = \left\{(x_5, x_6, x_7, x_4) \in \Re_+^4 | x_5 \geq 0, x_6 \geq 0, x_7 \geq 0, x_4 \geq 0, N_b \leq \frac{\Pi_2}{M_b}, x_4 \leq \frac{\Sigma_b}{\Theta}\right\}.$$

where $N_b(\tau) = x_5 + x_6 + x_7$

The techniques used to establish the invariance and boundedness of Ω_2 are the same as outlined in section (3).

4.2. Equilibrium points

In this section we investigate the existence of equilibria of sub-model (6). Solving the right hand side of the sub-model by equating it to zero, we obtan the disease free equilibrium given by

$$E_{0b} = \left(\frac{\Pi_2}{M_b}, 0, 0, 0\right).$$

The stability of E_{0b} is governed by the basic reproduction number which is obtained by the next generation operator [31, 32]. Following [31], the basic reproduction number of model (6) given by

$$R_{0b} = \frac{\Pi_2\ B_b\Phi_b}{M_b(\ E_b +\ M_b)(\ M_b + \Phi_b)} + \frac{\Psi_b\Pi_2\Sigma_b\Phi_b}{\Theta\ M_b(\ E_b +\ M_b)(\ M_b + \Phi_b)}.$$

Our R_{0b} is interpreted in the same way as R_{0c} in section (3).

To test the parameters that significantly affect the transmission dynamics of BTB infection in buffalo, sensitivity analysis on R_{ob} was carried out through differentiating R_{0b} with respect to parameters of R_{ob}. The following results were obtained

$$\begin{aligned}
\frac{\partial R_{0b}}{\partial \Psi_b} &= \frac{\Pi_2\Sigma_b\Phi_b}{\Theta\ M_b(\ E_b +\ M_b)(\ M_b + \Phi_b)} > 0,\\
\frac{\partial R_{0b}}{\partial \Sigma_b} &= \frac{\Pi_2\Psi_b\Phi_b}{\Theta\ M_b(\ E_b +\ M_b)(\ M_b + \Phi_b)} > 0,\\
\frac{\partial R_{0b}}{\partial \Theta} &= -\frac{\Psi_b\Pi_2\Sigma_b\Phi_b}{\Theta^2\ M_b(\ E_b +\ M_b)(\ M_b + \Phi_b)} < 0.
\end{aligned}$$

The explanation of the sensitivity analysis follows the same path as done in section (3)

The stability of E_{0b} is stated in the following theorem:

Theorem 3. *If $R_{0b} < 1$, the disease-free equilibrium E_{0b} of the sub-model (6) is locally asymptotically stable, and is unstable if $R_{0b} > 1$.*

Proof. The proof of theorem (3) follows the same procedure as outlined in section (3). □

4.2.1. The endemic equilibrium and its stability

Here, we study the existence and stability of the endemic equilibrium point. By straightforward computation, if $R_{0b} > 1$, then the buffalo sub-model (5) has a unique endemic equilibrium point given by $E_b^* = (x_5^*, x_6^*, x_7^*, x_4^*)$ in Ω_2 with

$$x_5^* = \frac{\Theta\Pi_2(\Theta\, B_b + \Psi_b\Sigma_b)}{M_b(R_{0b}-1)(\Theta\, B_b + \Psi_b\Sigma_b) + \Theta\, M_b(\Theta\, B_b + \Psi_b\Sigma_b)},$$

$$x_6^* = \frac{(\, M_b + \, E_b)\Sigma_b\, M_b(R_{0b}-1)}{\Phi_b(\Theta\, B_b + \Psi_b\sigma_b)},$$

$$x_7^* = \frac{M_b(R_{0b}-1)}{\Theta\, B_c + \Psi_b\Sigma_b}, \quad x_4^* = \frac{\Sigma_b\, M_b(R_{0b}-1)}{\Theta\, B_b + \Psi_b\Sigma_b}.$$

The approach used in section (3) to establish the local stability of the endemic equilibrium is also used in this section.

5. Analysis of a full model

This section covers the analysis of the full model (4). Positivity of the model will be established and the reproduction number will be determined. The association of the amplification or abating of the disease with the reproduction number in buffalo and cattle population will also be detailed.

5.1. Boundedness of the model

In this section, we establish the boundedness of the system (4) to ensure that all solutions remain in the feasible region Ω.

Proposition 1. *Let* $(x_1, x_2, x_3, x_4, x_5, x_6, x_7)$, *be a solution of the system (4) with initial conditions* $(x_1 \geq 0, x_2 \geq 0, x_3 \geq 0, x_4 \geq 0, x_5 \geq 0, x_6 \geq 0, x_7 \geq 0)$ *and a closed set*

$$\Omega = ((x_1, x_2, x_3, x_4, x_5, x_6, x_7) \in \Re_+^7, N_c \leq \Pi_1, N_b \leq \frac{\Pi_2}{M_b}, x_4 \leq \frac{\Sigma_c + \Sigma_b}{\Theta}),$$

then Ω *is positively invariant and attracting under the flow described by the system (4).*

Proof. Consider the Lyapunov function as used in [8]

$$H(\tau) = (N_c(\tau), N_b(\tau), x_4(\tau)) = x_1 + x_2 + x_3, x_5 + x_6 + x_7, x_4. \tag{7}$$

The time derivative of this equation is given by

$$\frac{dH}{d\tau} = (\Pi_1 - N_c - E_c x_3, \Pi_2 - M_b N_b - E_b x_7, \Sigma_c x_3 + \Sigma_b x_7 - \Theta x_4). \tag{8}$$

It is easy to prove that

$$\begin{aligned}
&\frac{dN_c}{d\tau} \leq \Pi_1 - N_c \leq 0 \quad \text{for} \quad N_c \geq \Pi_1 \\
&\frac{dN_b}{d\tau} \leq \Pi_2 - M_b N_b \leq 0 \quad \text{for} \quad N_b \geq \frac{\Pi_2}{M_b} \\
&\frac{dx_4}{d\tau} \leq \Sigma_c + \Sigma_b - \Theta x_4 \leq 0 \quad \text{for} \quad x_4 \geq \frac{\Sigma_c + \Sigma_b}{\Theta}
\end{aligned}$$

Thus it follows that $\frac{dH}{d\tau} \leq 0$ which implies that Ω is a positively invariant set. A standard comparison theorem [33] is used to show that

$$0 \leq (N_c, N_b, x_4) \leq \left(N_c(0)e^{-\tau} + \Pi_1(1 - e^{-\tau}), W, \frac{\Sigma_c + \Sigma_b}{\Theta} e^{-\Theta\tau}\right) \tag{9}$$

where $W = N_b(0)e^{-M_b\tau} + \frac{\Pi_2}{M_b}(1 - e^{-M_b\tau})$

Thus, as $\tau \to \infty$, $0 \leq (N_c, N_b, x_4) \leq (\Pi_1, \frac{\Pi_2}{M_b}, 0)$ and so Ω is an attracting set. □

5.2. Reproduction number

The disease-free equilibrium point of model system (4) is given by

$$E_{0f} = \left(\Pi_1, 0, 0, 0, \frac{\Pi_2}{M_b}, 0, 0\right).$$

Following [11, 31], the basic reproduction number of model (4) we obtain

$$F = \begin{pmatrix} 0 & B_c x_1^* & \Psi_c x_1^* & 0 & B_{cb} x_1^* \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & B_{bc} x_5^* & \Psi_b x_5^* & 0 & B_b x_5^* \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} \Phi_c + 1 & 0 & 0 & 0 & 0 \\ -\Phi_c & 1 + E_c & 0 & 0 & 0 \\ 0 & -\Sigma_c & \Theta & 0 & -\Sigma_b \\ 0 & 0 & 0 & \Phi_b + M_b & 0 \\ 0 & 0 & 0 & -\Phi_b & (M_b + E_b) \end{pmatrix},$$

The inverse of V is given by

$$V^{-1} = \begin{pmatrix} \frac{\Theta(1+E_c)}{\Theta(1+E_c)(1+\Phi_c)} & 0 & 0 & 0 & 0 \\ N_2 & \frac{\Theta(1+\Phi_c)}{\Theta(1+E_c)(1+\Phi_c)} & 0 & 0 & 0 \\ N_3 & \frac{\Sigma_c(1+\Phi_c)}{\Theta(1+E_c)(1+\Phi_c)} & \frac{(1+\Phi_c)(1+E_c)}{\Theta(1+E_c)(1+\Phi_c)} & N_4 & N_1 \\ 0 & 0 & 0 & \frac{1}{\Phi_b+M_b} & 0 \\ 0 & 0 & 0 & N_5 & \frac{1}{(M_b+E_b)} \end{pmatrix},$$

where

$$N_1 = \frac{\Sigma_c(1+\Phi_c)(1+E_c)}{(E_b+M_b)\Theta(1+E_c)(1+\Phi_c)}, \tag{10}$$

$$N_2 = \frac{\Theta\Phi_c(E_b+M_b)}{(E_b+M_b)\Theta(1+E_c)(1+\Phi_c)}, \tag{11}$$

$$N_3 = \frac{\Sigma_c\Phi_c(\Sigma_b+M_b)}{E_b+M_b\Theta(1+E_c)(1+\Phi_c)}, \tag{12}$$

$$N_4 = \frac{\Sigma_b\Phi_b(1+\Phi_c)(1+E_c)}{(E_b+M_b)(M_b+\Phi_b)\Theta(1+E_c)(1+\Phi_c)}, \tag{13}$$

$$N_5 = \frac{(1+E_c)(\Theta\Phi_c\Phi_b+\Theta\Phi_b)}{(E_b+M_b)\Theta(1+E_c)(1+\Phi_c)}. \tag{14}$$

Our next generation matrix of the system (4) is

$$FV^{-1} = \begin{pmatrix} m_{11} & m_{12} & m_{13} & m_{14} & m_{15} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ m_{41} & m_{42} & m_{43} & m_{44} & m_{45} \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

where

$$m_{11} = \frac{x_1^* B_c(\Theta E_b\Phi_c + \Theta M_b\Phi_c)}{(E_b + M_b)\Theta(1 + E_c)(1 + \Phi_c)} + \frac{x_1^*(E_b\Sigma_c\Phi_c + M_b\Sigma_c\Phi_c)\Psi_c}{(E_b + M_b)(1 + E_c)(1 + \Phi_c)\Theta}$$

$$m_{12} = \frac{x_1^* B_c\Theta(1 + \Phi_c)}{\Theta(1 + E_c)(1 + \Phi_c)} + \frac{x_1^*\Sigma_c\Psi_c(1 + \Phi_c)}{\Theta(1 + E_c)(1 + \Phi_c)}$$

$$m_{13} = \frac{x_1^*\Psi_c(1 + E_c)(1 + \Phi_1)}{\Theta(1 + E_c)(1 + \Phi_c)}$$

$$m_{14} = \frac{x_1^* B_{cb}(1 + E_c)(\Theta\Phi_c\Phi_c + \Theta\Phi_b)}{(E_b + M_b)(M_b + Phi_c)\Theta(1 + E_c)(1 + \Phi_c)} + \frac{x_1^*\Sigma_b\Phi_c\Psi_c(1 + E_c)(1 + \Phi_c)}{(E_b + M_b)(M_b + \Phi_b)\Theta(1 + E_c)(1 + \Phi_c)}$$

$$m_{15} = \frac{x_1^* B_{cb}}{E_b + M_b} + \frac{x_1^*\Sigma_b(1 + E_c)(1 + \Phi_c)\Psi_c}{(E_b + M_b)\Theta(1 + E_c)(1 + \Phi_c)}$$

$$m_{41} = \frac{x_5^* B_{bc}(\Theta E_b\Phi_c + \Theta M_b\Phi_c)}{(E_b + M_b)\Theta(1 + E_c)(1 + \Phi_c)} + \frac{x_5^*\Psi_b(E_b\Sigma_c\Phi_c + M_b\Sigma_c\Phi_c)}{(E_b + M_b)\Theta(1 + E_c)(1 + \Phi_c)}$$

$$m_{42} = \frac{x_5^* B_{bc}(\Theta + \Theta\Phi_c)}{\Theta(1 + E_c)(1 + \Phi_c)} + \frac{x_5^*\Psi_b(\Sigma_c + \Sigma_c\Phi_c)}{\Theta(1 + E_c)(1 + \Phi_c)}$$

$$m_{43} = \frac{x_5^*\Psi_b(1 + E_c)(1 + \Phi_c)}{\Theta(1 + E_c)(1 + \Phi_c)}$$

$$m_{44} = \frac{x_5^* B_b(1 + E_c)(\Theta\Phi_c\Phi_c + \Theta\Phi_b)}{(E_b + M_b)(M_b + Phi_c)\Theta(1 + E_c)(1 + \Phi_c)} + \frac{x_5^*\Sigma_b\Phi_b\Psi_b(1 + E_c)(1 + \Phi_c)}{(E_b + M_b)(M_b + \Phi_b)\Theta(1 + E_c)(1 + \Phi_c)}$$

$$m_{45} = \frac{x_5^* B_b}{E_b + M_b} + \frac{x_5^*\Sigma_b(1 + E_c)(1 + \Phi_c)\Psi_b}{(E_b + M_b)\Theta(1 + E_c)(1 + \Phi_c)}$$

So the basic reproduction number is given by

$$R_{0f} = \rho(FV^{-1}) = m_{11} + m_{44} + \sqrt{(m_{11} - m_{44})^2 + 4m_{14}m_{41}}, \qquad (15)$$

and ρ denotes the spectral radius.

The expression of R_{0f} contains two terms representing the direct transmission routes and the other two representing the cross-infection transmission routes. The components in our reproduction number can be interpreted as follows: m_{11} is the contribution of infected cattle and contaminated environment in the evolution and epidemiology of bovine tuberculosis in the cattle population only; m_{44}

is the contribution of infected buffalo and contaminated environment in the evolution and epidemiology of bovine tuberculosis in the buffalo population only; m_{14} is the contribution of infected buffalo and contaminated environment in the evolution and epidemiology of bovine tuberculosis in the cattle population; and m_{41} is the contribution of infected cattle and contaminated environment in the evolution and epidemiology of bovine tuberculosis in the buffalo population.

The inclusion of cross-infection and environment routes in the R_{0f} signifies the role these routes play in amplifying the infection in both cattle and buffalo populations. To lower the negative impacts of the infection on livestock industry, control measures should target reducing the mixing of cattle and buffalo at the wildlife-livestock interface.

5.3. Stability of disease free equilibrium point

Let

$$M = F - V = \begin{pmatrix} -(\Phi_c + 1) & B_c x_1^* & \Psi_c x_1^* & 0 & B_{bc} x_1^* \\ \Phi_c & -(1 + E_c) & 0 & 0 & 0 \\ 0 & \Sigma_c & -\Theta & 0 & \Sigma_b \\ 0 & B_{bc} x_5^* & \Psi_b x_5^* & -(\Phi_b + M_b) & B_b x_5^* \\ 0 & 0 & 0 & \Phi_b & -(M_b + E_b) \end{pmatrix}.$$

Define $s(M) = \max\{Re\lambda : \lambda \text{ is an eigenvalue of } M\}$, so $s(M)$ is a simple eigenvalue of M with positive eigenvector [11]. By **Theorem 2** of [31], these two equivalences hold

$$R_0 > 1 \Longleftrightarrow s(M) > 0, \quad R_0 < 1 \Longleftrightarrow s(M) < 0.$$

Theorem 4. *The bovine tuberculosis free equilibrium point, E_{0f}, is locally asymptotically stable if $R_{0f} < 1$ and unstable otherwise.*

Proof. To prove the local stability of disease free equilibrium of system (4), we verify the hypotheses (**A1** − **A5**) in [31]. Hypotheses (**A1** − **A4**) are easy to verify if all eigenvalues of 7×7 matrix

$$J \mid_{E_{0f}} = \begin{pmatrix} M & 0 \\ J_3 & J_2 \end{pmatrix}$$

are negative real parts, where $J_3 = -J_2$.

The matrix J_2 is given by

$$J_2 = \begin{pmatrix} -1 & 0 \\ 0 & -M_b \end{pmatrix}$$

The eigenvalues of J_2 are given by

$$s(J_2) = \max\{-1, -M_b\}$$

If $R_{0f} < 1$, then $s(M) < 0$ and $J \mid_{E_{0f}} < 0$, the disease free equilibrium of E_{0f} of system (4) is locally asymptotically stable. □

Theorem 4 implies that BTB infection can be eliminated from the community when $R_{0f} < 1$. Thus the initial sizes of the sub-populations of the model (4) are in the basin of attraction of the disease free equilibrium point.

To prove the global asymptotic stability of the disease free equilibrium point, we rewrite the model (4) in the form

$$\begin{cases} \frac{dX}{d\tau} &= F(X, Y), \\ \frac{dY}{d\tau} &= G(X, Y), \quad G(X, \mathbf{0}) = 0, \end{cases}$$

where $X = (x_1, x_5)^T$ and $Y = (x_2, x_3, x_4, x_6, x_7)^T$ with $X \in \Re_+^2$ denoting the number of susceptible cattle and buffalo and $Y \in \Re_+^5$ denoting the number of exposed cattle, infected cattle, contaminated environment, exposed buffalo and infected buffalo.

The disease-free equilibrium is now denoted by $E_{0f} = (X_0, \mathbf{0})$ where $\left(X_0 = \Pi_1, \frac{\Pi_2}{M_b}\right)$ and $\mathbf{0}$ is a zero vector. The following conditions should be satisfied to guarantee global asymptotic stability:

- $\mathbf{H_1}$: For $\frac{dX}{d\tau} = F(X_0, \mathbf{0})$, X_0 is globally asymptotically stable.
- $\mathbf{H_2}$: $G(X, Y) = AY - \tilde{G}(X, Y)$, $\tilde{G}(X, Y) \geq 0$ for $(X, Y) \in \Omega$, where $A = D_Y(G(X_0, \mathbf{0}))$ is an M-matrix.

If model (4) satisfies the conditions $\mathbf{H_1}$ and $\mathbf{H_2}$ [12], then the following result holds.

