A Mathematical model for Thelaziasis

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Abstract

In the present manuscript we present a mathematical model for thelaziasis in cattle. By appliyng different type of controls, we find optimal strategies to reduce the endemic levels.

Keywords: Thelaziasis, Mathematical Model, Parameter Estimation, Basic Reproductive number

1. Introduction

Thelaziasis is a vector neglected disease that affects mainly mammals, including humans and in a minor scales, birds. In humans, even it has been found in rare cases through the world, it has a higher presence in several areas of Asia, where it occurs in rural areas with high levels of poverty, and where the main hosts are children and the elderly [1, 2, 3]. The presence of these worms in its final hosts might result in excesive lacrimation, conjuntivitis, keratitis, epiphora and corneal ulcers [4], but in humans also can be cause of ocular morbidity [3].

Transmission takes place due to the presence of a vector, which are usually flies and they act as intermediate hosts [5]. Flies have a life expectancy of about 28 days, but it might live up to two months ([6]). The first larval stage (L1) of the worm is ingested by the fly when it feeds from lachrymal secretions, where in the internal organs, the worm develops into its second (L2) and third (L3) larval stages within 21 days post infection [7]. Other studies [8], show that flies infected with *Thelazia lacrymalis* can reach the infective stage in 12-15 days, while this takes 28-32 days for flies infected with *T. gulosa* [8]. Once in the infective stage, the fly releases L3 larvae into the definite host. Finally, once in the definite host, the L3 larvae matures within 3 to 6 weeks, where the new worm deposits new eggs into the definite host becoming infective [8]. Foxes lifespan is 2 years [9].

The transmission depends upon the presence of vectors and therefore thelaziasis has a seasonal occurrence [4]. In this work we focus on the control of the disease which occurs in one year season only.
A proper understanding in the control of thelaziasis in animals can be of great interest so to prevent possible future outbreaks in animals or humans. Control strategies for thelaziasis include treatment of infected individuals. Dog thelaziasis has been treated with a topical formulation of 10% imidacloprid and 2.5% moxidectin [10],

In [11], the authors comment control strategies to treat human thelaziosis. In [12] it was found the presence of *Thelazia gulosa* and *Thelazia lacrymalis* in cattle where the main responsible vector is the face fly (*Musca autumnalis*) in which of larvae of *Thelaszia spp* were found. Data from slaugtered cattle was collected from April to October 1978. In [13] the authors present a survey for different diseases in equids in Kentucky USA. In their study, they found the presence *Thelazia Lacrymalis* in which it is pressumed that the face fly (*Musca autumnalis*) is the vector responsible for transmission. Otranto et. al. [7] made a survey in different regions in Italy to observe the current status on dogs, cats and foxes. In their work they present the proportion of infected animals (by *Thelazia Callipaeda*) in each of the regions they studied. In [14] data about the proportions of mule deer from Wyoming and Utah by *T. californiensis* was reported. Asrat [4] sudy the prevalence of Thelaziasis in Ethiopia whereas Beitel [15] studied the prevalence of eyeworms in the columbian black tailed deer in Oregon, USA by *Thelazia californiensis*. Khedri et. al. [16] present a one year data about infected bovine in Southeast Iran (puede ser útil).
In [17], the authors present a study about the prevalence and intensity of *Thelazia spp* in a flies population in Alberta, Canada.

In [15] studied the prevalence of eyeworms in the Columbian Black-Tailed Deer in Oregon.

A special work was done in [12] were it was estimated the proportion of infected animals as well as the proportion of infected vectors.

1.1. Some questions to explore.

An important issue in this disease is that the propagation coincides with the presence of flies that carry the disease. If the life expectancy of the fly is reduced, then the complete cycle of the thelazia within the vector does not complete and therefore, the disease no longer can be transmitted. Therefore, it might be expected that as soon as the temperature of a place of study is

reduced, then the levels of the infected individuals with thelazia, must reach a final steady level.
In the mathematical side, analyse the model about stability, persistance, what would happen if stochasticity gets implemented? how?

