

Mathematics of FIV and BTB Dynamics in Buffalo and Lion Populations at Kruger National Park

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Abstract

A new deterministic model for the transmission dynamics of feline immunodeficiency virus (FIV) and bovine tuberculosis (BTB) in lion-buffalo population is designed and used to gain insight into the transmission dynamics of the two diseases in the population. The model is shown to undergo a backward bifurcation (a dynamic phenomenon characterized by the co-existence of the stable disease-free equilibrium and a stable endemic equilibrium when the associated reproduction number of the model is less than unity). Two sources for this dynamic phenomenon, namely the BTB re-infection of exposed buffalos and the BTB-FIV co-infection of lions, have been identified. It is shown that, for the special case of the model when backward bifurcation does not occur, the disease-free equilibrium of the resulting model is globally-asymptotically stable when the associated reproduction number is less than unity. Numerical simulations of the model, using initial and demographic data relevant to the BTB-FIV dynamics in Kruger National Park [6], show that control strategies, such as the isolation of lions with FIV symptoms or the treatment of lions and buffalos with BTB symptoms, can lead to the effective control or elimination of the disease in the lion-buffalo population if their effectiveness level is high enough. The time to elimination of any of the two diseases is significantly reduced if the two strategies are combined.

Keywords: BTB; FIV; equilibria; stability; backward bifurcation.

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1 Introduction

Feline immunodeficiency virus (FIV), a lentivirus that affects cats worldwide, is an endemic pathogen in many African lion (*Panthera leo*) populations in eastern and southern Africa [9, 14, 43, 45, 49, 53, 55, 59]. In particular, FIV has been found in the lion population at the Kruger National Park (KNP) of South Africa, dating back to the late 1980s [53]. The geographical distribution of FIV in all felines varies dramatically, with rates of prevalence of 2-5% in North America, 30% in Italy, Australia, and Japan, and up to over 80% in South Africa's KNP [15, 30, 50]. The high FIV prevalence in Africa can be attributed to a higher population density of free-roaming felines in Africa (FIV has been reported in leopards and cheetahs in South Africa [15, 30, 50, 62]), as well as variation among viral subtypes [15, 30, 50]. There are roughly 3,000 lions in South Africa, and approximately 2,000 lions roam KNP, a 7,253 square mile game reserve in northeastern South Africa. Antibody tests for FIV revealed that over 80% of the lions in KNP are infected with FIV, with a prevalence of 41% in the northern part and 80% in the southern part [43]. This disparity can be attributed to a higher population density of lions in the southern part of KNP [6]. Despite the high prevalence of FIV among felines, zoonotic transmission of FIV to humans remains doubtful [15].

Bovine tuberculosis (BTB) is a chronic bacterial disease, classified amongst the closely-related species that form the *M. tuberculosis* complex (MTBC) [20]. BTB, caused by *bovine bacillus* (*M. bovis*) [35], affects a wide range of hosts, including domestic livestock (such as cattle, goats, sheep, etc), wildlife (such as badgers, deer, bison, African buffalo, lion, etc) which can either be reservoir or spill-over, and humans [28]. BTB remains a major problem for animal health in many developing countries [31], and its widespread distribution has drastic negative socio-economic development in terms of public health, international trade, tourism, animal mortality and milk production [21]. For example, in Argentina, the annual economic loss due to BTB is estimated to be US\$ 63 million [11]. A cost benefit analysis of BTB eradication in the United States showed an actual cost of US\$ 538 million between 1917-1992 (current programs cost approximately US\$ 3.5-4.0 million *per year* [31]).

The African lion population is at an all-time low, with current estimate as low as 16,500 [22]. In fact, the lion population of Northern Africa has gone extinct [16, 22]. This certainly heightens the urgent need to monitor, conserve and protect the South African lion population. In addition to the laudable effort to preserve and conserve the lion species from extinction, the lion population (and other wildlife) at KNP serves as a major source of (and boost for) the South African economy, through tourism. Tourism has played a significant role in many African economies, and lions remain one of the premier attractions [59]. In fact, a number of South Africa's most impoverished communities remain reliant on the revenue generated through tourism, and would experience severe economic consequences if lions were no longer a part of

the safari experience for tourists [8]. For this, and numerous other reasons (e.g., the aforementioned ecological need for the preservation of the ecosystem), it is crucial that the lion population (one of world’s treasured animal species) in South Africa is not allowed to go extinct.

The principal mode of FIV transmission is through horizontal transfer, usually through saliva from the bite of an infected feline [37, 42]. Other reported modes of horizontal transfer are oral, transrectal and transvaginal (although these routes of transmission are not significant enough to be considered as secondary [50]). Vertical transmission through transplacental transfer has been reported as a potential mode of transmission (although transmission rate depends largely on the viral subtype present, and the likelihood of transmission in utero is reduced significantly in mothers producing FIV antibodies before conception) [13, 15]. Older, free-roaming lions are also the most likely to be infected with FIV, as they are more likely to engage in aggressive territorial fights, which increases the likelihood of transmitting the virus through a bite wound in the skin [13, 15]. Similar to the human immunodeficiency virus (HIV), FIV infects the target CD4+ T cells of the feline host, thereby compromising the host’s immune system and, subsequently, making the host to be vulnerable to opportunistic infections [5, 47]. As in cattle, the main source of BTB transmission in buffalo and lion is by direct contact, aerosol, oral, through a bite or contamination of a skin wound [28] (other means of transmission, such as vertical and pseudo-vertical [60], also occur).

A number of mathematical models have been developed in the literature and used to gain insight into the transmission dynamics of BTB in buffalo, human or lion populations (see, for instance, [7, 10, 25, 36, 38, 57, 60] and some of the references therein). However, none of these studies incorporate lions in the transmission dynamics of BTB. The objective of the current study is to gain insight into the qualitative dynamics of the two diseases (BTB and FIV) in a buffalo-lion population. The aim is to design and analyse a new realistic model (which extends some of the aforementioned studies in the literature) for BTB-FIV transmission dynamics in the lion-buffalo population at the KNP. The paper is organized as follows. The new model for the transmission dynamics of BTB-FIV in lion and buffalo population is formulated in Section 2 and rigorously analysed in Section 3. Sensitivity analysis is carried out in Section 4, and the effectiveness of control strategies are numerical-assessed in Section 5.

2 Model Formulation

The model is based on the transmission dynamics of FIV and BTB in the lion-buffalo population of South Africa’s Kruger National Park. The total lion population, at time t , denoted by N_L , is sub-divided into eleven mutually-exclusive compartments of susceptible lions ($S_L(t)$), lions infected with FIV only at early-stage of infection ($E_{LF1}(t)$), lions infected with FIV only at advanced-stage of infection ($E_{LF2}(t)$), lions infected with

FIV only that are isolated (and/or treated) ($J_F(t)$), lions infected with BTB only at early-stage of infection ($E_{LB1}(t)$), lions infected with BTB only at advanced-stage of infection ($E_{LB2}(t)$), infected lions with clinical symptoms of BTB ($I_{LB}(t)$), lions with BTB only that are treated against BTB ($W_{LB}(t)$), dually-infected lions with FIV and advanced-exposed to BTB ($D_{L1}(t)$), dually-infected lions with symptoms of both FIV and BTB ($D_{L2}(t)$) and treated/isolated dually-infected lions with symptoms of both diseases ($J_{FB}(t)$), so that

$$N_L(t) = S_L(t) + E_{LF1}(t) + E_{LF2}(t) + J_F(t) + E_{LB1}(t) + E_{LB2}(t) + I_{LB}(t) + W_{LB}(t) + D_{L1}(t) + D_{L2}(t) + J_{FB}(t).$$

Similarly, the total buffalo population in the herd at time t , denoted by $N_B(t)$, is divided into susceptible buffalos ($S_B(t)$), buffalos exposed to BTB infection ($E_{BB}(t)$), buffalos with BTB symptoms ($I_{BB}(t)$) and infected buffalos who recovered from BTB infection ($R_{BB}(t)$). Thus,

$$N_B(t) = S_B(t) + E_{BB}(t) + I_{BB}(t) + R_{BB}(t).$$

The susceptible lion population is generated *via* recruitment of lions (by birth or restocking) into the park (at a constant rate, Π_L per year). This population is decreased following the acquisition of infection with FIV, which can be acquired *via* effective contact with an infectious lion at a rate ($\lambda_F + f\lambda_{FB}$), or infection with BTB, following effective contact with BTB-infectious lion or buffalo, at a rate [$\lambda_B + (1 - f)\lambda_{FB}$] or $\theta_{BB}\lambda_{BB}$, respectively, where

$$\begin{aligned} \lambda_F &= \frac{\beta_F(E_{LF2} + \eta_{F1}J_F)}{N_L}, \quad \lambda_B = \frac{\beta_B(\eta_{B1}E_{LB1} + \eta_{B2}E_{LB2} + I_{LB})}{N_L}, \\ \lambda_{FB} &= \frac{\beta_{FB}(\eta_{FB}D_{L1} + D_{L2})}{N_L}, \quad \lambda_{BB} = \frac{\beta_{BB}I_{BB}}{N_B}. \end{aligned} \tag{2.1}$$

In (2.1), λ_F is the rate at which infected lions in advanced stage (E_{LF2}) of FIV infection and isolated lions with FIV (J_F) transmit FIV to susceptible lions or BTB-infected lions in the E_{LB2} and I_{LB} classes, and λ_B is the rate at which lions infected with BTB in the early (E_{LB1}) and late stage (E_{LB2}), as well as those with clinical symptoms of BTB (I_{LB}), transmit BTB to susceptible or exposed lions. Similarly, λ_{FB} is the rate at which dually-infected lions (in the D_{L1} and D_{L2} classes) transmit either BTB or FIV to susceptible lions or BTB-infected lions in the E_{LB2} and I_{LB} classes. Finally, λ_{BB} is the rate at which infected buffalos with clinical symptoms of BTB transmit BTB to susceptible buffalos or susceptible lions. The parameters β_F , β_B , β_{FB} and β_{BB} are the effective contact rates (contacts capable of leading to BTB or FIV infection) for the

transmission of FIV by infected lions, BTB by infected lions, BTB or FIV by dually-infected lions and BTB by infected buffalos, respectively. Furthermore, $0 \leq \eta_{F1} < 1$ is a modification parameter accounting for the assumed reduction in infectiousness of isolated lions, in comparison to lions infected with FIV only at advanced-stage of infection. The modification parameters $0 \leq \eta_{B1} < 1$ and $0 \leq \eta_{B2} < 1$ account for the assumed reduction in infectiousness of exposed lions, in the E_{LB1} and E_{LB2} classes in comparison to infected lions in the I_{LB} class. Similarly, η_{FB} accounts for the assumed reduction of the infectiousness of dually-infected lions in the D_{L1} class in comparison to those in the D_{L2} class. The parameter $0 < f < 1$ is the proportion of susceptible lions that are infected with FIV by dually-infected lions with both diseases. Natural death is assumed to occur in all lion compartments at a rate μ_L . Thus, the rate of change of the susceptible lion population is given by

$$\frac{dS_L}{dt} = \Pi_L - (\lambda_F + \lambda_B + \lambda_{FB} + \theta_{BB}\lambda_{BB})S_L - \mu_L S_L,$$

where $0 \leq \theta_{BB} < 1$ accounts for the expected reduced likelihood of infectious buffalos (in the I_{LB} class) transmitting BTB to susceptible lions (in comparison to BTB transmission from infected buffalo to a susceptible buffalo).

The population of lions infected with FIV only at early-stage of infection ($E_{LF1}(t)$) is generated by the infection of susceptible lions with FIV (at the rate $\lambda_F + f\lambda_{FB}$), and is decreased by the development of clinical symptoms of FIV (at a rate σ_F), co-infection with BTB (at a rate $\theta_B(\lambda_B + \lambda_{FB})$; where $0 \leq \theta_B < 1$ accounts for the assumption that co-infection of FIV infected lions with BTB occurs at a rate lower than primary infection of susceptible lions with BTB) and natural death, so that (the authors have found no evidence for BTB exogenous re-infection in the lion population, hence not included in this study):

$$\frac{dE_{LF1}}{dt} = (\lambda_F + f\lambda_{FB})S_L - \theta_B(\lambda_B + \lambda_{FB})E_{LF1} - (\sigma_F + \mu_L)E_{LF1}.$$

The population of lions infected with FIV only at advanced-stage of infection ($E_{LF2}(t)$) increases following the development of clinical symptoms of FIV by lions in E_{LF1} class (at the rate σ_F). This population is decreased by co-infection with BTB (at the rates $\theta_B(\lambda_B + \lambda_{FB})$), isolation (at a rate ξ_F) and natural death, this gives,

$$\frac{dE_{LF2}}{dt} = \sigma_F E_{LF1} - \theta_B(\lambda_B + \lambda_{FB})E_{LF2} - (\xi_F + \mu_L)E_{LF2}.$$

The population of lions infected with FIV only that are isolated (and/or treated) ($J_F(t)$) is generated by the isolations of lion with clinical symptoms of FIV (at the rate ξ_F). It is decreased by natural death. Hence,

$$\frac{dJ_F}{dt} = \xi_F E_{LF2} - \mu_L J_F.$$

Similarly, the population of lions infected with BTB only at early-stage of infection ($E_{LB1}(t)$) is generated by the infection of susceptible lions with BTB (at the rates $\lambda_B + (1 - f)\lambda_{FB} + \theta_{BB}\lambda_{BB}$), and is decreased by progressing to the advanced stage of infection with BTB (at a rate σ_{B1}) and natural death, so that

$$\frac{dE_{LB1}}{dt} = [\lambda_B + (1 - f)\lambda_{FB} + \theta_{BB}\lambda_{BB}]S_L - (\sigma_{B1} + \mu_L)E_{LB1}.$$

The population of lions infected with BTB only at advanced-stage of infection ($E_{LB2}(t)$) increases following the progression of lions infected with BTB only at early-stage of infection to advanced-stage (at the rate σ_{B1}). This population is decreased by FIV co-infection (at a rate $\theta_F(\lambda_F + \lambda_{FB})$; where $0 \leq \theta_F < 1$ accounts for the assumption that co-infection of BTB infected lions with FIV occurs at a rate lower than primary infection of susceptible lions with FIV), detection and isolation (at a rate ξ_F), development of clinical symptoms of BTB (at a rate σ_{B2}) and natural death, so that (it is assumed that FIV-infected lions placed in isolation are treated against FIV)

$$\frac{dE_{LB2}}{dt} = \sigma_{B1}E_{LB1} - \theta_F(\lambda_F + \lambda_{FB})E_{LB2} - (\sigma_{B2} + \mu_L)E_{LB2}.$$