Theorem 5. *The bovine tuberculosis free equilibrium point, E_{0f}, is globally asymptotically stable if $R_{0f} < 1$.*

Proof. Consider

$$F(X,0) = (\Pi_1 - x_1, \Pi_2 - M_b x_5), \quad G(X,Y) = AY - \tilde{G}(X,Y)$$

where

$$A = \begin{pmatrix} -(\Phi_c + 1) & B_c\Pi_1 & \Psi_c\Pi_1 & 0 & B_{cb}\Pi_1 \\ \Phi_c & -(1 + E_c) & 0 & 0 & 0 \\ 0 & \Sigma_c & -\Theta & 0 & \Sigma_b \\ 0 & \frac{B_{bc}\Pi_2}{M_b} & \frac{\Psi_b\Pi_2}{M_b} & -(\Phi_c + M_b) & \frac{B_b\Pi_2}{M_b} \\ 0 & 0 & 0 & \Phi_b & -(M_b + E_b) \end{pmatrix},$$

and

$$\tilde{G}(X,Y) = \begin{pmatrix} B_c x_3 + B_{cb} x_7 + \Psi_c x_4 \\ 0 \\ 0 \\ B_b x_7 + B_{bc} x_3 + \Psi_b x_4 \\ 0 \end{pmatrix}.$$

The first condition $\mathbf{H_1}$ is satisfied when X is a globally asymptotically stable equilibrium point of the equations

$$\frac{dx_1}{d\tau} = \Pi_1 - x_1, \frac{dx_5}{d\tau} = \Pi_2 - M_b x_5. \tag{16}$$

Solving (16) we obtain

$$x_1(\tau) = \Pi_1 - x_1(\tau)e^{-\tau}, x_5(\tau) = \frac{\Pi_2}{M_b} - x_5(\tau)e^{-M_b\tau}.$$

Taking limits as $\tau \to \infty$ we obtain,

$$\lim_{\tau\to\infty} x_1(\tau) = \Pi_1, \lim_{\tau\to\infty} x_5(\tau) = \frac{\Pi_2}{M_b}.$$

This suggests that, independent of the initial conditions, the solutions of the equations (16) converge to X_0. Thus, X_0 is a globally asymptotically equilibrium point of (16). To prove condition $\mathbf{H_2}$, we observe that $\tilde{G}(X,Y) \geq 0$, so this completes the proof of both conditions. □

The significance of Theorem (4) is that BTB infection can be eradicated completely from cattle and buffalo population in the long run whenever $R_{0f} < 1$. It naturally follows that the endemic equilibrium point is unstable.

5.4. Disease persistence

We now turn to the case where $R_{0f} > 1$. We only establish the uniform persistence for system (4) when $R_{0f} > 1$, by applying the following result established in [34].

Lemma 6. *Let $K_\tau : X \to X$ be a semiflow and $X_0 \subset X$ an open set. Define $\partial X_0 = X \backslash X_0$ and $M_\partial = \{x \in \partial X_0 : K_\tau x \in \partial X_0, \tau \geq 0\}$. Assume that*

(C_1) *$K_\tau X_0 \subset X_0$ and K_τ has a global attractor A;*

(C_2) *there exists a finite sequence $\mathbf{M} = \{M_1, ..., M_k\}$ of disjoint, compact, and isolated invariant sets in ∂X_0 such that*

- *(a) $\Omega(M_\partial) := \cup_{x \in M_\partial} \omega(x) \subset \cup_{i=1}^{k} M_i$;*
- *(b) no subset of $\mathbf{M}$ forms a cycle on ∂X_0;*
- *(c) M_i is isolated in X.*
- *(d) $W^s(M_i) \cap X_0 = \emptyset$ where $W^s(M_i) = \{x \in X_0 : \omega(x) \subset M_i\}$, for each $1 \leq i \leq k$.*

Then K_τ is uniformly persistent with respect to $(X_0, \partial X_0)$, i.e., there exists $\eta > 0$, such that $\liminf_{\tau \to \infty} d(K_\tau x, \partial X_0) \geq \eta$ for $x \in X_0$.

Theorem 7. *If $R_{0f} > 1$, then the system (4) is uniformly persistent, namely there exist $\eta > 0$ such that $\liminf_{\tau \to \infty} \{x_1(\tau), x_2(\tau), x_3(\tau), x_4(\tau), x_5(\tau), x_6(\tau), x_7(\tau)\} \geq \eta$ for initial conditions $x_1(0), x_2(0), x_3(0), x_4(0), x_5(0), x_6(0), x_7(0) > 0$*

Proof. Choose $X = \Re_+^7$, $X_0 = \{(x_1, x_2, x_3, x_4, x_5, x_6, x_7) \in X, x_2, x_3, x_4, x_6, x_7 > 0\}$ and $\partial X_0 = X \backslash X_0 = \{(x_1, x_2, x_3, x_4, x_5, x_6, x_7) \in X, x_2 = x_3 = x_4 = x_6 = x_7 = 0\}$. Let Φ_t be the semiflow induced by the solutions of system (4).

Proposition 2. *Let $(x_1, x_2, x_3, x_4, x_5, x_6, x_7)$, be a solution of the system (4) with initial conditions ($x_1 \geq 0, x_2 \geq 0, x_3 \geq 0, x_4 \geq 0, x_5 \geq 0, x_6 \geq 0, x_7 \geq 0$) and a closed set*

$$\Omega = ((x_1, x_2, x_3, x_4, x_5, x_6, x_7) \in \Re_+^7, N_c \leq \Pi_1, N_b \leq \frac{\Pi_2}{M_b}, x_4 \leq \frac{\Sigma_c + \Sigma_b}{\Theta}),$$

then Ω is positively invariant and attracting under the flow described by the system (4).

The proof of proposition 2 shows

$$H(\tau) = (N_c(\tau), N_b(\tau), x_4(\tau)) = x_1 + x_2 + x_3, x_5 + x_6 + x_7, x_4. \tag{17}$$

The time derivative of this equation is given by

$$\frac{dH}{d\tau} = (\Pi_1 - N_c - E_c x_3, \Pi_2 - M_b N_b - E_b x_7, \Sigma_c x_3 + \Sigma_b x_7 - \Theta x_4)\,. \tag{18}$$

It is easy to prove that

$$\begin{aligned}
&\frac{dN_c}{d\tau} \le \Pi_1 - N_c \le 0 \quad \text{for} \quad N_c \ge \Pi_1,\\
&\frac{dN_b}{d\tau} \le \Pi_2 - M_b N_b \le 0 \quad \text{for} \quad N_b \ge \frac{\Pi_2}{M_b},\\
&\frac{dx_4}{d\tau} \le \Sigma_c + \Sigma_b - \Theta x_4 \le 0 \quad \text{for} \quad x_4 \ge \frac{\Sigma_c + \Sigma_b}{\Theta}.
\end{aligned}$$

Thus it follows that $\frac{dH}{d\tau} \le 0$ which implies that Ω is a positively invariant set. A standard comparison theorem [33] is used to show that

$$0 \le (N_c, N_b, x_4) \le \left(N_c(0)e^{-\tau} + \Pi_1(1 - e^{-\tau}), W, \frac{\Sigma_c + \Sigma_b}{\Theta} e^{-\Theta\tau}\right), \tag{19}$$

where $W = N_b(0)e^{-M_b\tau} + \frac{\Pi_2}{M_b}(1 - e^{-M_b\tau})$

Thus, as $\tau \to \infty$, $0 \le (N_c, N_b, x_4) \le (\Pi_1, \frac{\Pi_2}{M_b}, 0)$ and so Ω is an attracting set.

that $K_t x \subset X_0$ and K_t is ultimately bounded in X_0; so there always exists a global attractor for K_t. It is obvious that E_{0f} is the unique boundary equilibrium on ∂X_0, which implies that E_{0f} is globally stable on ∂X_0. Moreover, (x_1, x_4, x_5) converges to $(\Pi_1, 0, \frac{\Pi_2}{M_b})$ on ∂X_0. Let $M_1 = \left\{E_{0f}\right\}$ and $\mathbf{M} = \{M_1\}$. Then $\cup_{x \in M_\partial} \omega(x) = M_1$ and no subset of $\mathbf{M}$ forms a cycle in ∂X_0. If $R_{0f} > 1$, then E_{0f} is unstable in X_0. Therefore conditions *c* and *d* are satisfied and the proof is complete. □

6. Numerical simulations

In this section, we present a detailed account on how the parameters used in this project are estimated. We then use the parameter values to carry out the numerical simulations that will enhance further understanding of the model's predictions.

Table 1: Table of parameter values used in the model

Name	Range	Reference	Name	Range	Reference
Π_1	[0.2, 0.9]	[4]	Σ_c	[.10, .20]	[27]
Π_2	[0.2, 0.8]	[36]	Θ	[0.1, 0.5]	[27]
Ψ_c	[0.01, 0.06]	Assumed	Φ_c	[0.3, 0.8]	[14]
Ψ_b	[0.1, 0.6]	Assumed	Φ_b	[0.3, 0.8]	[14]
B_c	[1, 5]	[4]	E_c	[0.1, 0.5]	[4]
B_b	[0.1, 0.53]	[14]	M_b	[0.1, 0.5]	[35]
B_{cb}	[0.1, 0.6]	Assumed	E_b	[0.1, 0.8]	[35]
B_{bc}	[0.01, 0.06]	Assumed	Σ_b	[.10, .20]	[27]

6.1. Parameter estimation

All parameter values used in the numerical simulations are given in Table 1 with their sources. Some parameter values are taken as they appear in literature while others are determined based on the given information in literature. Those with no known values from literature are determined by the conditions subjected to them in the model formulation. The values of B_c, B_b, M_b, E_c, E_b, Φ_c, Φ_b, Θ, Σ_c, Σ_b, Π_1 and Π_2 are obtained from [4, 14, 25, 27, 35, 36]. There is a paucity of data on B_{cb}, B_{cb}, Ψ_c and Ψ_b. However as the infection rate through environment and other species is small [16, 21], we make estimations in line with this constraint. This suggests that data have to be collected on the processes to reasonably estimate the parameters. This in turn gives reasonable predictions about the future scenarios of the system of interest.

6.2. Simulations

We present numerical simulations of the full model (3) to explore the impact of various transmission mechanisms of bovine tuberculosis in both cattle and buffalo populations. We first examine the role of the between cattle transmission rate β_c on the levels of the infectious unit in the environment and the overall epidemiology of BTB infection in the cattle population only. This is followed by the exploration of the impact of the between cattle transmission rate on the evolution of BTB infection in cattle and buffalo populations and the level of infectious unit in the environment. Thirdly, we investigate the role of the between buffalo transmission rate β_b on the levels of infectious unit and the time varying behaviour of BTB infection in the buffalo population only. Lastly, we examine the transmission dynamics of BTB infection in both cattle and buffalo populations when the between buffalo transmission rate is varied.

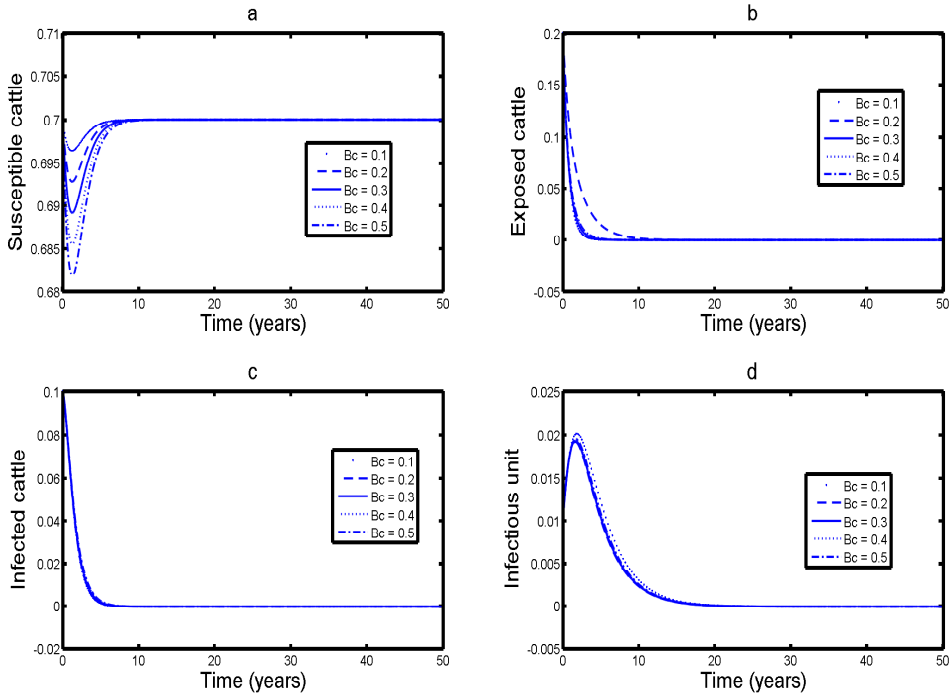

Figure 2: Graph showing the effect of varying only the between cattle transmission rate B_c on the evolution of BTB infection in cattle only. $x_1 = 0.7, x_2 = 0.2, x_3 = 0.1, x_4 = 0.01, \Pi_1 = 0.7, \Psi_c = 0.05,\ E_c = 0.1, \Phi_c = 0, \Sigma_c = 0.15, \Theta = 0.3.$

Figure 2 displays the effects of varying the between cattle transmission rate B_c on the evolution of BTB infection in the cattle population and the levels of the infectious unit in the environment. Increasing B_c, leads to a decrease of the proportion of exposed and infected cattle in Figure 2 (b) and (c). This also corresponds to a decrease in the amount of infectious unit in the environment as shown in Figure 2 (d). If it is only horizontal transmission route involved, the disease eventually dies out from the community. This implies that one route of disease transmission cannot sustain the infection in cattle. This agrees well with the observation made in [1] that cattle are dead hosts, implying that the disease cannot persist without the external infection sources.

Figure 3 shows the effects of varying the between cattle transmission rate B_b on the transmission dynamics of BTB infection in cattle population and also on the levels of the infectious unit in the environment. The results show that the intensity of BTB infection is aggravated in cattle population when all transmis-

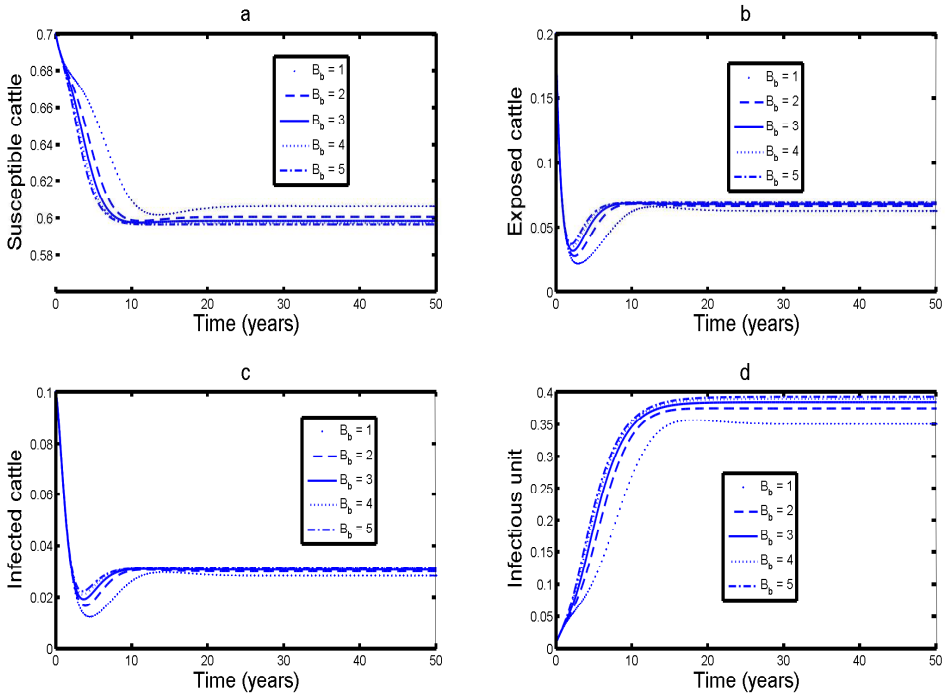

Figure 3: Graph showing the effect of varying only the between cattle transmission rate B_b on the evolution of BTB infection in cattle population and the levels of pathogen concentration in the environment. $x_1 = 0.7, x_2 = 0.2, x_3 = 0.1, x_4 = 0.01, x_5 = 0.7, x_6 = 0.2, x_7 = 0.1, \Pi_1 = 0.7, \Psi_c = 0.05,\ E_c = 0.1, \Phi_c = 0.5, \Sigma_c = 0.15, \Theta = 0.3,\ B_{cb} = 0.5,\ B_b = 0.25, \Sigma_b = 0.15, \Pi_2 = 0.43,\ B_{bc} = 0.01, \Psi_b = 0.5, \Phi_b = 0.5,\ M_b = 0.135,\ E_c = 0.2.$

sion routes are incorporated in the model (4). The proportions of the exposed and the infected cattle rise to endemic levels as shown in Figure 3 (b) and (c). Even the concentration of pathogens in the environment has gone up in Figure 3. The simulations suggests that the impact of cross-infection and environment transmission routes which is more severely felt in cattle population as evidenced in plots (a)-(d) in Figure 3. The reader is advised to compare Figure 3 to Figure 2 to appreciate the role of cross-infection on the epidemiology of BTB infection in cattle population. The results further suggest that the environment is seriously contaminated when the practices that promote the mixing of cattle and buffalo are encouraged.