1.2. Model parameters

We will use the model to fit two data sets. One referring to a multi-host case given by dogs and foxes and the second in a one host study, particularly the case of cattle.

1.2.1. Cattle only.

The problem can be seen as a simple host or multi-host when considering beef and milk cattle. Some considerations about the life expectancy of the individuals. A common technique to detect thelazia in farming animals is done by sacrificing the animal. In this case, the infected individual is no longer part of the infection cycle and basically out of the dynamics. In this work we consider that the sample used to observe the proportion of infected individuals is of little to neglected significance respect to the total population. The life expectancy of beef cattle is approximately 16 to 24 months (and can be up to 30 months [18]), whereas for diary cattle is 5 to 6 years. The natural cattle life expectancy is 18 to 22 years.

2. Mathematical Model

Our model is based on the interaction of flies and cattle. For the model, we consider that infected cattle shows visual presence of worms. A sample of the herd is taken per time unit and the animals are revised if there is presence of worms. Then vaccination proceeds. Following the formulation in Esteva

[19] we obtain the following SI vector host model for cattle and flies.

$$\begin{aligned}
\dot{S}_f &= \Lambda_f - \frac{\beta_f}{N_c^\infty} I_c S_f - \mu_f S_f \\
\dot{L}_f &= \frac{\beta_f}{N_c^\infty} I_c S_f - \left(k_f + \mu_f\right) L_f \\
\dot{I}_f &= k_f L_f - \mu_f I_f \\
\dot{S}_c &= \Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \mu_c S_c \\
\dot{L}_c &= \frac{\beta_c}{N_c^\infty} I_f S_c - \left(\mu_c + k_c\right) L_c \\
\dot{I}_c &= k_c L_c - \mu_c + \delta I_c
\end{aligned} \tag{1}$$

$$\begin{aligned}
\dot{S}_f &= \Lambda_f - \frac{\beta_f}{N_c^\infty} I_c S_f - (\mu_f + w(t)) S_f \\
\dot{L}_f &= \frac{\beta_f}{N_c^\infty} I_c S_f - \left(k_f + w(t) + \mu_f\right) L_f \\
\dot{I}_f &= k_f L_f - (w(t) + \mu_f) I_f \\
\dot{S}_c &= \Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \left(\mu_c + v(t)\right) S_c + \rho T_c \\
\dot{L}_c &= \frac{\beta_c}{N_c^\infty} I_f S_c - \left(\mu_c + v(t) + k_c\right) L_c \\
\dot{I}_c &= k_c L_c - (\mu_c + v(t) + \delta u(t)) I_c \\
\dot{T}_c &= \delta u(t) I_c - \left(\rho + \mu_c\right) T_c
\end{aligned} \tag{2}$$

A second version of the model takes into account two different disease stages for the definite host (cows). Such stages refer to the severity of the worms parasitism. The main idea is to have different control measures depending on the severity of the disease. Therefore, we define two different infected classes for infected cows, I_{cl} and I_{ch} which refer infected cows with light and heavy worm burden, respectively. Once a vector has transmitted some larvae into some susceptible individuals they become infected and depending on the amount of deposited larvae, a fraction θ of the susceptible hosts move to the I_{cl} class and the complement $1-\theta$, move to the I_{ch} class. An individual in the I_{cl} class might move to the I_{ch} class as it keep continuously in contact with vectors which remain depositing larvae into the eyes in such way that eventually the light worm burden becomes high and then a change to the class I_{ch}. Our model in this case becomes