The population of lions with clinical symptoms of BTB ($I_{LB}(t)$) increases following the development of clinical symptoms of BTB by lions infected with BTB only at the advanced-stage of infection (at the rate σ_{B2}). This population is decreased by co-infection with FIV (at the rate $\theta_F(\lambda_F + \lambda_{FB})$), treatment (at a rate ξ_B), natural death and BTB-induced death (at a rate δ_B), so that

$$\frac{dI_{LB}}{dt} = \sigma_{B2}E_{LB2} - \theta_F(\lambda_F + \lambda_{FB})I_{LB} - (\xi_B + \mu_L + \delta_B)I_{LB}.$$

The population of lions with BTB only that are treated against BTB ($W_{LB}(t)$) is generated by the treatment of lions with clinical symptoms of BTB (at the rate ξ_B). It is decreased by natural death. Hence,

$$\frac{dW_{LB}}{dt} = \xi_B I_{LB} - \mu_L W_{LB}.$$

The population of dually-infected lions with FIV and advanced-exposed to BTB (D_{L1}) is generated by the co-infection of lions in the E_{LF1} class with BTB (at the rate $\theta_B(\lambda_B + \lambda_{FB})$) and lions in E_{LB2} class with FIV (at the rate $\theta_F(\lambda_F + \lambda_{FB})$). This population is decreased by the progression to the class of dually-infected lions with symptoms of both FIV and BTB (at a rate σ_D) and by natural death, so that

$$\frac{dD_{L1}}{dt} = \theta_B(\lambda_B + \lambda_{FB})E_{LF1} + \theta_F(\lambda_F + \lambda_{FB})E_{LB2} - (\sigma_D + \mu_L)D_{L1}.$$

The population of dually-infected lions with symptoms of both FIV and BTB (D_{L2}) is generated by the development of symptoms of both FIV and BTB by lions in D_{L1}

class and co-infection of lion in E_{LF2} class with BTB (at the rate $\theta_B(\lambda_B + \lambda_{FB})$) and lions in I_{LB} class with FIV (at the rate $\theta_F(\lambda_F + \lambda_{FB})$). It is decreased by treatment (at a rate ξ_D) and natural death, this gives

$$\frac{dD_{L2}}{dt} = \sigma_D D_{L1} + \theta_B(\lambda_B + \lambda_{FB})E_{LF2} + \theta_F(\lambda_F + \lambda_{FB})I_{LB} - (\xi_D + \mu_L)D_{L2}.$$

The population of treated lions population (J_{FB}) is increased by the treatment of lions with symptoms of both diseases (at the rate ξ_D) and decreased due to natural death. Hence,

$$\frac{dJ_{FB}}{dt} = \xi_D D_{L2} - \mu_L J_{FB}.$$

Similarly, the population of susceptible buffalos ($S_B(t)$) is generated by the recruitment of buffalos (either by birth or re-stocking from other herds) at a rate Π_B . The population of susceptible buffalos is decreased by the acquisition of BTB infection (following effective contact with buffalos infected with BTB), at the rate λ_{BB} , and by natural death (at a rate μ_B ; buffalos in each epidemiological compartment are assumed to suffer natural death at this rate). Thus,

$$\frac{dS_B}{dt} = \Pi_B - \lambda_{BB}S_B - \mu_B S_B.$$

The population of buffalos exposed to BTB ($E_{BB}(t)$) is increased by the infection of susceptible buffalos with BTB (at the rate λ_{BB}). This population is decreased by exogenous re-infection with BTB (at a rate $\theta_{EB}\lambda_{BB}$; with $0 \leq \theta_{EB} < 1$ accounting for the assumption that re-infection of exposed buffalos with BTB occurs at a rate lower than primary infection of susceptible buffalos with BTB), development of clinical symptoms of BTB (at a rate σ_{BB}) and natural death, so that

$$\frac{dE_{BB}}{dt} = \lambda_{BB}S_B - \theta_{EB}\lambda_{BB}E_{BB} - (\sigma_{BB} + \mu_B)E_{BB}.$$

The population of buffalos with clinical symptoms of BTB ($I_{BB}(t)$) is increased by the development of clinical symptoms of exposed buffalos with BTB (at the rate σ_{BB}) and by the exogenous re-infection of exposed buffalos (at the rate $\theta_{EB}\lambda_{BB}$). It is decreased by recovery (at a rate ξ_{BB}), natural death and by BTB-induced mortality (at a rate δ_{BB}). Thus,

$$\frac{dI_{BB}}{dt} = \sigma_{BB}E_{BB} + \theta_{EB}\lambda_{BB}E_{BB} - (\xi_{BB} + \mu_B + \delta_{BB})I_{BB}.$$

Finally, the recovered buffalos population (R_{BB}) is generated by the recovery of buffalos with symptoms of BTB (at the rate ξ_{BB}) and decrease by natural death. Hence,

$$\frac{dR_{BB}}{dt} = \xi_{BB}I_{BB} - \mu_B R_{BB}.$$

In summary, the BTB-FIV transmission model is given by the following system of non-linear differential equations (a flow diagram of the model is given in Figure 1 and the associated variables and parameters are described in Tables 1 and 2, respectively):

$$\left. \begin{aligned}
& \frac{dS_L}{dt} = \Pi_L - (\lambda_F + \lambda_B + \lambda_{FB} + \theta_{BB}\lambda_{BB})S_L - \mu_L S_L, \\
& \frac{dE_{LF1}}{dt} = (\lambda_F + f\lambda_{FB})S_L - \theta_B(\lambda_B + \lambda_{FB})E_{LF1} - (\sigma_F + \mu_L)E_{LF1}, \\
& \frac{dE_{LF2}}{dt} = \sigma_F E_{LF1} - \theta_B(\lambda_B + \lambda_{FB})E_{LF2} - (\xi_F + \mu_L)E_{LF2}, \\
& \frac{dJ_F}{dt} = \xi_F E_{LF2} - \mu_L J_F, \\
& \frac{dE_{LB1}}{dt} = [\lambda_B + (1-f)\lambda_{FB} + \theta_{BB}\lambda_{BB}]S_L - (\sigma_{B1} + \mu_L)E_{LB1}, \\
& \frac{dE_{LB2}}{dt} = \sigma_{B1}E_{LB1} - \theta_F(\lambda_F + \lambda_{FB})E_{LB2} - (\sigma_{B2} + \mu_L)E_{LB2}, \\
& \frac{dI_{LB}}{dt} = \sigma_{B2}E_{LB2} - \theta_F(\lambda_F + \lambda_{FB})I_{LB} - (\xi_B + \mu_L + \delta_B)I_{LB}, \\
& \frac{dW_{LB}}{dt} = \xi_B I_{LB} - \mu_L W_{LB}, \\
& \frac{dD_{L1}}{dt} = \theta_B(\lambda_B + \lambda_{FB})E_{LF1} + \theta_F(\lambda_F + \lambda_{FB})E_{LB2} - (\sigma_D + \mu_L)D_{L1}, \\
& \frac{dD_{L2}}{dt} = \sigma_D D_{L1} + \theta_B(\lambda_B + \lambda_{FB})E_{LF2} + \theta_F(\lambda_F + \lambda_{FB})I_{LB} - (\xi_D + \mu_L)D_{L2}, \\
& \frac{dJ_{FB}}{dt} = \xi_D D_{L2} - \mu_L J_{FB},
\end{aligned} \right\} \text{Lions} \quad (2.2)$$

$$\left. \begin{aligned}
& \frac{dS_B}{dt} = \Pi_B - \lambda_{BB}S_B - \mu_B S_B, \\
& \frac{dE_{BB}}{dt} = \lambda_{BB}S_B - \theta_{EB}\lambda_{BB}E_{BB} - (\sigma_{BB} + \mu_B)E_{BB}, \\
& \frac{dI_{BB}}{dt} = \sigma_{BB}E_{BB} + \theta_{EB}\lambda_{BB}E_{BB} - (\xi_{BB} + \mu_B + \delta_{BB})I_{BB}, \\
& \frac{dR_{BB}}{dt} = \xi_{BB}I_{BB} - \mu_B R_{BB}.
\end{aligned} \right\} \text{Buffalos}$$

Some of the main assumptions made in the formulation of the model (2.2) include:

- (i) Homogeneous mixing is assumed within and between the two (lion and buffalo) populations [43]. This assumption may not be entirely realistic in the lion population (since lions typically live in patches). However, the current study consider the study area (KNP) to be a single herd (the authors plan to extend this study by using a multi-patch modeling approach which accounts for the non-uniform mixing of the lion population).

- (ii) Infectious buffalos can transmit BTB to susceptible lions (*via* lions preying on buffalos infected with BTB), but infectious lion do not transmit FIV to susceptible buffalos (this is owing to the fact that contact between lion and buffalo resulted in the death of buffalo [6]).
- (iii) Susceptible lions acquire FIV infection only through contacts with FIV infectious lions (E_{LF2} and J_F) [56].
- (iv) Exposed buffalos can experience exogenous re-infection with BTB (following effective contact with symptomatic buffalos) [36].
- (v) No BTB exogenous re-infection in the lion population is assumed (the authors could not find any evidence for this at the current time).

For mathematical tractability, other FIV transmission pathways in the lion population (such as vertical transmission and infection acquired *via* lion-to-lion fights for territory/resources [55]) are not considered in this study. The model (2.2), to the authors' knowledge, is the first to incorporate buffalos and lions in the transmission dynamics of BTB and FIV. The model (2.2) extends numerous models for FIV and BTB transmission in the literature, such as those in [10, 36, 38, 39, 43, 57, 60], by, *inter alia*,

- (i) Including the dynamics of early- and advanced- infected lions with FIV (this was not considered in [39, 43]).
- (ii) Allowing for BTB and FIV transmission by exposed and lions (this was not considered in [38, 57, 60]).
- (iii) Allowing for the re-infection of exposed buffalos (this was not considered in [10, 38, 39, 60]).
- (iv) Allowing for the co-infection of BTB and FIV in lion populations (this was not considered in [39, 43]).

3 Analysis of the Model

3.1 Basic Properties

For the model (2.2) to be epidemiologically meaningful, it is important to prove that all its solutions remain non-negative for all non-negative initial data (i.e., its state variables remain non-negative for all time t , since it monitors animal populations).

Lemma 1 *Let the initial data $S_L(0) > 0$, $E_{LF1}(0) \geq 0$, $E_{LF2}(0) \geq 0$, $J_F(0) \geq 0$, $E_{LB1}(0) \geq 0$, $E_{LB2}(0) \geq 0$, $I_{LB}(0) \geq 0$, $W_{LB}(0) \geq 0$, $D_{L1}(0) \geq 0$, $D_{L2}(0) \geq 0$, $J_{FB}(0) \geq 0$, $S_B(0) > 0$, $E_{BB}(0) \geq 0$, $I_{BB}(0) \geq 0$, $R_{BB}(0) \geq 0$, then the solutions $S_L(t)$, $E_{LF1}(t)$, $E_{LF2}(t)$*

$J_F(t)$, $E_{LB1}(t)$, $E_{LB2}(t)$, $I_{LB}(t)$, $W_{LB}(t)$, $D_{L1}(t)$, $D_{L2}(t)$, $J_{FB}(t)$, $S_B(t)$, $E_{BB}(t)$, $I_{BB}(t)$ and $R_{BB}(t)$ of the model (2.2) are positive for all $t \geq 0$.

Proof. Consider the first equation in model (2.2), given by

$$\frac{dS_L}{dt} = \Pi_L - (\lambda_F + \lambda_B + \lambda_{FB} + \theta_{BB}\lambda_{BB})S_L - \mu_L S_L,$$

which is equivalent to

$$\frac{dS_L}{dt} + [(\lambda_F + \lambda_B + \lambda_{FB} + \theta_{BB}\lambda_{BB}) + \mu_L]S_L = \Pi_L > 0. \quad (3.1)$$

Consider the integrating factor

$$\rho(t) = \exp \left\{ \mu_L t + \int_0^t [\lambda_F(\tau) + \lambda_B(\tau) + \lambda_{FB}(\tau) + \theta_{BB}\lambda_{BB}(\tau)] d\tau \right\} > 0.$$

Multiplying both sides of equation (3.1) by $\rho(t)$ gives

$$\rho(t) \left[\frac{dS_L}{dt} + \{(\lambda_F + \lambda_B + \lambda_{FB} + \theta_{BB}\lambda_{BB}) + \mu_L\} S_L \right] = \frac{d(\rho(t)S_L(t))}{dt} = \rho(t)\Pi_L,$$

so that

$$\frac{d(\rho(t)S_L(t))}{dt} = \rho(t)\Pi_L,$$

from which it follows that,

$$S_L(t) = \frac{1}{\rho(t)} \left[S_L(0) + \Pi_L \int_0^t \rho(\tau) d\tau \right] \geq 0.$$

Thus, $S_L(t) > 0$ for all $t \geq 0$. Similarly, it can be shown that $E_{LF1}(t) \geq 0$, $E_{LF2}(t) \geq 0$, $J_F(t) \geq 0$, $E_{LB1}(t) \geq 0$, $E_{LB2}(t) \geq 0$, $I_{LB}(t) \geq 0$, $W_{LB}(t) \geq 0$, $D_{L1}(t) \geq 0$, $D_{L2}(t) \geq 0$, $J_{FB}(t) \geq 0$, $S_B > 0$, $E_{BB} \geq 0$, $I_{BB} \geq 0$, $R_{BB} \geq 0$. \blacksquare

Lemma 2 *The following biologically-feasible region of the model (2.2) is positively-invariant.*

$$\Gamma = \left\{ (S_L, E_{LF1}, E_{LF2}, J_F, E_{LB1}, E_{LB2}, I_{LB}, W_{LB}, D_{L1}, D_{L2}, J_{FB}, S_B, E_{BB}, I_{BB}, R_{BB}) \right. \\ \left. \in \mathbb{R}_+^{15} : N_L \leq \frac{\Pi_L}{\mu_L}, N_B \leq \frac{\Pi_B}{\mu_B} \right\}.$$

Proof. The equations for the lion and buffalo components of the model (2.2) gives

$$\frac{dN_L(t)}{dt} = \Pi_L - \mu_L N_L - \delta_B I_{LB} \quad \text{and} \quad \frac{dN_B(t)}{dt} = \Pi_B - \mu_B N_B - \delta_{BB} I_{BB}, \quad (3.2)$$

so that,

$$\frac{dN_L(t)}{dt} \leq \Pi_L - \mu_L N_L \quad \text{and} \quad \frac{dN_B(t)}{dt} \leq \Pi_B - \mu_B N_B. \quad (3.3)$$