To explore the role of the between buffalo transmission rate B_b on the dynamics of BTB infection in buffalo only and of the infectious unit in the environment,

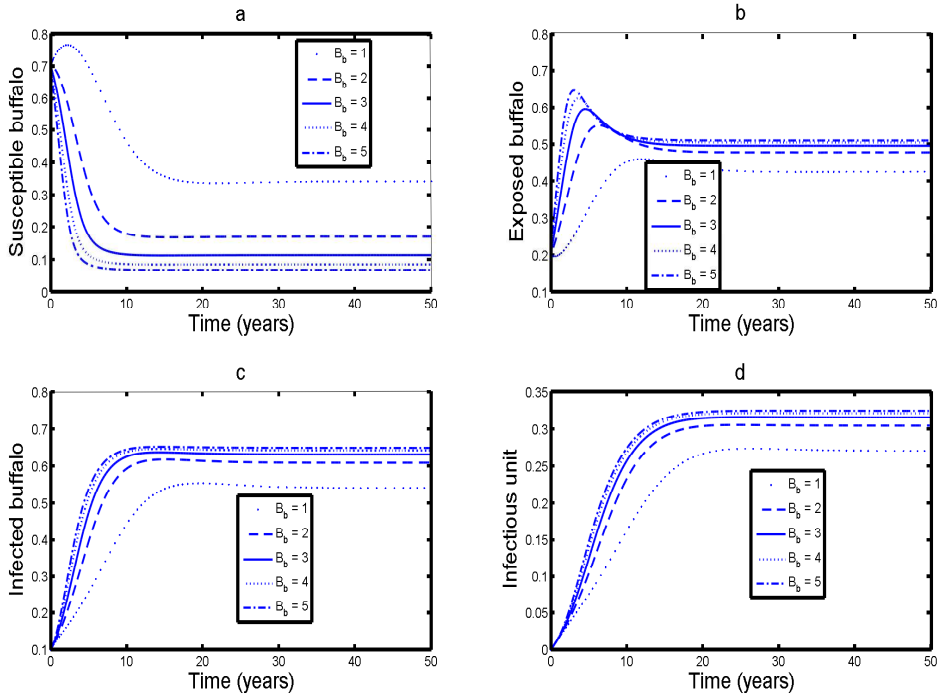

Figure 4: Graph showing the effect of increasing the between buffalo transmission rate B_b on the evolution of BTB infection in buffalo population only. $x_4 = 0.01, x_5 = 0.7, x_6 = 0.2, x_7 = 0.1, \Pi_2 = 0.23, \Psi_b = 0,\ M_b = 0.135,\ E_b = 0.2, \Phi_b = 0.3, \Sigma_b = 0.15, \Theta = 0.3.$

B_b was varied. The results show an increase in the proportion of the exposed and the infected buffalo in Figure 4 (b) and (c). The pathogen concentration in the environment as shown in Figure 4 (d), has also gone up. This observation agrees well with the observations made in [1], which show that buffalo are reservior hosts. This implies that buffalo stay with the infection in absence of external infection sources. Susceptible buffalo too decrease as B_b is being varied as it is indicated in Figure 4 (a).

Figure 5 investigates the effects of varying the between cattle transmission rate B_c on the evolution of BTB infection on buffalo population and the levels of the pathogens in the environment. The simulations show a very little effect on the epidemiology of BTB infection in buffalo population. An increase in B_c results in a very small increase in the proportion of the exposed and the infected buffalo as shown in Figure 5 (b) and (c). A small increase in the levels of the pathogen in

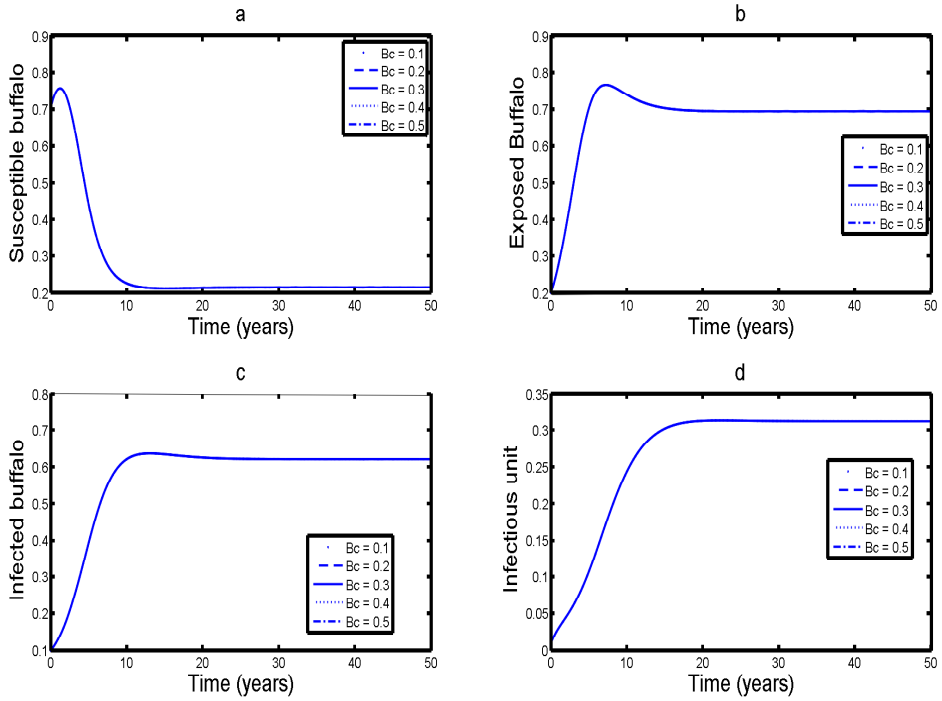

Figure 5: Graph showing the effect of increasing the between cattle transmission rate B_c on the evolution of BTB infection in buffalo population and the levels of pathogen in the environment. $x_1 = 0.7, x_2 = 0.2, x_3 = 0.1, x_4 = 0.01, x_5 = 0.7, x_6 = 0.2, x_7 = 0.1, \Pi_1 = 0.7, \Psi_c = 0.05,\ E_c = 0.1, \Phi_c = 0.3, \Sigma_c = 0.15, \Theta = 0.3,\ B_{cb} = 0.2,\ B_b = 2, \Sigma_b = 0.15, \Pi_2 = 0.33,\ B_{bc} = 0.2, \Psi_b = 0.5, \Phi_b = 0.3,\ M_b = 0.135,\ E_c = 0.2.$

the environment is also observed in Figure 5 (d). The simulations further show that all parameter values of B_c have the same effect on the dynamics of BTB infection in all classes of buffalo population and on the levels of pathogen in the environment. A significant impact of varying B_c is only observed when the birth rate of the buffalo population increases.

7. Discussion

A deterministic model for the transmission of bovine tuberculosis in cattle and buffalo populations was formulated and analysed. The reproduction numbers (R_{0c}, R_{0b}) for cattle only and buffalo only models were determined and used in qualitative analyses. The disease free equilibrium for both models were proven to be locally stable when their respective reproduction numbers were less than one.

Sensitivity analysis was carried on both reproductive numbers (R_{0c}, R_{0b}). The results indicated that Ψ_b, Ψ_b, Σ_c and Σ_b contribute positively towards the epidemiology of bovine tuberculosis in both buffalo and cattle populations, Thus the risk measure of the outbreak of BTB is increased when the infective rate due to contaminated environment and the shedding rate of infectious mycobacterium bovis into the environment are increased. The results also showed that both R_{0c} and R_{0b} are reduced if the decaying rate of the infectious unit increases.

The endemic equilibrium points of both sub-models were found to be locally stable. This ecologically implies that the disease remains in the community if there are no interventions.

The reproduction number R_{0f} for the full model was then determined. It was used to establish the global stability of the disease free equilibrium point when $R_{0f} < 1$. When $R_{0f} > 1$, the disease persists in both populations of cattle and buffalo. The reproduction number of the full model comprised of cross-infection parameters and contaminated environment parameter. This suggests that the transmission dynamics of bovine tuberculosis are enhanced by the cross-infection and contaminated environment parameters.

The numerical simulations also showed that the infection is only sustained in cattle and buffalo population when all transmission routes are involved. The disease has a minimal negative impact in cattle or buffalo when there is no cross-infection between the two populations. This suggests that the cross-infection route promotes the persistence of BTB infection in cattle and buffalo populations. The fact that buffalo populations are maintenance host of *M. bovis* pathogen, more devastating effect is observed on cattle population when all routes are involved. This ecologically implies that the disease can only be eradicated if the practices that promote the mixing of cattle and buffalo are discouraged.

Finally, it is necessary to mention that our mathematical model considers the evolution of bovine tuberculosis in cattle and buffalo populations. However, it is of paramount importance to enhance our understanding about the disease by incorporating factors like treatment, seasonality, and vertical transmission route.

The role of temperature on the survival of microbes in the environment and age classes of both cattle and buffalo populations should also be considered. These are the subjects of future work.

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Chapter 4

Modelling the spatial heterogeneity of bovine tuberculosis in buffalo

Modelling the spatial heterogeneity of bovine tuberculosis in buffalo.

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Abstract

A metapopulation model is developed to describe the spread of bovine tuberculosis (BTB) between two patches connected by movement. Disease reproduction numbers specific to the patches are given, considering scenarios of isolated and connected patches. The relationship of the reproduction numbers to disease spread and stability is discussed. The disease free equilibrium point is globally stable whenever the corresponding patch specific disease reproduction numbers are less than one and unstable otherwise. Patch specific endemic equilibrium points are unique, locally asymptotically stable, and only exist when the corresponding disease reproduction numbers are greater than one. The numerical results show that the disease is more explosive in patch 1 than in patch 2 if there is no movement. The severity of the disease in patch 2 is exacerbated when there is movement of susceptible and exposed buffalo from patch 1. Synchronous fluctuation of the population is observed when there is unrestricted movement of both susceptible and exposed buffalo across the patches. Our results suggest that movement to and from endemic areas should be minimised if the propensity of the disease spread is to be ameliorated. Otherwise, with continued movement, the infection may potentially worsen even in patches where disease prevalence is low.

Keywords: Metapopulation, Movement, Buffalo, Patch, Prevalence, Shedding.

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1. Introduction

African buffalo are the maintenance host for mycobacteriun bovis (*M. bovis*) in the endemically infected Kruger National Park (KNP). Studies carried out on bovine tuberculosis (BTB) incorporate both descriptive epidemiology and mathematical modelling approaches. Descriptive epidemiology focuses on issues of transmission modes [13, 14, 15, 16, 17, 18, 19], susceptible hosts to infection [4, 12], economic impact of the infection [16, 17, 23, 24, 25], the diagnostic tests used to detect the infection [14, 17, 20], global statistics of the infection [3, 22] and the risk factors that promote the spread of BTB infection to wildlife, livestock and human beings. Mathematical modelling approaches focus on converting the biological system into a mathematical structure that mimics the dynamics of the system of interest. Mathematical modelling is an important tool in analysing the epidemiological characteristics of infectious diseases and can provide useful control measures [23].

Various models have been formulated to explore different aspects of BTB infection. A non-linear transmission model consisting of susceptible and infected possum populations was developed by Barlow[24]. The model was used to explain bovine tuberculosis dynamics in a heterogeneous possum population, taking into account the patchy distribution of the infection. A deterministic/stochastic model was developed to explore the factors that drive the spread of BTB infection in possum populations and social contact was found to promote the spread of BTB infection. A spatial stochastic model was developed in [25] to assess fertility control as a means of controlling bovine tuberculosis in badgers. The results showed that fertility control alone can not completely eradicate BTB infection from badger population. The article [14] focussed on the impact of imported cattle into the herd on the dynamics of bovine tuberculosis. The results indicated the attainment of the unique endemic equilibrium by the model when the infected cattle are imported into the herd.

Many mathematical models see for instance [23, 24, 25] assume that space is homogeneous and investigations are confined to a population. In reality infectious diseases spread geographically over time. For example, West Nile virus, SARS and Swine Flu (PH1N1) spread from one country to another through movement of infected people [5, 6]. The same trend also occurs in BTB infection in buffalo populations in the Kruger National Park. The disease initially started at the Southern tip of the Kruger National park and has spread spread towards the Northern part of the park. When spatial homogeneity does not adequately accommodate the observed behavior or disease transmission, spatial modelling be-

comes necessary to account the spatially distinct individual characteristics. Some of these characteristics include differences in mixing behaviour as well as migration which requires a heterogeneous model [7]. Spatial structure and the spatial scale roughly operates in three major classes of heterogeneities namely: environment, which covers geography and space including climate and hydrological factors; contact, which involves contact patterns between hosts and pathogens including movement of hosts; and host/pathogen heterogeneity [8, 26]. Hence, spatial modelling has been widely applied to study disease behaviour to account for the degree of uniqueness in one patch relative to another.

We use metapopulation models that capture homogeneity within a patch and accounts for spatial heterogeneity through migration between patches. The approach uses ordinary differential equations [7, 8]. We seek to understand the effects of migration between patches on the spread of bovine tuberculosis, an aspect that has not been considered by previous studies on BTB. For instance, studies carried out in [23, 24, 25] based their investigations on one population. We consider an SEI metapopulation model for bovine tuberculosis describing disease spread between two patches connected by movement. In the bovine tuberculosis transmission dynamics, we assume that only the exposed are capable of moving from one patch to another. The patches considered in the model are assumed to differ in the level of disease prevalence, the epidemiological features existing in Kruger National park. The disease in the park is more prevalent in the southern part of the park where the infection initially begun. The transmission of *M. bovis* from the environment is affected by environmental factors such as temperature and relative humidity. This effect is represented by a constant parameter η_j for $1 \leq j \leq 2$ in our model. We also assume that the movement between populations depends on the density of the population and the distance separating the adjunct patches.

This manuscript is organised as follows: in section 2, we develop the mathematical model and give a comprehensive mathematical analysis. In section 3 we derive the equilibrium points and evaluate the patch specific disease threshold values for the case of isolated and non-isolated patches. In section 4, numerical results are given and discussed, and in section 5 we present concluding comments.

2. The mathematical model

We shall use two spatial patches of Kruger National Park. Patch 1 is the southern part of the park and patch 2 is the center of the park. The two regions of the park are separated by the river. The Figure 1 shows the map of Kruger National Park. The northern part of the park is ignored in our work because the prevalence

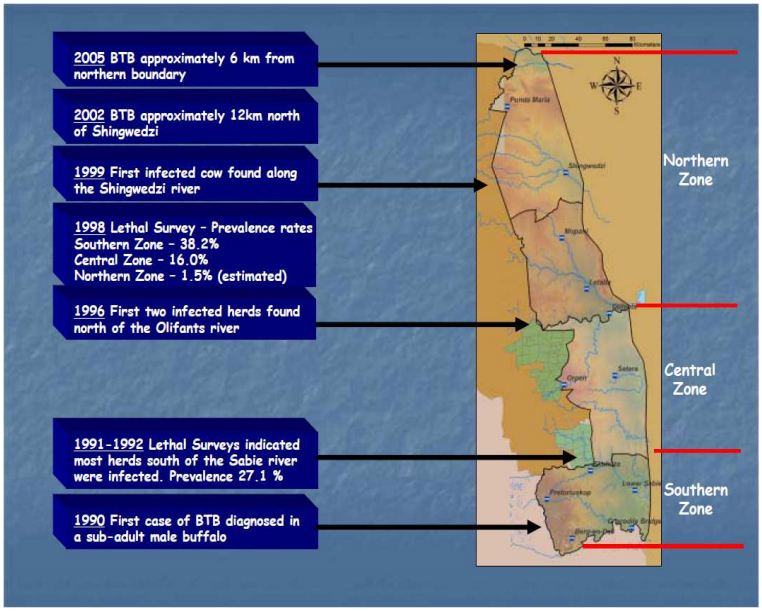

Figure 1: The map showing the spread trends of BTB infection in KNP from 1970 to 2003

of the BTB infection in the region is almost zero. The sub-population in a single patch denoted by N_j is compartmentalised into a susceptible population, B_{js}, those exposed to mycobacterium bovis (*M. bovis*), B_{je}, and those buffalo which are infected, B_{ji}, for $1 \leq j \leq 2$. Within a patch, the sub-populations are assumed to be mixing homogeneously. Our metapopulation model for bovine tuberculosis accounts for two movement patterns. Firstly, the movement of susceptible buffalo from one patch to the other at rate m_j. The rate m_1 is assumed to be greater than m_2. This is due to the availability of water sources in the central part of the park. It is assumed that no infection occurs en route when the susceptible individuals migrate. The recruitment of new susceptibles into patches occurs at rates π_1 and π_2 for patch 1 and patch 2 respectively. This recruitment is done via immigration and new births. Secondly, there is movement of the exposed buffalo from one patch to the other. These play a pivotal role in the metapopulation transmission modelling of bovine tuberculosis dynamics through the generation of the

infectious buffalo. The infectious buffalo take part in the spread of the infection through buffalo to buffalo transmission as well as shedding of *M. bovis* in the environment. The overall transmission dynamics of the general population are accounted for by the contribution from both sub-populations of the two patches. We assume that the infected buffalo population do not move from one patch to the other due to weakness induced by the disease. The susceptible population in patch one is reduced in size following contact from environment *M. bovis* at rate Ψ_1 as well as through buffalo-to buffalo contact at rate β_1. The infection with the contact with *M. bovis* in the environment occurs when the concentration of *M. bovis* is very high in the environment. The rate η_1 represent the probability of the survival time of the *M. bovis* in the environment in patch one. The higher the survival probability time, the more likely that environment transmission occurs. The exposed population in patch one progress to the infectious class at rate ϕ_1. The infected population in patch 1 suffers both natural and disease induced mortality at rates μ_1 and ϵ_1. The susceptible and exposed populations in patch one suffer only natural mortality at rate μ_1. The infected buffalo in the first patch shed pathogens into the environment at rate σ_1. This shedding rate in the patch depends on the level of the disease prevalence. The state variable U_1 represents the concentration of *M. bovis* in patch one. The parameter θ_1 is the decay rate of *M. bovis* in patch one. The susceptible population in patch two is reduced in size following contact from environment *M. bovis* at rate Ψ_2 as well as through buffalo-to- buffalo contact at rate β_2. The infection with the contact with *M. bovis* in the environment occurs when the concentration of *M. bovis* is very high in the environment. The rate η_2 represents the probability of the survival time of *M. bovis* in the environment in patch 1. The exposed population in patch two progresses to the infectious class at rate ϕ_2. The infectious population in patch two suffers both natural and disease induced mortality at rates μ_2 and ϵ_2. The susceptible and exposed populations in patch two suffer only natural mortality at rate μ_2. The infected buffalo in the second patch shed pathogens into the environment at rate σ_2. This shedding rate in the patch depends on the level of the disease prevalence. The state variable U_2 represents the concentration of *M. bovis* in patch two. The parameter θ_2 is the decay rate of *M. bovis* in patch two. The flow diagram of the model is given in Figure 2. The resulting system of

equations for the sub-population in patch 1 is given by

$$\begin{aligned}
\frac{dB_{1s}}{dt} &= \pi_1 + m_2 B_{2s} - \beta_1 B_{1s} B_{1i} - \eta_1 \Psi_1 U_1 B_{1s} - (\mu_1 + m_1) B_{1s}, \\
\frac{dB_{1e}}{dt} &= \beta_1 B_{1s} B_{1i} + \eta_1 \Psi_1 U_1 B_{1s} + \alpha_2 B_{2e} - (\mu_1 + \phi_1 + \alpha_1) B_{1e}, \\
\frac{dB_{1i}}{dt} &= \phi_1 B_{1e} - (\mu_1 + \epsilon_1) B_{1i}, \\
\frac{dU_1}{dt} &= \sigma_1 B_{1i} - \theta_1 U_1.
\end{aligned} \tag{1}$$

and for patch 2 is given by

$$\begin{aligned}
\frac{dB_{2s}}{dt} &= \pi_2 + m_1 B_{1s} - \beta_2 B_{2s} B_{2i} - \eta_2 \Psi_2 U_2 B_{2s} - (\mu_2 + m_2) B_{2s}, \\
\frac{dB_{2e}}{dt} &= \beta_2 B_{2s} B_{2i} + \eta_2 \Psi_2 U_2 B_{2s} + \alpha_1 B_{1e} - (\mu_2 + \phi_2 + \alpha_2) B_{2e}, \\
\frac{dB_{2i}}{dt} &= \phi_2 B_{2e} - (\mu_2 + \epsilon_2) B_{2i}, \\
\frac{dU_2}{dt} &= \sigma_2 B_{2i} - \theta_2 U_2.
\end{aligned} \tag{2}$$

