

Optimal Control of a Model of Gambiense Sleeping Sickness in Humans and Cattle

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Abstract: Human African trypanosomiasis (HAT) generally known as sleeping sickness is a fatal parasitic disease which appears mostly in sub-Saharan Africa, threatening millions of people and animals. Sleep disorders are a major feature of the (most) advanced stage of the disease, when the central nervous system is affected. In the absence of treatment, the outcome is always fatal. The parasite is transmitted to humans or animals through the bite of a tsetse fly previously infected by humans or animals carrying the parasite. We look for different scenarios to control the epidemic by integrating in our model terms that model the different control techniques.

Keywords: Trypanosoma Brucei Gambiense, Sleeping Sickness, Glossina, Optimization, Control, Modeling, Optimal Control

1. Introduction

Recently, a number of studies were carried out to explore the optimal control theory in some mathematical models for infectious diseases including the HIV virus [45, 46], tuberculosis [48] and vector-borne diseases [47]. Authors in [47] derive the optimal control efforts for treatment and prevention in order to prevent the spread of a vector-borne disease using a system of ordinary differential equations (ODEs) for the host and vector populations. Authors in [9] investigated such optimal strategies for prevention, treatment and vector control using two systems of ODEs which consist of a stage-structured model for the vector and a SI/SIR-type model for the vector/host population. In this paper, using models described in [39] for the tsetse fly population dynamics and the transmission virus, we formulate the associated control model in order to derive an optimal prevention and treatment strategies with minimal implementation costs. Controls used here are based on five main actions applied in the epidemics. There are optimal strategies for prevention, treatment and vector control for humans and cattle using two systems of ODEs which consist

of a stage-structured model for the vector and a SEI/SEIRS-type model for the vector/host populations (human and cattle).

The paper is organized as follows. In section 2, we present the compartmental models used in [39] to describe the tsetse fly population dynamics and HAT transmission between tsetse flies, humans and cattle. In section 3, we formulate an optimal control problem; first, we investigate the existence of an optimal control, then we derive the optimality system which characterizes the optimal control using Pontryagin's Maximum Principle [49]. In section 4 numerical results illustrate our theoretical results.

2. The Basic Model

2.1. Modeling the Growth Dynamics of the Tsetse Fly

We first model the growth dynamics of the tsetse fly. From the life cycle of the tsetse fly, it is sufficient to consider two life stages, namely the pupae and the adult flies.

Let $L(t)$ be the number of pupae at time t and $A(t)$ be the number of (male and female) adult flies at time t . The dynamics of L and A is modeled by the following system

$$\frac{dL}{dt} = b_L W A \left(1 - \frac{L}{K_L}\right) - (\sigma_L + d_L)L \quad (1)$$

$$\frac{dA}{dt} = \sigma_L L - d_F A \quad (2)$$

Here, b_L is the rate at which female flies give birth to larvae; W is the proportion of female flies in the population of adult flies; K_L is the pupae carrying the capacity of the nesting site; σ_L is the transfer rate from pupae to adult tsetse flies, so $\frac{1}{\sigma_L}$ is the average time as a pupa; d_L and d_F are the mortality rate of pupae and adult flies, respectively; with all parameters assumed positive.

2.1.1. Equilibrium Points

The threshold defined by

$$r = \frac{\sigma_L}{\sigma_L + d_L} \frac{b_L W}{d_F} \quad (3)$$

is important when calculating the equilibrium points of system (1)–(2), as shown in the following result. Parameter r can be interpreted as the probability of surviving the pupal stage multiplied by the birthrate divided by the death rate. If $r < 1$, the population of tsetse flies will be extinguished, otherwise they evolve toward an equilibrium given by

$$(L^*, A^*) = \left(1 - \frac{1}{r}\right) \left(\frac{K_L}{\frac{\sigma_L}{d_F} K_L}\right) \quad (4)$$

Details as regards the stability of this model are given in [39].

2.1.2. Formulation of the Full Model

For our full model, we assume that $r > 1$ and that the flies are in equilibrium (L^*, A^*) . Trypanosomiasis in the fly population is modeled by an SEI compartmental model. It is assumed that a fly once infected will never recover or be removed. So we subdivide the adult fly population into three compartments, S_F susceptible tsetse flies, E_F exposed tsetse flies infected but not yet infectious, and I_F infectious tsetse flies that are able to transmit the disease once they bite a susceptible host. Thus the total adult fly population is

$$A^* = S_F + E_F + I_F \quad (5)$$

The human and cattle host populations are described by a Malthus model. We denote by N_H and N_C the total size of the human and cattle host populations, respectively, at time t and b_H , b_C , d_H , d_C are the rates of birth and mortality of the human and cattle host populations, respectively. The dynamics of N_H and N_C is governed by

$$\frac{dN_H}{dt} = (b_H - d_H)N_H = \alpha_H N_H \quad (6)$$

$$\frac{dN_C}{dt} = (b_C - d_C)N_C = \alpha_C N_C \quad (7)$$

Where $\alpha_H = b_H - d_H$ and $\alpha_C = b_C - d_C$ are the growth rates of the human and cattle population respectively. If $\alpha_H < 0$ ($\alpha_C < 0$), the human (cattle) population will be extinguished, it will remain constant if $\alpha_H = 0$ ($\alpha_C = 0$), and will grow exponentially if $\alpha_H > 0$ ($\alpha_C > 0$). We assume that $\alpha_H = 0$ ($\alpha_C = 0$),

i.e. $b_H = d_H$ ($b_C = d_C$), so that the human (cattle) population is constant over the period of the study and that there is no human and cattle death due to HAT. Trypanosomiasis in the human and cattle host populations is modeled by SEIRS compartmental models, each with four compartments:

- susceptible hosts S_H (S_C): humans (cattle) at risk and disease free;
- Exposed hosts E_H (E_C): humans (cattle) in the latent stage of the disease. they are infected but unable to transmit the disease;
- Infectious hosts I_H (I_C), humans (cattle) able to transmit the disease to tsetse flies if they are bitten. These compartments contain hosts in the first stage of the disease with only minor symptoms or not aware if they are infected;
- Removed hosts R_H (R_C) consist of humans (cattle) in the second stage of the disease, very sick and not exposed to flies, so that they do not pass on infection, as well as humans (cattle) undergoing treatment and not exposed to flies. We assume that treatment starts at the beginning of stage 2, since this is usually when hosts become symptomatic. These compartments also contain removed humans (cattle) that have developed temporary immunity after recovery from stage 2 or treatment and they can neither transmit nor acquire HAT, but they will become susceptible again after the period of temporary immunity has passed.

The constant total human and cattle populations are defined by:

$$N_H = S_H + E_H + I_H + R_H \quad (8)$$

$$N_C = S_C + E_C + I_C + R_C \quad (9)$$

The dynamics of *T. b. Gambiense* in the tsetse fly population, assuming that transmission to flies occurs from humans and cattle in only the first stage of HAT, is given by the system

$$\frac{dS_F}{dt} = \sigma_L L^* - d_F S_F - (1-p)ac \frac{I_H}{N_H} S_F - pav \frac{I_C}{N_C} S_F \quad (10)$$

$$\frac{dE_F}{dt} = (1-p)ac \frac{I_H}{N_H} S_F + pav \frac{I_C}{N_C} S_F - (q_F + d_F)E_F \quad (11)$$

$$\frac{dI_F}{dt} = q_F E_F - d_F I_F \quad (12)$$

Here a is the vector blood feeding rate, c is the probability that a fly becomes infected after biting an infectious human, v is the probability that a fly becomes infected after biting infectious cattle, $\frac{1}{q_F}$ is the incubation period in the fly, d_F is the natural mortality rate of adult flies and p is the proportion of tsetse fly bites on cattle (thus $(1-p)$ is the proportion of bites on humans). This proportion is assumed to be constant as in Funk et al. [40]. For a discussion of this assumption see Rock et al. [10, Section 3.3].