Thus, $dN_L/dt < 0$ if $N_L(t) > \Pi_L/\mu_L$ and $dN_B/dt < 0$ if $N_B(t) > \Pi_B/\mu_B$. It follows from the inequalities in (3.3), and the Gronwall lemma [40], that

$$N_L(t) \leq N_L(0)e^{-\mu_L t} + \frac{\Pi_L}{\mu_L} [1 - e^{-\mu_L t}] \quad \text{and} \quad N_B(t) \leq N_B(0)e^{-\mu_B t} + \frac{\Pi_B}{\mu_B} [1 - e^{-\mu_B t}].$$

In particular, $N_L(t) \leq \Pi_L/\mu_L$ if $N_L(0) \leq \Pi_L/\mu_L$ and $N_B(t) \leq \Pi_B/\mu_B$ if $N_B(0) \leq \Pi_B/\mu_B$. Thus, the region Γ is positively-invariant with respect to the model (2.2). \blacksquare

3.2 Local Asymptotic Stability of Disease-free Equilibrium (DFE)

The DFE of the model (2.2) is given by

$$\begin{aligned} \mathcal{E}_0 &= (S_L^*, E_{LF1}^*, E_{LF2}^*, J_F^*, E_{LB1}^*, E_{LB2}^*, I_{LB}^*, W_{LB}^*, D_{L1}^*, D_{L2}^*, J_{FB}^*, S_B^*, E_{BB}^*, I_{BB}^*, R_{BB}^*) \\ &= \left(\frac{\Pi_L}{\mu_L}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, \frac{\Pi_B}{\mu_B}, 0, 0, 0 \right). \end{aligned}$$

The linear stability of \mathcal{E}_0 can be established using the next generation operator on the system (2.2). Using the notation in [58], the matrices F and V , for the new infection terms and the remaining transfer terms, are, respectively, given by

$$F = \begin{pmatrix} F_{4 \times 6}^{(11)} & F_{4 \times 6}^{(12)} \\ \mathbf{0}_{8 \times 11} & F_{8 \times 1}^{(22)} \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} V_{7 \times 6}^{(1)} & \mathbf{0}_{6 \times 6} \\ \mathbf{0}_{5 \times 6} & V_{6 \times 6}^{(2)} \end{pmatrix},$$

where $F^{(22)} = (0, 0, 0, 0, 0, 0, \beta_{BB}, 0)^T$,

$$F^{(11)} = \begin{pmatrix} 0 & \beta_F & \beta_F \eta_{F1} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_B \eta_{B1} & \beta_B \eta_{B2} & \beta_B \end{pmatrix},$$

$$F^{(12)} = \begin{pmatrix} 0 & f \beta_{FB} \eta_{FB} & f \beta_{FB} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & (1-f) \beta_{FB} \eta_{FB} & (1-f) \beta_{FB} & 0 & 0 & \frac{\theta_{BB} \beta_{BB} S_L^*}{N_B^*} \end{pmatrix},$$

$$V^{(1)} = \begin{pmatrix} K_1 & 0 & 0 & 0 & 0 & 0 \\ -\sigma_F & K_2 & 0 & 0 & 0 & 0 \\ 0 & -\xi_F & \mu_L & 0 & 0 & 0 \\ 0 & 0 & 0 & K_3 & 0 & 0 \\ 0 & 0 & 0 & -\sigma_{B1} & K_4 & 0 \\ 0 & 0 & 0 & 0 & -\sigma_{B2} & K_5 \\ 0 & 0 & 0 & 0 & 0 & -\xi_B \end{pmatrix}$$

and,

$$V^{(2)} = \begin{pmatrix} \mu_L & 0 & 0 & 0 & 0 & 0 \\ 0 & K_6 & 0 & 0 & 0 & 0 \\ 0 & -\sigma_D & K_7 & 0 & 0 & 0 \\ 0 & 0 & -\xi_D & \mu_L & 0 & 0 \\ 0 & 0 & 0 & 0 & K_8 & 0 \\ 0 & 0 & 0 & 0 & -\xi_{BB} & K_9 \end{pmatrix},$$

with $K_1 = \sigma_F + \mu_L$, $K_2 = \xi_F + \mu_L$, $K_3 = \sigma_{B1} + \mu_L$, $K_4 = \sigma_{B2} + \mu_L$, $K_5 = \xi_B + \mu_L + \delta_B$, $K_6 = \sigma_D + \mu_L$, $K_7 = \xi_D + \mu_L$, $K_8 = \sigma_{BB} + \mu_B$ and $K_9 = \xi_{BB} + \mu_B + \delta_{BB}$. Thus, the associated (overall) reproduction number of the model (denoted by \mathcal{R}_0) is given by

$$\mathcal{R}_0 = \rho(FV^{-1}) = \max\{\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3\}, \quad (3.4)$$

where

$$\mathcal{R}_1 = \frac{\beta_F \sigma_F (\eta_{F1} \xi_F + \mu_L)}{\mu_L K_1 K_2}, \quad (3.5)$$

$$\mathcal{R}_2 = \frac{\beta_B [\sigma_{B1} (K_5 \eta_{B2} + \sigma_{B2}) + \eta_{B1} K_4 K_5]}{K_3 K_4 K_5}, \quad (3.6)$$

$$\mathcal{R}_3 = \frac{\beta_{BB} \sigma_{BB}}{K_8 K_9}. \quad (3.7)$$

are the constituent reproduction threshold quantities associated with FIV transmission in the lion population, BTB transmission in the lion population and BTB transmission in the buffalo population, respectively. The result below follows from Theorem 2 of [58]:

Theorem 1 *The disease-free equilibrium, \mathcal{E}_0 , of the model (2.2), is locally-asymptotically stable (LAS) if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$.*

The threshold quantity \mathcal{R}_0 measures the average number of new infections generated by a single infected lion or buffalo in a completely susceptible lions and buffalos population [58]. Thus, Theorem 1 implies that both BTB and FIV can be eliminated from the lions and buffalos population (when $\mathcal{R}_0 < 1$) if the initial sizes of the sub-populations of the model (2.2) are in the basin of attraction of the DFE (\mathcal{E}_0).

3.2.1 Interpretation of reproduction number

The reproduction threshold (\mathcal{R}_0) can be epidemiologically interpreted as follows. Susceptible lions can acquire FIV infection following effective contacts with FIV-infectious lions either at the advanced-stage of FIV infection (E_{LF2}) or those that are isolated/treated for FIV (i.e., those in the J_F class).

Interpretation of \mathcal{R}_1

(i) *New FIV cases generated by FIV-infected lions in the E_{LF2} class:*

The average number of new FIV cases in lion population generated by an FIV-infectious lion in the E_{LF2} class (near the DFE) is the product of the infection rate of infected lions in the E_{LF2} class ($\beta_F \frac{S_L^*}{N_L^*} = \beta_F$, since $S_L^*/N_L^* = 1$), the probability that a lion in the E_{LF2} class survived the E_{LF1} class and moved to the advanced (E_{LF2}) stage (σ_F/K_1) and the average duration in the E_{LF2} class ($1/K_2$). Thus, the average number of new cases generated by a lion in the E_{LF2} class is given by

$$\mathcal{R}_{01} = \beta_F \left(\frac{\sigma_F}{K_1} \right) \left(\frac{1}{K_2} \right) \quad (3.8)$$

(ii) *New FIV cases generated by lions in the J_F class:*

Similarly, the average number of new FIV cases in the lion population by an infected lion in the J_F class (near the DFE) is the product of the infection rate of lion in the J_F class ($\beta_F \eta_{F1} \frac{S_L^*}{N_L^*} = \beta_F \eta_{F1}$), the probability that an FIV-infected lion survives the E_{LF1} and E_{LF2} stages and moved to the isolated class J_F ($\frac{\sigma_F \xi_F}{K_1 K_2}$) and the average duration in the J_F class ($\frac{1}{\mu_L}$). Thus, the average number of new FIV infections generated by a lion in the J_F class is given by:

$$\mathcal{R}_{02} = (\beta_F \eta_{F1}) \left(\frac{\sigma_F}{K_1} \right) \left(\frac{\xi_F}{K_2} \right) \left(\frac{1}{\mu_L} \right). \quad (3.9)$$

The sum of the expressions in Equations (3.8) and (3.9) gives \mathcal{R}_1 .

Interpretation of \mathcal{R}_2

Susceptible lions can acquire BTB infection following effective contacts with BTB-infectious lions in either the early (E_{LB1}) or advanced (E_{LB2}) stage of BTB infection or BTB-infectious lions with clinical symptoms of BTB (i.e., lions in the I_{LB} class).

(i) *New BTB cases generated by lions in the E_{LB1} class:*

The average number of new BTB-infected lions generated by an infected lion in the E_{LB1} class is the product of the infection rate of an infected lion in the early-stage (E_{LB1}) of BTB infection ($\beta_B \eta_{B1} \frac{S_L^*}{N_L^*} = \beta_B \eta_{B1}$) and the average duration in the E_{LB1} class ($\frac{1}{K_3}$). Thus, the number of new BTB cases in lions generated by a BTB-infected lion in the E_{LB1} class is given by

$$\mathcal{R}_2^{(01)} = (\beta_B \eta_{B1}) \left(\frac{1}{K_3} \right). \quad (3.10)$$

(ii) *New BTB cases generated by lions in the E_{LB2} class:*

This is given by the product of the infection rate of BTB-infected lions in the advanced (E_{LB2}) stage of BTB infection ($\beta_B \eta_{B2} \frac{S_L^*}{N_L^*} = \beta_B \eta_{B2}$), the probability that an infected lion with BTB survived the early-stage of infection and moved to the advanced-stage ($\frac{\sigma_{B1}}{K_3}$) and the average duration in the E_{LB2} stage ($\frac{1}{K_4}$). Thus, the average number of BTB infections in the lion population generated by an infected lion in the E_{LB2} class is given by:

$$\mathcal{R}_2^{(02)} = (\beta_B \eta_{B2}) \left(\frac{\sigma_{B1}}{K_3} \right) \left(\frac{1}{K_4} \right). \quad (3.11)$$

(iii) *New BTB cases generated by lions in the I_{LB} class:*

Finally, the average number of new BTB-infected lions generated by an infectious lions with clinical symptoms of BTB (in the I_{LB} class) is the product of the infection rate of infectious lions in the I_{LB} class ($\beta_B \frac{S_L^*}{N_L^*} = \beta_B$), the probability that an infected lion survived the early (E_{LB1}) and advanced (E_{LB2}) stages and moved to the infectious (I_{LB}) stage ($\frac{\sigma_{B1}}{K_3} \frac{\sigma_{B2}}{K_4}$) and the average duration in the infectious (I_{LB}) stage ($\frac{1}{K_5}$). Thus, the average number of new BTB infections in lions generated by lions in the I_{LB} class is given by:

$$\mathcal{R}_2^{(03)} = (\beta_B) \left(\frac{\sigma_{B1}}{K_3} \right) \left(\frac{\sigma_{B2}}{K_4} \right) \left(\frac{1}{K_5} \right). \quad (3.12)$$

The sum of the expressions in Equations (3.10), (3.11) and (3.12) gives \mathcal{R}_2 .

It should be noted that lions in the dually-infected classes D_{L1} and D_{L2} do not contribute to \mathcal{R}_0 (since the two classes are populated *via* secondary, and not primary, infection).

3.2.2 Interpretation of \mathcal{R}_3

Susceptible buffalos can acquire BTB infection following effective contacts with infectious buffalos in the I_{BB} class. The average number of new BTB infections in the buffalo population generated by an infectious buffalo (near the DFE) is given by the product of the BTB infection rate of buffalos ($\beta_{BB} \frac{S_B^*}{N_B^*} = \beta_{BB}$, since $\frac{S_B^*}{N_B^*} = 1$), the probability that an exposed buffalo survived the exposed (E_{BB}) class and moved to the infectious (I_{BB}) class ($\frac{\sigma_{BB}}{K_8}$) and the average duration in the I_{BB} class ($\frac{1}{K_9}$). Hence, the average number of new BTB cases generated by an infected buffalo is given by:

$$\mathcal{R}_3 = (\beta_{BB}) \left(\frac{\sigma_{BB}}{K_8} \right) \left(\frac{1}{K_9} \right). \quad (3.13)$$

The maximum of \mathcal{R}_1 , \mathcal{R}_2 and \mathcal{R}_3 gives \mathcal{R}_0 .

3.3 Backward Bifurcation Analysis

Some models for disease transmission, particularly those that include the re-infection of exposed individuals (such as model (2.2)), are known to exhibit the phenomenon of backward bifurcation (where the stable DFE co-exists with at least one stable endemic equilibrium when the associated reproduction threshold of the model is less than unity; see, for instance, [19, 33, 46]). It is, therefore, instructive, to explore the possibility of the existence of such phenomenon in the model (2.2). This is explored below.

3.3.1 Existence

Let,

$$\mathcal{E}_e = (S_L^{**}, E_{LF1}^{**}, E_{LF2}^{**}, J_F^{**}, E_{LB1}^{**}, E_{LB2}^{**}, I_{LB}^{**}, W_{LB}^{**}, D_{L1}^{**}, D_{L2}^{**}, J_{FB}^{**}, S_L^{**}, E_{BB}^{**}, I_{BB}^{**}, R_{BB}^{**})$$

represents any arbitrary endemic equilibrium of the model (2.2) (that is, an equilibrium in which at least one of the infected components is non-zero). We claim the following result (the proof, based on using center manifold theory [19], is given in Appendix A):

Theorem 2 *The model (2.2) exhibits backward bifurcation at $\mathcal{R}_0 = 1$ whenever the bifurcation coefficient, \tilde{a} , given by Equation (A.2) in Appendix A, is positive.*

The phenomenon of backward bifurcation of the model (2.2) is numerically illustrated (Figure 2) (using a set of arbitrarily-chosen parameter values that satisfy the conditions for the existence of the backward bifurcation specified in Appendix A). The epidemiological implication of the phenomenon of backward bifurcation is that the classical requirement of $\mathcal{R}_0 < 1$ is, although necessary, no longer sufficient for the effective control of the BTB-FIV in the lion-buffalo population. Hence, the presence of backward

bifurcation makes the feasibility of the effective control of BTB and FIV in the lion-buffalo population difficult. To the authors' knowledge, this is the first time such a dynamic phenomenon is established in the transmission dynamics of BTB-FIV. The possible cause(s) of this phenomenon is(are) explored below.