The initial conditions of the model are such that $B_{1s} > 0, B_{1e} \geq 0, B_{1i} \geq 0$ and $U_1(0) \geq 0$ for the first patch and $B_{2s} > 0, B_{2e} \geq 0, B_{2i} \geq 0$ and $U_2(0) \geq 0$ for the second patch. The total population in each sub-population is $N_j = B_{js} + B_{je} + B_{ji}$ and the total population in both patches is given by $N = N_1 + N_2$. In the absence of movement i.e when $m_j = 0 = \alpha_j$ is given by

$$\frac{dN_j}{dt} = \pi_j - \mu_1 N_j - \epsilon_j B_{ji} \leq \pi_1 - \mu_1 N_1 \tag{3}$$

The solution to equation (3) is given by $N_j \leq \frac{\pi_j}{\mu_j} + (N_{0j} - \frac{\pi_j}{\mu_j}) e^{-\mu_j t}$, where N_{0j} are initial populations. The solution of all equations from the systems (1) and (2) remain non negative for all $t \geq 0$. The total populationis bounded by $\frac{\pi_j}{\mu_j}$. In the presence of animal movement the rate of change of the overall total population is given by

$$\frac{dN}{dt} = \pi_1 + \pi_2 - (\mu_1 N_1 + \mu_2 N_2).$$

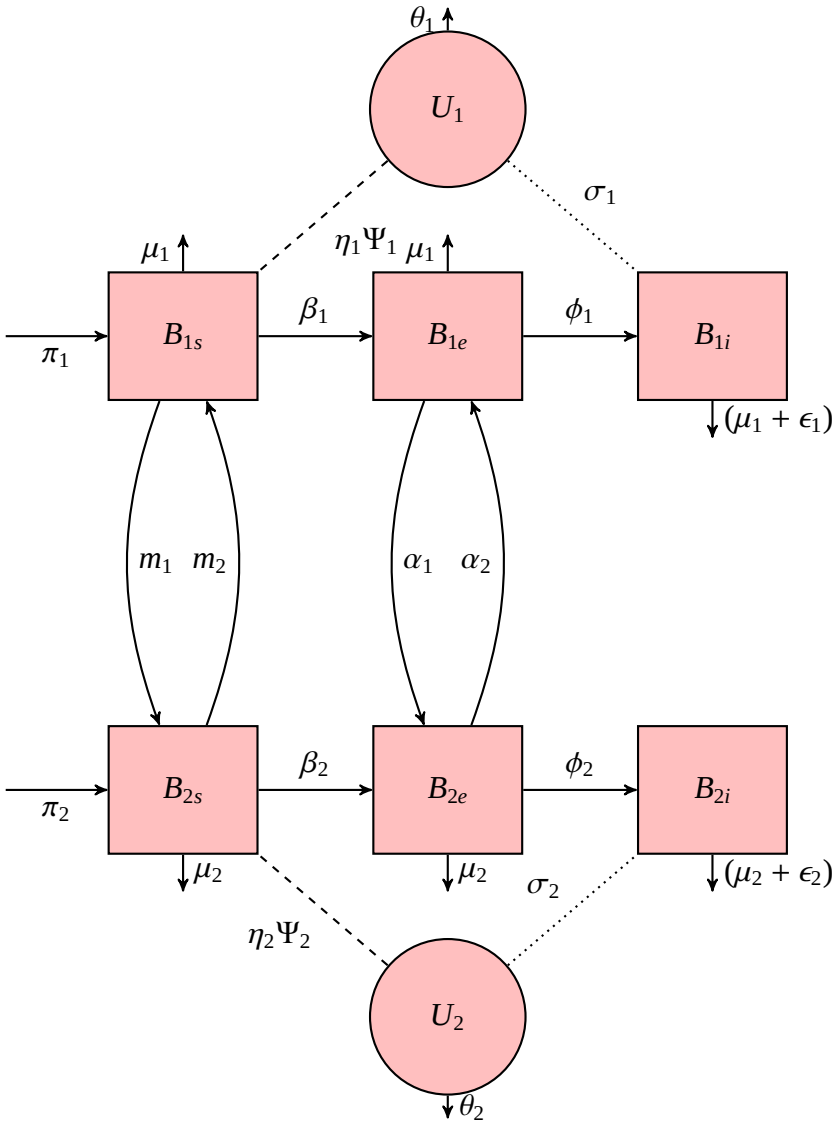

Figure 2: The flowchart of the transmission dynamics of bovine tuberculosis in two patched buffalo population . The dashed lines represent the environment transmission route. The dotted lines represent the shedding off of *M. bovis* in the environment.

If we let $\mu^* = \min\{\mu_1, \mu_2\}$, then it can be shown that

$$\limsup_{t\to\infty} \leq \frac{\pi_1 + \pi_2}{\mu^*}.$$

The phase space of the model is given by

$$\Omega := \left\{ (B_{1s}, B_{1e}, B_{1i}, U_1, B_{2s}, B_{2e}, B_{2i,U_2}) | B_{1s} + B_{1e} + B_{1i} + B_{2s} + B_{2e} + B_{2i} \leq \frac{\pi_1 + \pi_2}{\mu^*} \right\}$$

The solutions in Ω are all non negative and bounded. Hence the domain of the biological importance is positively invariant and attracting. Therefore all solutions start and remain in Ω. The guide to the proof of positivity and boundedness of solutions can be found in [2, 9, 10, 11].

3. Equilibrium points

Our model has four equilibrium points given by

$$E_0 = (B_{1s}^*, 0, 0, 0, B_{2s}^*, 0, 0, 0), \tag{4}$$
$$E_1 = (B_{1s}^*, B_{1e}^*, B_{1i}^*, U_1^*, B_{2s}^*, 0, 0, 0), \tag{5}$$
$$E_2 = (B_{1s}^*, 0, 0, 0, B_{2s}^*, B_{2e}^*, B_{2i}^*, U_2^*), \tag{6}$$
$$E_3 = (B_{1s}^*, B_{1e}^*, B_{1i}^*, U_1^*, B_{2s}^*, B_{2e}^*, B_{2i}^*, U_2^*), \tag{7}$$

of which E_0 is the disease free equilibrium point. The equilibrium points E_1 and E_2 represent the first and second boundary endemic equilibria, whereas E_3 represents the interior endemic equilibrium point in the domain Ω.

The disease free equilibrium point E_0 in both patches is obtained from both sub-models (1) and (2). At this equilibrium point we assume that there is no *M. bovis* in both environments, and that there are no infected buffalo in both patches. Therefore, the sub-models (1) and (2) reduce to

$$\frac{dB_{1s}}{dt} = \pi_1 + m_2 B_{2s} - (m_1 + \mu_1) B_{1s}, \tag{8}$$
$$\frac{dB_{2s}}{dt} = \pi_2 + m_1 B_{1s} - (m_2 + \mu_2) B_{2s}. \tag{9}$$

Equating the right hand of equations (8-9) to zero and solving for the equilibrium points we obtain

$$B_{1s}^* = \frac{\pi_1(m_2 + \mu_2) + m_2\pi_2}{m_2\mu_1 + \mu_2 m_1 + \mu_2\mu_1} \quad B_{2s}^* = \frac{\pi_2(m_1 + \mu_1) + m_1\pi_1}{m_1\mu_2 + \mu_1 m_2 + \mu_2\mu_1} \tag{10}$$

3.1. The Reproduction number

The basic reproduction number for the model is obtained using the next generation matrix method described in [27]. If there is no movement of animals, the patch specific basic reproduction numbers are

$$R_{01} = \frac{\pi_1\phi_1(\beta_1\theta_1 + \eta_1\sigma_1\Psi_1)}{\mu_1\theta_1(\epsilon_1 + \mu_1)(\mu_1 + \phi_1)}, \quad \text{and} \quad R_{02} = \frac{\pi_2\phi_2(\beta_2\theta_2 + \eta_2\sigma_2\Psi_2)}{\mu_2\theta_2(\epsilon_2 + \mu_2)(\mu_2 + \phi_2)} \tag{11}$$

for the first and second patch respectively. The values R_{01} and R_{02} apply to completely isolated patches. If the infection exists in a single patch which is linked to another patch through movement, the phenomenon related to the movement of buffalo should be factored into the disease threshold. When the patches are connected by movement, the patch specific basic reproduction numbers are given by

$$R_{01m} = \frac{(\pi_1(\mu_1 + m_2) + m_2\pi_2)Q_1}{m_2\mu_1 + \mu_2 m_1 + \mu_2\mu_1}, \quad \text{and} \quad R_{02m} = \frac{(\pi_2(\mu_1 + m_1) + m_1\pi_2)Q_2}{m_1\mu_2 + \mu_1 m_2 + \mu_2\mu_1}.$$

where

$$\begin{aligned} Q_1 &= \phi_1\theta_1(\beta_1\theta_1 + \eta_1\sigma_1\Psi_1)(\epsilon_1 + \mu_1)(\mu_1 + \phi_1 + \alpha_1), \\ Q_2 &= \phi_2\theta_2(\beta_2\theta_2 + \eta_2\sigma_2\Psi_2)(\epsilon_2 + \mu_2)(\mu_2 + \phi_2 + \alpha_2). \end{aligned}$$

The overall model reproduction number is given by

$$R_0 = \frac{1}{2}m_{44} + \frac{1}{2}m_{11} + \frac{1}{2}\sqrt{m_{44}^2 - 2m_{44}m_{11} + m_{11} + 4m_{41}m_{14}} \tag{12}$$

where

$$
\begin{aligned}
m_{11} &= \frac{(\pi_1(\mu_2+m_2)+\pi_2 m_2)\phi_1(\mu_2+\phi_2+\alpha_2)(\theta_1\beta_1+\eta_1\Psi_1\sigma_1)}{\theta_1(\mu_2\mu_1+m_2\mu_1+\mu_2 m_1)(\mu_1+\epsilon_1)(\mu_2+\phi_2)(\mu_1+\phi_1)},\\
m_{12} &= \frac{(\pi_1(\mu_2+m_2)+\pi_2 m_2)(\theta_1\beta_1+\eta_1\Psi_1\sigma_1)}{\theta_1(\mu_1+\epsilon_1)(\mu_2\mu_1+m_2\mu_1+\mu_2 m_1)},\\
m_{13} &= \frac{\eta_1\Psi_1(\pi_1(\mu_2+m_2)+\pi_2 m_2)}{\theta_1(\mu_2\mu_1+m_2\mu_1+\mu_2 m_1)},\\
m_{14} &= \frac{(\pi_1(\mu_2+m_2)+\pi_2 m_2)\phi_1\alpha_2(\theta_1\beta_1+\eta_1\Psi_1\sigma_1)}{\theta_1(\mu_1+\epsilon_1)(\mu_2+\phi_2)(\mu_1+\phi_1)(\mu_2\mu_1+m_2\mu_1+\mu_2 m_1)},\\
m_{41} &= \frac{(\pi_2(\mu_1+m_1)+m_1\pi_1)\phi_2\alpha_1(\theta_2\beta_2+\eta_2\Psi_2\sigma_2)}{\theta_2(\mu_2+\phi_2)(\mu_1+\phi_1)(\mu_2\mu_1+m_2\mu_1+\mu_2 m_1)},\\
m_{44} &= \frac{(\pi_2(\mu_1+m_1)+m_1\pi_1)\phi_2(\mu_1+\phi_1+\alpha_1)(\theta_2\beta_2+\eta_2\Psi_2\sigma_2)}{\theta_2(\mu_2+\epsilon_2)(\mu_2+\phi_2)(\mu_1+\phi_1)(\mu_2\mu_1+m_2\mu_1+\mu_2 m_1)},\\
m_{45} &= \frac{(\pi_2(\mu_1+m_1)+m_1\pi_1)(\theta_2\beta_2+\eta_2\Psi_2\sigma_2)}{\theta_2(\mu_2+\epsilon_2)(\mu_2\mu_1+m_2\mu_1+\mu_2 m_1)},\\
m_{46} &= \frac{(\pi_2(\mu_1+m_1)+m_1\pi_1)\eta_2\Psi_2}{\theta_2(\mu_2\mu_1+m_2\mu_1+\mu_2 m_1)}.
\end{aligned}
$$

Note that the movement aspect of buffalo from one patch to another increases the basic reproduction number. This may drive the establishment of the infection in both patches or extinction of the infection in one of the patches.

3.1.1. Global stability of the disease free equilibrium E_0

To prove the global asymptotic stability of the disease free equilibrium point, we use an approach used in [30] to rewrite the sub-models 1 and 2 in the form

$$
\begin{cases}
\dfrac{dX}{dt} &= F(X,Y),\\
\dfrac{dY}{dt} &= G(X,Y), \quad G(X,\mathbf{0})=0,
\end{cases}
$$

where $X=(B_{1s},B_{2s})^T$ and $Y=(B_{1e},B_{1i},U_1,B_{2e},B_{2i},U_2)^T$ with $X\in\mathfrak{R}_+^2$ denoting the number of susceptible buffalo in both patches and $Y\in\mathfrak{R}_+^6$ denoting the number of exposed buffalo, infected buffalo and contaminated environment in both patches.

The disease-free equilibrium is now denoted by $E_0=(X_0,\mathbf{0})$ where $\left(X_0=\dfrac{\pi_1}{\mu_1},\dfrac{\pi_2}{mu_2}\right)$ and $\mathbf{0}$ is a zero vector. The following conditions should be satisfied to guarantee global asymptotic stability:

- $\mathbf{H_1}$: For $\frac{dX}{dt} = F(X_0, \mathbf{0})$, X_0 is globally asymptotically stable.
- $\mathbf{H_2}$: $G(X, Y) = AY - \tilde{G}(X, Y)$, $\tilde{G}(X, Y) \geq 0$ for $(X, Y) \in \Omega$, where $A = D_Y(G(X_0, \mathbf{0}))$ is an M-matrix.

If sub-models (1) and (2) satisfy the conditions $\mathbf{H_1}$ and $\mathbf{H_2}$, then the following result holds.

Theorem 1. *The disease free equilibrium point, E_0, is globally asymptotically stable if $R_0 < 1$ and unstable otherwise.*

Proof. Consider

$$F(X, 0) = (\pi_1 - (\mu_1 + m_1)B_{1s}, \pi_2 - (\mu_2 + m_2)B_{2s}), \quad G(X, Y) = AY - \tilde{G}(X, Y)$$

where

$$A = \begin{pmatrix} -R & \frac{\beta_1\pi_1}{\mu_1} & S & \alpha_2 & 0 & 0 \\ \phi_1 & -(\mu_1 + m_1) & 0 & 0 & 0 & 0 \\ 0 & \sigma_1 & -\theta_1 & 0 & 0 & 0 \\ \alpha_2 & 0 & 0 & -(\mu_2 + m_2) & \frac{\beta_2\pi_2}{\mu_2} & 0 \\ 0 & 0 & 0 & \phi_2 & -(\mu_2 + \epsilon_2) & 0 \\ 0 & 0 & 0 & 0 & \sigma_2 & -\phi_2 \end{pmatrix},$$

where

$$R = (\mu_1 + \phi_1 + m_1), \quad S = \frac{\Psi_1\pi_1\eta_1}{\mu_1} \quad T = \frac{\Psi_2\pi_2\eta_2}{\mu_2}.$$

and

$$\tilde{G}(X, Y) = \begin{pmatrix} \beta_1 B_{1i} + \eta_1\Psi_1 U_1 \\ 0 \\ 0 \\ \beta_2 B_{2i} + \eta_2\Psi_2 U_2 \\ 0 \\ 0 \end{pmatrix}.$$

The condition $\mathbf{H_1}$ is satisfied when X is a globally asymptotically stable equilibrium point of the equations

$$\frac{dB_{1s}}{dt} = \pi_1 - (\mu_1 + m_1), \quad \frac{dB_{2s}}{dt} = \pi_2 - \mu_2 + m_2 B_{2s}. \tag{13}$$

Solving (13) we obtain

$$B_{1s}(t) = \frac{\pi_1}{\mu_1} - B_{1s}(t)e^{-(\mu_1+m_1)t}, \quad B_{2s}(t) = \frac{\pi_2}{\mu_2} - B_{2s}(t)e^{-(\mu_2+m_2)t}.$$

Taking limits as $t \to \infty$ we obtain,

$$\lim_{t\to\infty} B_{1s}(t) = \frac{\pi_1}{\mu_1}, \quad \lim_{t\to\infty} B_{2s}(t) = \frac{\pi_2}{\mu_2}.$$

This suggests that, independent of the initial conditions, the solutions of the equations (13) converge to X_0. Thus, X_0 is a globally asymptotically equilibrium point of (13). To prove condition $\mathbf{H_2}$, we observe that $\tilde{G}(X, Y) \geq 0$, so this completes the proof of both conditions. □

3.2. Patch 1 endemic equilibrium point E_1 and its stability

The sub-model (1) has a unique boundary patch one endemic equilibrium point E_1 in Ω whenever $R_{01m} > 1$. The statement implies that bovine tuberculosis persists in the first sub-population but dies in the second sub-population. The components of the endemic equilibrium point are:

$$U_1^* = \frac{\sigma_1 B_{1i}^*}{\theta_1}, \quad B_{1e}^* = \frac{(\mu_1 + \epsilon_1)B_{1i}^*}{\phi_1}$$
$$B_{1i}^* = \frac{1}{F}\left(\frac{1}{C}\left(\frac{W}{D} + m_2 m_1\right)(m_1 + \mu_1)(R_{01m} - 1)\right)$$

where

$$W = (m_2\mu_1 + \mu_2 m_1 + \mu_2\mu_1)(\pi_1(\mu_2 + m_2) + m_2\pi_2), \quad C = (\mu_2 + m_2), \quad D = \pi_1(m_2 + \mu_2) + m_2\pi_2$$
$$F = \theta_1(\mu_1 + \phi_1 + \alpha_1)(\mu_1 + \epsilon_1).$$

Therefore, when $R_{01m} > 1$ we have a unique disease persistent equilibrium localised in the first patch.