$$\begin{aligned}
\dot{S}_f &= \Lambda_f - \frac{S_f}{N_c^{\infty}}\left(\beta_f I_{cl} + \tilde{\beta}_f I_{ch}\right) - \mu_f S_f \\
\dot{L}_f &= \frac{S_f}{N_c^{\infty}}\left(\beta_f I_{cl} + \tilde{\beta}_f I_{ch}\right) - \left(k_f + \mu_f\right) L_f \\
\dot{I}_f &= k_f L_f - \mu_f I_f \\
\dot{S}_c &= \Lambda_c - \frac{\beta_c}{N_c^{\infty}} I_f S_c - \mu_c S_c \\
\dot{L}_c &= \frac{\beta_c}{N_c^{\infty}} I_f S_c - \left(\mu_c + k_c\right) L_c \\
\dot{I}_{cl} &= \theta k_c L_c - \frac{\tilde{\beta}_c}{N_c^{\infty}} I_{cl} I_f - \mu_c I_{cl} \\
\dot{I}_{ch} &= (1-\theta) k_c L_c + \frac{\tilde{\beta}_c}{N_c^{\infty}} I_{cl} I_f - \mu_c I_{ch}
\end{aligned} \tag{3}$$

In order to control the presence of eyeworms we focus our strategy based on [**?**], in which there are considered three levels of worm burden. For those scenarios, the two less severe are treated with medication, whereas the most severe consist on direct removal. In our model, we focus on two generic strategies. The use of medicationine, which is applied for light to medium levels as one single class (I_{cl}) and removal for the heavy worm burden (I_{ch}).

Under these hyphothesis our model with applied control becomes,

$$\begin{aligned}
\dot{S}_f &= \Lambda_f - \frac{S_f}{N_c^{\infty}}\left(\beta_f I_{cl} + \tilde{\beta}_f I_{ch}\right) - \left(\mu_f + w_f(t)\right) S_f \\
\dot{L}_f &= \frac{S_f}{N_c^{\infty}}\left(\beta_f I_{cl} + \tilde{\beta}_f I_{ch}\right) - \left(k_f + \mu_f + w_f(t)\right) L_f \\
\dot{I}_f &= k_f L_f - \left(w_f(t) + \mu_f\right) I_f \\
\dot{S}_c &= \Lambda_c - \frac{\beta_c}{N_c^{\infty}} I_f S_c - \mu_c S_c + v_h(t) I_{ch} + \rho T_c \\
\dot{L}_c &= \frac{\beta_c}{N_c^{\infty}} I_f S_c - \left(\mu_c + k_c\right) L_c \\
\dot{I}_{cl} &= \theta k_c L_c - \frac{\tilde{\beta}_c}{N_c^{\infty}} I_{cl} I_f - (\mu_c + v_l(t)) I_{cl} \\
\dot{I}_{ch} &= (1-\theta) k_c L_c + \frac{\tilde{\beta}_c}{N_c^{\infty}} I_{cl} I_f - (\mu_c + v_h(t)) I_{ch} \\
\dot{T}_c &= v_l(t) I_{cl} - \left(\mu_c + \rho\right) T_c
\end{aligned} \tag{4}$$

where $w_f(t)$ represents fly fumigation, $v_l(t)$ is cow treatment by medication and $v_h(t)$ consists on worm removal.

For the uncontrolled model (System 1), the basic reproductive number is given by

$$R_0 = \left(\frac{\beta_c \beta_f k_c k_f N_f^{\infty}}{\mu_f(\mu_c + k_c)(\mu_c + \delta_c)(\mu_f + k_f) N_c^{\infty}}\right)^{1/4} \tag{5}$$

where $N_f^{\infty} = \dfrac{\Lambda_f}{\mu_f}$ and $N_c^{\infty} = \dfrac{\Lambda_c}{\mu_c}$. Table 1 shows the meaning and values of the parameters considered in this study.

3. Local and global stability analysis

In system 1, we observe that the equations for the total cow and fly populations are given by:

$$\begin{aligned}
\dot{N}_f &= \Lambda_f - \mu_f N_f \\
\dot{N}_c &= \Lambda_c - \mu_c N_c,
\end{aligned}$$

Parameter	Meaning	Interval	Reference
N_c	Total number of individuals at time t	1000	This study
Λ_f	Fly recruitment rate		This study
Λ_c	Cattle recruitment rate		This study
β_c	Number of successful contacts of a fly that infects a cattle host		This study
β_f	Number of successful contacts in which a fly gets infected by a cattle host		This study
k_v^{-1}	average latency time for vectors	14-21 days	[20]
		12-15 days (*T. Lacrymalis*)	[8]
		28-32 days (*T. Gulosa*)	[8]
k_i^{-1}	average latency time for hosts $i = 1, 2$	$\approx$ 35 days	[20]
		21-42 days	[8]
μ_v^{-1}	vector average lifespan	30-60 months	[6]
μ_c^{-1}	cows average lifespan	1080 days	[21]