3.3.2 Non-existence

Consider the model (2.2) for the case where BTB-infected lions do not acquire FIV infection (i.e., $\theta_F = 0$), FIV-infected lions do not acquire BTB infection (i.e., $\theta_B = 0$), and exposed buffalos with BTB do not acquire BTB re-infection ($\theta_{EB} = 0$). It follows, by substituting $\theta_B = \theta_F = \theta_{EB} = 0$ into the expression for the backward bifurcation coefficient (\tilde{a}), given by Equation (A.2) in Appendix A (and simplifying), that the associated backward bifurcation coefficient (\tilde{a}) reduces to (noting, from Appendix A, that the eigenvectors $w_1, \dots, w_8, w_{13}, w_{14}, w_{15}$ and v_1, \dots, v_{15} are all positive):

$$\begin{aligned} \tilde{a} = & -\frac{2\mu_B\mu_L}{\Pi_B\Pi_L} \left[\frac{\Pi_B}{\mu_B} \beta_F^* (\eta_{F1}w_4 + w_3) \left(v_2 \sum_{i=2}^8 w_i \right) + \frac{\Pi_B}{\mu_B} \beta_B (\eta_{B1}w_5 + \eta_{B2}w_6 + w_7) \left(v_5 \sum_{i=2}^8 w_i \right) \right. \\ & \left. + \frac{\Pi_L}{\mu_L} \beta_{BB} w_{14} [v_{13}(w_{13} + w_{14} + w_{15})] \right] < 0. \end{aligned} \quad (3.14)$$

Thus, it follows from Theorem 4.1 of [19], that the model (2.2) does not undergo a backward bifurcation at $\mathcal{R}_0 = 1$ in the absence of BTB-FIV co-infection in lions and re-infection of exposed buffalos (this result is consistent with that in [19, 36, 51], on the transmission dynamics of *mycobacterium tuberculosis* and BTB in human and buffalo populations).

It is worth stating, however, that the backward bifurcation phenomenon persists even if the aforementioned co-infection assumption is relaxed. In other words, backward bifurcation still occurs in the FIV-BTB dynamics even if $\theta_F = \theta_B = 0$, provided that $\theta_{EB} \neq 0$. Hence, this study identifies two sufficient conditions for the existence of backward bifurcation in the model (2.2), namely the FIV-BTB co-infection in lions and the re-infection of exposed buffalos. To further confirm the absence of backward bifurcation in the model (2.2) for the aforementioned special case (i.e, the model (2.2) with $\theta_F = \theta_B = \theta_{EB} = 0$), a global asymptotic stability of the DFE is established for this case below.

Theorem 3 *The DFE, \mathcal{E}_0 , of the model (2.2) with $\theta_F = \theta_B = \theta_{EB} = 0$ is globally-asymptotically stable (GAS) in Γ if $\mathcal{R}_0 \leq 1$.*

Proof. Consider the BTB-FIV model (2.2) in the absence of FIV-BTB co-infection in the lion population (i.e., $\theta_F = \theta_B = 0$) and re-infection of exposed buffalos (i.e., $\theta_{EB} = 0$). It follows first of all, by setting $\theta_F = \theta_B = \theta_{EB} = 0$ in the model (2.2), that $D_{L1}(t) \rightarrow 0$, $D_{L2}(t) \rightarrow 0$ and $J_{FB}(t) \rightarrow 0$, as $t \rightarrow \infty$ (i.e., the equations for

$D_{L1}(t)$, $D_{L2}(t)$ and $J_{FB}(t)$ decouple from the model). Furthermore, consider the following linear Lyapunov function

$$\begin{aligned} \mathcal{F} = & \mathcal{R}_1 E_{LF1} + \frac{K_1}{\sigma_F} E_{LF2} + \frac{\eta_{F1} \beta_F}{\mu_L} J_F + \mathcal{R}_2 E_{LB1} + \frac{\beta_B (K_5 \eta_{B2} + \sigma_{B2})}{K_4 K_5} E_{LB2} + \frac{\beta_B}{K_5} I_{LB} \\ & + \mathcal{R}_3 E_{BB} + \frac{\beta_{BB}}{K_9} I_{BB}, \end{aligned}$$

with Lyapunov derivative given by (where a dot represents differentiation with respect to t)

$$\begin{aligned}
\dot{\mathcal{F}} &= \mathcal{R}_1 \dot{E}_{LF1} + \frac{K_1}{\sigma_F} \dot{E}_{LF2} + \frac{\eta_{F1}\beta_F}{\mu_L} \dot{J}_F + \mathcal{R}_2 \dot{E}_{LB1} + \frac{\beta_B(K_5\eta_{B2} + \sigma_{B2})}{K_4K_5} \dot{E}_{LB2} + \frac{\beta_B}{K_5} \dot{I}_{LB} \\
&\quad + \mathcal{R}_3 \dot{E}_{BB} + \frac{\beta_{BB}}{K_9} \dot{I}_{BB}, \\
&= \mathcal{R}_1 \left(\lambda_F S_L - K_1 E_{LF1} \right) + \frac{K_1}{\sigma_F} \left(\sigma_F E_{LF1} - K_2 E_{LF2} \right) + \frac{\eta_{F1}\beta_F}{\mu_L} \left(\xi_F E_{LF2} - \mu_L J_F \right) \\
&\quad + \mathcal{R}_2 \left(\lambda_B S_L - K_3 E_{LB1} \right) + \frac{\beta_B(K_5\eta_{B2} + \sigma_{B2})}{K_4K_5} \left(\sigma_{B1} E_{LB1} - K_4 E_{LB2} \right) \\
&\quad + \frac{\beta_B}{K_5} \left(\sigma_{B2} E_{LB2} - K_5 I_{LB} \right) + \mathcal{R}_3 \left(\lambda_{BB} S_B - K_8 E_{BB} \right) + \frac{\beta_{BB}}{K_9} \left(\sigma_{BB} E_{BB} - K_9 I_{BB} \right), \\
&= \mathcal{R}_1 \left[\frac{\beta_F(E_{LF2} + \eta_{F1}J_F)}{N_L} S_L - K_1 E_{LF1} \right] + \frac{K_1}{\sigma_F} \mathcal{R}_1 \left(\sigma_F E_{LF1} - K_2 E_{LF2} \right) \\
&\quad + \frac{\eta_{F1}\beta_F}{\mu_L} \left(\xi_F E_{LF2} - \mu_L J_F \right) + \mathcal{R}_2 \left[\frac{\beta_B(\eta_{B1}E_{LB1} + \eta_{B2}E_{LB2} + I_{LB})}{N_L} S_L - K_3 E_{LB1} \right] \\
&\quad + \frac{\beta_B(K_5\eta_{B2} + \sigma_{B2})}{K_4K_5} \left(\sigma_{B1} E_{LB1} - K_4 E_{LB2} \right) + \frac{\beta_B}{K_5} \left(\sigma_{B2} E_{LB2} - K_5 I_{LB} \right) \\
&\quad + \mathcal{R}_3 \left[\frac{\beta_{BB}I_{BB}}{N_B} S_B - K_8 E_{BB} \right] + \frac{\beta_{BB}}{K_9} \left(\sigma_{BB} E_{BB} - K_9 I_{BB} \right), \\
&= \beta_F \left(\mathcal{R}_1 \frac{S_L}{N_L} - 1 \right) E_{LF2} + \beta_F \eta_{B2} \left(\mathcal{R}_1 \frac{S_L}{N_L} - 1 \right) J_F + \beta_B \eta_{B1} \left(\mathcal{R}_2 \frac{S_L}{N_L} - 1 \right) E_{LB1} \\
&\quad + \beta_B \eta_{B2} \left(\mathcal{R}_2 \frac{S_L}{N_L} - 1 \right) E_{LB2} + \beta_B \left(\mathcal{R}_2 \frac{S_L}{N_L} - 1 \right) I_{LB} + \beta_{BB} \left(\mathcal{R}_3 \frac{S_B}{N_B} - 1 \right) I_{BB}, \\
&\leq \beta_F (E_{LF2} + \eta_{F1}J_F)(\mathcal{R}_1 - 1) + \beta_B (\eta_{B1}E_{LB1} + \eta_{B2}E_{LB2} + I_{LB})(\mathcal{R}_2 - 1) \\
&\quad + \beta_{BB} I_{BB}(\mathcal{R}_3 - 1), \text{ since } S_L(t) \leq N_L(t) \text{ and } S_B(t) \leq N_B(t) \text{ for all } t \geq 0 \text{ in } \Gamma. \\
&\leq 0, \text{ for } \mathcal{R}_0 = \max\{\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3\} \leq 1.
\end{aligned}$$

Thus, $\dot{\mathcal{F}} \leq 0$ if $\mathcal{R}_0 = \max\{\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3\} \leq 1$ with $\dot{\mathcal{F}} = 0$ if and only if $E_{LF1}(t) = E_{LF2}(t) = J_F(t) = E_{LB1}(t) = E_{LB2}(t) = I_{LB}(t) = E_{BB}(t) = I_{BB}(t) = 0$. Substituting $E_{LF1}(t) = E_{LF2}(t) = J_F(t) = E_{LB1}(t) = E_{LB2}(t) = I_{LB}(t) = E_{BB}(t) = I_{BB}(t) = 0$ in the equations for $\dot{S}_L, \dot{W}_{LB}, \dot{S}_B, \dot{R}_{BB}$ in the model (2.2) shows that $S_L(t) \rightarrow \Pi_L/\mu_L, S_B(t) \rightarrow \Pi_B/\mu_B, W_{LB}(t) \rightarrow 0$ and $R_{BB}(t) \rightarrow 0$, as $t \rightarrow \infty$. Furthermore, noting that $D_{L1}(t) \rightarrow 0, D_{L2}(t) \rightarrow 0$ and $J_{FB}(t) \rightarrow 0$, as $t \rightarrow \infty$ (when

$\theta_F = \theta_B = \theta_{EB} = 0$), the largest compact invariant set in $\{(S_L, E_{LF1}, E_{LF2}, J_F, E_{LB1}, E_{LB2}, I_{LB}, W_{LB}, D_{L1}, D_{L1}, J_{FB}, S_B, E_{BB}, I_{BB}, R_{BB}) \in \Gamma : dF/dt = 0\}$ is the singleton $\{\mathcal{E}_0\}$. It follows, from the LaSalle's Invariance Principle [41], that every solution to the equations in the model (2.2), with initial conditions in Γ , converges to the DFE (\mathcal{E}_0) as $t \rightarrow \infty$. ■

This result shows that, in the absence of BTB-FIV co-infection in lions and the re-infection of exposed buffalos, the DFE of the model (2.2) is GAS (thus, both FIV and BTB will be effectively controlled or eliminated from the lion and buffalo population if $\mathcal{R}_0 \leq 1$).

4 Uncertainty and Sensitivity Analysis

The expression for the reproduction number (\mathcal{R}_0) of the model (2.2), given by the equations in (3.5), contains numerous parameters, and uncertainties in the estimates of these parameters (hence, uncertainties in the estimate for \mathcal{R}_0) are expected to occur. The effect of such uncertainties on the numerical simulation results obtained will be assessed using Latin Hypercube Sampling (LHS). Furthermore, sensitivity analysis (using Partial Rank Correlation Coefficients (PRCC)) will be carried out to determine the parameters that have the most effect (positive or negative) on \mathcal{R}_0 [4]. The reproduction number \mathcal{R}_0 is chosen as the response function for these (uncertainty and sensitivity) analyses because the dynamics of the model (2.2) is governed by the value of \mathcal{R}_0 (the diseases can be effectively controlled, in the absence of backward bifurcation, if \mathcal{R}_0 is less than unity, and they will persist if the threshold quantity exceeds unity). LHS, a statistical method for generating a sample of plausible collections of parameter values from a multidimensional distribution [4], treats the model's inputs (i.e., the model parameters) as random variables. Thus, appropriate probability distributions (such as uniform, normal, gamma, triangular etc.) are chosen for each parameter. The LHS procedure is implemented by dividing the range of values for each given parameter into equally-probable intervals, and one selected at random from each interval with the objective of uniformly filling the input space [4]. On the other hand, as noted by Marino *et al.* [3], "PRCC is a robust sensitivity measure for nonlinear but monotonic relationships between input and output, as long as little to no correlation exists between the inputs" (in other words, PRCC is considered to be more powerful at determining the sensitivity of a parameter that is strongly monotonic yet highly nonlinear [1]). The magnitude, as well as the statistical significance, of the PRCC value of a parameter indicates that parameter's contribution to the model's prediction imprecision [4]. The parameters with large PRCC values (typically ≥ 0.5 or ≤ -0.5) are considered to be the most important (in determining the value/size of the chosen response function) [2]. Thus, a PRCC approaching -1 or $+1$ indicates a strong effect of the corresponding

parameter to the response function (\mathcal{R}_0 in this case). The sign indicates the qualitative relationship between the parameter inputs and \mathcal{R}_0 (a negative sign indicates that the LHS parameter is inversely proportional to \mathcal{R}_0 , while a positive sign shows that the response function increases with increasing values of that parameter).