The dynamics of *T. b. gambiense* in the human host population is governed by the system

$$\left\{ \begin{array}{l} \frac{dS_H}{dt} = b_H N_H + \kappa_H R_H - (1-p)ab \frac{I_F}{N_H} S_H - b_H S_H \\ \frac{dE_H}{dt} = (1-p)ab \frac{I_F}{N_H} S_H - (q_H + b_H)E_H \\ \frac{dI_H}{dt} = q_H E_H - (\gamma_H + b_H)I_H \\ \frac{dR_H}{dt} = \gamma_H I_H - (b_H + \kappa_H)R_H \end{array} \right.$$

Where b is the probability that an infectious fly infects a human host, b_H is the birth rate of the human population, $b_H = d_H$ is the human mortality rate, $\frac{1}{q_H}$ is the average incubation period for a human host, $\frac{1}{\gamma_H}$ is the average length of stage 1 for humans corresponding to the infectious period. For untreated humans, $\frac{1}{\kappa_H}$ is the sum of the average length of stage 2 and the average temporary immunity period. For treated humans, $\frac{1}{\kappa_H}$ is the sum of the average length of treatment and the average temporary immunity period. Note that we assume that the average length of treatment is equal to the average length of stage 2. Similarly, the dynamics of *T. b. Gambiense* in the cattle host population is governed by the system

$$\begin{aligned} \frac{dS_C}{dt} &= b_C N_C + \kappa_C R_C - pau \frac{I_F}{N_C} S_C - b_C S_C \\ \frac{dE_C}{dt} &= pau \frac{I_F}{N_C} S_C - (q_C + b_C)E_C \\ \frac{dI_C}{dt} &= q_C E_C - (\gamma_C + b_C)I_C \\ \frac{dR_C}{dt} &= \gamma_C I_C - (b_C + \kappa_C)R_C \end{aligned}$$

where u is the probability that an infectious fly infects a cattle host, b_C is the birth rate of the cattle population, $d_C = b_C$ is the cattle mortality rate, $\frac{1}{q_C}$ is the average incubation period for cattle, $\frac{1}{\gamma_C}$ is the average length of stage 1 for cattle corresponding to the infectious period. For the untreated cattle, $\frac{1}{\kappa_C}$ is the sum of the average length of stage 2 and the average temporary immunity period. For the cattle treated, $\frac{1}{\kappa_C}$ is the sum of the average length of treatment and the average temporary immunity period. As for humans, we assume that the average length of treatment is equal to the average length of stage 2 for cattle.

Thus, the dynamics of the transmission of sleeping sickness is then described by the system of equations below, where we have assumed that there is no death due to the disease, no vertical transmission, and all parameters are positive, except κ_H and κ_C which are non negative.

$$\frac{dE_F}{dt} = (1-p)ac \frac{I_H}{N_H} S_F + pav \frac{I_C}{N_C} S_F - \tilde{q}_F E_F \quad (13)$$

$$\frac{dI_F}{dt} = q_F E_F - d_F I_F \quad (14)$$

$$\frac{dE_H}{dt} = pau \frac{I_F}{N_C} S_C - \tilde{q}_H E_H \quad (15)$$

$$\frac{dI_H}{dt} = q_H E_H - \tilde{q}_H I_H \quad (16)$$

$$\frac{dE_C}{dt} = pau \frac{I_F}{N_C} S_C - \tilde{q}_C E_C \quad (17)$$

$$\frac{dI_C}{dt} = q_C E_C - \tilde{\gamma}_C I_C \quad (18)$$

$$\frac{dS_F}{dt} = \sigma_L L^* - d_F S_F - (1-p)ac \frac{I_H}{N_H} S_F - pav \frac{I_C}{N_C} S_F \quad (19)$$

$$\frac{dS_H}{dt} = b_H N_H + \kappa_H R_H - (1-p)ab \frac{I_F}{N_H} S_H - b_H S_H \quad (20)$$

$$\frac{dS_C}{dt} = b_C N_C + \kappa_C R_C - pau \frac{I_F}{N_C} S_C - b_C S_C \quad (21)$$

$$\frac{dR_H}{dt} = \gamma_H I_H - (b_H + \kappa_H)R_H \quad (22)$$

$$\frac{dR_C}{dt} = \gamma_C I_C - (b_C + \kappa_C)R_C \quad (23)$$

Where $\tilde{\gamma}_i = \gamma_i + b_i$; $\tilde{q}_i = q_i + b_i$ for $i \in \{H, C\}$ and $\tilde{q}_F = q_F + d_F$

Figure 1 shows a flow diagram for this system and Table 1 describes the model parameters. Note that all cross transmission terms are normalized with respect to the host population as it is common in vector-borne disease models [19, Section 14.3]. Non negative initial conditions with $E_F + I_F + E_H + I_H + E_C + I_C$ positive and small complete the formulation of our HAT model in the invariant region

$$\Gamma = \left\{ (E_F, I_F, E_H, I_H, E_C, I_C, S_F, S_H, R_H, S_C, R_C) \in \mathbb{R}_+^{11} \cap \left(\begin{array}{l} E_F + I_F + S_F = A^* \\ E_H + I_H + S_H + R_H = N_H \\ E_C + I_C + S_C + R_C = N_C \end{array} \right) \right\} \quad (24)$$

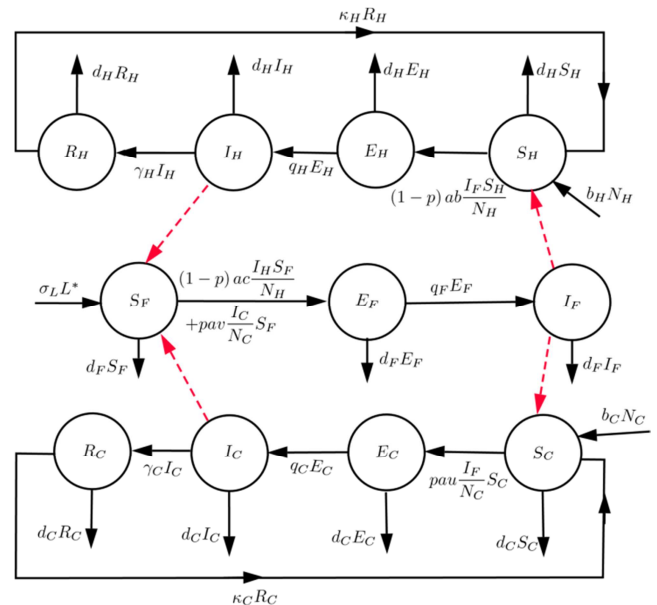


Figure 1. Flow diagram of HAT transmission dynamics.

2.2. Model Equilibrium and Stability

In [39] A. M. Ndondo et al. showed that system (13)–(23) always reaches the disease free equilibrium (DFE), $X_0^* = (0, 0, 0, 0, 0, 0, A^*, N_H, N_C, 0, 0)$. Considering the local

stability of X_0^* , they followed the notation of [7] and only considered the infected compartments given by (13)–(18) and the calculation of the basic reproduction number gave

$$\mathcal{R}_0 = \sqrt{\frac{(1-p)^2 a^2 b c q_F q_H A^*}{\check{q}_F d_F \check{q}_H \check{q}_H N_H} + \frac{p^2 a^2 u v q_F q_C A^*}{\check{q}_F d_F \check{q}_C \check{q}_C N_C}}$$

3. Optimal Control

In this section, we discuss the control measures to limit the impact of the tsetse fly in the transmission of HAT. We consider model (13)–(23) with different control measures:

- The first control measure noted μ_1 models efforts to prevent the spread of infection. It brings together the various strategies used in order to reduce the number of vector-human contacts. We can cite in particular the use of repellents, mosquito nets (since the tsetse flies are mostly active in the late afternoon and early morning) or suggest that humans wear long-sleeved clothing to cover the exposed parts of the body, and prevent cattle from being bitten by dipping them in fly repellent solutions. Moreover, control μ_1 also takes into account the municipality efforts to raise awareness of the danger of the tsetse fly and HAT in the population. Our action is limited in the interval $[0, T]$.
- The second control measure μ_2 is the treatment of human patients on the interval $[0, T]$. It also models the isolation of patients in treatment places (hospitals and isolation areas) to avoid all possible new contamination cases.
- The third control measure μ_3 specifically models the vector control on the interval $[0, T]$. It includes actions under the responsibility of vector control services and is intended to kill the pupae through the use of larvicides whose action is specifically directed against the pupae. It also includes the community effort to destroy potential breeding sites around homes and deprive the tsetse flies of the breeding sites in which their larvae can develop (in hot weather, at midday, tsetse hide in shelters to avoid high temperatures). Houses and huts also provide a fresh environment and many tsetse flies find refuge there in the dry season. Tsetse flies normally leave their refuge in the late afternoon to find blood meal [15], thus to avoid being bitten or to prevent tsetse flies from entering or facilitating their exit from habitations. The control measure μ_3 can also model the efforts to trap tsetse flies, reducing the larvae capacity K_L . There is also the idea of introducing a sterile population of flies to reduce the number of clutches (since the females are in general fertilized only once).
- The fourth control noted μ_4 models efforts to prevent the spread of infection. It brings together the various strategies used in order to reduce the number of cattle-vector contacts. It brings together the different strategies used in order to reduce the number of contacts between vectors and cattle on the interval $[0, T]$.