Theorem 2. *If $R_{01m} > 1$, the endemic equilibrium E_1 of the model (1) is locally asymptotically stable in Ω.*

Proof. In order to explore the local stability of the endemic equilibrium point E_1, we evaluate the Jacobian $J(B_{1s}^*, B_{1e}^*, B_{1i}^*, U_1^*)$ at the endemic equilibrium point and we get

$$J(E_1) = \begin{pmatrix} -D_1 & 0 & -\beta_1 B_{1s}^* & -\eta_1 \Psi_1 B_{1s}^* \\ D_2 & -(\mu_1 + \phi_1 + \alpha_1) & \beta_1 B_{1s}^* & \eta_1 \Psi_1 B_{1s} \\ 0 & \phi_1 & -(\mu_1 + \epsilon_1) & 0 \\ 0 & 0 & \sigma_1 & -\theta_1 \end{pmatrix}.$$

$$D_1 = -\beta_1 B_{1i}^* - \eta_1 \Psi_1 U_1^* - \mu_1 - m_1$$
$$D_2 = \beta_1 B_{1s}^* + \eta_1 \Psi_1 U_1^*$$

After doing the row operation on the Jacobian matrix we obtain

$$\begin{pmatrix} -C_1 & 0 & -C_2 & -C_3 \\ 0 & -C_1 C_5 & C_1 C_2 - C_2 C_4 & C_1 C_3 - C_3 C_4 \\ 0 & 0 & P_1 & P_2 \\ 0 & 0 & 0 & -\theta_1 P_1 + \sigma_1 P_2 \end{pmatrix},$$

where

$$P1 = \phi_1(C_1 C_2 - C_2 C_4) - C_1 C_5 C_6; \quad P_2 = \phi_1(C_1 C_3 - C_3 C_4).$$

The eigenvalues of $J(E_1)$ are calculated using $Det(J(E_1 - \lambda I_4)) = 0$

$$Det\begin{pmatrix} -C_1 - \lambda & 0 & -C_2 & -C_3 \\ 0 & -C_1 C_5 - \lambda & C_1 C_2 - C_2 C_4 & C_1 C_3 - C_3 C_4 \\ 0 & 0 & P_1 - \lambda & P_2 \\ 0 & 0 & 0 & -\theta_1 P_1 + \sigma_1 P_2 - \lambda \end{pmatrix} = 0.$$

$$C_1 = \beta_1 B_{1i}^* + \eta_1 \Psi_1 U_1^* + \mu_1 + m_1; \quad C_2 = \beta_1 B_{1s}^*; \quad C_3 = \eta_1 \Psi_1 B_{1s}^*;$$
$$C_4 = \beta_1 B_{1i}^* + \eta_1 \Psi_1 U_1^*; \quad C_5 = \mu_1 + \phi_1 + \alpha_1; \quad C_6 = \mu_1 + \epsilon_1.$$

The first two eigenvalues of the Jacobian matrix are $\lambda_1 = -C_1$ and $\lambda_2 = -C_1 C_5$. The other two eigenvalues are

$$\lambda_3 = \phi_1 C_1 C_2 - \phi_1 C_2 C_4 - C_1 C_5 C_6; \quad \lambda_4 = \theta_1 P_1 + \sigma_1 P_2.$$

The eigenvalues $\lambda_{3,4}$ are both negative when $\phi_1 C_1 C_2 < \theta_1 C_2 C_3 + C_1 C_5 C_6$ and $\theta_1 \phi_1 C_2 C_3 + \sigma_1 \phi_1 C_1 C_3 < \theta_1 \phi_1 C_2 C_3 + \theta_1 C_1 C_5 C_6 + \sigma_1 \phi_1 C_3 C_4$ hold. This implies that all four eigenvalues of our Jacobian matrix are negative, which proves the local stability of endemic equilibrium point E_1. □

3.3. Endemic equilibrium point E_2 and its stability

The sub-model (2) has a unique boundary endemic equilibrium point E_1 in Ω whenever $R_{02m} > 1$. The statement implies that bovine tuberculosis persists in the second sub-population but dies in the first sub-population. The process to establish the existence of E_2 and its components is same as in (3.2). We conclude:

Theorem 3. *If $R_{02m} > 1$, the endemic equilibrium E_2 of the model (2) is locally asymptotically stable in Ω.*

Proof. The proof for Theorem (3) follows the same procedure as outlined in (3.2). □

3.4. Existence of interior endemic equilibrium point E_3

We consider two scenarios to establish the existence of the interior endemic equilibrium point. We first assume that $m_1 = m_2 = 0$. The interior endemic equilibrium point can be expressed in closed form so we express our endemic equilibrium point denoted by $E_{31} = \left(B^*_{1s}, B^*_{1e}, B^*_{1i}, U^*_1, B^*_{2s}, B^*_{2e}, B^*_{2i}, U^*_2\right)$ in terms of the forces of infection $(\lambda^*_1, \lambda^*_2)$ using the approach in [29] as follows:

$$B^*_{1s} = \frac{\pi_1}{\lambda^*_1 + \mu_1}, \quad B^*_{2s} = \frac{\pi_2}{\lambda^*_2 + \mu_2}, \tag{14}$$

$$B^*_{1e} = \frac{\pi_1\lambda^*_1}{(\lambda^*_1 + \mu_1)(\mu_1 + \phi_1 + \alpha_1)} + \frac{\alpha_2 B^*_{2e}}{\mu_1 + \phi_1 + \alpha_1}, \tag{15}$$

$$B^*_{1i} = \frac{s\pi_1\lambda^*_1}{rb(\lambda^*_1 + \mu_1)} + \frac{s\alpha_2\pi_2\lambda^*_2}{rab(\lambda^*_2 + \mu_2)}, \quad U^*_1 = \frac{ws\pi_1\lambda^*_1}{rb(\lambda^*_1 + \mu_1)} + \frac{ws\alpha_2\pi_2\lambda^*_2}{rab(\lambda^*_2 + \mu_2)}, \tag{16}$$

$$B^*_{2e} = \frac{\pi_2\lambda^*_2}{(\lambda^*_2 + \mu_2)(\mu_2 + \phi_2 + \alpha_2)} + \frac{\alpha_1 B^*_{1e}}{\mu_2 + \phi_2 + \alpha_2}, \tag{17}$$

$$B^*_{2i} = \frac{d\pi_2\lambda^*_2}{ac(\lambda^*_2 + \mu_2)} + \frac{d\alpha_1\pi_1\lambda^*_1}{abc(\lambda^*_1 + \mu_1)}, \quad U^*_2 = \frac{ed\pi_2\lambda^*_2}{ac(\lambda^*_2 + \mu_2)} + \frac{ed\alpha_1\pi_1\lambda^*_1}{abc(\lambda^*_1 + \mu_1)}, \tag{18}$$

where

$$a = \mu_2 + \phi_2 + \alpha_2; \quad b = \mu_1 + \phi_1 + \alpha_1; \quad c = 1 - \frac{\alpha_1\alpha_2}{ab}; \quad d = \frac{\phi_2}{\mu_2 + \epsilon_2}; \quad e = \frac{\sigma_2}{\theta_2}.$$

Substituting the equations (16) and (18) into the forces of infection we obtain

$$\lambda_1 = \frac{\nu_{11}\lambda^*_1}{\lambda^*_1 + \mu_1} + \frac{\nu_{21}\lambda^*_2}{\lambda^*_2 + \mu_2}; \quad \lambda_2 = \frac{n_{11}\lambda^*_2}{\lambda^*_2 + \mu_2} + \frac{n_{12}\lambda^*_1}{\lambda^*_1 + \mu_1},$$

where

$$f = \frac{\beta_2 d\pi_2}{ac}; \quad g = \frac{\beta_2 d\alpha_1\pi_1}{abc}; \quad h = \frac{\eta_2\Psi_2 ed\pi_2}{ac}; \quad k = \frac{\eta_2\Psi_2 ed\alpha_1\pi_1}{abc}; \quad n_{11} = f + h;$$

$$n_{12} = g + k \quad r = 1 - \frac{\alpha_2\alpha_1}{ab}; \quad s = \frac{\phi_1}{\mu_1 + \epsilon_1}; \quad w = \frac{\sigma_1}{\theta_1}; \quad y_1 = \frac{\beta_1 s\pi_1}{rb}; \quad y_2 = \frac{\beta_1 s\alpha_2\pi_2}{rab};$$

$$y_3 = \frac{\eta_1\Psi_1 ws\pi_1}{rb}; \quad y_4 = \frac{\eta_1\Psi_1 ws\alpha_2\pi_2}{rab}; \quad v_{11} = y_1 + y_3; \quad v_{21} = y_2 + y_4.$$

The equilibrium points of sub-model (1) and sub-model (2) can be obtained by finding the fixed points of equations $\vartheta(\lambda_1, \lambda_2) = \begin{pmatrix} \vartheta_1(\lambda_1, \lambda_2) \\ \vartheta_2(\lambda_1, \lambda_2) \end{pmatrix}$ and are given by

$$\vartheta_1(\lambda_1, \lambda_2) = \frac{v_{11}\lambda_1}{\lambda_1 + \mu_1} + \frac{v_{21}\lambda_2}{\lambda_2 + \mu_2} \tag{19}$$

$$\vartheta_2(\lambda_1, \lambda_2) = \frac{n_{11}\lambda_2}{\lambda_2 + \mu_2} + \frac{n_{12}\lambda_1}{\lambda_1 + \mu_1} \tag{20}$$

Clearly, $(\lambda_1^*, \lambda_2^*) = (0, 0)$ is a fixed point of equations (19)-(20) which corresponds to the disease free equilibrium point.

Theorem 4. *There exists a unique fixed point* $\left(\lambda_1^*, \lambda_2^2\right), \lambda_1^* > 0, \lambda_2^* > 0$ *satisfying*

$$\vartheta(\lambda_1, \lambda_2) = \begin{pmatrix} \lambda_1^* \\ \lambda_2^* \end{pmatrix}$$

corresponding to the interior endemic equilibrium point E_{31}.

Proof. For each $\lambda_2 > 0$ we consider the following real valued function depending on λ_1:

$$\vartheta_1^{\lambda_2}(\lambda_1) = \frac{v_{11}\lambda_1}{\lambda_1 + \mu_1} + \frac{v_{21}\lambda_2}{\lambda_2 + \mu_2}$$

Clearly,

$$\vartheta_1^{\lambda_2}(0) = \frac{v_{21}\lambda_2}{\lambda_2 + \mu_2} > 0,$$

and

$$\lim_{\lambda_1 \to \infty} \vartheta_1^{\lambda_2}(\lambda_1) = v_{11} < \infty.$$

Thus $0 < \vartheta_1^{\lambda_2}(\lambda_1) < \infty$, which implies that the real valued function $\vartheta_1^{\lambda_2}(\lambda_1)$ is bounded for every fixed $\lambda_2 > 0$.

The first derivative of $\vartheta_1^{\lambda_2}(\lambda_1)$ with respect to λ_1 is given by

$$\frac{\partial \vartheta_1^{\lambda_2}(\lambda_1)}{\partial \lambda_1} = \frac{\nu_{11}\mu_1}{(\lambda_1+\mu_1)^2} > 0, \tag{21}$$

and the second derivative $\vartheta_1^{\lambda_2}(\lambda_1)$ with respect to λ_1 is given by

$$\frac{\partial^2 \vartheta_1^{\lambda_2}(\lambda_1)}{\partial \lambda_1^2} = -\frac{2\nu_{11}\mu_1}{(\lambda_1+\mu_1)^3} < 0. \tag{22}$$

Since $\frac{\partial \vartheta_1^{\lambda_2}(\lambda_1)}{\partial \lambda_1} > 0$ and $\frac{\partial^2 \vartheta_1^{\lambda_2}(\lambda_1)}{\partial \lambda_1^2} < 0$, the function $\vartheta_1^{\lambda_2}(\lambda_1)$ is an increasing concave down function which has no change in convexity in the bounded domain. This implies that there exists a unique point $\lambda_1^* > 0$ satisfying $\vartheta_1^{\lambda_2}(\lambda_1^*) = \lambda_1^*$

For $\lambda_1 > 0$ we consider the following real valued function depending on λ_2 :

$$\vartheta_2^{\lambda_1}(\lambda_2) = \frac{n_{11}\lambda_2}{\lambda_2+\mu_2} + \frac{n_{12}\lambda_1}{\lambda_1+\mu_1}$$

Now

$$\vartheta_2^{\lambda_1}(0) = \frac{n_{12}\lambda_1}{\lambda_1+\mu_1} > 0,$$

$$\lim_{\lambda_2 \to \infty} \vartheta_1^{\lambda_1}(\lambda_2) = n_{11} < \infty.$$

Thus $0 < \vartheta_2^{\lambda_1}(\lambda_2) < \infty$, which implies that the function $\vartheta_2^{\lambda_1}(\lambda_2)$ is bounded for every fixed $\lambda_1 > 0$. The first derivative of $\vartheta_1^{\lambda_1}(\lambda_2)$ with respect to λ_2 is given by

$$\frac{\partial \vartheta_1^{\lambda_1}(\lambda_2)}{\partial \lambda_2} = \frac{n_{11}\mu_2}{(\lambda_2+\mu_2)^2} > 0, \tag{23}$$

and the second derivative $\vartheta_1^{\lambda_1}(\lambda_2)$ with respect to λ_1 is given by

$$\frac{\partial^2 \vartheta_1^{\lambda_1}(\lambda_2)}{\partial \lambda_2^2} = -\frac{2n_{11}\mu_2}{(\lambda_2+\mu_2)^3} < 0. \tag{24}$$

Since $\frac{\partial \vartheta_1^{\lambda_1}(\lambda_2)}{\partial \lambda_2} > 0$ and $\frac{\partial^2 \vartheta_1^{\lambda_1}(\lambda_2)}{\partial \lambda_2^2} < 0$, the function $\vartheta_1^{\lambda_1}(\lambda_2)$ is an increasing concave down function which has no change in convexity in the bounded domain. This implies that there exists a unique point $\lambda_2^* > 0$ satisfying $\vartheta_1^{\lambda_1}(\lambda_2^*) = \lambda_2^*$. Hence, we have a unique fixed point $(\lambda_1^*, \lambda_2^*)$ corresponding to the endemic equilibrium point. □

3.5. Stability analysis of equilibrium points

The Jacobian matrix of the equations (19)-(20) evaluated at the equilibrium point $(0, 0)$ is given by

$$J(0,0) = \begin{pmatrix} \frac{v_{11}}{\mu_1} & \frac{v_{21}}{\mu_2} \\ \\ \frac{n_{12}}{\mu_1} & \frac{n_{11}}{\mu_2} \end{pmatrix},$$

whose characteristics equation is

$$\lambda^2 - \left(\frac{n_{11}}{\mu_2} + \frac{v_{11}}{\mu_1}\right)\lambda + \frac{v_{11}n_{11}}{\mu_1\mu_2} - \frac{n_{12}v_{21}}{\mu_1\mu_2} \tag{25}$$

The solutions for equation (25) are

$$\lambda_1 = \left(\frac{n_{11}}{\mu_2} + \frac{v_{11}}{\mu_1}\right) + \sqrt{\frac{1}{4}\left(\frac{n_{11}}{\mu_2} - \frac{v_{11}}{\mu_1}\right)^2 + \frac{n_{12}v_{21}}{\mu_1\mu_2}}; \lambda_2 = \left(\frac{n_{11}}{\mu_2} + \frac{v_{11}}{\mu_1}\right) - \sqrt{\frac{1}{4}\left(\frac{n_{11}}{\mu_2} - \frac{v_{11}}{\mu_1}\right)^2 + \frac{n_{12}v_{21}}{\mu_1\mu_2}}$$

where

$$v_{11} = \frac{\phi_1\pi_1(\mu_2 + \phi_2 + \alpha_2)(\theta_1\beta_1 + \eta_1\Psi_1\sigma_1)}{\mu_1\theta_1(\mu_1 + \epsilon_1)(\mu_2 + \phi_2)(\mu_1 + \phi_1)}; \quad n_{11} = \frac{\phi_2\pi_2(\mu_1 + \phi_1 + \alpha_1)(\theta_2\beta_2 + \eta_2\Psi_2\sigma_2)}{\mu_2\theta_2(\mu_2 + \epsilon_2)(\mu_2 + \phi_2)(\mu_1 + \phi_1)}, \tag{26}$$

$$n_{12} = \frac{\alpha_1\pi_1\phi_2(\theta_2\beta_2 + \eta_2\Psi_2\sigma_2)}{\theta_2(\mu_2 + \epsilon_2)(\mu_2 + \phi_2)(\mu_1 + \phi_1)}; \quad v_{21} = \frac{\alpha_2\pi_2\phi_1(\theta_1\beta_1 + \eta_1\Psi_1\sigma_1)}{\theta_1(\mu_1 + \epsilon_1)(\mu_2 + \phi_2)(\mu_1 + \phi_1)}. \tag{27}$$

For stability, we need $max\{|\lambda_1|, |\lambda_2|\} < 1$. Thus the equilibrium point $(0, 0)$ is stable when the dominant eigenvalue $\lambda_1 < 1$.