The aforementioned analyses are implemented on the model (2.2) by, first of all, drawing 10,000 parameter samples (for the 19 parameters in the expressions for \mathcal{R}_0) from the range of parameter values tabulated in Table 3. Boxplots for the constituent reproduction numbers, \mathcal{R}_1 , \mathcal{R}_2 and \mathcal{R}_3 , as functions of the LHS runs carried out, are depicted in Figures 3(a), 3(b) and 4(a), respectively, from which the following mean values of the constituent reproduction numbers were obtained: $\mathcal{R}_1 \approx 1.2735$ with 95% CI (0.7121, 1.9760), $\mathcal{R}_2 \approx 0.7129$ with 95% CI (0.3690, 1.4884) and $\mathcal{R}_3 \approx 1.1972$ with 95% CI (0.4538, 3.5986). Similarly, a boxplot of \mathcal{R}_0 , depicted in Figure 4(b), shows that the mean value of the overall reproduction number (\mathcal{R}_0) is $\mathcal{R}_0 \approx 1.5961$ with 95% CI (0.8009, 3.5986). The epidemiological implication of these simulation results is that, based on the assumptions made in the study and the current levels of control strategies implemented, the two diseases will persist in the Kruger National Park (since the mean value of \mathcal{R}_0 is above unity). Furthermore, Table 4 depicts the results of the sensitivity analyses carried out, using the constituent reproduction thresholds \mathcal{R}_1 , \mathcal{R}_2 and \mathcal{R}_3 , and the overall reproduction number $\mathcal{R}_0 = \max\{\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3\}$, as the response functions. The results obtained show that three parameters have the highest effect on the overall reproduction number \mathcal{R}_0 (hence, the burden of the two diseases), namely the rate of FIV transmission by infected lions (β_F), the modification parameter accounting for the assumed reduction in infectiousness of isolated/treated lions, in comparison to infected lions with clinical symptoms of FIV (η_{F1}) and the natural death of lions (μ_L) (these same parameters also have the highest impact on the constituent reproduction number, \mathcal{R}_1 , for FIV transmission by lions; this is due to the fact, for the choice of parameter values and ranges in Table 3, \mathcal{R}_1 is the maximum of the three constituent reproduction numbers. Hence, $\mathcal{R}_0 = \mathcal{R}_1$; and the dynamics of the model is governed by the size of \mathcal{R}_1). Thus, this study identifies the parameters that have the greatest influence on the FIV-BTB dynamics in the Kruger National Park, and controlling the impact of these parameters will play a major role in determining the outcome (persistence or effective control of the two diseases in the lion-buffalo population). In other words, this study shows that the two diseases can be effectively controlled by implementing a strategy that minimizes β_F and η_{F1} . The parameter β_F can be reduced by minimizing contact between FIV-infected and susceptible lions or by, perhaps, vaccinating susceptible lions against FIV infection (when such a vaccine becomes available). Similarly, the parameter β_F can be reduced by the rapid detection, isolation and treatment of lions with symptoms of FIV. The parameter μ_L is important in the sense that susceptible lions form a pool of target for FIV (and BTB) infection. Hence, depleting them (by increasing their natural death rate, μ_L) will invariably reduce FIV transmission (hence, reduce

the size of \mathcal{R}_1). Table 4 further shows that BTB dynamics within the lion population (governed by the size of the constituent reproduction number \mathcal{R}_2) is most affected by the parameters associated with BTB transmission in lions (β_B), progression rate of advanced-exposed lions with BTB only to symptomatic stage (σ_{B2}) and the modification parameters accounting for the assumed reduction in infectiousness of early and advanced exposed lions, in comparison to infected lions with clinical symptoms of BTB (η_{B1} and η_{B2} , respectively). Here, too, a strategy based on minimizing contacts between BTB-infected lions and susceptible lions (i.e., minimize β_B), rapid detection and treatment of BTB-infected lions in the early and advanced-exposed stages (i.e., reduce σ_{B2} , η_{B1} and η_{B2}) will be very effective in controlling the BTB burden in the lion population. Finally, it is shown (as expected) that the BTB burden in the buffalo population is most affected by the contact rate of infected buffalos with susceptible buffalos (β_{BB}). Here, too, a strategy that minimizes contacts between BTB-infected and susceptible buffalos (such as quarantine, isolation and treatment of infected cases) will curb the burden of BTB among the buffalo population in the herd.

5 Assessment of Control Strategies

Control strategies against the spread of the two diseases in the buffalo-lion population are typically based on two main strategies, namely

- (a) detecting and isolating lions with FIV symptoms (it is assumed that when lions with FIV are detected and isolated, they are given relevant treatment against FIV);
- (b) detecting and treating lions and buffalos with BTB symptoms;
- (c) detecting and treating dually-infected lions with symptoms of both diseases.

The model (2.2) will now be simulated, using the data in Table 3 (unless otherwise stated) to assess the effectiveness of these strategies (implemented singly or in combination). Since we are interested in exploring the feasibility of disease elimination, these simulations are carried out for the special case of the model where backward bifurcation does not occur (i.e., the special case where reinfection and co-infection rates are negligible ($\theta_B = \theta_F = \theta_{ED} \approx 0$); so that (by Theorem 3) the disease-free equilibrium of the model is globally-asymptotically stable, when the reproduction number (\mathcal{R}_0) is less than unity).

5.1 Effect of isolation of lions with FIV symptoms

Here, the singular effect of the detection and isolation of lions with FIV symptoms is assessed. Numerical simulations of the model, in the absence of intervention against

BTB (i.e., in the absence of the treatment of lions and buffalos with symptoms of BTB; so that, $\xi_B = \xi_{BB} = 0$), are carried out for the following three arbitrarily-chosen (but plausible) effectiveness levels of the isolation-only strategy against FIV infection in the lion population:

- (I) low effectiveness level: $\xi_F = 0.1$ (i.e., it takes 10 days on average to detect and isolate a lion symptomatic with FIV), so that $\mathcal{R}_1 = 1.6957$;
- (II) moderate effectiveness level: $\xi_F = 0.2$ (i.e., it takes 5 days on average to detect and isolate a lion symptomatic with FIV), so that $\mathcal{R}_1 = 1.2529$;
- (III) high effectiveness level: $\xi_F = 0.5$ (i.e., it takes 2 days on average to detect and isolate a lion symptomatic with FIV), $\mathcal{R}_1 = 0.8691$.

The simulation results obtained, depicted in Figure 5A, show that an increase in the isolation rate of lions with FIV symptoms (ξ_F) leads to a decrease in the associated reproduction number (\mathcal{R}_1). This, consequently, results in a decrease in the FIV burden in the lion population. Although the low and moderate effectiveness levels fail to reduce \mathcal{R}_1 to a value less than unity, the high effectiveness level of this strategy reduces $\mathcal{R}_1 = 0.8691 < 1$. Thus, the implementing the high effectiveness level of this strategy can lead to the effective control of FIV in the lion population. In fact, elimination of the disease is feasible (in the absence of backward bifurcation) in this case (Figure 5B shows that such elimination can be achieved in about 100 years).

5.2 Effect of treatment of lions and buffalos against BTB

The singular effect of the treatment of BTB-infected lions and buffalos with symptoms of BTB (i.e., $\xi_B \neq 0$ and $\xi_{BB} \neq 0$, respectively) is monitored by simulating the model under the following three effectiveness levels of the treatment-only strategy (for these simulations, the parameter associated with the isolation of lions with FIV symptoms, ξ_F , is set to zero):

- (I) low effectiveness level: $\xi_B = \xi_{BB} = 0.1$ (i.e., it takes 10 days on average to detect and treat a lion or buffalo with symptoms of BTB), so that $\mathcal{R}_2 = 2.3084$ and $\mathcal{R}_3 = 1.5638$;
- (II) moderate effectiveness level: $\xi_B = \xi_{BB} = 0.2$ (i.e., it takes 5 days on average to detect and treat a lion or buffalo with symptoms of BTB), so that $\mathcal{R}_2 = 1.5821$ and $\mathcal{R}_3 = 0.9135$;
- (III) high effectiveness level: $\xi_B = \xi_{BB} = 0.5$ (i.e., it takes 2 days on average to detect and treat a lion or buffalo with symptoms of BTB), so that $\mathcal{R}_2 = 0.9470$ and $\mathcal{R}_3 = 0.4064$.

These simulations (depicted in Figures 6A and 6B) show that, while the low and moderate effectiveness levels of this strategy fail to bring the associated reproduction numbers (\mathcal{R}_2 and \mathcal{R}_3) to values less than unity, the high effectiveness level of this strategy reduces \mathcal{R}_2 and \mathcal{R}_3 to values less than unity. Thus, BTB can be effectively controlled in (or eliminated from) the buffalo-lion population in the herd using the high effectiveness level of this strategy (Figure 7 shows that such elimination can be achieved in about 140 years).

5.3 Effect of hybrid isolation-treatment strategy against both diseases

Here, the impact of a hybrid strategy, that combines the above two singular strategies, is assessed. In particular, it entails the isolation of lions with symptoms of FIV, the treatment of lions and buffalos with symptoms of BTB and dually-infected lions with symptoms of both diseases. The following effectiveness levels of the hybrid strategy are considered:

- (I) low effectiveness level: $\xi_F = \xi_B = \xi_D = \xi_{BB} = 0.1$ (so that $\mathcal{R}_1 = 1.6957$, $\mathcal{R}_2 = 2.3020$, $\mathcal{R}_3 = 1.5638$ and $\mathcal{R}_0 = \mathcal{R}_2 = 2.3084$);
- (II) moderate effectiveness level: $\xi_F = \xi_B = \xi_D = \xi_{BB} = 0.2$ (so that $\mathcal{R}_1 = 1.2529$, $\mathcal{R}_2 = 1.5821$, $\mathcal{R}_3 = 0.9135$ and $\mathcal{R}_0 = \mathcal{R}_2 = 1.5821$);
- (III) high effectiveness level: $\xi_F = \xi_B = \xi_D = \xi_{BB} = 0.5$ (so that $\mathcal{R}_1 = 0.8691$, $\mathcal{R}_2 = 0.9470$, $\mathcal{R}_3 = 0.4064$ and $\mathcal{R}_0 = \mathcal{R}_2 = 0.9470$).

As expected, this strategy fares much better than any of the singular strategies discussed above (Figure 8A). In particular, Figure 8 shows that the high effectiveness level of this (hybrid) strategy can lead to the elimination of the two diseases in a much sooner duration (80 years), in comparison to time to elimination using any of the two singular strategies.

Conclusions

A new model for the transmission dynamics of FIV and BTB in a herd, consisting of lions and buffalos, is constructed and analysed. Some of the main findings of this study are summarized below:

- (i) The BTB-FIV model undergoes the phenomenon of backward bifurcation (a dynamic phenomenon characterized by the co-existence of two stable attractors when the associated reproduction number of the model is less than unity).

Two sufficient conditions for the emergence of this phenomenon (namely the co-infection with the two diseases and the BTB re-infection of exposed buffalos) have been identified.

- (ii) In the absence of the BTB-FIV co-infection of lions and the re-infection of exposed buffalos (i.e., in the absence of the backward bifurcation phenomenon), the disease-free equilibrium of the resulting model is shown to be globally-asymptotically stable, whenever the associated reproduction number is less than unity.
- (iii) Numerical simulations of the model (2.2), using data relevant to BTB-FIV dynamics in South Africa's Kruger National Park, show that (for the case where backward bifurcation does not occur) the highest effectiveness levels of the aforementioned singular strategies (i.e., the isolation of lions against FIV or the treatment of buffalos and lions against BTB) can lead to the effective control or elimination of the respective disease (FIV elimination in about 100 years; and elimination of BTB in about 140 years). The hybrid strategy, which combines both singular strategies, as well as the treatment/isolation of dually-infected lions with symptoms of both diseases, eliminates both diseases in about 80 years. In other words, each of the three strategies considered in this study can lead to the elimination of the respective disease or diseases it targets, and such elimination can be achieved much sooner if the hybrid strategy is implemented.
- (iv) The effect of uncertainties in the estimates of the parameters of the model, on the numerical simulation results obtained, were assessed using Latin Hypercube Sampling on the reproduction number, \mathcal{R}_0 (as the response function). These analyses reveal that the mean value of the reproduction number (\mathcal{R}_0) is $\mathcal{R}_0 \approx 1.5961$ with 95% CI (0.8009, 3.5986). This result shows that, based on the parameter values and ranges used in the simulation of the novel model developed in this study, the current levels of control strategies implemented in the Kruger National Park are insufficient to lead to the effective control of the two diseases in the buffalo-lion population (although, since the mean value of $\mathcal{R}_0 \approx 1.6$, it seems that not much extra control efforts will be needed to bring the reproduction number to a value less than unity, thereby enhancing the prospect of the effective control, or elimination, of both diseases). It is further shown, *via* sensitivity analysis, that the transmission dynamics of the two diseases in the herd (as measured in terms of the size of the overall reproduction number, \mathcal{R}_0) is most affected by changes in three parameters of the model. These parameters are the rate of FIV transmission by infected lions (β_F), the modification parameter accounting for the assumed reduction in infectiousness of isolated/treated lions, in comparison to infected lions with clinical symptoms of FIV (η_{F1}) and the natural death of lions (μ_L). Thus, a control strategy that focuses on minimizing β_F and η_{F1} (such as

minimizing contacts between FIV-infected and susceptible lions, rapid detection, quarantine, isolation and effective treatment of FIV-infected lions) will lead to the effective control of both diseases in the herd.

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Appendix A: Proof of Theorem 2

Proof. The existence of backward bifurcation will be explored using the Centre Manifold theory [18, 19, 58]. To apply this theory, it is convenient to carry out the following change of variables. Consider the model (2.2). Let $S_L = x_1$, $E_{LF1} = x_2$, $E_{LF2} = x_3$, $J_F = x_4$, $E_{LB1} = x_5$, $E_{LB2} = x_6$, $I_{LB} = x_7$, $W_{LB} = x_8$, $D_{L1} = x_9$, $D_{L2} = x_{10}$, $J_{FB} = x_{11}$, $S_B = x_{12}$, $E_{BB} = x_{13}$, $I_{BB} = x_{14}$ and $R_{BB} = x_{15}$. Thus, $N_L = \sum_{i=1}^{15} x_i$.