Table 1: Parameter meaning and values.

so it implies that, for a sufficiently large time, the fly and cow populations will tend to $N_f^{\infty} = \dfrac{\Lambda_f}{\mu_f}$ and $N_c^{\infty} = \dfrac{\Lambda_c}{\mu_c}$, respectively. In consequence, we can

114 reduce system 1,obtaining:

$$
\begin{aligned}
\dot{L}_f &= \frac{\beta_f}{N_c^\infty} I_c \left(N_f^\infty - L_f - I_f\right) - (k_f + \mu_f) L_f \\
\dot{I}_f &= k_f L_f - \mu_f I_f \\
\dot{S}_c &= \Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \mu_c S_c + \rho \left(N_c^\infty - S_c - L_c - I_c\right) \\
\dot{L}_c &= \frac{\beta_c}{N_c^\infty} I_f S_c - (\mu_c + k_c) L_c \\
\dot{I}_c &= k_c L_c - (\mu_c + \delta) I_c
\end{aligned}
\tag{6}
$$

System 6 has two equilibrium points in $\Omega = \{(L_f, I_f, S_c, L_c, I_c) \in \mathbb{R}^5 : 0 \leq L_f + I_f \leq N_f^\infty, 0 \leq S_c + L_c + I_c \leq N_c^\infty\}$. The disease free equilibrium

$$S_1 = \left(L_{f1}^*, I_{f1}^*, S_{c1}^*, L_{c1}^*, I_{c1}^*\right) = \left(0, 0, \frac{\Lambda_c}{\mu_c}, 0, 0\right)$$

and the endemic equilibrium

$$S_2 = (L_{f2}^*, I_{f2}^*, S_{c2}^*, L_{c2}^*, I_{c2}^*) = .$$

Theorem. The disease free equilibrium point S_1 is globally asymptotically stable in Ω, if $R_0 < 1$.
Proof: Consider the Lyapunov function

$$V(L_f, I_f, S_c, L_c, I_c) = a_1 \left(S_c - N_c^\infty - N_c^\infty \ln \frac{S_c}{N_c^\infty}\right) + a_2 L_f + I_f + a_3 L_c + a_4 I_c \ ,$$

with

$$a_1 = a_2 = \frac{k_c}{\mu_c + k_c}, \ a_3 = \left(\frac{k_f}{\mu_f + k_f}\right)\left(\frac{k_c}{\mu_c + k_c}\right)\frac{\beta_c}{\mu_f}, \ a_4 = \left(\frac{k_c}{\mu_c + k_c}\right)\frac{\beta_c}{\mu_f} \ .$$

115 The derivative of V is as follows:

$$
\begin{aligned}
\dot{V} = {} & a_1 \left(1 - \frac{N_c^\infty}{S_c}\right)\left[\Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \mu_c S_c + \rho \left(N_c^\infty - S_c - L_c - I_c\right)\right] \\
& + a_2 \left[\frac{\beta_c}{N_c^\infty} I_f S_c - (\mu_c + k_c) L_c\right] + \left[k_c L_c - (\mu_c + \delta) I_c\right] \\
& + a_3 \left[\frac{\beta_f}{N_c^\infty} I_c \left(N_f^\infty - L_f - I_f\right) - (k_f + \mu_f) L_f\right] + a_4 \left[k_f L_f - \mu_f I_f\right]
\end{aligned}
\tag{7}
$$