Remark 1.

(i) We observe that when $\alpha_1 = 0 = \alpha_2$ the effect of n_{12} and v_{21} in equations (30)-(31) disappears. This means that the disease dynamics in both patches are driven by the factors within the specific patches. The analysis further shows that v_{11} and n_{11} in equations (26)-(27) correspond to the patch 1 and patch 2 specific reproduction numbers.

(ii) The contribution of the movement is observed when the movement of the exposed buffalo is allowed between patches. The equations (26)-(27) show the role of movement in the transmission dynamics of BTB infection in both patches.

The Jacobian of $\vartheta(\lambda_1, \lambda_2)$ evaluated at the unique fixed point $\left(\lambda_1^*, \lambda_2^*\right)$ is given as

$$J(\lambda_1^*, \lambda_2^*) = \begin{pmatrix} \frac{\partial \vartheta_1}{\partial \lambda_1}(\lambda_1, \lambda_2)|_(\lambda_1^*, \lambda_2^*) & \frac{\partial \vartheta_1}{\partial \lambda_2}(\lambda_1, \lambda_2)|_(\lambda_1^*, \lambda_2^*) \\ \\ \frac{\partial \vartheta_2}{\partial \lambda_1}(\lambda_1, \lambda_2)|_(\lambda_1^*, \lambda_2^*) & \frac{\partial \vartheta_2}{\partial \lambda_2}(\lambda_1, \lambda_2)|_(\lambda_1^*, \lambda_2^*) \end{pmatrix},$$

where

$$\frac{\partial \vartheta_1}{\partial \lambda_1}(\lambda_1, \lambda_2|_(\lambda_1^*, \lambda_2^*) = \left(\frac{\nu_{11}\mu_1}{\lambda_1^* + \mu_1}\right)^2; \quad \frac{\partial \vartheta_1}{\partial \lambda_2}(\lambda_1, \lambda_2|_(\lambda_1^*, \lambda_2^*) = \left(\frac{\nu_{12}\mu_2}{\lambda_2^* + \mu_2}\right)^2; \qquad (28)$$

$$\frac{\partial \vartheta_2}{\partial \lambda_1}(\lambda_1, \lambda_2|_(\lambda_1^*, \lambda_2^*) = \left(\frac{n_{12}\mu_1}{\lambda_1^* + \mu_1}\right)^2; \quad \frac{\partial \vartheta_2}{\partial \lambda_2}(\lambda_1, \lambda_2|_(\lambda_1^*, \lambda_2^*) = \left(\frac{n_{11}\mu_2}{\lambda_2^* + \mu_2}\right)^2. \qquad (29)$$

The characteristic equation of $J(\lambda_1^*, \lambda_2^*)$ is given as

$$\lambda^2 - \lambda\left(\frac{\partial \vartheta_1}{\partial \lambda_1} + \frac{\partial \vartheta_2}{\partial \lambda_2}\right)|_{(\lambda_1^*, \lambda_2^*)} + \left(\frac{\partial \vartheta_1}{\partial \lambda_1}\frac{\partial \vartheta_2}{\partial \lambda_2} - \frac{\partial \vartheta_1}{\partial \lambda_2}\frac{\partial \vartheta_2}{\partial \lambda_1}\right)|_{(\lambda_1^*, \lambda_2^*)} = 0. \qquad (30)$$

The solutions of the characteristic equation are given as

$$G_1 = \frac{1}{2}\left(X_0 + \sqrt{X_0^2 - 4X_1}\right); \quad G_2 = \frac{1}{2}\left(X_0 - \sqrt{X_0^2 - 4X_1}\right), \qquad (31)$$

where

$$X_0 = \left(\frac{\partial \vartheta_1}{\partial \lambda_1} + \frac{\partial \vartheta_2}{\partial \lambda_2}\right)|_{(\lambda_1^*, \lambda_2^*)}; \quad X_1 = \left(\frac{\partial \vartheta_1}{\partial \lambda_1}\frac{\partial \vartheta_2}{\partial \lambda_2} - \frac{\partial \vartheta_1}{\partial \lambda_2}\frac{\partial \vartheta_2}{\partial \lambda_1}\right)|_{(\lambda_1^*, \lambda_2^*)}.$$

The equilibrium point $(\lambda_1^*, \lambda_2^*)$ is therefore stable when $max\,(G_1, G_2) < 1$.

The second scenario considers movement of both susceptible and exposed buffalo populations between the patches. As before, the interior endemic equilibrium point is written in terms of the forces of infection $(\lambda_1^*, \lambda_2^*)$. The coordinates

of the equilibrium point are given as follows:

$$B^*_{2s} = \frac{\pi_2\lambda_1 + d}{\lambda_2\lambda_1 + a\lambda_2 + b\lambda_1 + c}; \quad B^*_{2e} = \frac{n_1\lambda_2\lambda_1^2 + n_2\lambda_2\lambda_1 + n_3\lambda_1^2 + n_4\lambda_1 + n_5\lambda_2}{g\lambda_2\lambda_1^2 + 2k_1\lambda_1\lambda_2 + k_2\lambda_1^2 + k_3\lambda_2 + k_4\lambda_1 + k_5};$$
$$B^*_{2i} = \frac{v_1n_1\lambda_2\lambda_1^2 + v_1n_2\lambda_2\lambda_1 + v_1n_3\lambda_1^2 + v_1n_4\lambda_1 + v_1n_5\lambda_2}{g\lambda_2\lambda_1^2 + 2k_1\lambda_1\lambda_2 + k_2\lambda_1^2 + k_3\lambda_2 + k_4\lambda_1 + k_5};$$
$$U^*_2 = \frac{v_2n_1\lambda_2\lambda_1^2 + v_2n_2\lambda_2\lambda_1 + v_2n_3\lambda_1^2 + v_2n_4\lambda_1 + v_2n_5\lambda_2}{g\lambda_2\lambda_1^2 + 2k_1\lambda_1\lambda_2 + k_2\lambda_1^2 + k_3\lambda_2 + k_4\lambda_1 + k_5}; \quad B_{1s} = \frac{\pi + m_2B^*_{2s}}{\lambda_1 + a};$$
$$B^*_{1e} = \frac{S_{11}}{S_{12}}; \quad B^*_{1i} = \frac{\theta_1S_{11}}{(\mu_1 + \epsilon_1)S_{12}}; \quad U^*_1 = \frac{\sigma_1\phi_1S_{11}}{\theta_1(\mu_1 + \epsilon_1)S_{12}};$$

where the constants in the coordinates of our endemic equilibrium are defined in the appendix.

Our forces of infection become

$$\lambda_1 = \frac{RS_{11}}{S_{12}}, \tag{32}$$
$$\lambda_2 = \frac{Gv_1n_1\lambda_2\lambda_1^2 + Gv_1n_2\lambda_2\lambda_1 + Gv_1n_3\lambda_1^2 + Gv_1n_4\lambda_1 + Gv_1n_5\lambda_2}{g\lambda_2\lambda_1^2 + 2k_1\lambda_1\lambda_2 + k_2\lambda_1^2 + k_3\lambda_2 + k_4\lambda_1 + k_5}. \tag{33}$$

The equilibrium points of sub-model 1 and sub-model 2 can be obtained by finding the fixed points of equations $\Upsilon(\lambda_1, \lambda_2) = \begin{pmatrix} \Upsilon_1(\lambda_1, \lambda_2) \\ \Upsilon_2(\lambda_1, \lambda_2) \end{pmatrix}$ and are given by

$$\Upsilon_1(\lambda_1, \lambda_2) = \frac{RS_{11}}{S_{12}}, \tag{34}$$
$$\Upsilon_2(\lambda_1, \lambda_2) = \frac{Gv_1n_1\lambda_2\lambda_1^2 + Gv_1n_2\lambda_2\lambda_1 + Gv_1n_3\lambda_1^2 + Gv_1n_4\lambda_1 + Gv_1n_5\lambda_2}{g\lambda_2\lambda_1^2 + 2k_1\lambda_1\lambda_2 + k_2\lambda_1^2 + k_3\lambda_2 + k_4\lambda_1 + k_5}. \tag{35}$$

Clearly, $(\lambda^*_1, \lambda^*_2) = (0, 0)$ is a fixed point of equations (34)-(35) which corresponds to the disease free equilibrium point.

Theorem 5. *There exists a unique fixed point* $\left(\lambda^*_1, \lambda^*_2\right), \lambda^*_1 > 0, \lambda^*_2 > 0$ *satisfying*

$$\Upsilon(\lambda_1, \lambda_2) = \begin{pmatrix} \lambda^*_1 \\ \lambda^*_2 \end{pmatrix}$$

corresponding to the interior endemic equilibrium point E_{32}, whenever the following conditions are satisfied

$$\frac{c_1d_2}{c_2d_1}>1;\quad \frac{c_1d_3}{c_3d_1}>1;\quad \frac{c_2d_3}{c_3d_2}>1;\quad \frac{2d_1k_3}{d_3k_1}+\frac{d_2k_2}{2k_1d_3}>1;\quad \frac{2d_2k_3}{k_2d_3}>1.$$
$$\frac{a_1b_2}{a_2b_1}>1;\quad \frac{a_1b_3}{a_3b_1}>1;\quad \frac{a_2b_3}{a_3b_2}>1;\quad \frac{2b_1r_3}{b_3r_1}+\frac{b_2r_2}{2r_1b_3}>1;\quad \frac{2b_2r_3}{r_2b_3}>1.$$

Proof. For each $\lambda_1>0$ we consider the following real valued function depending on λ_2:

$$\Upsilon_1^{\lambda_1}(\lambda_2)=\frac{RS_{11}}{S_{12}}$$

Clearly,

$$\Upsilon_1^{\lambda_1}(0)=\frac{R(u_{10}\lambda_1^4+u_{11}\lambda_1^3+u_{12}\lambda_1^2+u_{13}\lambda_1)}{z_{10}\lambda_1^4+z_{11}\lambda_1^3+z_{12}\lambda_1^2+z_{13}\lambda_1+z_{16}}>0,$$

and

$$\lim_{\lambda_2\to\infty}\Upsilon_1^{\lambda_1}(\lambda_2)=\frac{R(u_1\lambda_1^4+u_2\lambda_1^3+u_4\lambda_1^2+u_8\lambda_1+u_{15})}{z_1\lambda_1^4+z_2\lambda_1^3+z_4\lambda_1^2+z_8\lambda_1+z_{14}}<\infty.$$

Thus $0<\Upsilon_1^{\lambda_1}(\lambda_2)<\infty$, which implies that the real valued function $\Upsilon_1^{\lambda_1}(\lambda_2)$ is bounded for every fixed $\lambda_1>0$. If we fix λ_1 we obtain the following equation

$$\Upsilon_1^{\lambda_1}(\lambda_2)=\frac{c_1\lambda_2^2+c_2\lambda_2+c_3}{d_1\lambda_2^2+d_2\lambda_2+d_3},\tag{36}$$

where

$$\begin{aligned}
c_1&=R(u_1\lambda_1^4+u_2\lambda_1^3+u_4\lambda_1^2+u_8\lambda_1+u_{15}),\\
c_2&=R(u_3\lambda_1^5+u_6\lambda_1^2+u_7\lambda_1^4+u_9\lambda_1+u_5\lambda_1^3+u_{14}),\\
c_3&=R(u_{10}\lambda_1^4+u_{11}\lambda_1^3+u_{12}\lambda_1^2+u_{13}\lambda_1),\\
d_1&=z_1\lambda_1^4+z_2\lambda_1^3+z_4\lambda_1^2+z_8\lambda_1+z_{14},\\
d_2&=z_3\lambda_1^5+z_5\lambda_1^3+z_6\lambda_1^2+z_7\lambda_1^4+z_9\lambda_1+z_{15},\\
d_3&=z_{10}\lambda_1^4+z_{11}\lambda_1^3+z_{12}\lambda_1^2+z_{13}\lambda_1+z_{16}.
\end{aligned}$$

The first derivative of $\Upsilon_1^{\lambda_1}(\lambda_2)$ with respect to λ_2 is given by

$$\frac{\partial\Upsilon_1^{\lambda_1}(\lambda_2)}{\partial\lambda_2}=\frac{(c_1d_2-c_2d_1)\lambda_2^2+(2c_1d_3-2c_3d_1)\lambda_2+c_2d_3-c_3d_2}{(d_1\lambda_2^2+d_2\lambda_2+d_3)^2}>0\tag{37}$$

provided the following holds

$$\frac{c_1 d_2}{c_2 d_1} > 1; \quad \frac{c_1 d_3}{c_3 d_1} > 1; \quad \frac{c_2 d_3}{c_3 d_2} > 1,$$

and the second derivative $\Upsilon_1^{\lambda_1}(\lambda_2)$ with respect to λ_2 is given by

$$\frac{\partial^2 \Upsilon_1^{\lambda_1}(\lambda_2)}{\partial \lambda_2^2} = \frac{-2k_1 d_1 \lambda_2^3 - 3k_2 d_1 \lambda_2^2 + (-4d_1 k_3 - d_2 k_2 + 2k_1 d_3)\lambda_2 + k_2 d_3 - 2d_3 k_3}{(d_1 \lambda_2^2 + d_2 \lambda_2 + d_3)^3} < 0, \tag{38}$$

where

$$k_1 = c_1 d_2 - c_2 d_1; \quad k_2 = 2c_1 d_3 - 2c_3 d_1; \quad k_3 = c_2 d_3 - c_3 d_2.$$

The second derivative in (38) is negative if the following conditions hold

$$\frac{2d_1 k_3}{d_3 k_1} + \frac{d_2 k_2}{2k_1 d_3} > 1; \quad \frac{2d_2 k_3}{k_2 d_3} > 1.$$

Since $\frac{\partial \Upsilon_1^{\lambda_1}(\lambda_2)}{\partial \lambda_2} > 0$ and $\frac{\partial^2 \Upsilon_1^{\lambda_1}(\lambda_2)}{\partial \lambda_2^2} < 0$, the function $\Upsilon_1^{\lambda_1}(\lambda_2)$ is an increasing concave down function which has no change in convexity in the bounded domain. This implies that there exists a unique point $\lambda_2^* > 0$ satisfying $\Upsilon_1^{\lambda_1}(\lambda_2^*) = \lambda_2^*$.

For each $\lambda_2 > 0$ we consider the following real valued function depending on λ_1:

$$\Upsilon_2^{\lambda_2}(\lambda_1) = \frac{Gv_1 n_1 \lambda_2 \lambda_1^2 + Gv_1 n_2 \lambda_2 \lambda_1 + Gv_1 n_3 \lambda_1^2 + Gv_1 n_4 \lambda_1 + Gv_1 n_5 \lambda_2}{g\lambda_2 \lambda_1^2 + 2k_1 \lambda_1 \lambda_2 + k_2 \lambda_1^2 + k_3 \lambda_2 + k_4 \lambda_1 + k_5}.$$

Clearly,

$$\Upsilon_2^{\lambda_2}(0) = \frac{Gv_1 n_5 \lambda_2}{k_3 \lambda_2 + k_5} > 0,$$

and

$$\lim_{\lambda_1 \to \infty} \Upsilon_2^{\lambda_2}(\lambda_1) = \frac{Gv_1 n_1 \lambda_2 + Gv_1 n_3}{g\lambda_2 + k_2} < \infty.$$

Thus $0 < \Upsilon_2^{\lambda_2}(\lambda_1) < \infty$, which implies that the real valued function $\Upsilon_2^{\lambda_2}(\lambda_1)$ is bounded for every fixed $\lambda_2 > 0$. If we fix λ_2 we obtain the following equation

$$\Upsilon_2^{\lambda_2}(\lambda_1) = \frac{a_1 \lambda_1^2 + a_2 \lambda_1 + a_3}{b_1 \lambda_1^2 + b_2 \lambda_1 + b_3}, \tag{39}$$

where

$$a_1 = Gv_1n_1\lambda_2 + Gv_1n_3; \quad a_2 = Gv_1n_2\lambda_2 + Gv_1n_4; \quad a_3 = Gv_1n_5\lambda_2$$
$$b_1 = g\lambda_2 + k_2; \quad b_2 = 2k_1\lambda_2 + k_4; \quad b_3 = k_3\lambda_2 + k_5.$$

The first derivative of $\Upsilon_1^{\lambda_2}(\lambda_1)$ with respect to λ_1 is given by

$$\frac{\partial\Upsilon_1^{\lambda_2}(\lambda_1)}{\partial\lambda_1} = \frac{(a_1b_2 - a_2b_1)\lambda_1^2 + (2c_1b_3 - 2a_3b_1)\lambda_1 + a_2b_3 - a_3b_2}{(b_1\lambda_1^2 + b_2\lambda_1 + b_3)^2} > 0 \qquad (40)$$

provided the following holds

$$\frac{a_1b_2}{a_2b_1} > 1; \quad \frac{a_1b_3}{a_3b_1} > 1; \quad \frac{a_2b_3}{a_3b_2} > 1.$$

and the second derivative $\Upsilon_1^{\lambda_2}(\lambda_1)$ with respect to λ_1 is given by

$$\frac{\partial^2\Upsilon_2^{\lambda_2}(\lambda_1)}{\partial\lambda_1^2} = \frac{-2r_1b_1\lambda_1^3 - 3r_2b_1\lambda_1^2 + (-4b_1r_3 - b_2r_2 + 2r_1b_3)\lambda_1 + r_2b_3 - 2b_2r_3}{(b_1\lambda_1^2 + b_2\lambda_1 + b_3)^3} < 0, \qquad (41)$$

where

$$r_1 = a_1b_2 - a_2b_1; \quad r_2 = 2c_1b_3 - 2a_3b_1; \quad r_3 = a_2b_3 - a_3b_2.$$

The second derivative in (41) is negative if the following conditions hold

$$\frac{2b_1r_3}{b_3r_1} + \frac{b_2r_2}{2r_1b_3} > 1; \quad \frac{2b_2r_3}{r_2b_3} > 1.$$

Since $\frac{\partial\Upsilon_2^{\lambda_2}(\lambda_1)}{\partial\lambda_1} > 0$ and $\frac{\partial^2\Upsilon_2^{\lambda_2}(\lambda_1)}{\partial\lambda_1^2} < 0$, the function $\Upsilon_2^{\lambda_2}(\lambda_1)$ is an increasing concave down function which has no change in convexity in the bounded domain. This implies that there exists a unique point $\lambda_1^* > 0$ satisfying $\Upsilon_2^{\lambda_2}(\lambda_1^*) = \lambda_1^*$. Hence, we have a unique fixed point $(\lambda_1^*, \lambda_2^*)$ corresponding to the endemic equilibrium point. □

3.6. Stability analysis

The process for stability analysis is as carried out in section 3.5.