Further, by using the vector notation

$\mathbf{X} = (x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8, x_9, x_{10}, x_{11}, x_{12}, x_{13}, x_{14}, x_{15})^T$, the model (2.2) can be written in the form $\frac{d\mathbf{X}}{dt} = (f_1, f_2, f_3, f_4, f_5, f_6, f_7, f_8, f_9, f_{10}, f_{11}, f_{12}, f_{13}, f_{14}, f_{15})^T$, as

follows

$$\begin{aligned}
\frac{dx_1}{dt} &= \Pi_L - (\lambda_F + \lambda_B + \lambda_{FB})x_1 - \mu_L x_1 = f_1, \\
\frac{dx_2}{dt} &= (\lambda_F + f\lambda_{FB})x_1 - \theta_B(\lambda_B + \lambda_{FB})x_2 - (\sigma_F + \mu_L)x_2 = f_2, \\
\frac{dx_3}{dt} &= \sigma_F x_2 - \theta_B(\lambda_B + \lambda_{FB})x_3 - (\xi_F + \mu_L)x_3 = f_3, \\
\frac{dx_4}{dt} &= \xi_F x_3 - \mu_L x_4 = f_4, \\
\frac{dx_5}{dt} &= [\lambda_B + (1-f)\lambda_{FB}]x_1 - (\sigma_{B1} + \mu_L)x_5 = f_5, \\
\frac{dx_6}{dt} &= \sigma_{B1}x_5 - \theta_F(\lambda_F + \lambda_{FB})x_6 - (\sigma_{B2} + \mu_L)x_6 = f_6, \\
\frac{dx_7}{dt} &= \sigma_{B2}x_6 - \theta_F(\lambda_F + \lambda_{FB})x_7 - (\xi_B + \mu_L + \delta_B)x_7 = f_7, \\
\frac{dx_8}{dt} &= \xi_B x_7 - \mu_L x_8 = f_8, \\
\frac{dx_9}{dt} &= \theta_B(\lambda_B + \lambda_{FB})x_2 + \theta_F(\lambda_F + \lambda_{FB})x_6 - (\sigma_D + \mu_L)x_9 = f_9, \\
\frac{dx_{10}}{dt} &= \sigma_D x_9 + \theta_B(\lambda_B + \lambda_{FB})x_3 + \theta_F(\lambda_F + \lambda_{FB})x_7 - (\xi_D + \mu_L)x_{10} = f_{10}, \\
\frac{dx_{11}}{dt} &= \xi_D x_{10} - \mu_L x_{11} = f_{11}, \\
\frac{dx_{12}}{dt} &= \Pi_B - \lambda_{BB}x_{12} - \mu_B x_{12} = f_{12}, \\
\frac{dx_{13}}{dt} &= \lambda_{BB}x_{12} - \theta_{EB}\lambda_{BB}x_{13} - (\sigma_{BB} + \mu_B)x_{13} = f_{13}, \\
\frac{dI_{14}}{dt} &= \sigma_{BB}x_{13} + \theta_{EB}\lambda_{BB}x_{13} - (\xi_{BB} + \mu_B + \delta_{BB})x_{14} = f_{14}, \\
\frac{dx_{15}}{dt} &= \xi_{BB}x_{14} - \mu_B x_{15} = f_{15},
\end{aligned} \tag{A.1}$$

with the associated forces of infection given by

$$\begin{aligned}
\lambda_F &= \frac{\beta_F(x_3 + \eta_{F1}x_4)}{\sum_{i=1}^{11} x_i}, \quad \lambda_B = \frac{\beta_B(\eta_{B1}x_5 + \eta_{B2}x_6 + x_7)}{\sum_{i=1}^{11} x_i}, \\
\lambda_{FB} &= \frac{\beta_{FB}(\eta_{FB}x_9 + x_{10})}{\sum_{i=1}^{11} x_i} \quad \text{and} \quad \lambda_{BB} = \frac{\beta_{BB}x_{14}}{\sum_{i=12}^{15} x_i}.
\end{aligned}$$

Consider the case with $\mathcal{R}_0 = 1$. Choose, without loss of generality, β_F^* as the bifurcation parameter. Solving for β_F from $\mathcal{R}_0 = 1$ gives

$$\beta_F = \beta_F^* = \frac{\mu_L K_1 K_2}{\sigma_F (\eta_{F1} \xi_F + \mu_L)},$$

be chosen as a bifurcation parameter. The Jacobian of the system (A.1), evaluated at the DFE (\mathcal{E}_0) with $\beta_F = \beta_F^*$ (denoted by J^*), is given by

$$J^* = \begin{bmatrix} q_1 & q_2 \\ 0 & q_3 \end{bmatrix},$$

where,

$$q_1 = \begin{bmatrix} -\mu_L & 0 & -\beta_F & -\beta_F \eta_{F1} & -\beta_B \eta_{B1} & -\beta_B \eta_{B2} & -\beta_B & 0 \\ 0 & -K_1 & \beta_F & \beta_F \eta_{F1} & 0 & 0 & 0 & 0 \\ 0 & \sigma_F & -K_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \xi_F & -\mu_L & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \beta_B \eta_{B1} - K_3 & \beta_B \eta_{B2} & \beta_B & 0 \\ 0 & 0 & 0 & 0 & \sigma_{B1} & -K_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \sigma_{B2} & -K_5 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \xi_B & -\mu_L \end{bmatrix},$$

$$q_2 = \begin{bmatrix} -\beta_{FB} \eta_{FB} & -\beta_{FB} & 0 & 0 & 0 & -A_1 & 0 \\ f \beta_{FB} \eta_{FB} & f \beta_{FB} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ q \beta_{FB} \eta_{FB} & q \beta_{FB} & 0 & 0 & 0 & A_1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

and,

$$q_3 = \begin{bmatrix} -K_6 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \sigma_D & -K_7 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \xi_D & -\mu & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\mu_B & -\beta_{BB}\eta_{\eta_{FB}} & -\beta_{BB} & 0 & 0 \\ 0 & 0 & 0 & 0 & \beta_{BB}\eta_{\eta_{FB}} - K_8 & \beta_{BB} & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma_{BB} & -K_9 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \xi_{BB} & -\mu_B & 0 \end{bmatrix},$$

with, $A_1 = \frac{\Pi_L \mu_B \theta_{BB} \beta_{BB}}{\mu_L \Pi_B}$. The Jacobian (J^*) of the linearized system has a simple zero eigenvalue (with all other eigenvalues having negative real part). Hence, the centre manifold theory [19, 58] can be used to analyse the dynamics of the system (A.1) around $\beta_F = \beta_F^*$. Using the notation in [19], the following computations are carried out.

Eigenvectors of J^* $\Big|_{\beta_F = \beta_F^*}$

For the case when $\mathcal{R}_0 = 1$, it can be shown that the Jacobian, J^* , has a right eigenvector (corresponding to the simple zero eigenvalue), given by

$\mathbf{w} = [w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8, w_9, w_{10}, w_{11}, w_{12}, w_{13}, w_{14}, w_{15}]^T$, where,

$$\begin{aligned} w_1 &= -\frac{\beta_F^*(w_3 + \eta_{F1}w_4) + \beta_B(\eta_{B1}w_5 + \eta_{B2}w_6 + w_7) + A_1w_{14}}{\mu_L}, \quad w_2 = w_2, \quad w_3 = \frac{\sigma_F w_2}{K_2}, \\ w_4 &= \frac{\xi_F \sigma_F w_2}{\mu_L K_2}, \quad w_5 = w_5, \quad w_6 = \frac{\sigma_{B1} w_5}{K_4}, \quad w_7 = \frac{\sigma_{B1} \sigma_{B2} w_5}{K_4 K_5}, \quad w_8 = \frac{\xi_B \sigma_{B1} \sigma_{B2} w_5}{\mu_L K_4 K_5}, \\ w_9 &= w_{10} = w_{11} = 0, \quad w_{12} = \frac{-\beta_{BB} w_{14}}{\mu_B}, \quad w_{14} = \frac{\sigma_{BB} w_{13}}{K_9}, \quad w_{13} = w_{13}, \quad w_{15} = \frac{\xi_{BB} \sigma_{BB} w_{13}}{\mu_B K_9}. \end{aligned}$$

Similarly, the components of the left eigenvector of J^* (corresponding to the simple zero eigenvalue), denoted by $\mathbf{v} = [v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8, v_9, v_{10}, v_{11}, v_{12}, v_{13}, v_{14}, v_{15}]$, are given by,

$$\begin{aligned} v_3 &= \frac{K_1 v_2}{\sigma_F}, \quad v_4 = \frac{\beta_F^* \eta_{F1} v_2}{\mu_L}, \quad v_5 = \frac{K_5 v_7}{\beta_B}, \quad v_6 = \frac{\beta_B \eta_{B2} v_5 + \sigma_{B2} v_7}{K_4}, \quad v_{14} = \frac{A_1 v_5 + \beta_{BB} v_{13}}{K_9}, \\ v_1 &= v_8 = v_{11} = v_{12} = v_{15} = 0, \quad v_2 > 0, \quad v_7 > 0, \quad v_{13} > 0. \end{aligned}$$

It is worth mentioning that the free right eigenvectors, w_2 , and w_5 , and left eigenvectors, v_2 and v_7 , are chosen to be

$$w_2 = \frac{\mu_L^2 K_1}{2\mu_L^2 K_1 + \beta_F \eta_{F1} \sigma_F}, w_5 = \frac{\beta_B K_4^2 K_5}{K_5^2 (K_4^2 + \eta_{B2} \beta_B \sigma_{B1}) + \beta_B \sigma_{B1} \sigma_{B2} (K_4 + K_5)}, w_{13} = 1,$$

$$v_2 = \frac{1}{4}, v_7 = \frac{1}{4} \text{ and } v_{13} = \frac{1}{2}, \text{ so that } \mathbf{v} \cdot \mathbf{w} = 1 \text{ (in line with [19])}.$$

It can be shown, by computing the non-zero partial derivatives of the right-hand side functions of the model (A.1), $f_i (i = 1, \dots, 15)$, that the associated backward bifurcation coefficients, a and b , are given, respectively, by (see Theorem 4.1 in [19]):

$$\begin{aligned} \tilde{a} &= \sum_{k,i,j=1}^{15} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j} (0, 0), \\ &= -\frac{2\mu_B \mu_L}{\Pi_B \Pi_L} \left[\frac{\Pi_B}{\mu_B} \beta_F^* (\eta_{F1} w_4 + w_3) \left\{ \theta_F [(w_6 (v_6 - v_9) + w_7 (v_7 - v_{10})) + v_2 \sum_{i=2}^8 w_i] \right\} \right. \\ &\quad + \frac{\Pi_B}{\mu_B} \beta_B (\eta_{B1} w_5 + \eta_{B2} w_6 + w_7) \left\{ \theta_B [w_2 (v_2 - v_9) + w_3 (v_3 - v_{10})) + v_5 \sum_{i=2}^8 w_i] \right\} \\ &\quad \left. + \frac{\Pi_L}{\mu_L} \beta_{BB} w_{14} [\theta_{EB} w_{13} (v_{13} - v_{14}) + v_{13} (w_{13} + w_{14} + w_{15})] \right], \end{aligned} \tag{A.2}$$

and,

$$b = \sum_{k,i=1}^{15} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta_B^*} (0, 0) = v_2 (\eta_{F1} w_4 + w_3) > 0.$$

Since the bifurcation coefficient, b , is automatically positive, it follows from Theorem 4.1 of [19] that the model (2.2) (or its transformed equivalent, given by model (A.1)) will undergo a backward bifurcation at $\mathcal{R}_0 = 1$ whenever the bifurcation coefficient, \tilde{a} , given by Equation (A.2), is positive. ■

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Variable	Interpretation
S_L	Population of susceptible lions
E_{LF1}	Population of lions infected with FIV only at early-stage of infection
E_{LF2}	Population of lions infected with FIV only at advanced-stage of infection
J_F	Population of lions infected with FIV only that are isolated (and/or treated)
E_{LB1}	Population of lions infected with BTB only at early-stage of infection
E_{LB2}	Population of lions infected with BTB only at advanced-stage of infection
I_{LB}	Population of lions Infected with clinical symptom of BTB
W_{LB}	Population of lions with BTB only that are treated against BTB
D_{L1}	Population of dually-infected lions with FIV and advanced-exposed to BTB
D_{L2}	Population of dually-infected lions with symptoms of both FIV and BTB
J_{FB}	Population of treated/isolated dually-infected lions with symptoms of FIV and BTB
S_B	Population of susceptible buffalos
E_{BB}	Population of buffalos exposed (infected but not yet show a symptoms) to BTB infection
I_{BB}	Population of buffalos with clinical symptoms of BTB
R_{BB}	Population of buffalos who recovered from BTB infection

Table 1: Description of state variables of the model (2.2).

Parameter	Interpretation
Π_L	Recruitment rate of lions
Π_B	Recruitment rate of buffalos
$\frac{1}{\mu_L}$	Average lifespan of lions
$\frac{1}{\mu_B}$	Average lifespan of buffalos
$\beta_B (\beta_F)$	Effective contact rates for BTB (FIV) transmission
β_{FB}	Effective contact rate for FIV or BTB transmission from dually infected lions to susceptible lions or BTB transmission from infected buffalos to infected lions
β_{BB}	Effective contact rate for BTB transmission from infected buffalos to susceptible buffalos
σ_F	Progression rate of early-exposed lions with FIV only to advanced-exposed stage
σ_{B1}	Progression rate of early-exposed lions with BTB only to advanced-exposed stage
σ_{B2}	Progression rate of advanced-exposed lions with BTB only to symptomatic stage
σ_{BB}	Progression rate of exposed buffalos with BTB infectious stage
σ_D	Progression rate of dually-infected lions with FIV and advanced-exposed with BTB to symptomatic stage of both FIV and BTB
f	Proportion of lions that are infected with FIV by dually-infected lions with both diseases
ξ_F	Isolation rate of advanced-exposed lions with FIV
ξ_B	Treatment rate of infected lions with BTB
ξ_{BB}	Treatment rate of infected buffalos with BTB
ξ_D	Treatment rate of dually-infected lions with clinical symptoms of both diseases
η_{F1}	Modification parameter accounting for the assumed reduction in infectiousness of isolated lions with FIV, in comparison to infected lions at advanced-stage of FIV infection
$\eta_{B1} (\eta_{B2})$	Modification parameter accounting for the assumed reduction in infectiousness of early (advanced) exposed lions, in comparison to infected lions with clinical symptoms of BTB
η_{FB}	Modification parameter accounting for the assumed reduction in infectiousness of dually-infected lions, in comparison to dually-infected lions with symptoms of FIV and BTB
$\theta_F (\theta_B)$	Modification parameter accounting for the assumption that co-infection of BTB (FIV) infected lions with FIV (BTB) occurs at a rate lower than primary infection of susceptible lions with FIV (BTB)
θ_{BB}	Modification parameter accounting for the assumed reduced likelihood of BTB transmission from buffalos to lions in relation to BTB transmission from a buffalo to buffalo
θ_{EB}	Modification parameter accounting for the assumed reduced likelihood of exogenous reinfection for buffalos in the exposed class in relation to the primary infection of buffalos in the susceptible class
δ_B	BTB-induced death rate of lions
δ_{BB}	BTB-induced death rate of buffalos

Table 2: Description of parameters of the model (2.2).