Substituting the values of a_1, a_2, a_3 and a_4, we simplify equation 7,

$$\begin{aligned}\dot{V} = &-a_1 \frac{(S_c - N_c^\infty)^2}{S_c} - a_1 \rho \left(N_c^\infty - S_c - I_c - L_c\right)\left(\frac{N_c^\infty - S_c}{S_c}\right) \\ &- a_3 \beta_f \frac{I_c}{N_c^\infty}\left(L_f + I_f\right) - (\mu_c + k_c)\left[1 - \frac{\beta_c \beta_f k_c k_f N_f^\infty}{\mu_f(\mu_c + k_c)(\mu_c + \delta_c)(\mu_f + k_f) N_c^\infty}\right] I_c\end{aligned}$$

Replacing the expression for $\mathcal{R}_0$ given in (5), we conclude that $\dot{V} < 0$ for $\mathcal{R}_0 < 1$. Finally, as S_1 is the only invariant set in Ω such that $\dot{V} = 0$, from the La Salle-Lyapunov theorem, it follows that if $\mathcal{R}_0 < 1$, then S_1 is globally asymptotically stable in Ω.

Theorem. A unique endemic equilibrium exists when $R_0 > 1$.

Proof: Solving the equations for the state variables, we end up with the following relationships

$S_f = \frac{\Lambda_f}{\left(\frac{\beta_f}{N_c^\infty} I_c + \mu_f\right)}$; $L_f = \left(\frac{\beta_f}{N_c^\infty(\lambda_f + \mu_f)}\right)\left(\frac{\Lambda_f}{\left(\frac{\beta_f}{N_c^\infty} I_c + \mu_f\right)}\right) I_c$;

$I_f = \left(\frac{\lambda_f}{\mu_f}\right)\left(\frac{\beta_f}{N_c^\infty(\lambda_f + \mu_f)}\right)\left(\frac{\Lambda_f}{\left(\frac{\beta_f}{N_c^\infty} I_c + \mu_f\right)}\right) I_c$; $S_c = \frac{(\mu_c+\lambda_c)(\mu_c+\delta)(\lambda_f+\mu_f)\mu_f (N_c^\infty)^2 \left(\frac{\beta_f}{N_c^\infty} I_c + \mu_f\right)}{\lambda_c \beta_c \lambda_f \beta_f \Lambda_f}$;

$T_c = \frac{\delta T_c}{\rho + \mu_c}$; $L_c = \frac{(\mu_c + \delta) I_c}{\lambda_c}$ and $I_c = \frac{A}{B}\left(R_0^4 - 1\right)$, with

$A = \frac{\mu_c \mu_f^2 (\mu_c+\lambda_c)(\mu_c+\delta)(\lambda_f+\mu_f)(N_c^\infty)^2}{\lambda_c \beta_c \lambda_f \beta_f \Lambda_f}$ and $B = \frac{(\mu_c+\lambda_c)(\mu_c+\delta)}{\lambda_c}\left[1 + \frac{\mu_c(\lambda_f+\mu_f)\mu_c N_c^\infty}{\beta_c}\right] - \frac{\rho\delta}{\rho+\mu_c}$.

Clearly, $\frac{(\mu_c+\lambda_c)(\mu_c+\delta)}{\lambda_c} > \delta$, $1 + \frac{\mu_c(\lambda_f+\mu_f)\mu_c N_c^\infty}{\beta_c} > 1$ and $\frac{\rho\delta}{\rho+\mu_c} < \delta$. Therefore, $I_c > 0$ if and only if $R_0 > 1$.

Observe that the endemic equilibrium is preserved when no control is applied into the model ($\rho = \delta = 0$). For this particular case it is possible to show global stability for the endemic equilibrium

Theorem 1. *The endemic equilibrium for the model with no control (*$\rho = \delta = 0$*) is asymptotically globally stable.*

Proof. Following the ideas in [22], we consider the Lyapunov function

$$V = \sum_{i=1}^{6} a_i \left(X_i - \overline{X}_i \ln \frac{X_i}{\overline{X}_i}\right),$$

where X_i are the components of the vector $(S_f, L_f, I_f, S_c, L_c, I_c)$ and $\overline{X} = (\overline{S}_f, \overline{L}_f, \overline{I}_f, \overline{S}_c, \overline{L}_c, \overline{I}_c)$ are the coordinates of the endemic equilibrium.