- The fifth control noted μ_5 measures the treatment of infected cattle on the interval $[0, T]$. It also models the isolation of infected cattle in treatment places (isolated areas) to avoid all possible new contamination cases.

We will consider a situation where:

$$\mathcal{R}_0 = \sqrt{\frac{(1-p)^2 a^2 b c q_F q_H A^*}{\check{q}_F d_F \check{q}_H \check{q}_H N_H} + \frac{p^2 a^2 u v q_F q_C A^*}{\check{q}_F d_F \check{q}_C \check{q}_C N_C}}$$

is greater than 1, and we are not at a stable disease free equilibrium??, and there is need to apply a treatment to control the epidemic. Under these conditions, the optimal control problem is formulated as follows:

$$\frac{dL}{dt} = b_L W A \left(1 - \frac{L}{K_L}\right) - (\sigma_L + d_L + d_C \mu_3) L \quad (25)$$

$$\frac{dA}{dt} = \sigma_L L - d_F A \quad (26)$$

$$\frac{dE_F}{dt} = (1 - \mu_1)(1 - p)ac \frac{I_H}{N_H} S_F + (1 - \mu_4)pav \frac{I_C}{N_C} S_F - (\check{q}_F + d_F \mu_3) E_F \quad (27)$$

$$\frac{dI_F}{dt} = q_F E_F - (d_F + d_F \mu_3) I_F \quad (28)$$

$$\frac{dE_H}{dt} = (1 - \mu_1)(1 - p)ab \frac{I_F}{N_H} S_H - (\check{q}_H + \mu_2 \gamma_H) E_H \quad (29)$$

$$\frac{dI_H}{dt} = q_H E_H - (\tilde{\gamma}_H + \mu_2 \gamma_H) I_H \quad (30)$$

$$\frac{dE_C}{dt} = (1 - \mu_4)pau \frac{I_F}{N_C} S_C - (\check{q}_C + \gamma_C \mu_5) E_C \quad (31)$$

$$\frac{dI_C}{dt} = q_C E_C - (\tilde{\gamma}_C + \gamma_C \mu_5) I_C \quad (32)$$

$$\frac{dS_F}{dt} = \sigma_L L^* - (d_F + d_F \mu_3) S_F - (1 - \mu_1)(1 - p)ac \frac{I_H}{N_H} S_F - (1 - \mu_4)pav \frac{I_C}{N_C} S_F \quad (33)$$

$$\frac{dS_H}{dt} = b_H N_H + \kappa_H R_H - (1 - \mu_1)(1 - p)ab \frac{I_F}{N_H} S_H - b_H S_H \quad (34)$$

$$\frac{dS_C}{dt} = b_C N_C + \kappa_C R_C - (1 - \mu_4)pau \frac{I_F}{N_C} S_C - b_C S_C \quad (35)$$

$$\frac{dR_H}{dt} = \gamma_H I_H - (b_H + \kappa_H) R_H \quad (36)$$

$$\frac{dR_C}{dt} = \gamma_C I_C - (b_C + \kappa_C) R_C \quad (37)$$

Where

$\mu_1 \in [0, 1]$ corresponds to prevention. So if $\mu_1 = 1$, then the number of human-vector contacts is zero and if $\mu_1 = 0$, the infection rate is maximum and equal to ab or ac ;

$\mu_2 \in [0, 1]$ corresponds to the treatment

γ_H is the proportion of actual treatment (so $\mu_2 \gamma_H$ gives the proportion of humans cured with treatment)

$\mu_3 \in [0, 1]$ corresponds to the vector control. $d_F \mu_3$ is the mortality rate of tsetse flies due to the use of chemicals or destruction of breeding sites.

$\mu_4 \in [0, 1]$ corresponds to prevention. So if $\mu_4 = 1$, then the number of cattle-vector contacts is zero and if $\mu_4 = 0$, the infection rate is maximum and equal to av or au ;

$\mu_5 \in [0, 1]$ corresponds to the cattle treatment and γ_C is

the proportion of actual treatment (so $\gamma_C \mu_5$ gives the proportion of cattle cured with treatment);

Proposition 3 $D \times \Gamma$ is positively invariant for system (17-29)

Proof

First we have:

Using Grönwall's inequality, we deduce easily that while all variables in this system are positive, we have moreover

$$\begin{aligned} \frac{dL}{dt} &\leq b_L W A \left(1 - \frac{L}{K_L}\right) - (\sigma_L + d_L)L \\ \frac{dA}{dt} &\leq \sigma_L L - d_F A \\ \frac{dE_F}{dt} &\leq (1-p)ac \frac{I_H}{N_H} S_F + pav \frac{I_C}{N_C} S_F - \tilde{q}_F E_F \\ \frac{dI_F}{dt} &\leq q_F E_F - d_F I_F \\ \frac{dE_H}{dt} &\leq pau \frac{I_F}{N_C} S_C - \tilde{q}_H E_H \\ \frac{dI_H}{dt} &\leq q_H E_H - \tilde{q}_H I_H \\ \frac{dE_C}{dt} &\leq pau \frac{I_F}{N_C} S_C - \tilde{q}_C E_C \\ \frac{dI_C}{dt} &\leq q_C E_C - \tilde{\gamma}_C I_C \\ \frac{dS_F}{dt} &\leq \sigma_L L^* - d_F S_F - (1-p)ac \frac{I_H}{N_H} S_F - pav \frac{I_C}{N_C} S_F \\ \frac{dS_H}{dt} &\leq b_H N_H + \kappa_H R_H - (1-p)ab \frac{I_F}{N_H} S_H - b_H S_H \\ \frac{dS_C}{dt} &\leq b_C N_C + \kappa_C R_C - pau \frac{I_F}{N_C} S_C - b_C S_C \\ \frac{dR_H}{dt} &\leq \gamma_H I_H - (b_H + \kappa_H) R_H \\ \frac{dR_C}{dt} &\leq \gamma_C I_C - (b_C + \kappa_C) R_C \end{aligned}$$

The right side of these inequalities is exactly the HAT transmission model (13-23) without control. Since the solutions of system (13-23) were defined in $D \times \Gamma$. So, as done before, using Grönwall's inequality, we deduce that the solutions of the last system are bounded.

We associate to system (27-37), the optimal control problem coupled with the following cost function:

$$J(\mu_1, \mu_2, \mu_3, \mu_4, \mu_5) = \int_0^T \left(A_1 I_H + A_2 I_F + A_3 I_C + \frac{1}{2} B_1 \mu_1^2 + \frac{1}{2} B_2 \mu_2^2 + \frac{1}{2} B_3 \mu_3^2 + \frac{1}{2} B_4 \mu_4^2 + \frac{1}{2} B_5 \mu_5^2 \right) dt \quad (38)$$

The first terms represent the costs for populations I_H , I_C and I_F that we want to reduce. The constants B_1, B_2, B_3, B_4 and B_5 are positive and correspond to the ratio used to regulate the control for the prevention, treatment and vector control in human and cattle population respectively. As given in the literature, the cost functions are assumed to be quadratic functions. In fact, a quadratic cost function is a natural way that allows the analogy with the expended energy for all those dimensions.