Parameter	Range (day ⁻¹)	Baseline (day ⁻¹)	Distribution	Reference
Π_L	[0.5, 0.8]	0.6	Uniform	[62]
Π_B	[2, 2.7]	2.3	Uniform	[36, 52]
μ_L	[0.0002, 0.000274]	0.00025	Uniform	[62]
μ_B	[0.0001, 0.00015]	0.00013	Uniform	[61]
β_F	[0.0003, 0.0007]	0.0005	Uniform	[62]
β_B	[0.1, 0.2]	0.15	Uniform	[62]
β_{FB}	[0.4, 0.6]	0.5	Not in \mathcal{R}_0	[62]
β_{BB}	[0.4, 0.6]	0.5	Uniform	[25, 36]
σ_F	[0.4, 0.5]	0.45	Uniform	[62]
σ_{B1}	[0.45, 0.55]	0.5	Uniform	[62]
σ_{B2}	[0.25, 0.35]	0.3	Uniform	[62]
σ_{BB}	[0.25, 0.44]	0.4	Uniform	[36, 48]
σ_D	[0.30, 0.40]	0.35	Uniform	Assumed
η_{F1}	[0.5, 0.7] (dimensionless)	0.6	Uniform	Assumed
η_{B1}	[0.01, 0.03] (dimensionless)	0.5	Uniform	Assumed
η_{B2}	[0.6, 0.8](dimensionless)	0.7	Uniform	Assumed
η_{FB}	[0.01, 0.03] (dimensionless)	0.7	Not in \mathcal{R}_0	Assumed
f	[0.01, 0.1] (dimensionless)	0.5	Not in \mathcal{R}_0	Assumed
ξ_F	[0.1, 1]	0.7	Uniform	Assumed
ξ_B	[0.1, 1]	0.7	Uniform	Assumed
ξ_{BB}	[0.1, 1]	0.75	Uniform	Assumed
ξ_D	[0.1, 1]	0.7	Uniform	Assumed
θ_F	[0.01, 0.022] (dimensionless)	0.02	Not in \mathcal{R}_0	Assumed
θ_B	[0.01, 0.022] (dimensionless)	0.02	Not in \mathcal{R}_0	Assumed
θ_{BB}	[0.025, 0.05] (dimensionless)	0.03	Not in \mathcal{R}_0	[62]
θ_{EB}	[0.024, 0.030] (dimensionless)	0.0271	Not in \mathcal{R}_0	[23, 36]
δ_B	[0.018, 0.022]	0.02	Uniform	[27]
δ_{BB}	[0.018, 0.022]	0.02	Uniform	[17, 23, 36]

Table 3: Ranges and baseline values for parameters of the model (2.2).

Parameter	\mathcal{R}_1	\mathcal{R}_2	\mathcal{R}_3	$\mathcal{R}_0 = \max\{\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3\}$
μ_L	-0.9191	-0.0059	-0.0067	-0.8518
μ_B	0.0120	0.0085	-0.0051	0.0069
β_F	0.9884	0.0041	0.0031	0.9773
β_B	0.0053	0.9931	-0.0027	0.0965
β_{BB}	-0.0015	0.0010	0.9703	0.0575
σ_F	0.0144	0.0145	-0.0115	0.0075
σ_{B1}	0.0041	-0.4355	0.0001	-0.0089
σ_{B2}	0.0046	-0.8884	-0.0110	-0.0398
σ_{BB}	-0.0157	-0.0117	0.0103	-0.0240
σ_D	0.0148	-0.0061	0.0034	0.0159
η_{F1}	0.9290	0.0071	-0.0011	0.8687
η_{B1}	-0.0004	0.7004	-0.0067	0.0167
η_{B2}	-0.0180	0.8565	-0.0042	0.0201
ξ_F	-0.0173	-0.0078	0.0206	-0.0098
ξ_B	-0.0024	-0.8926	-0.0107	-0.0405
ξ_{BB}	-0.0131	-0.0106	-0.9856	-0.0995
ξ_D	-0.0066	0.0043	0.0112	-0.0094
δ_B	0.0075	-0.0287	0.0111	0.0031
δ_{BB}	0.0074	0.0052	-0.0572	-0.0023

Table 4: PRCC plots of the various parameters of the model, using the various reproduction thresholds ($\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3$ and \mathcal{R}_0) as the response functions. Parameter values and ranges used are as given in Table 3.

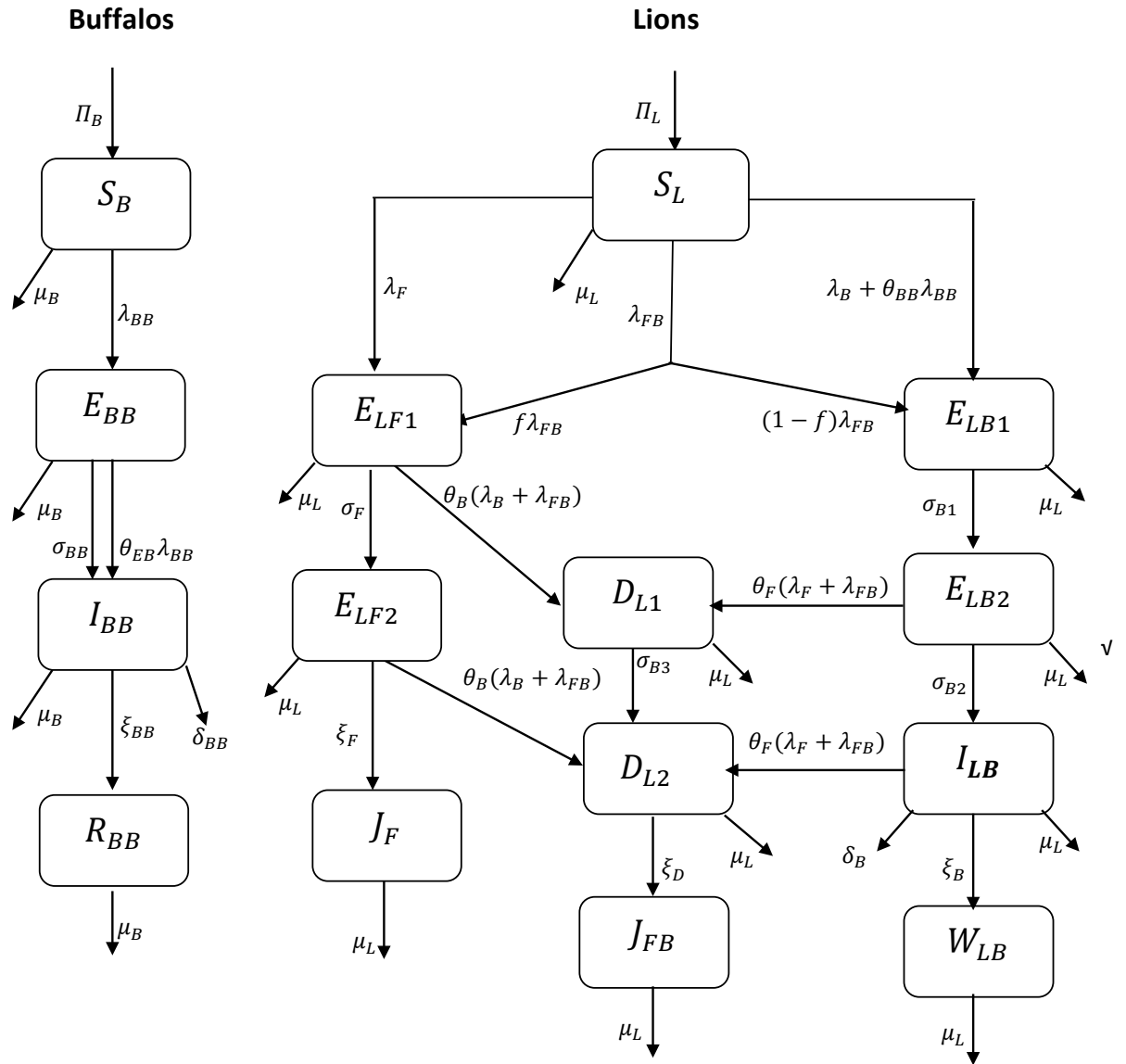
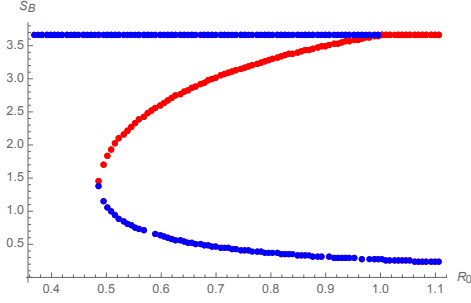
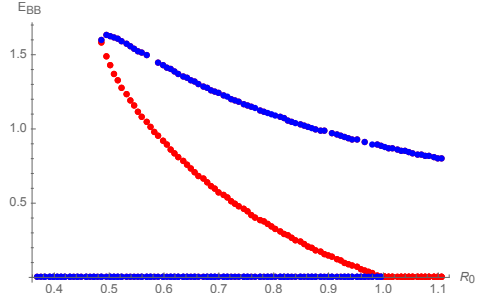


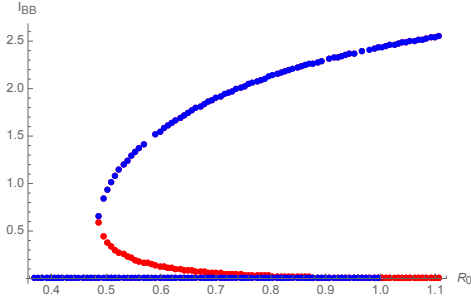
Figure 1: Flow diagram of the model (2.1)



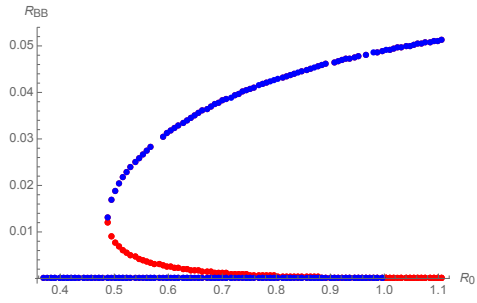
(a) Susceptible buffalos



(b) Exposed buffalos



(c) Infectious buffalos



(d) Recovered buffalos

Figure 2: Backward bifurcation diagram of the model (2.2). Parameter values used are: $\Pi_L = 20, \Pi_B = 40, \eta_{F1} = 0.05, \eta_{B1} = 0.6, \eta_{B2} = 0.4, \eta_{FB} = 0.5, \sigma_F = 0.5, \sigma_{B1} = 0.4, \sigma_{B2} = 0.53, \sigma_D = 0.4, \sigma_{BB} = 0.63, \theta_{BB} = 0.2, \theta_B = 0.3, \theta_F = 0.25, \theta_{EB} = 0.22, \delta_B = 0.1, \delta_{BB} = 0.1, \mu_L = 0.94, \mu_B = 10.94, \xi_F = 0.002, \xi_B = 0.25, \xi_D = 0.3, \xi_{BB} = 0.22, \beta_{FB} = 100, f = 0.994, \beta_B = 0.6019422435\beta_F^*$ and $\beta_{BB} = 76.23141982\beta_F^*$, $\beta_F^* = 2.712671416$ (so that, $\mathcal{R}_1 = \mathcal{R}_2 = \mathcal{R}_3 = 1$ and $\tilde{a} = 4.053619135 \times 10^{37} > 0$).

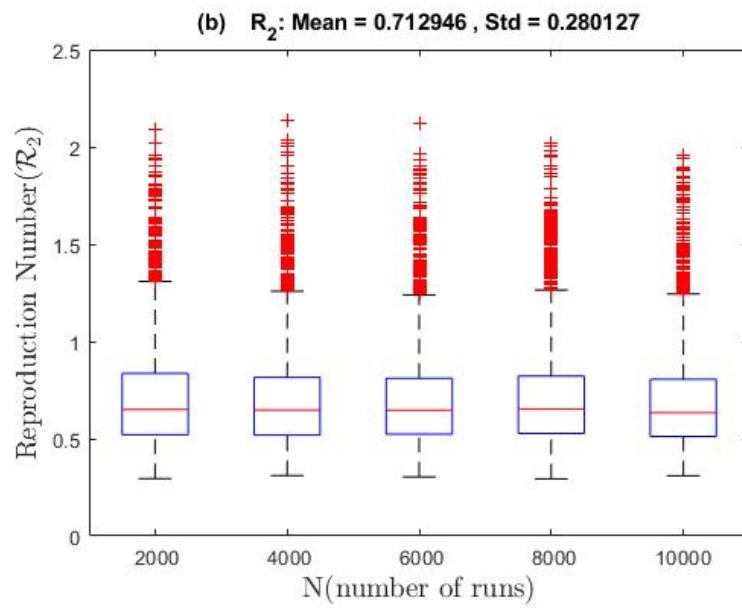
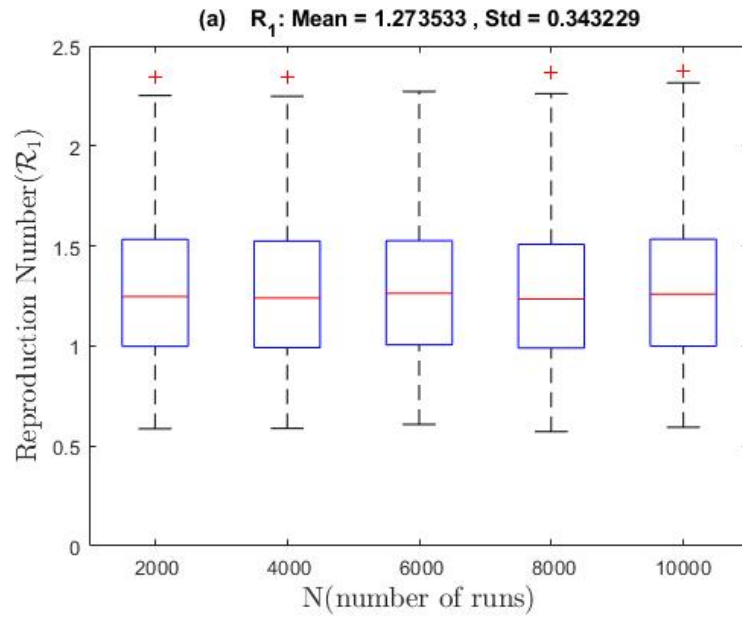


Figure 3: Boxplots of constituent reproduction numbers \mathcal{R}_1 and \mathcal{R}_2 . Parameter values and ranges used are as given in Table 3.