At the endemic equilibrium point, the following equalities hold

$$\Lambda_f = \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty} + \mu_f \overline{S}_f \qquad \Lambda_c = \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty} + \mu_c \overline{S}_c \qquad \mu_f + k_f = \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty \overline{L}_f}$$

$$\mu_c + k_c = \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty \overline{L}_c} \qquad \mu_f = k_f \frac{\overline{L}_f}{\overline{I}_f} \qquad \mu_c = k_c \frac{\overline{L}_c}{\overline{I}_c} \tag{8}$$

From this information, we obtain

$$\dot{V}(t) = a_1 \left(\Lambda_f - \frac{\beta_f}{N_c^\infty} I_c S_f - \mu_f S_f \right) \left(1 - \frac{\overline{S}_f}{S_f} \right) + a_2 \left(\frac{\beta_f}{N_c^\infty} I_c S_f - (k_f + \mu_f) L_f \right) \left(1 - \frac{\overline{L}_f}{L_f} \right)$$

$$+ a_3 (k_f L_f - \mu_f I_f) \left(1 - \frac{\overline{I}_f}{I_f} \right) + a_4 \left(\Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \mu_c S_c \right) \left(1 - \frac{\overline{S}_c}{S_c} \right)$$

$$+ a_5 \left(\frac{\beta_c}{N_c^\infty} I_f S_c - (\mu_c + k_c) L_c \right) \left(1 - \frac{\overline{L}_c}{L_c} \right) + a_6 (k_c L_c - \mu_c I_c) \left(1 - \frac{\overline{I}_c}{I_c} \right).$$

Then, by taking the scaled variables

$$s_f^* = \frac{S_f}{\overline{S}_f}; \quad l_f^* = \frac{L_f}{\overline{L}_f}; \quad i_f^* = \frac{I_f}{\overline{I}_f}; \quad s_c^* = \frac{S_c}{\overline{S}_c}; \quad l_c^* = \frac{L_c}{\overline{L}_c}; \quad i_c^* = \frac{I_c}{\overline{I}_c}$$

and the use of the equalities in 8, our last expression becomes

$$\dot{V}(t) = -a_1 \frac{\mu_f \overline{S}_f}{s_f^*} \left(s_f^* - 1 \right)^2 - a_4 \frac{\mu_c \overline{S}_c}{s_c^*} \left(s_c^* - 1 \right)^2 + a_1 \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty} (1 - s_f^* i_c^*) - a_1 \frac{\beta_f \overline{S}_f \overline{I}_c}{s_f^* N_c^\infty} (1 - s_f^* i_c^*)$$

$$+ a_2 \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty} \left(s_f^* i_c^* - l_f^* \right) \left(1 - \frac{1}{l_f^*} \right) + a_3 k_f \overline{L}_f \left(1 - \frac{1}{i_f^*} \right) \left(l_f^* - i_f^* \right)$$

$$+ a_4 \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty} \left(1 - \frac{1}{s_c^*} \right) \left(1 - i_f^* s_c^* \right) + a_5 \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty} \left(1 - \frac{1}{l_c^*} \right) \left(i_f^* s_c^* - l_c^* \right)$$

$$+ a_6 k_c \overline{L}_c \left(1 - \frac{1}{i_c^*} \right) \left(l_c^* - i_c^* \right).$$

After rearranging terms we end up with

$$\dot{V}(t) = -a_1 \frac{\mu_f \overline{S}_f}{s_f^*}\left(s_f^* - 1\right)^2 - a_4 \frac{\mu_c \overline{S}_c}{s_c^*}\left(s_c^* - 1\right)^2 + \left(a_3 k_f \overline{L}_f - a_2 \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty}\right) l_f^*$$

$$+ \left(a_4 \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty} - a_3 k_f \overline{L}_f\right) i_f^* + \left(a_6 k_c \overline{L}_c - a_5 \frac{\beta_c \overline{I}_f \overline{S}_c}{N_c^\infty}\right) l_c^* + \left(a_1 \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty} - a_6 k_c \overline{L}_c\right) i_c^*$$