The objective is to limit the spread of the disease by reducing the number of flies and infected humans. We then look for the control terms $(\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*)$ that minimize the cost:

$$\begin{aligned} J(\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*) = \\ \min \{ J(\mu_1, \mu_2, \mu_3, \mu_4, \mu_5) | (\mu_1, \mu_2, \mu_3, \mu_4, \mu_5) \in \Lambda \} \\ \text{where } \Lambda = (\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*), a_i \leq \mu_i \leq b_i, \\ i \in \{1, 2, 3, 4, 5\} \\ \text{with } \mu_i \text{ a piecewise continuous function on } [0, T] \\ \text{and } i = 1, 2, 3, 4, 5 \end{aligned}$$

The aim is not only to reduce the populations of infected humans and infected vectors I_H , I_C and I_F after a time T but also over $[0, T]$ to act simultaneously on prevention (contact vectors-infected humans/cattle), treatment (infected humans/cattle), I_H , I_C and the vector control. The First, second and third terms of the functional J model the human population, the cattle population and the accumulated infected vectors from the initial time $T_0 = 0$ to the final time $T_f = T$.

The fourth, fifth, sixth, seventh and eighth terms model the cumulative costs of prevention, treatment and vector control. All of them vary according to time.

The choice of positive parameters $A_1, A_2, A_3, B_1, B_2, B_3, B_4$ and B_5 depends on a subjective assessment of the relative importance given by the technical staff to reduce the population of infected human, infected cattle, infected flies by prevention, treatment of infected humans and cattle, and vector control (the weight or weighting for regulating the control). Λ is the set of controls and a_i, b_i are constants belonging to $[0, 1]$, $i = 1, 2, 3, 4, 5$

The optimal control problem is solved when we determine $(\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*) \in \Lambda$ that minimizes the function (38). Hence our work will consist of the following steps:

- to show the existence of an optimal control;
- to give a characterization of the optimal control;
- to obtain numerical representations

3.1. Existence of the Optimal Control

Proposition 3.1 Consider the control problem associated with problem (25-37). There is a control $(\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*)$ and a corresponding solution $(L^*, A^*, E_F^*, I_F^*, E_H^*, I_H^*, E_C^*, I_C^*, S_F^*, S_H^*, R_H^*, S_C^*, R_C^*)$ which minimizes $J(\mu_1, \mu_2, \mu_3, \mu_4, \mu_5)$ on Λ such that

$$\min_{(\mu_1, \mu_2, \mu_3, \mu_4, \mu_5) \in \Lambda} J(\mu_1, \mu_2, \mu_3, \mu_4, \mu_5) = J(\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*)$$

Proof

According to W. H. Fleming [1], Theorem 3.4.1, we need to check the following conditions:

1. The set of controls and corresponding solutions is not empty;
2. The set of controls of Λ is convex and closed in $L^2(0, T)$;
3. The vector set of the state system is bounded by a linear function of control;
4. the integrand of the objective function is convex;
5. there exist constants c_1, c_2 and $\beta > 0$ such that the objective function integrand is bounded by $c_1(|\mu_1|^2 + |\mu_2|^2 + |\mu_3|^2 + |\mu_4|^2 + |\mu_5|^2)^{\beta-2} - c_2$

We check that $\mu_1 = \mu_2 = \mu_3 = \mu_4 = \mu_5 = 0$ is a control in Λ and $(L^*, A^*, E_F^*, I_F^*, E_H^*, I_H^*, E_C^*, I_C^*, S_F^*, S_H^*, R_H^*, S_C^*, R_C^*)$ is a solution corresponding to control $\mu_1 = \mu_2 = \mu_3 = \mu_4 = \mu_5 = 0$, so the set of all controls and corresponding solutions is not empty, which satisfies condition 1.

- The set Λ is bounded by definition, so condition 2 is

$$A_1 I_H(t) + A_2 I_F(t) + A_3 I_C(t) + \frac{1}{2} B_1 \mu_1^2(t) + \frac{1}{2} B_2 \mu_2^2(t) + \frac{1}{2} B_3 \mu_3^2(t) + \frac{1}{2} B_4 \mu_4^2(t) + \frac{1}{2} B_5 \mu_5^2(t) \geq c_1(|\mu_1|^2 + |\mu_2|^2 + |\mu_3|^2 + |\mu_4|^2 + |\mu_5|^2)^{\frac{\beta}{2} - c_2}$$

Since variables I_H, I_C, I_F are bounded, we deduce then the existence of an optimal control $(\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*)$ which minimizes the cost function $J(\mu_1, \mu_2, \mu_3, \mu_4, \mu_5)$.

In summary, for this minimization problem, the necessary convexity condition required for the functional J with parameters $I_H, I_F, I_C, \mu_1, \mu_2, \mu_3, \mu_4$ and μ_5 holds. The right set of the system of equations (25-37) is linearly bounded because of the fact that a priori variable T is bounded, which implies that other state variables are also bounded. Boundedness and the fact that the bounds are finite guarantee the required compactness for the existence of optimal

satisfied.

- The system vector field (25-37) satisfies condition 3 because it is bounded.
- there exist $c_1, c_2 > 0$ and $\beta > 1$ satisfying

control. The initial conditions are $I_H(0), I_C(0), I_F(0)$.

Since now we have assured the existence of an optimal control, we can use Pontryagin's Maximum principle to solve the optimal control problem.

3.2. Characterization of Optimal Control

Theorem 4 The optimal control which minimizes the functional J given in (38) under the constraints given by the system of differential equations (25-37) is given by:

$$\begin{aligned} \mu_1^* &= \max \left\{ a_1, \min \left\{ b_1, \frac{1}{B_1} \left[(\lambda_3 - \lambda_9)(1-p)ac \frac{I_H}{N_H} S_F + (\lambda_5 - \lambda_{10})(1-p)ab \frac{I_F}{N_H} S_H \right] \right\} \right\} \\ \mu_2^* &= \max \left\{ a_2, \min \left\{ b_2, \frac{\gamma_H}{B_2} [\lambda_5 E_H + \lambda_6 I_H] \right\} \right\} \\ \mu_3^* &= \max \left\{ a_3, \min \left\{ b_3, \frac{1}{B_3} [\lambda_1 d_C L + \lambda_3 d_F E_F - \lambda_4 d_F I_F + \lambda_9 d_F S_F] \right\} \right\} \\ \mu_4^* &= \max \left\{ a_4, \min \left\{ b_4, \frac{1}{B_4} \left[(\lambda_3 - \lambda_9)pav \frac{I_C}{N_C} S_F + (\lambda_7 - \lambda_{11})pau \frac{I_F}{N_C} S_C \right] \right\} \right\} \\ \mu_5^* &= \max \left\{ a_5, \min \left\{ b_5, \frac{\gamma_C}{B_5} [\lambda_8 I_C + \lambda_7 E_C] \right\} \right\} \end{aligned}$$

Proof

Let $Z = (L, A, E_F, I_F, E_H, I_H, E_C, I_C, S_F, S_H, R_H, S_C, R_C) \in D \times \Gamma, U = (\mu_1, \mu_2, \mu_3, \mu_4, \mu_5) \in \Lambda$ and $\Pi = (\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7, \lambda_8, \lambda_9, \lambda_{10}, \lambda_{11}, \lambda_{12}, \lambda_{13})$ be the adjoint variables. We define the Lagrangian (Hamiltonian increased penalties) associated with the problem defined above:

$$\begin{aligned} \mathcal{L}(Z, U, \pi) &= A_1 I_H + A_2 I_F + A_3 I_C + \frac{1}{2} B_1 \mu_1^2 + \frac{1}{2} B_2 \mu_2^2 + \frac{1}{2} B_3 \mu_3^2 + \frac{1}{2} B_4 \mu_4^2 + \frac{1}{2} B_5 \mu_5^2 + \lambda_1 [b_L W A \left(1 - \frac{L}{K_L} \right) - (\sigma_L + d_L + d_C \mu_3) L] + \lambda_2 [\sigma_L L \\ &\quad - d_F A] + \lambda_3 [(1 - \mu_1)(1 - p)ac \frac{I_H}{N_H} S_F + (1 - \mu_4)pav \frac{I_C}{N_C} S_F - (\tilde{q}_F + d_F \mu_3) E_F] + \lambda_4 [q_F E_F - (d_F + d_F \mu_3) I_F] \\ &\quad + \lambda_5 [(1 - \mu_1)(1 - p)ab \frac{I_F}{N_H} S_H - (\tilde{q}_H + \mu_2 \gamma_H) E_H] + \lambda_6 [q_H E_H - (\tilde{y}_H + \mu_2 \gamma_H) I_H] \\ &\quad + \lambda_7 [(1 - \mu_4)pau \frac{I_F}{N_C} S_C - (\tilde{q}_C + \gamma_C \mu_5) E_C] + \lambda_8 [q_C E_C - (\tilde{y}_C + \gamma_C \mu_5) I_C] \\ &\quad + \lambda_9 [\sigma_L L^* - (d_F + d_F \mu_3) S_F - (1 - \mu_1)(1 - p)ac \frac{I_H}{N_H} S_F - (1 - \mu_4)pav \frac{I_C}{N_C} S_F] \\ &\quad + \lambda_{10} [b_H N_H + \kappa_H R_H - (1 - \mu_1)(1 - p)ab \frac{I_F}{N_H} S_H - b_H S_H] + \lambda_{11} [b_C N_C + \kappa_C R_C - (1 - \mu_4)pau \frac{I_F}{N_C} S_C - b_C S_C] \\ &\quad + \lambda_{12} [b_C N_C + \kappa_C R_C - (1 - \mu_4)pau \frac{I_F}{N_C} S_C - b_C S_C] + \lambda_{13} [\gamma_H I_H - (b_H + \kappa_H) R_H] + w_1 (\mu_1 - a_1) + w_2 (b_1 - \mu_1) \\ &\quad + w_3 (\mu_2 - a_2) + w_4 (b_2 - \mu_2) + w_5 (\mu_3 - a_3) + w_6 (b_3 - \mu_3) + w_7 (\mu_4 - a_4) + w_8 (b_4 - \mu_4) + w_9 (\mu_5 - a_5) \\ &\quad + w_{10} (b_5 - \mu_5) \end{aligned}$$

Where $\omega_1, \omega_2, \omega_3, \omega_4, \omega_5, \omega_6, \omega_7, \omega_8, \omega_9$ and ω_{10} are penalty variables (multipliers) attached to control $\mu_1, \mu_2, \mu_3, \mu_4$ and μ_5 . These penalty multipliers must meet the following conditions:

$$\begin{aligned}\omega_1(t)(\mu_1(t) - a_1) &= 0; \omega_2(t)(b_1 - \mu_1(t)) = 0 \\ \omega_3(t)(\mu_2(t) - a_2) &= 0; \omega_4(t)(b_2 - \mu_2(t)) = 0 \\ \omega_5(t)(\mu_3(t) - a_3) &= 0; \omega_6(t)(b_3 - \mu_3(t)) = 0 \\ \omega_7(t)(\mu_4(t) - a_4) &= 0; \omega_8(t)(b_4 - \mu_4(t)) = 0 \\ \omega_9(t)(\mu_5(t) - a_5) &= 0; \omega_{10}(t)(b_5 - \mu_5(t)) = 0\end{aligned}$$

In addition, the differential equations which govern the adjoint variables are obtained by differentiating the Lagrangian (as per Maximum Principle):

$$\begin{aligned}\frac{d\lambda_1}{dt} &= -\frac{\partial \mathcal{L}}{\partial L}; \frac{d\lambda_2}{dt} = -\frac{\partial \mathcal{L}}{\partial A}; \frac{d\lambda_3}{dt} = -\frac{\partial \mathcal{L}}{\partial E_F}; \frac{d\lambda_4}{dt} = -\frac{\partial \mathcal{L}}{\partial I_F}; \frac{d\lambda_5}{dt} = -\frac{\partial \mathcal{L}}{\partial E_H}; \\ \frac{d\lambda_6}{dt} &= -\frac{\partial \mathcal{L}}{\partial I_H}; \frac{d\lambda_7}{dt} = -\frac{\partial \mathcal{L}}{\partial E_C}; \frac{d\lambda_8}{dt} = -\frac{\partial \mathcal{L}}{\partial I_C}; \frac{d\lambda_9}{dt} = -\frac{\partial \mathcal{L}}{\partial S_F}\end{aligned}$$

For these adjoint variables, we must have $\lambda_i(T) = 0$, $i = 1, 2, \dots, 9$, these are the transversality conditions called also marriage conditions.

The value of the optimal control can be characterized at each time $t \in [0, T]$ noting that it minimizes the Lagrangian (Pontryagin's Maximum Principle) and that's at this optimal control, variables must satisfy the necessary condition:

$$\frac{\partial \mathcal{L}}{\partial \phi^*} = 0 \text{ with } \phi^* = (\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*) \text{ where } \phi^* = ((\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*)) \text{ is the optimal quintuplet.}$$

Given that

$$\begin{aligned}\mathcal{L} &= \frac{1}{2}B_1\mu_1^2 + \frac{1}{2}B_2\mu_2^2 + \frac{1}{2}B_3\mu_3^2 + \frac{1}{2}B_4\mu_4^2 + \frac{1}{2}B_5\mu_5^2 + \lambda_1[-d_C\mu_3L] + \lambda_3[(1-\mu_1)(1-p)ac\frac{I_H}{N_H}S_F + (1-\mu_4)pav\frac{I_C}{N_C}S_F - d_F\mu_3E_F] \\ &\quad + \lambda_4[-(d_F\mu_3)I_F] + \lambda_5[(1-\mu_1)(1-p)ab\frac{I_F}{N_H}S_H - (\mu_2\gamma_H)E_H] + \lambda_6[-(\mu_2\gamma_H)I_H] \\ &\quad + \lambda_7\left[(1-\mu_4)pau\frac{I_F}{N_C}S_C - (\gamma_C\mu_5)E_C\right] + \lambda_8[-(\gamma_C\mu_5)I_C] \\ &\quad + \lambda_9\left[-(d_F\mu_3)S_F - (1-\mu_1)(1-p)ac\frac{I_H}{N_H}S_F - (1-\mu_4)pav\frac{I_C}{N_C}S_F\right] + \lambda_{10}\left[-(1-\mu_1)(1-p)ab\frac{I_F}{N_H}S_H\right] \\ &\quad + \lambda_{11}\left[-(1-\mu_4)pau\frac{I_F}{N_C}S_C\right] + \lambda_{12}\left[-(1-\mu_4)pau\frac{I_F}{N_C}S_C\right] + w_1(\mu_1 - a_1) + w_2(b_1 - \mu_1) + w_3(\mu_2 - a_2) \\ &\quad + w_4(b_2 - \mu_2) + w_5(\mu_3 - a_3) + w_6(b_3 - \mu_3) + w_7(\mu_4 - a_4) + w_8(b_4 - \mu_4) + w_9(\mu_5 - a_5) + w_{10}(b_5 - \mu_5) \\ &\quad + (\text{terms without } \mu_1 \text{ nor } \mu_2 \text{ nor } \mu_3 \text{ nor } \mu_4 \text{ nor } \mu_5)\end{aligned}$$

Differentiating \mathcal{L} with respect to $\mu_1, \mu_2, \mu_3, \mu_4$ and μ_5 gives respectively:

$$\begin{aligned}\frac{\partial \mathcal{L}}{\partial \mu_1} &= B_1\mu_1 - \lambda_3(1-p)ac\frac{I_H}{N_H}S_F - \lambda_5(1-p)ab\frac{I_F}{N_H}S_H + \lambda_9(1-p)ac\frac{I_H}{N_H}S_F + \lambda_{10}(1-p)ac\frac{I_F}{N_H}S_H + w_1 - w_2 \\ \frac{\partial \mathcal{L}}{\partial \mu_2} &= B_2\mu_2 - \lambda_5\gamma_H E_H - \lambda_6\gamma_H I_H + w_3 - w_4 \\ \frac{\partial \mathcal{L}}{\partial \mu_3} &= B_3\mu_3 - \lambda_1 d_C L - \lambda_3 d_F E_F + \lambda_4 d_F I_F - \lambda_9 d_F S_F + w_5 - w_6 \\ \frac{\partial \mathcal{L}}{\partial \mu_4} &= B_4\mu_4 - \lambda_3 pav\frac{I_C}{N_C}S_F - \lambda_7 pau\frac{I_F}{N_C}S_C + \lambda_9 pav\frac{I_C}{N_C}S_F + \lambda_{11} pau\frac{I_F}{N_C}S_C + w_7 - w_8 \\ \frac{\partial \mathcal{L}}{\partial \mu_5} &= B_5\mu_5 - \lambda_7 \gamma_C E_C - \lambda_8 \gamma_C I_C + w_9 - w_{10}\end{aligned}$$