4. Numerical simulations

In this section, we present a detailed account on how the parameters used in this study are estimated. We then use the parameter values to carry out numerical simulations that will provide more insights into dynamics of BTB infection that is modelled via our metapopulation model.

4.1. Parameter estimation

All parameter values used in the numerical simulations are given in Table 1 including their sources. Some parameter values are taken as they appear in literature while others are determined based on the given information in literature. Those with no known values from literature are determined by the conditions subjected to them in the model formulation. The values of $\pi_1, \pi_2, \mu_1, \mu_2, \epsilon_1$ and ϵ_2 are obtained in [31] and parameter values of β_1, β_2, ϕ_1 and ϕ_2 are obtained from [16]. The parameters values of η_1 and η_2 are estimated based on survival data of *M. bovis* in the environment. *M. bovis* takes the survival period of 88 days [28]. The parameter value of η_j, for $1 \leq j \leq 2$, is then estimated by dividing the number of the survival days by the number of days in a year. The decaying rate of *M. bovis* in the environment is calculated by simply subtracting the survival rate from 1. The spread trends of BTB infection in the Kruger National Park and the observations made in [1, 21] about the rate at which buffalo contract *M. bovis* from the environment guide us to assume appropriate values for $\Psi_1, \Psi_2, \alpha_1, \alpha_2, m_1$ and m_2.

Table 1: Table of parameter values used in the model

Name	Range	Reference	Name	Range	Reference
π_1	[400, 1460]	[31]	π_2	[400, 1460]	[31]
β_1	[0.01, 0.053]	[16]	β_2	[0.01, 0.053]	[16]
Ψ_1	[0.01, 0.06]	Assumed	η_2	[0.11, 0.25]	[28]
η_1	[0.11, 0.25]	[28]	Ψ_2	[0.01, 0.06]	[Assumed]
μ_1	[0.03, 0.05]	[31]	ϕ_2	[0.056, 1]	[17]
α_1	[0.01, 0.05]	Assummed	α_2	[0.01, 0.06]	Assumed
ϵ_1	[0.657, 0.803]	[31]	ϵ_2	[0.657, 0.803]	[31]
θ_1	[0.7, 0.8]	calculated	θ_2	[0.7, 0.8]	calculated
σ_1	[0.1, 0.6]	Assumed	μ_2	[0.03, 0.05]	[31]
m_1	[0.01, 0.05]	Assumed	σ_2	[0.1, 0.6]	Assumed
ϕ_1	[0.056, 1]	[16]	m_2	[0.01, 0.05]	Assumed

4.2. Simulations

We present numerical simulations of models (1) and (2) to explore the impact of various scenarios of migration on the disease dynamics in both patches. The first scenario to be explored is the patch specific disease dynamics when there is no between them. The second scenario to be investigated is the impact of movement of patch 1 susceptible and exposed buffalo into patch 2 on its disease dynamics. The third scenario to be investigated is the impact of movement of patch 2 susceptible and exposed buffalo into patch 1 on its disease dynamics. Finally, we explore the impact of the two way movement of susceptible and exposed buffalo on the patch specific disease dynamics and also the role of environment on the dynamics of BTB infection in both patches.

Figure 3 displays the patch specific disease dynamics when there is no movement. As expected the disease dynamics are more explosive in patch 1 with higher disease prevalence than patch 2 with low disease prevalence. This is indicated by a higher level of patch 1 infected buffalo and higher concentration levels of *M. bovis* than in patch 2. We used Figure 3 as a control in order to compare to other figures to examine the impact of movement on the on the dynamics of BTB infection in both patches.

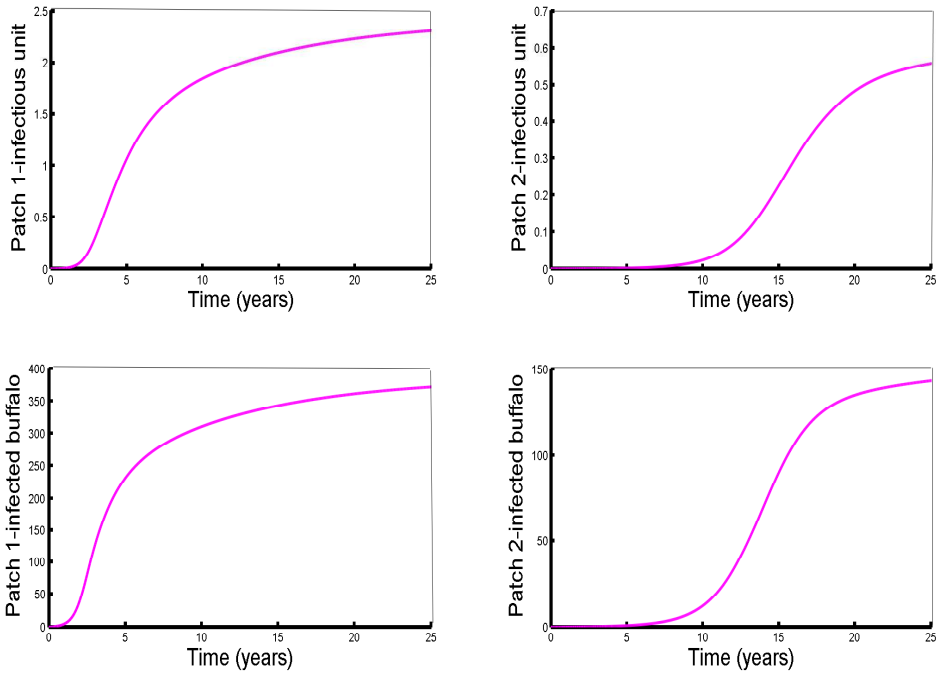

Figure 3: Comparison of infectious unit and infected buffalo in both patches when there is no movement

Figure 4 illustrates the scenario of allowing one-way movement of patch 1 susceptible buffalo into patch 2. The scenario affects the disease dynamics of patch 2. The movement of patch 1 susceptible buffalo into patch 2, increases the number of susceptible buffalo in the patch 2. The observation is illustrated by the higher levels of patch 2 infected buffalo and patch 2 *M. bovis* concentration. This is explained by the arrival of patch 1 susceptible buffalo that act as raw material for the infection. However, in patch 1 the infection rate decreases due to the decline of susceptible buffalo.

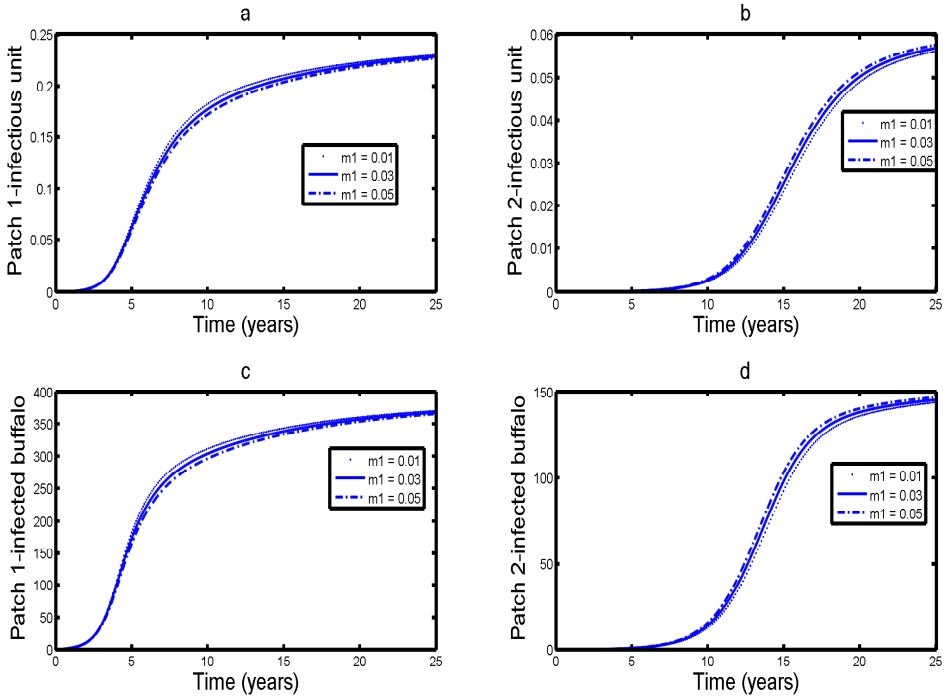

Figure 4: Comparison of infectious unit and infected buffalo across patches assuming movement of patch 1 susceptible buffalo into patch 2 only.

Figure 5 illustrates the impact of the movement of patch 1 exposed buffalo to patch 2 only. This scenario results in an increase of exposed buffalo in patch 2, which in turn increases the infection rate. The patch 1 infection rate is not greatly affected. This is due to the number of susceptible buffalo in patch 1 is not perturbed by the movement. Note that it is the movement of patch 1 susceptible buffalo into patch 2 that significantly decreases the infection rate in patch 1.

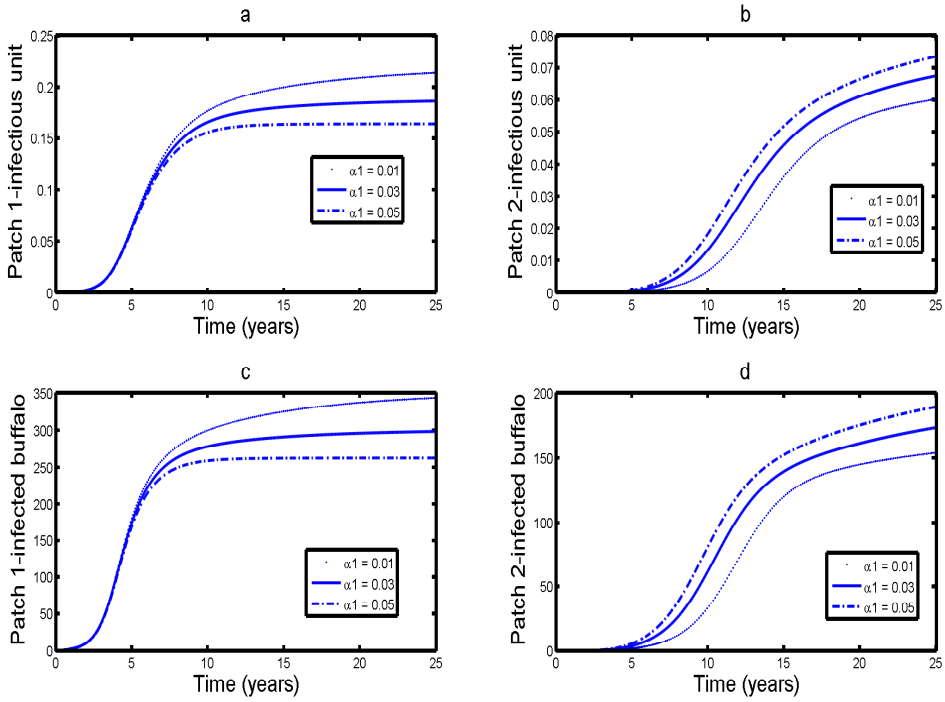

Figure 5: Comparison of infectious unit and infected buffalo across patches assuming movement of patch 1 exposed buffalo into patch 2 only. The parameters describing the movement are $\alpha_1 > 0$ and $m_1, m_2, \alpha_2 = 0$.

Figure 6 shows the effect of movement of patch 2 exposed buffalo to a patch 1. The disease dynamics in patch 1 are greatly perturbed due to the increased number of exposed buffalo in patch 1 that eventually generate more infected buffalo in the patch. The propensity of disease dynamics in patch 2 is reduced due to the decrease of the exposed buffalo via movement. These are responsible to generate the infected buffalo that increase the force of infection.

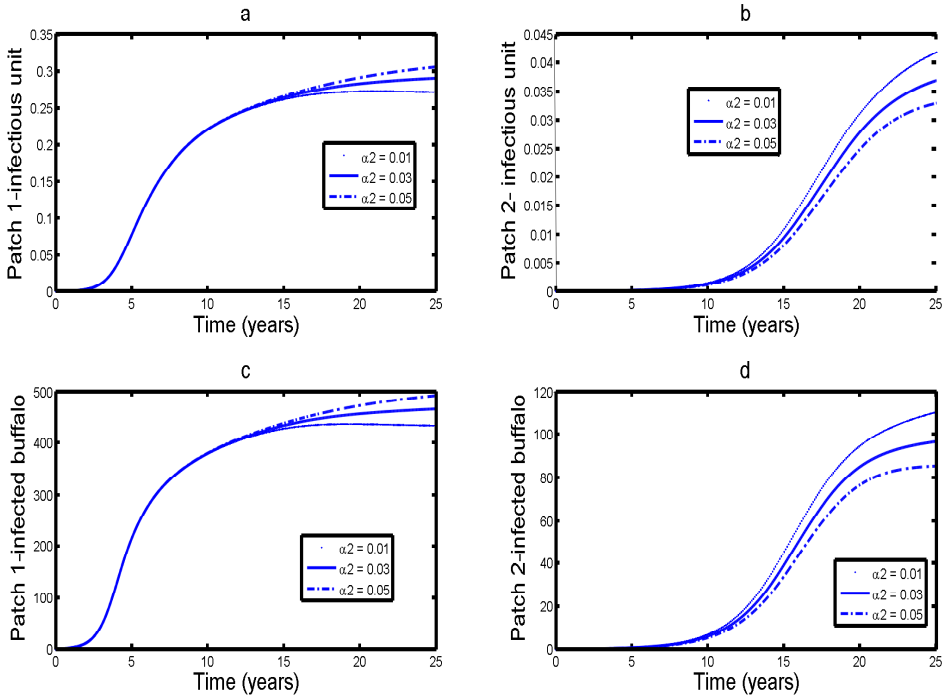

Figure 6: Comparison of infectious unit and infected buffalo across patches assuming movement of patch 1 exposed buffalo into patch 2 only. The parameters describing the movement are $\alpha_1 > 0$ and $m_1, m_2, \alpha_2 = 0$.

In Figure 7, the impact of the movement of patch 2 susceptible buffalo into patch 1 is shown. The simulations show the increase of the propensity of the BTB infection in patch 1 which is as a result of an increase in number of the infected buffalo and an increase in the concentration of *M. bovis* pathogens in the environment. This however, has decreased the gravity of the disease in patch 2 due to a decrease of the susceptible buffalo in patch 1. This implies that the concentration of *M. bovis* pathogens in the environment and the number infected buffalo in patch 1 are at low levels as illustrated in Figure 7 (b) and (d).

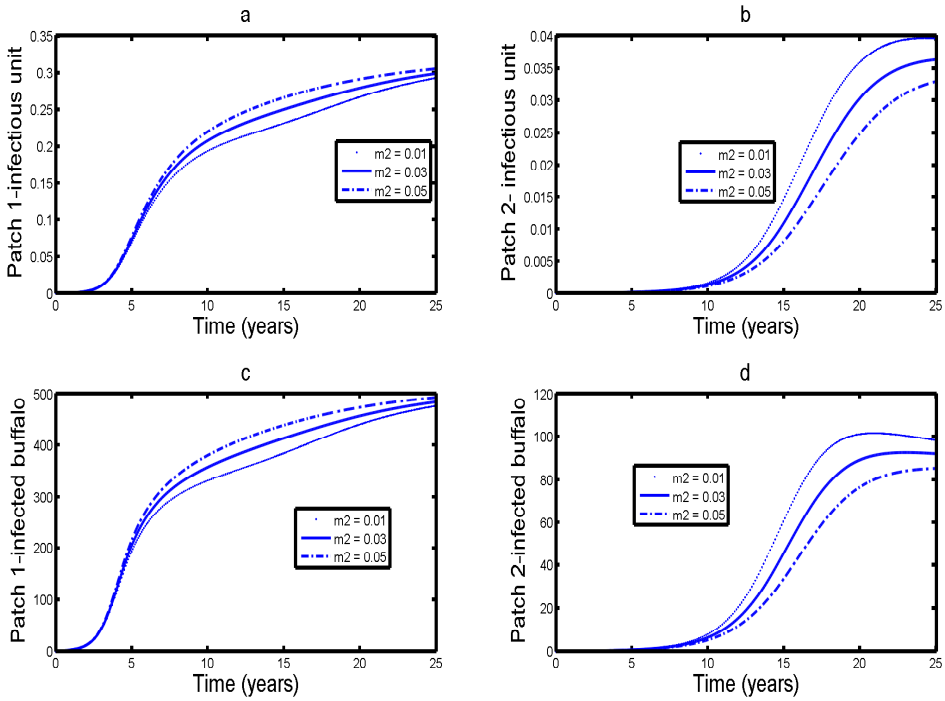

Figure 7: Comparison of infectious unit and infected buffalo across patches assuming movement of patch 2 susceptible buffalo into patch 1 only. The parameters describing the movement are $m_2 > 0$ and $m_1, \alpha_1, \alpha_2 = 0$.

Figure 8 shows the dynamic trends of all classes of buffalo including the pathogen concentration in the environment in both patches when movement of both susceptible and exposed buffalo into both patches is allowed. The simulations show the synchronous changes in all classes of interest. In both patches the intensity of the BTB infection slightly increased, but the impact is more pronounced in patch 1 where the disease prevalence is low. All simulations involving the mixing of buffalo agree well with the analytical results where the reproduction number is directly related to exposed movement parameter. This relation increases the reproduction number when there an increase in the exposed buffalo movement parameters.