$$+ (a_2 - a_1) \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty} s_f^* i_c^* + (a_5 - a_4) \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty} i_f^* s_c^* + a_1 \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty} + a_2 \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty}$$

$$+ a_3 k_f \overline{L}_f + a_4 \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty} + a_5 \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty} + a_6 k_c \overline{L}_c - a_1 \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty}\left(\frac{1}{s_f^*}\right) - a_2 \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty}\left(\frac{s_f^* i_c^*}{l_f^*}\right)$$

$$- a_3 k_f \overline{L}_f \left(\frac{l_f^*}{i_f^*}\right) - a_4 \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty}\left(\frac{1}{s_c^*}\right) - a_5 \frac{\beta_c \overline{S}_c \overline{I}_f}{N_c^\infty}\left(\frac{s_c^* i_f^*}{l_c^*}\right) - a_6 k_c \overline{L}_c \left(\frac{l_c^*}{i_c^*}\right)$$

By taking the constant values as

$$a_2 = a_1; \quad a_3 = \frac{\beta_f \overline{I}_c \overline{S}_f}{k_f \overline{L}_f N_c^\infty} a_1; \quad a_4 = \frac{\beta_f \overline{I}_c \overline{S}_f}{\beta_c \overline{I}_f \overline{S}_c} a_1; \quad a_5 = a_4; \quad a_6 = \frac{\beta_f \overline{I}_c \overline{S}_f}{k_c \overline{L}_c N_c^\infty} a_1$$

, we obtain

$$\dot{V} = -a_1 \frac{\mu_f \overline{S}_f}{s_f^*}\left(s_f^* - 1\right)^2 - a_4 \frac{\mu_c \overline{S}_c}{s_c^*}\left(s_c^* - 1\right)^2 + a_1 \frac{\beta_f \overline{S}_f \overline{I}_c}{N_c^\infty}\left[6 - \left(\frac{1}{s_f^*} + \frac{s_f^* i_c^*}{l_f^*} + \frac{l_f^*}{i_f^*} + \frac{1}{s_c^*} + \frac{i_f^* s_c^*}{l_c^*} + \frac{l_c^*}{i_c^*}\right)\right]$$

Now, because the arithmetic mean is larger than the geometric mean, implies that $\frac{1}{6}\left(\frac{1}{s_f^*} + \frac{s_f^* i_c^*}{l_f^*} + \frac{l_f^*}{i_f^*} + \frac{1}{s_c^*} + \frac{i_f^* s_c^*}{l_c^*} + \frac{l_c^*}{i_c^*}\right) \geq 1$, and therefore $\dot{V} \leq 0$. Clearly, $\dot{V} = 0$ only at the endemic equilibrium.

□

3.1. Persistance

4. Optimal Controlled Model

According to [23], thelazia management is closed related to animal husbandry practices, grazing management, barn cleaning, anthelmintic treatment, among others. However, when cattle show symptoms as excessive lacrimation, conjunctivitis, corneal opacity, ulceration of the eyes, the authors in [2] report the choice of a control strategy according to the number of worms detected in the cattle eyes. Thus, if a cattle have between 1 and 100 worms, then the control treatment is Ciplox eye drops and Neomec injection [2]. When the number of worms is between 11 and 20, the treatment consists in to apply Levamisole, and if the number of worm eyes exceeds 21 worms then proceeds by manual removal of worms with anesthesia.

We consider this practices to obtain a optimal controlled model. Let $w_f(t)$ denotes the race of mortality of flies due to fumigation. Denote by $v_l(t)$ the use of medicament treatment in cattle with light and medium worm burden and let $v_h(t)$ the manual removal of worms. By convenience we assume that w_f, v_l and v_h lies in the space of measurable functions

$$
\begin{aligned}
\mathcal{U}[0,T] := \{ \ (w_f(t), v_l(t), v_h(t))^\top : \ \text{measurable and} \\
w_{f_{min}} \leq w_f(t) \leq w_{f_{max}}, \ v_{l_{min}} \leq v_l(t) \leq v_{l_{max}}, \\
v_{h_{min}} \leq v_h(t) \leq v_{h_{max}} \ \}
\end{aligned}
\tag{9}
$$