At $(\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*)$, we have $\frac{\partial \mathcal{L}}{\partial \mu_1} = \frac{\partial \mathcal{L}}{\partial \mu_2} = \frac{\partial \mathcal{L}}{\partial \mu_3} = \frac{\partial \mathcal{L}}{\partial \mu_4} = \frac{\partial \mathcal{L}}{\partial \mu_5} = 0$

These equalities give:

$$\begin{cases} B_1\mu_1 - \lambda_3(1-p)ac\frac{I_H}{N_H}S_F - \lambda_5(1-p)ab\frac{I_F}{N_H}S_H + \lambda_9(1-p)ac\frac{I_H}{N_H}S_F + \lambda_{10}(1-p)ab\frac{I_F}{N_H}S_H + w_1 - w_2 = 0 \\ B_2\mu_2 - \lambda_5\gamma_H E_H - \lambda_6\gamma_H I_H + w_3 - w_4 = 0 \\ B_3\mu_3 - \lambda_1 d_C L - \lambda_3 d_F E_F + \lambda_4 d_F I_F - \lambda_9 d_F S_F + w_5 - w_6 = 0 \\ B_4\mu_4 - \lambda_3 pav\frac{I_C}{N_C}S_F - \lambda_7 pau\frac{I_F}{N_C}S_C + \lambda_9 pav\frac{I_C}{N_C}S_F + \lambda_{11}pau\frac{I_F}{N_C}S_C + w_7 - w_8 = 0 \\ B_5\mu_5 - \lambda_7\gamma_C E_C - \lambda_8\gamma_C I_C + w_9 - w_{10} = 0 \end{cases}$$

Hence, we get the optimum

$$\begin{aligned} \mu_1^* &= \frac{1}{B_1} \left[(\lambda_3 - \lambda_9)(1-p)ac\frac{I_H}{N_H}S_F + (\lambda_5 - \lambda_{10})(1-p)ab\frac{I_F}{N_H}S_H - w_1 + w_2 \right] \\ \mu_2^* &= \frac{\gamma_H}{B_2} [\lambda_5 E_H + \lambda_6 I_H - w_3 + w_4] \\ \mu_3^* &= \frac{1}{B_3} [\lambda_1 d_C L + \lambda_3 d_F E_F - \lambda_4 d_F I_F + \lambda_9 d_F S_F - w_5 + w_6] \\ \mu_4^* &= \frac{1}{B_4} \left[(\lambda_3 - \lambda_9)pav\frac{I_C}{N_C}S_F + (\lambda_7 - \lambda_{11})pau\frac{I_F}{N_C}S_C - w_7 + w_8 \right] \\ \mu_5^* &= \frac{\gamma_C}{B_5} [\lambda_8 I_C + \lambda_7 E_C - w_9 + w_{10}] \end{aligned}$$

For a more explicit formula for optimal controls without $\omega_1, \omega_2, \omega_3, \omega_4, \omega_5$ and ω_6 , we use standard techniques. For this purpose, we consider 15 cases, with 3 cases for each optimal control:

1) Case 1

In the set $\{t, a_1 < \mu_1^* < b_1\}$, $w_1(\mu_1^* - a_1) = w_2(b_1 - \mu_1^*) = 0 \Rightarrow w_1 = w_2 = 0$

So the optimal control is

$$\mu_1^* = \frac{1}{B_1} \left[(\lambda_3 - \lambda_9)(1-p)ac\frac{I_H}{N_H}S_F + (\lambda_5 - \lambda_{10})(1-p)ab\frac{I_F}{N_H}S_H \right]$$

2) Case 2

In the set $\{t, \mu_1^* = b_1\}$, $b_1 = \mu_1^* = \frac{1}{B_1} \left\{ (\lambda_3 - \lambda_9)(1-p)ac\frac{I_H}{N_H}S_F + (\lambda_5 - \lambda_{10})(1-p)ab\frac{I_F}{N_H}S_H + w_2 \right\}$

So the optimal control is $\mu_1^* = \frac{1}{B_1} \left\{ (\lambda_3 - \lambda_9)(1-p)ac\frac{I_H}{N_H}S_F + (\lambda_5 - \lambda_{10})(1-p)ab\frac{I_F}{N_H}S_H \right\} \leq b_1$

With $w_2(t) \geq 0$

3) Case 3

In the set $\{t, \mu_1^* = a_1\}$, $w_1(\mu_1^* - a_1) = w_2(b_1 - \mu_1^*) = 0 \Rightarrow w_2 = 0$, from where

$$a_1 = \mu_1^* = \frac{1}{B_1} \left\{ (\lambda_3 - \lambda_9)(1-p)ac\frac{I_H}{N_H}S_F + (\lambda_5 - \lambda_{10})(1-p)ab\frac{I_F}{N_H}S_H - w_1 \right\}$$

and therefore $\mu_1^* = \frac{1}{B_1} \left\{ (\lambda_3 - \lambda_9)(1-p)ac\frac{I_H}{N_H}S_F + (\lambda_5 - \lambda_{10})(1-p)ab\frac{I_F}{N_H}S_H \right\} \geq a_1$

With $w_1(t) \geq 0$

4) Case 4

In the set $\{t, a_2 < \mu_2^* < b_2\}$, $w_3(\mu_2^* - a_2) = w_4(b_2 - \mu_2^*) = 0 \Rightarrow w_3 = w_4 = 0$

So the optimal control is $\mu_2^* = \frac{\gamma_H}{B_2} [\lambda_5 E_H + \lambda_6 I_H]$

5) Case 5

In the set $\{t, \mu_2^* = b_2\}$, $w_3(\mu_2^* - a_2) = w_4(b_2 - \mu_2^*) = 0 \Rightarrow w_3(t) = 0$, hence

$b_2 = \mu_2^* = \frac{\gamma_H}{B_2} [\lambda_5 E_H + \lambda_6 I_H + w_4]$. As $w_4(t) \geq 0$, so the optimal control is

$$\mu_2^* = \frac{\gamma_H}{B_2} [\lambda_5 E_H + \lambda_6 I_H] \leq b_2.$$

6) Case 6

In the set $\{t, \mu_2^* = a_2\}$, $w_3(\mu_2^* - a_2) = w_4(b_2 - \mu_2^*) = 0 \Rightarrow w_4(t) = 0$, hence

$a_2 = \mu_2^* = \frac{\gamma_H}{B_2} [\lambda_5 E_H + \lambda_6 I_H - w_3]$. As $w_3(t) \geq 0$, so the optimal control is

$$\mu_2^* = \frac{\gamma_H}{B_2} [\lambda_5 E_H + \lambda_6 I_H] \geq a_2.$$

With these three cases, we rewrite the expression of the second control:

$$\mu_2^* = \max \left\{ a_2, \min \left\{ b_2, \frac{\gamma_H}{B_2} [\lambda_5 E_H + \lambda_6 I_H] \right\} \right\}$$

7) *Case 7*

In the set $\{t, a_3 < \mu_3^* < b_3\}$, $w_5(\mu_3^* - a_3) = w_6(b_3 - \mu_3^*) = 0 \Rightarrow w_5(t) = w_6(t) = 0$

So the optimal control is $\mu_3^* = \frac{1}{B_3} [\lambda_1 d_C L + \lambda_3 d_F E_F - \lambda_4 d_F I_F + \lambda_9 d_F S_F]$

8) *Case 8*

In the set $\{t, \mu_3^* = b_3\}$, $w_5(\mu_3^* - a_3) = w_6(b_3 - \mu_3^*) = 0 \Rightarrow w_5(t) = 0$, hence

$b_3 = \mu_3^* = \frac{1}{B_3} [\lambda_1 d_C L + \lambda_3 d_F E_F - \lambda_4 d_F I_F + \lambda_9 d_F S_F + w_6]$. As $w_6(t) \geq 0$, so the optimal control is

$$\mu_3^* = \frac{1}{B_3} [\lambda_1 d_C L + \lambda_3 d_F E_F - \lambda_4 d_F I_F + \lambda_9 d_F S_F] \leq b_3.$$

9) *Case 9*

In the set $\{t, \mu_3^* = a_3\}$, $w_5(\mu_3^* - a_3) = w_6(b_3 - \mu_3^*) = 0 \Rightarrow w_6(t) = 0$, hence