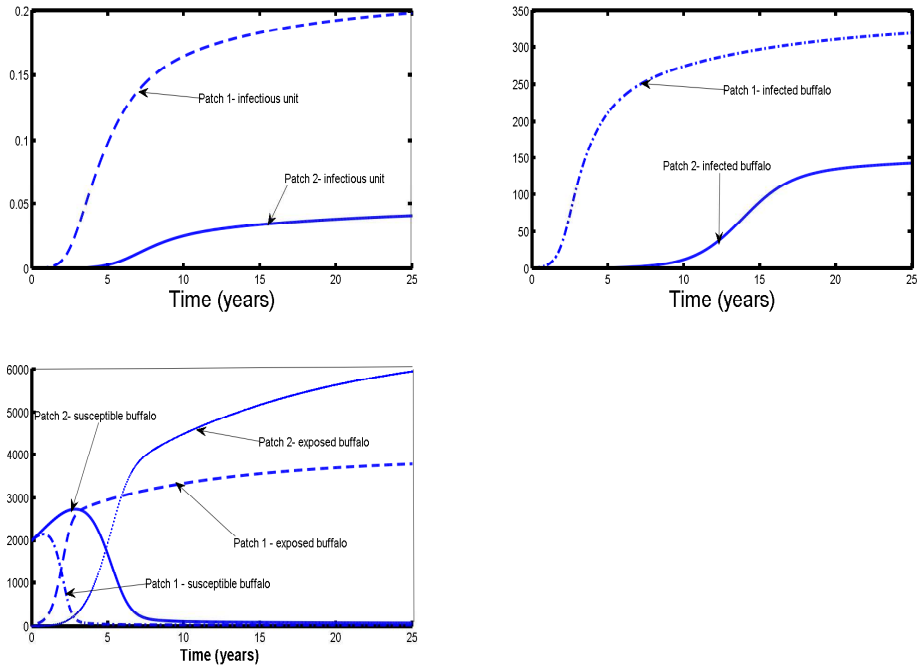

Figure 8: Comparison of susceptible, exposed and infected buffalo populations and pathogen concentration in the environment across patches assuming movement of both susceptible and exposed buffalo populations between patches. The parameter describing movement are such that $m_1 > m_2$ and $\alpha_1 > \alpha_2$.

The effect of environment was explored, the results showed no significant change in the transmission dynamics of BTB infection in both patches. The observation agrees well with what was observed in [21]. Figure 9 puts the scenario in the right context.

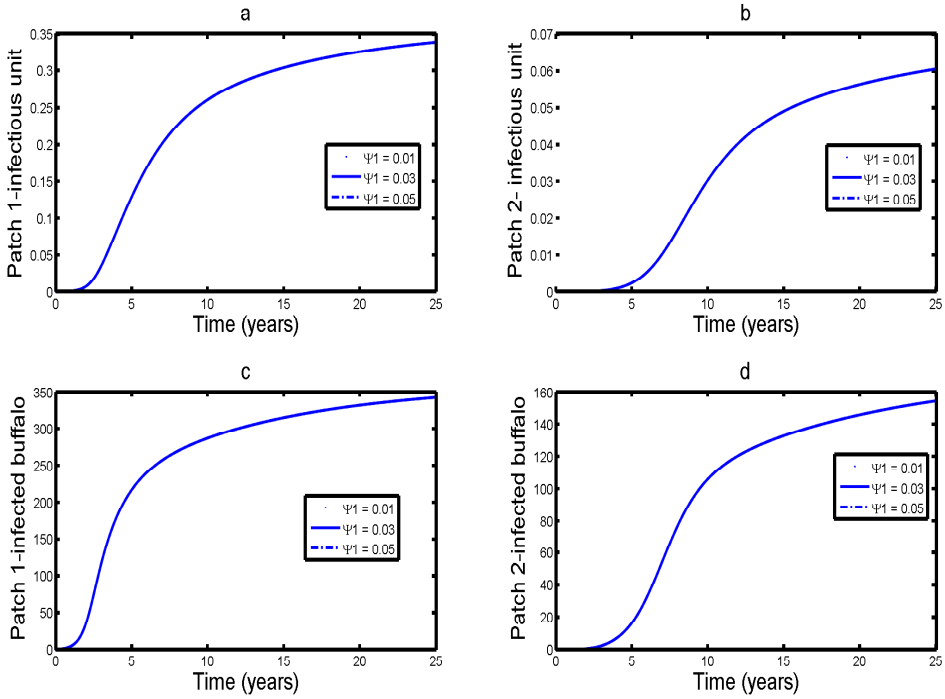

Figure 9: Comparison of infectious unit and the infected buffalo across patches assuming movement of both susceptible and exposed buffalo between patches when the environment transmission rate Ψ_J, for $1 \leq j \leq 2$ is varied. The parameter describing movement are such that $m_1 > m_2$ and $\alpha_1 > \alpha_2$.

5. Conclusion

A deterministic model for bovine tuberculosis dynamics between linked patches was presented. Very important mathematical characteristics like the invariant region of biological importance, patch specific reproduction numbers for isolated, non-isolated patches linked by migration as well as the model disease reproduction number were presented. The disease free and the boundary endemic equilibrium points are presented. The disease free equilibrium point was established to be globally stable whenever the patch specific disease reproduction numbers are less than one. This suggests that whenever the patch specific disease reproduction numbers are less than one, the following generation of the infective will be less than their predecessor, and thus the disease can not persist. The boundary endemic equilibria were determined, shown to be unique, and locally asymptotically stable when the non-isolated patch specific reproduction numbers are

greater than one. The interior endemic equilibrium point was also determined using the fixed point theorem.

The effect of movement of both susceptible and exposed buffalo on bovine tuberculosis transmission dynamics has been explored via numerical simulations. Our results show that when the patches are isolated the disease would be more severe in a patch if it has high disease prevalence. Endemic bovine tuberculosis is manifested by high levels of infected buffalo and *M. bovis* concentration in the environment. The disease may remain persistent in both cases when the patch specific disease reproduction numbers are greater than one. When patches are linked by migration, main features observed in the long term dynamics of the BTB infection are: First, there is a probability of the disease wrecking more damage in the patch with relatively low disease prevalence. This case results from an increase in the number of susceptible buffalo as well as the exposed buffalo (due to migration) hence an increase in the probability of buffalo to buffalo contact as well as contact with *M. bovis* in the environment. Secondly, migration of both susceptible and infected buffalo results in synchronous fluctuation of subpopulations in both patches. Therefore, free migration in bovine tuberculosis hit areas may eventuate in introduction of the disease in unaffected areas or even worsening it in less affected areas. Therefore, from the management perspective, it may be reasonable to restrict movement to and from bovine tuberculosis endemic areas if disease is to be easily contained.

Finally, it is reasonable to state that our metapopulation model considers the effect of migration on the evolution of bovine tuberculosis in buffalo in two patches. However, it is important to enhance our understanding about the disease by carrying out sensitivity analysis of the within-patch transmission rates and other parameters on disease dynamics. The future work will also extend our two patched model to three patched model or multi-patched model. This will give more insights into the spatial propagation of the disease in the multi-patched model. Age-structured metapopulation dynamics model is another fertile area to be investigated in future.

6. Appendix

$$a = \mu_1 + m_1; \quad b = \mu_2 + mu_2; \quad c = \mu_2\mu_1 + \mu_2 m_1 + mu_2\mu_1; \quad d = \mu_1\pi_2 + m_1\pi_2 + m_1\pi_1;$$
$$f = \mu_1 + \phi_1 + \alpha_1; \quad g = fb + \alpha_2 a; \quad n_1 = f\pi_2 + \alpha_1\pi_1; \quad n_2 = fd + af\pi_2 + a\alpha_1\pi_1;$$
$$n_3 = b\alpha_1\pi_1 + \alpha_1 m_2\pi_2; \quad n_4 = c\alpha_1\pi_1 + d\alpha_1 m_2; \quad n_5 = afd; \quad k_1 = ag; \quad k_2 = bg; \quad k_3 = a^2 g;$$
$$k_4 = gab; \quad k_5 = gac; \quad v_1 = \frac{\phi_2}{\mu_2 + \epsilon_2}; \quad v_2 = \frac{\sigma_2}{\theta_2}; \quad G = \beta_2 + \eta_2\Psi_2 v_2; \quad x_{11} = \alpha_2 n_1;$$
$$x_{12} = \alpha_2 n_2 + a\alpha_2 n_1; \quad x_{13} = \alpha_2 n_5 + a\alpha_2 n_2; x_{14} = \alpha_2 n_4 + a\alpha_2 n_3; \quad x_{15} = \alpha_2 n_3; x_{16} = a\alpha_2 n_4;$$
$$x_{17} = a\alpha_2 n_5; \quad y_{11} = gm_2\pi_2; \quad y_{12} = m_2\pi_2 2k_1 + dg; \quad y_{13} = k_3 m_2\pi_2 + 2k_1 d;$$
$$y_{14} = k_2 m_2\pi_2 + k_2 d; \quad y_{15} = k_5 m_2\pi_2 + 2k_1 d; \quad y_{16} = k_2 m_2\pi_2; \quad y_{17} = k_3 d; \quad y_{18} = k_5 d$$
$$l_1 = x_{12} + ax_{11}; \quad l_2 = x_{13} + x_{17} + ax_{13}; \quad l_3 = x_{14} + ax_{15} + cx_{11} + bx_{12}; \quad l_4 = x_{15} + bx_{11};$$
$$l_5 = x_{16} + ax_{14} + bx_{13} + cx_{12}; \quad l_6 = ax_{12}; \quad l_7 = ax_{16} + bx_{17} + cx_{13}; \quad l_8 = ax_{17};$$
$$l_9 = bx_{14} + cx_{15}; \quad l_{10} = bx_{15}; \quad l_{11} = bx_{16} + cx_{14}; \quad l_{12} = cx_{16}; \quad l_{13} = cx_{17}; \quad f_1 = l_4 + y_{12}$$
$$f_2 = l_5 + y_{13}; \quad f_3 = l_7 + y_{17}; \quad f_4 = l_9 + y_{14}; \quad f_5 = l_{10} + y_{16}; \quad f_6 = l_{11} + y_{15}; \quad f_7 = l_{12} + y_{15}$$
$$h_1 = 2k_1 + ag; \quad h_2 = k_3 + 2k_1 a + gc; \quad h_3 = k_4 + 2k_1 b + gc; \quad h_4 = k_5 + k_3 b + k_4 a + 2k_1 c$$
$$h_5 = k_2 a + bg; \quad h_6 = ak_5 + ck_3; \quad h_7 = bk_5 + ck_4; \quad h_8 = ck_5; \quad u_1 = \pi_1 g + x_{11}; \quad h_1\pi_1 + l_1;$$
$$u_3 = k_2\pi_1; \quad u_4 = h_2\pi_1 + l_6; \quad u_5 = \pi_1 h_3 + f_1; \quad u_6 = \pi_1 h_4 + f_2; \quad u_7 = \pi_1 h_3 + y_{11};$$
$$u_8 = \pi_1 k_3 a + l_3; \quad u_9 = \pi_1 h_6 + f_3; \quad u_{10} = \pi_1 ck_2 + f_5; \quad u_{11} = \pi_1 k_4 + f_4; \quad u_{12} = \pi_1 h_7 + f_6;$$
$$u_{13} = \pi_1 h_8 + f_7; u_{14} = l_{13}; \quad z_1 = bg; \quad z_2 = bh_1 + bag; \quad z_3 = bk_2; z_4 = bh_2 + bah_1;$$
$$z_5 = bh_3 + bah_5; z_6 = bh_4 + bah_3; \quad z_7 = bh_5 + bak_2; \quad z_8 = bk_3 a + bah_2; \quad z_9 = bh_6 + bah_4;$$
$$z_{10} = bck_2; z_{11} = bk_4 + back_2; \quad z_{12} = bh_7 + bak_4; \quad z_{13} = bh_8 + bah_8; \quad z_{14} = bak_3; \quad z_{15} = bah_6;$$
$$z_{16} = bah_8;$$
$$S_{11} = u_1\lambda_1^4\lambda_2^2 + u_2\lambda_2^2\lambda_1^3 + u_3\lambda_2\lambda_1^5 + u_4\lambda_2^2\lambda_1^2 + u_5\lambda_1^3\lambda_2 + u_6\lambda_2\lambda_1^2 + u_7\lambda_2\lambda_1^4 + u_8\lambda_2^2 + u_9\lambda_2\lambda_1 + u_{10}\lambda_1^4;$$
$$+ u_{11}\lambda_1^3 + u_{12}\lambda_1^2 + u_{13}\lambda_1 + u_{14}\lambda_2 + u_{15}\lambda_2^2;$$
$$S_{12} = z_1\lambda_2^2\lambda_1^4 + z_2\lambda_2^2\lambda_1^3 + z_3\lambda_2\lambda_1^5 + z_4\lambda_2^2\lambda_1^2 + z_5\lambda_2\lambda_1^3 + z_6\lambda_1^2\lambda_2 + z_7\lambda_2\lambda_1^4 + z_8\lambda_2^2\lambda_1 + z_9\lambda_1\lambda_2 + z_{10}\lambda_1^4;$$
$$+ z_{11}\lambda_1^3 + z_{12}\lambda_1^2 + z_{13}\lambda_1 + z_{14}\lambda_2^2 + z_{15}\lambda_2 + z_{16};$$
$$R = \frac{\theta_1\beta_1\phi_1 + \eta_1\Psi_1\sigma_1\phi_1}{\theta_1(\mu_1 + \epsilon_1)}.$$

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Chapter 5

Conclusion and future work

This thesis focused on developing epidemiological mathematical models to enhance the understanding of the transmission dynamics of bovine tuberculosis (BTB) in buffalo and cattle populations. Considering the biology and natural history of the BTB infection, various aspects of the infection were incorporated into the models developed.

Chapter 1 gave a detailed account of the background of the BTB infection. Important aspects of the disease highlighted are background information, epidemiology of bovine tuberculosis in Africa and other continents, epidemiology of bovine tuberculosis in Kruger National Park, bovine tuberculosis in cattle population, the biology of the causative agent of the infection, the concept of metapopulation and the statistics for the BTB infection globally and in Kruger National Park, motivation of the study, objectives of the study, outline of the study and publications that have built the thesis.

In Chapter 2, we considered the role of buffalo carriers in the transmission dynamics of BTB infection in buffalo population. The results suggest that the infection of susceptible buffalo via buffalo carriers increase the number of infected buffalo population, which subsequently increase the prevalence of bovine tuberculosis in buffalo community. This can be the other reason for BTB infection persistence in the buffalo population and unsuccessful efforts to eradicate the disease so far. This implies that the control efforts should target mechanisms that can detect the buffalo carriers to successfully improve efforts to control the infection. The work done in

[32] attempted to study the dynamics of bovine tuberculosis via a mathematical model that did not include the role of buffalo carriers. Their results showed the existence of BTB infection in buffalo population, but their model could not explain the reason for disease existence.

Our study also investigated the aspect of cross-infection between cattle and buffalo populations in Chapter 3. Its inclusion in the model has given new insights into the evolution of BTB infection in cattle and buffalo populations. The results show that the prevalence of BTB infection is high particularly in the cattle population when there is cross-infection of BTB infection between cattle and buffalo populations. Our model results on cross-infection can be a suitable explanation for the observed [82] high prevalence of BTB infection in cattle population at the interface areas compared to areas that are far from the wildlife-livestock interface areas. The same aspect was also considered in [53] to study the dynamics of brucellosis between cattle and sheep on a public farm. Similar observations were also made that the cross-infection transmission mechanism increased the disease prevalence in both populations, but the intensity of the increase of the prevalence differs from our study which considered the movement of buffalo on an uncontrolled site.

In Chapter 4, we investigated the role of movement of susceptible and exposed buffalo from one patch to another in Kruger National Park. To the best of our knowledge this is the first study that explores the effect of movement of susceptible and exposed buffalo from one patch to another. The results show that the intensity of the disease in a low prevalence patch 2 increases when the susceptible and exposed buffalo from patch 1 move into it. It is the movement of the exposed buffalo from patch 1 to patch 2 that poses a serious threat regarding the spread of the BTB infection northwards. This underpins the fact that the disease spread in Kruger National Park is moving northwards from the southern part where the infection initially started. The study [32] attempted to look at the transmission dynamics of bovine tuberculosis in buffalo population but their work did not consider the aspect of movement of susceptible and exposed buffalo from one patch to another. Their model results did not manage to explain why BTB infection is increasing northwards in Kruger National Park, an observation our model has managed to show.

These findings have very important implications for bovine tuberculosis control: We recommend

that if bovine tuberculosis is to be eliminated, advanced test techniques should be developed to be able to diagnose the buffalo carriers to reduce the transmission of the infection from carrier buffalo. This will accelerate the eradication of BTB infection from the buffalo population. We also recommend that strict control and monitoring measures should be used at the interface to reduce or block the cross-infection of bovine tuberculosis to either cattle population or buffalo population. We also recommend that control measures that prevent the movement of buffalo from one patch to another should be implemented.

Our study has managed to provide significant improvement to the existing knowledge regarding the spread mechanisms of the BTB infection in both cattle and buffalo populations. Our work can be enhanced by considering the following aspects :

- The stochasticity of the BTB infection was not incorporated into our models. Generally, the disease is stochastic in nature, outbreaks of the disease are commonly observed in drought times where animals converge at water drinking sites. This situation increases the chances of spreading the BTB infection. The model would be more realistic if a stochastic component was factored in the model.

- Another important driving factor of the infection not included in the model is pseudo-vertical transmission route. The age specific disease prevalence suggests that young animals get the infection via sucking milk from their mothers. This biological aspect of the infection if incorporated in the model can improve the understanding of the transmission dynamics of bovine tuberculosis. Bovine tuberculosis prevalence is high in buffalo aged less than two years [18] and this explains why the pseudo-vertical transmission route should be considered in our models.

- The further understanding of the BTB infection would be enhanced if in-host modelling is carried out. This type of modelling gives very significant insights into the characteristics of *M. bovis*; the knowledge can be used to develop the right medication for the infection.

- The model validation is a crucial step in the modelling process. This step is achieved when the models are fitted to data; the process helps to estimate the appropriate values

of the model parameters. Model validation provides more confidence in trusting the model prediction. A current challenges is that data is scarce in the case of BTB.

- The zoonotic effect of the disease was not considered in the models developed in this thesis. People in rural settings close to the interface between the park and the rural areas reside closer to their livestock and they can easily become hosts for BTB.

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