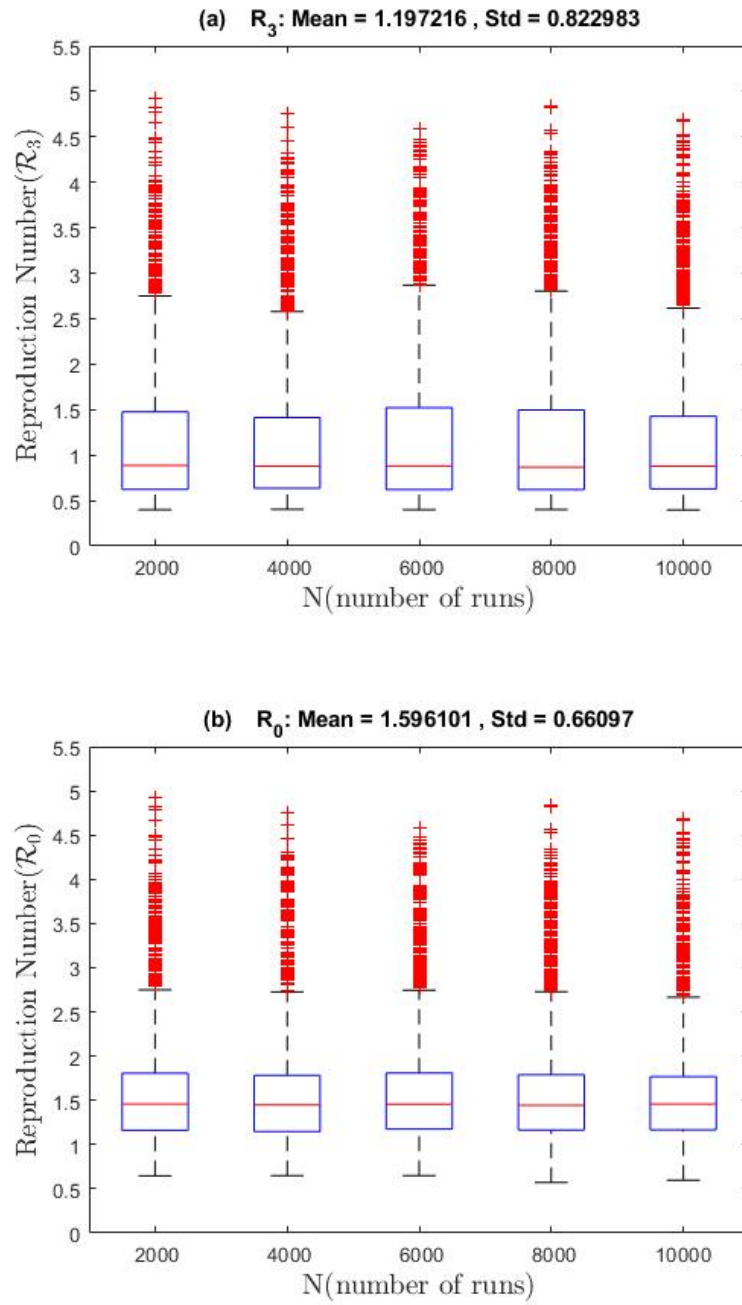


Figure 4: Boxplots of the reproduction numbers \mathcal{R}_3 and \mathcal{R}_0 . Parameter values and ranges used are as given in Table 3.

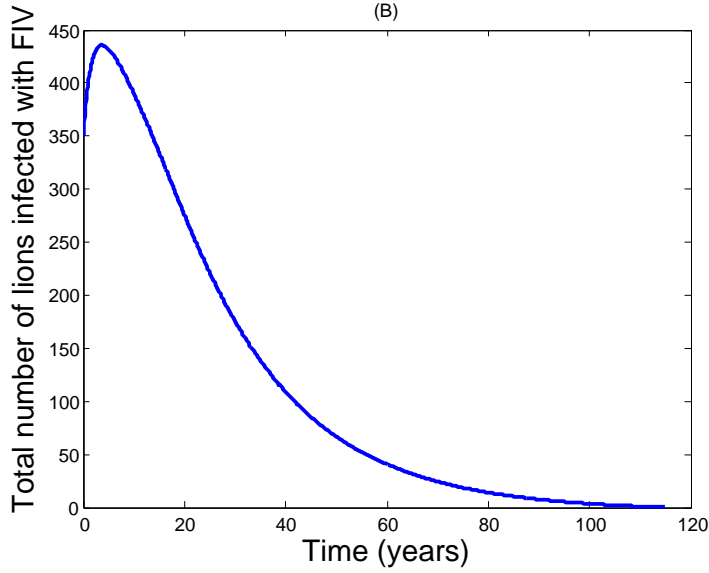
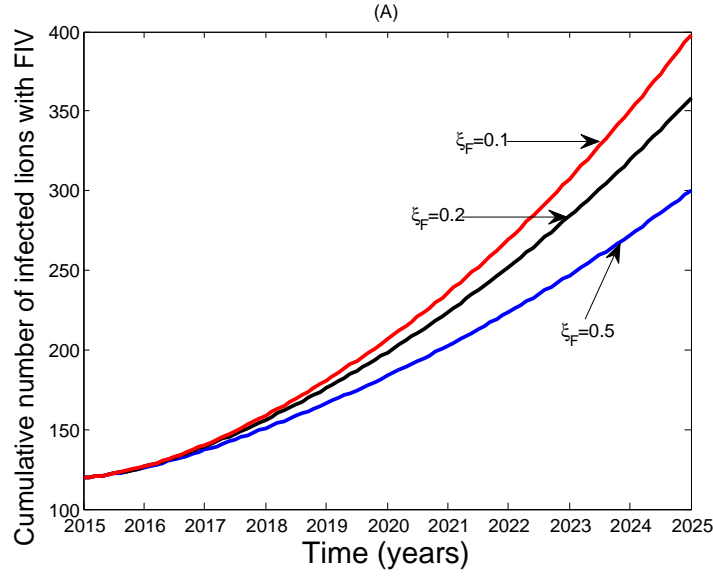


Figure 5: Simulations of the model (2.2), showing the (A) cumulative number of lions infected with FIV (B) time to FIV elimination using the high effectiveness level of the isolation-only strategy. Parameter values used are as given in Table 3, with (A) various values of ξ_F and (B) $\xi_F = 0.5$, $\xi_B = \xi_{BB} = \xi_D = 0$ (so that, $\mathcal{R}_1 = 0.8691 < 1$), $\theta_F = \theta_B = \theta_{EB} = 0$.

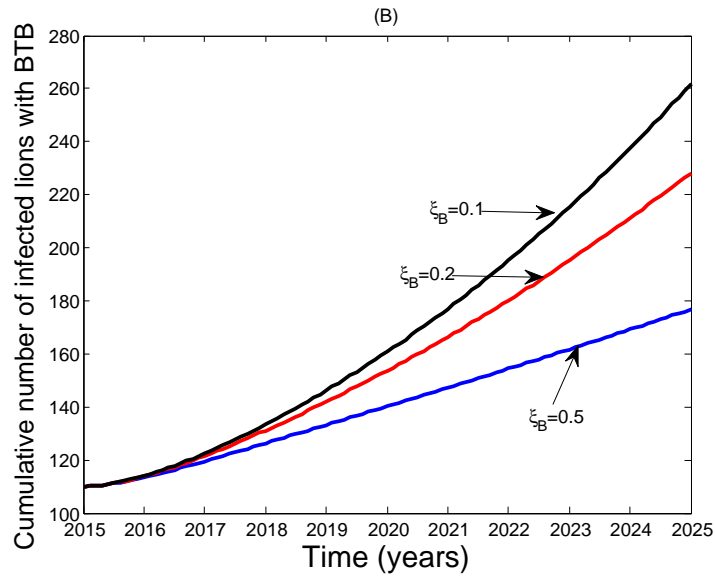
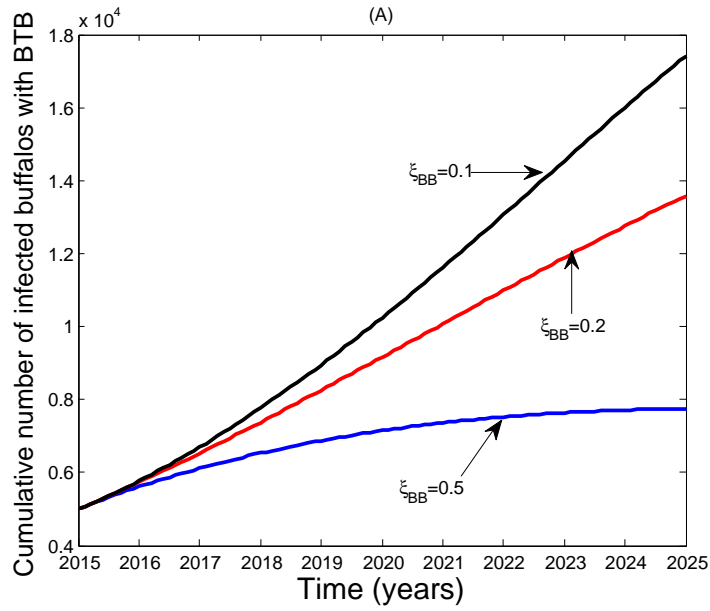


Figure 6: Simulations of the model (2.2), showing the cumulative number of (A) buffaloes infected with BTB (B) lions infected with BTB. Parameter values used are as given in Table 3, with various values of (A) ξ_{BB} and (B) ξ_B .

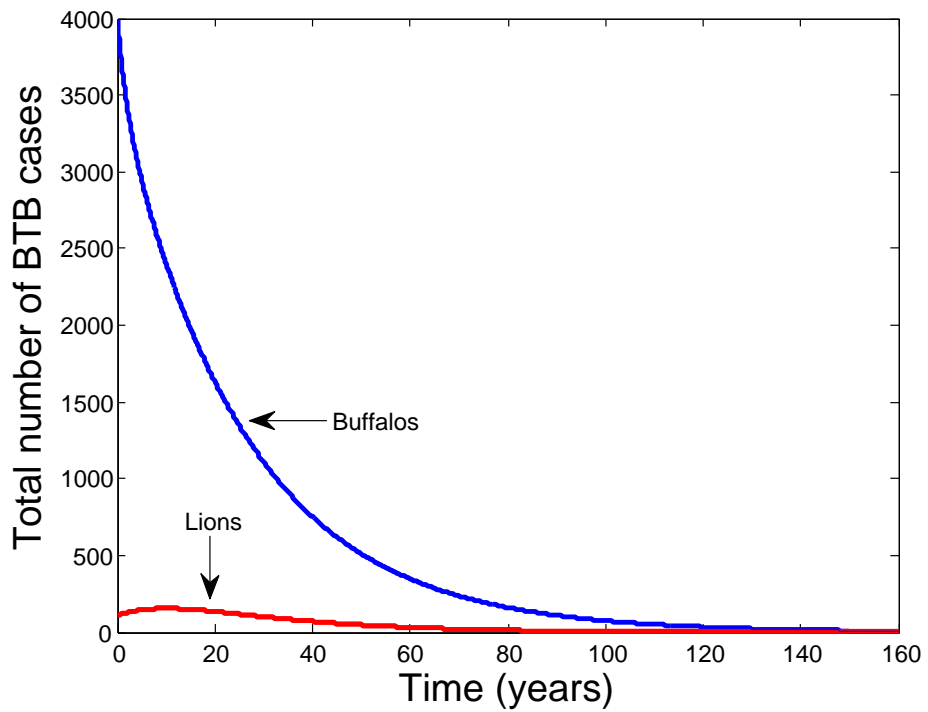


Figure 7: Simulations of the model (2.2), showing the time to BTB elimination using the high effectiveness level of the treatment-only strategy. Parameter values used are as given in Table 3 with $\theta_F = \theta_B = \theta_{EB} = 0$, $\xi_F = 0$, $\xi_B = \xi_{BB} = \xi_D = 0.5$ (so that, $\mathcal{R}_2 = 0.9470 < 1$ and $\mathcal{R}_3 = 0.4064 < 1$).

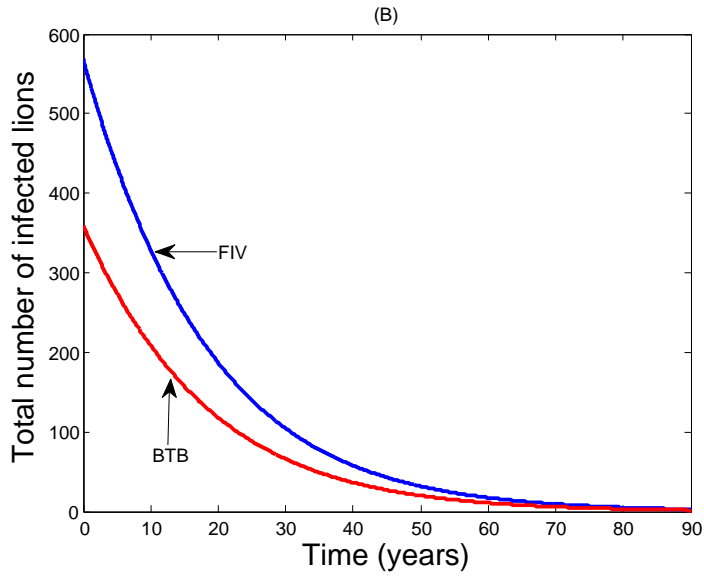
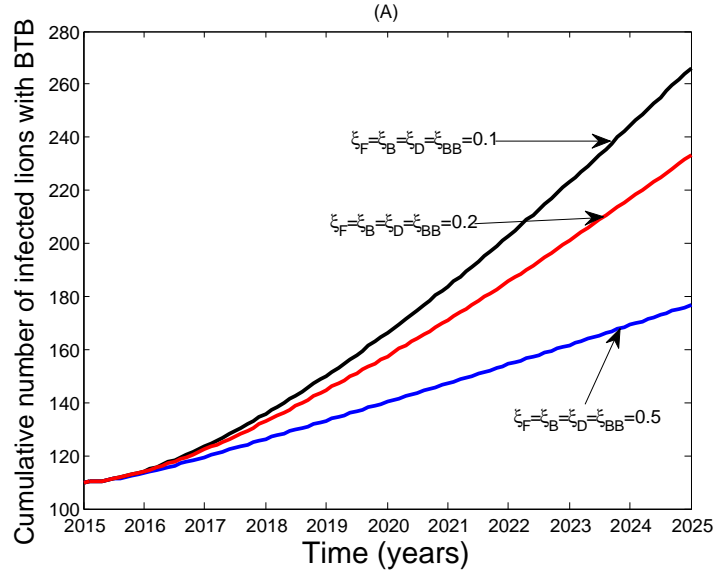


Figure 8: Simulations of the model (2.2) showing the (A) cumulative number of lions infected with BTB (B) time to FIV and BTB elimination using the high effectiveness level of the combined isolation-treatment strategy. Parameter values used are as given in Table 3, with $\theta_F = \theta_B = \theta_{EB} = 0$, $\xi_F = \xi_B = \xi_{BB} = \xi_D = 0.5$ (so that, $\mathcal{R}_0 = 0.9470 < 1$).