$a_3 = \mu_3^* = \frac{1}{B_3} [\lambda_1 d_C L + \lambda_3 d_F E_F - \lambda_4 d_F I_F + \lambda_9 d_F S_F - w_5]$. As $w_5(t) \geq 0$, so the optimal control is

$$\mu_3^* = \frac{1}{B_3} [\lambda_1 d_C L + \lambda_3 d_F E_F - \lambda_4 d_F I_F + \lambda_9 d_F S_F] \geq a_3.$$

With these nine cases, we rewrite the expression of the third control:

$$\mu_3^* = \max \left\{ a_3, \min \left\{ b_3, \frac{1}{B_3} [\lambda_1 d_C L + \lambda_3 d_F E_F - \lambda_4 d_F I_F + \lambda_9 d_F S_F] \right\} \right\}$$

10) *Case 10*

In the set $\{t, a_4 < \mu_4^* < b_4\}$, $w_7(\mu_4^* - a_4) = w_8(b_4 - \mu_4^*) = 0 \Rightarrow w_7(t) = w_8(t) = 0$

So the optimal control is $\mu_4^* = \frac{1}{B_4} \left[(\lambda_3 - \lambda_9) p a v \frac{I_C}{N_C} S_F + (\lambda_7 - \lambda_{11}) p a u \frac{I_F}{N_C} S_C \right]$

11) *Case 11*

In the set $\{t, \mu_4^* = b_4\}$, $w_7(\mu_4^* - a_4) = w_8(b_4 - \mu_4^*) = 0 \Rightarrow w_7(t) = 0$, hence

$b_4 = \mu_4^* = \frac{1}{B_4} \left[(\lambda_3 - \lambda_9) p a v \frac{I_C}{N_C} S_F + (\lambda_7 - \lambda_{11}) p a u \frac{I_F}{N_C} S_C + w_8 \right]$. As $w_8 \geq 0$,

So the optimal control is $\mu_4^* = \frac{1}{B_4} \left[(\lambda_3 - \lambda_9) p a v \frac{I_C}{N_C} S_F + (\lambda_7 - \lambda_{11}) p a u \frac{I_F}{N_C} S_C \right] \leq b_4$

12) *Case 12*

In the set $\{t, \mu_4^* = a_4\}$, $w_7(\mu_4^* - a_4) = w_8(b_4 - \mu_4^*) = 0 \Rightarrow w_8(t) = 0$, hence

$a_4 = \mu_4^* = \frac{1}{B_4} \left[(\lambda_3 - \lambda_9) p a v \frac{I_C}{N_C} S_F + (\lambda_7 - \lambda_{11}) p a u \frac{I_F}{N_C} S_C - w_7 \right]$. As $w_7 \geq 0$,

So the optimal control is $\mu_4^* = \frac{1}{B_4} \left[(\lambda_3 - \lambda_9) p a v \frac{I_C}{N_C} S_F + (\lambda_7 - \lambda_{11}) p a u \frac{I_F}{N_C} S_C \right] \geq a_4$

With these three cases, we rewrite the expression of the third control:

$$\mu_4^* = \max \left\{ a_4, \min \left\{ b_4, \frac{1}{B_4} \left[(\lambda_3 - \lambda_9) p a v \frac{I_C}{N_C} S_F + (\lambda_7 - \lambda_{11}) p a u \frac{I_F}{N_C} S_C \right] \right\} \right\}$$

13) *Case 13*

In the set $\{t, a_5 < \mu_5^* < b_5\}$, $w_9(\mu_5^* - a_5) = w_{10}(b_5 - \mu_5^*) = 0 \Rightarrow w_9(t) = w_{10}(t) = 0$

So the optimal control is $\mu_5^* = \frac{\gamma_C}{B_5} [\lambda_8 I_C + \lambda_7 E_C]$

14) *Case 14*

In the set $\{t, \mu_5^* = b_5\}$, $w_9(\mu_5^* - a_5) = w_{10}(b_5 - \mu_5^*) = 0 \Rightarrow w_9(t) = 0$, hence

$b_5 = \mu_5^* = \frac{\gamma_C}{B_5} [\lambda_8 I_C + \lambda_7 E_C + w_{10}]$. As $w_{10}(t) \geq 0$, so the optimal control is

$$\mu_5^* = \frac{\gamma_C}{B_5} [\lambda_8 I_C + \lambda_7 E_C] \leq b_5$$

15) Case 15

In the set $\{t, \mu_5^* = a_5\}$, $w_9(\mu_5^* - a_5) = w_{10}(b_5 - \mu_5^*) = 0 \Rightarrow w_{10}(t) = 0$, hence $a_5 = \mu_5^* = \frac{\gamma_C}{B_5} [\lambda_8 I_C + \lambda_7 E_C - w_9]$. As $w_9(t) \geq 0$, so the optimal control is

$$\mu_5^* = \frac{\gamma_C}{B_5} [\lambda_8 I_C + \lambda_7 E_C] \geq a_5.$$

With these three cases, we rewrite the expression of the third control:

$$\mu_5^* = \max \left\{ a_5, \min \left\{ b_5, \frac{\gamma_C}{B_5} [\lambda_8 I_C + \lambda_7 E_C] \right\} \right\}$$

In summary, we obtain the control $(\mu_1^*, \mu_2^*, \mu_3^*, \mu_4^*, \mu_5^*)$ that optimizes the functional J under the constraints given by the system of differential equations (25-37), its expression is given by the optimal quintuplet defined by:

$$\begin{aligned} \mu_1^* &= \max \left\{ a_1, \min \left\{ b_1, \frac{1}{B_1} \left[(\lambda_3 - \lambda_9)(1-p)ac \frac{I_H}{N_H} S_F + (\lambda_5 - \lambda_{10})(1-p)ab \frac{I_F}{N_H} S_H \right] \right\} \right\} \\ \mu_2^* &= \max \left\{ a_2, \min \left\{ b_2, \frac{\gamma_H}{B_2} [\lambda_5 E_H + \lambda_6 I_H] \right\} \right\} \\ \mu_3^* &= \max \left\{ a_3, \min \left\{ b_3, \frac{1}{B_3} [\lambda_1 d_C L + \lambda_3 d_F E_F - \lambda_4 d_F I_F + \lambda_9 d_F S_F] \right\} \right\} \\ \mu_4^* &= \max \left\{ a_4, \min \left\{ b_4, \frac{1}{B_4} \left[(\lambda_3 - \lambda_9)pa v \frac{I_C}{N_C} S_F + (\lambda_7 - \lambda_{11})pa u \frac{I_F}{N_C} S_C \right] \right\} \right\} \\ \mu_5^* &= \max \left\{ a_5, \min \left\{ b_5, \frac{\gamma_C}{B_5} [\lambda_8 I_C + \lambda_7 E_C] \right\} \right\} \end{aligned}$$

This completes the proof of the Theorem.

4. Numerical Results

Table 1. Description of model parameters, indicating baselines, ranges and references.

Parameter	Description	Baseline value	Value range with time unit = 1 day
σ_L	Rate of maturation from pupal to adult fly	1/30	1/60 to 1/22 [30]
b_H	Human population birth rate = death rate	1/(50 x 360)	10 to 40 births per 1000 per year [40]
b_C	Cattle population birth rate = death rate	1/(15 x 360)	guess
d_F	Fly death rate	1/33	1/30 to 1/62 [4]
W	Proportion of female flies	6/10	guess, female flies are more abundant than males
d_L	Pupa death rate	1/100	guess; in natural conditions very few pupae die
K_L	Pupa carrying capacity	300000	guess
b_L	Larva birth rate	0.6/9	An adult female is expected to produce one larva every 9 days. [10, 39]
q_F	Incubation rate of the flies	1/25	1/30 to 1/25 [5]
q_H, q_C	Incubation rate of humans, cattle	1/12	
a	Fly biting rate	1/4	1/10 to 1/3: a fly is expected to have 1 bite every 3-10 days [36]
p	Proportion of tsetse fly bites on cattle	0.7	Table 2 [35]
b, u	Probability that an infectious fly infects a human, cattle	0.62	Table 2 [35]
c, v	Probability that a fly becomes infected after biting an infectious human, cattle	0.01	Table 2 [35]
γ_H, γ_C	Human, cattle rate of progression from stage 1 to stage 2	1/30; 1/25	Table 2 [35]
κ_H, κ_C	Human, cattle rate of progression from stage 2 to recovery and loss of temporary immunity for untreated humans, cattle	1/90; 1/75	Table 2 [35]

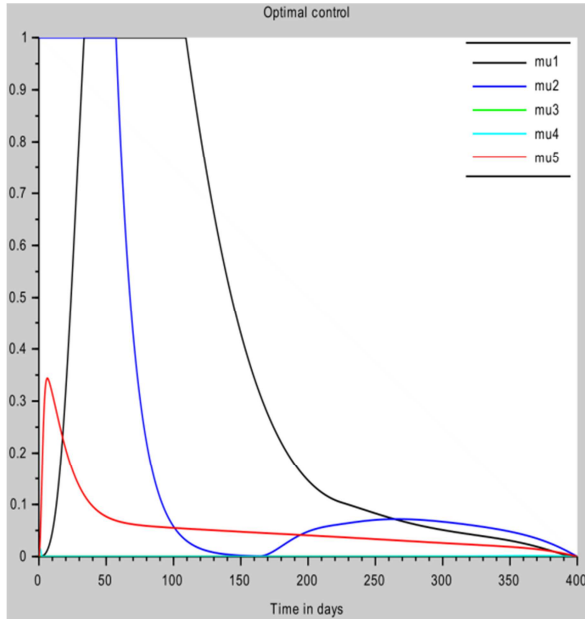


Figure 2. Control with $p = 1.0$ and $a = 0.25$.

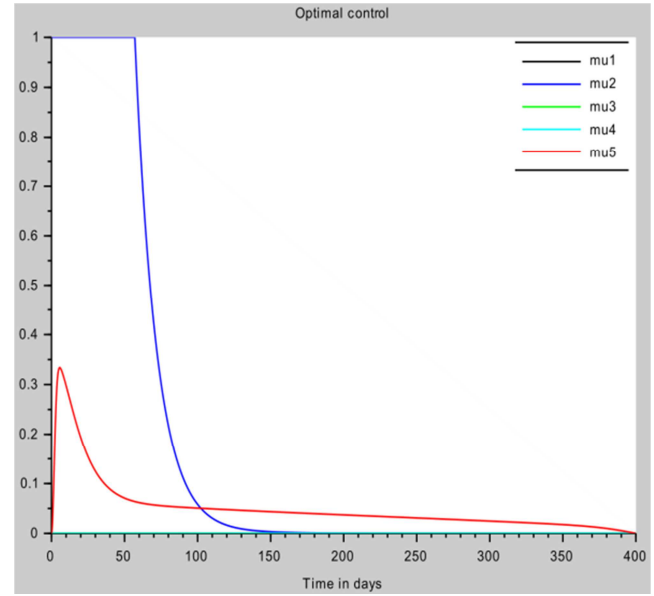


Figure 4. Control with $p = 0.7$ and $a = 0.25$.

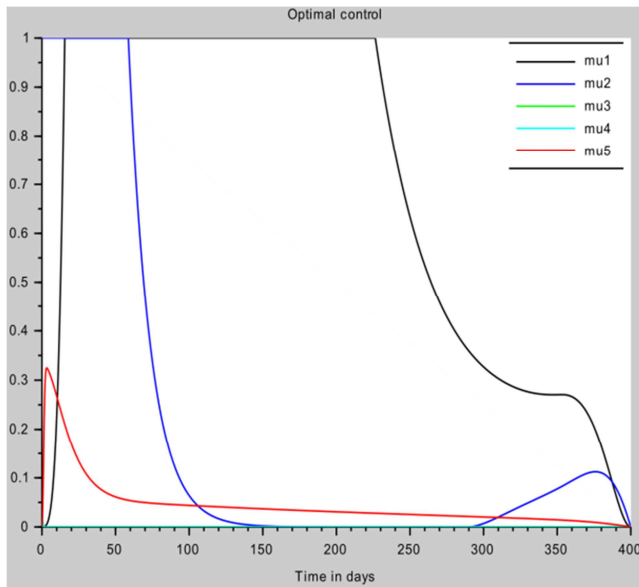


Figure 3. Control with $p = 0.7$ and $a = 1.00$.

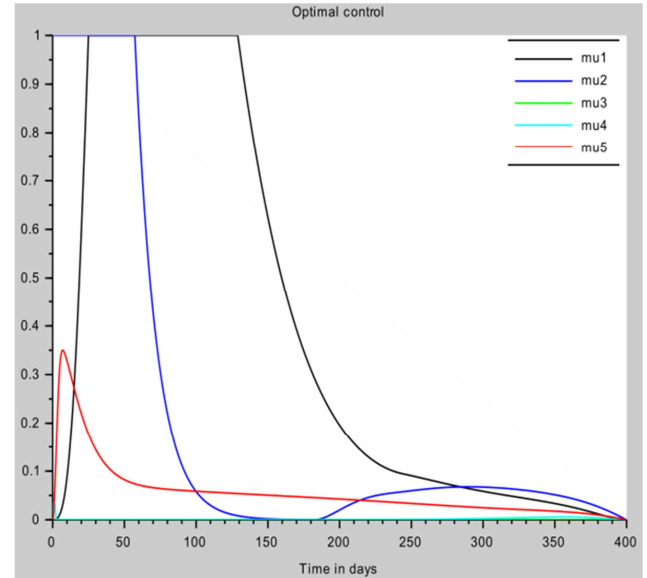


Figure 5. Control with $p = 0.7$ and $a = 1.00$.

Figures 2, 3, 4 and 5 are plots with different values of a and p . The value $a = 0.25$ means that flies take one blood meal in four days and the value $a = 1$ means flies take one blood meal very day. In the other hand, the value $p = 0.7$ shows the preference of blood meal taken by flies on cattle as given below. We assume the carrying capacity of the tsetse pupae $K_L = 300000$, the human population $N_H = 300$, and the cattle population $N_C = 50$. Baseline parameter values given in Table 1 were collected from the literature on HAT in West Africa as cited, and values that were not found in the literature were estimated. Values from Table 1 gives $r = 1.0154$, the number of larvae $L^* = 4545$, and the number of adult flies $A^* = 5000$. Note that since by our assumptions compartments R_H and R_C contain hosts in stage 2 (or in

treatment) and recovered hosts, $\frac{1}{\gamma_H} + \frac{1}{\kappa_H} = 30 + 90$ days and $\frac{1}{\gamma_C} + \frac{1}{\kappa_C} = 25 + 75$ days have the same values as given by Rogers [35] for the sums of the duration of infection and immunity in species 1 and 2, although the definitions of our parameters are different. Stage 1 of *T. b. gambiense* HAT in humans in Africa may last for several months [2] (i.e. γ_H may be much smaller than the above value). Thus our baseline values apply more to our model with treatment giving control reproduction numbers.

5. Concluding

We have built a model that includes the most important mechanisms of transmission of sleeping sickness between a

host population and a vector population. First fly growth dynamics is modeled. We use it because unlike most flies, once fertilized the tsetse fly generally keeps its eggs and each birth, one larva is hatched. In addition, the tsetse flies of both sexes are blood-sucking insects. A SEI model was used to express the different states of infection of the tsetse fly. For the host population, we modeled the dynamics of a SEIRS model. A coupled model was obtained and analyzed. A mathematical analysis of the model was made. The equilibrium points of the model were calculated and presented. The study of the system's stability of these equilibrium points was presented. A numerical simulation of the system illustrates the theoretical results obtained and discussed throughout this study.

We built optimal control problem to assess the efficiency of three control measures to reduce the number of infections in the human population. The study of the proposed model allows us to know when the controls efforts should be applied, and the importance to be given to each of these vector control efforts, the treatment to administer to patients infected by the sleeping disease and the various means of prevention to avoid or reduce the host-vector contact. These efforts can obviously be applied to a finite time interval $[0, T]$. The model does not allow us to make long-term predictions of the disease dynamics. We have shown the existence of optimal controls for the cost minimization problem (quadratic) to reduce the densities of infected individuals in the population, namely the individuals who constitute the germ reservoir and the essential agents in the spread of infection.

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