Applying the above strategies implies economic cost and profit, in order to optimize this balance, we define the functional

$$
\begin{aligned}
J(x,u) &:= \int_0^T A_{l_c} L_c + A_{cl} I_{cl} + A_{ch} I_{ch} + B_{wf} w_f^2 + B_{vl} v_l^2 + B_{vh} v_h^2 ds, \\
x &:= (S_f, L_f, I_f, S_c, L_c, I_{cl}, I_{ch}, T_c)^\top, \\
u &:= (w_f, v_l, v_h)^\top.
\end{aligned}
\tag{10}
$$

In other words, J describe the cost of manage the cattle infected classes L_c, I_{cl}, I_{ch} by fumigation, medical treatment and manual removal or worms. The positive constants A_{l_c}, A_{cl}, B_{wf}, B_{vl}, B_{vh} adjust the cost contribution due to the respective class or strategy.

Then, our problem will be minimize J in the space $\mathcal{U}[0,T]$ subject to the controlled dynamics governed by Equation (4), that is, we have to solve the following optimization problem.

$$
\begin{aligned}
\min_{u\in\mathcal{U}[0,T]} J(x,u) := \int_0^T & \left(A_{l_c}L_c + A_{cl}I_{cl} + A_{ch}I_{ch}\right. \\
& \left. + B_{wf}w_f^2 + B_{vl}v_l^2 + B_{vh}v_h^2\right) ds \\
\text{subject to} & \\
\dot{S}_f &= \Lambda_f - \frac{S_f}{N_c^\infty}\left(\beta_f I_{cl} + \tilde{\beta}_f I_{ch}\right) - (\mu_f + w_f)\, S_f \\
\dot{L}_f &= \frac{S_f}{N_c^\infty}\left(\beta_f I_{cl} + \tilde{\beta}_f I_{ch}\right) - (k_f + \mu_f + w_f)\, L_f \\
\dot{I}_f &= k_f L_f - (w_f + \mu_f)\, I_f \\
\dot{S}_c &= \Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \mu_c S_c + v_h I_{ch} + \rho T_c \\
\dot{L}_c &= \frac{\beta_c}{N_c^\infty} I_f S_c - (\mu_c + k_c)\, L_c \\
\dot{I}_{cl} &= \theta k_c L_c - \frac{\tilde{\beta}_c}{N_c^\infty} I_{cl} I_f - (\mu_c + v_l) I_{cl} \\
\dot{I}_{ch} &= (1-\theta) k_c L_c + \frac{\tilde{\beta}_c}{N_c^\infty} I_{cl} I_f - (\mu_c + v_h) I_{ch} \\
\dot{T}_c &= v_l I_{cl} - (\mu_c + \rho)\, T_c. \\
S_f(0) = S_{f_0}, \qquad & L_f = L_{f_0}, \qquad I_f(0) = I_{f_0}, \\
S_c(0) = S_{c_0}, \qquad & L_c = L_{c_0}, \qquad I_{cl}(0) = I_{cl_0}, \\
I_c h(0) = I_{ch_0}, \qquad & T_c(0) = T_{c_0}, \\
w_f(t) \in (0,1],\ & v_l(t) \in (0,1],\ v_h(t) \in (0,1],\ \forall t \in [0,T].
\end{aligned} \tag{11}
$$

We solve this optimization problem applying an indirect method. To this end, first we have to assure existence of a optimal pair (x^*, u^*), that solves the problem (11). This is the statement of the following result.

Theorem 2. *There exist at least a optimal measurable control* $u^*(t) = (w_f(t)^*, v_l(t)^*, v_h(t)^*)^\top$ *and a corresponding optimal path* $x^*(t) = (S_f^*, L_f^*, I_f^*, S_c^*, L_c^*, I_{cl}^*, I_{ch})^\top$ *that solves problem*(11).

Proof. According to the Cesari existence result [24, p. 69 Col 4.2], we verify that

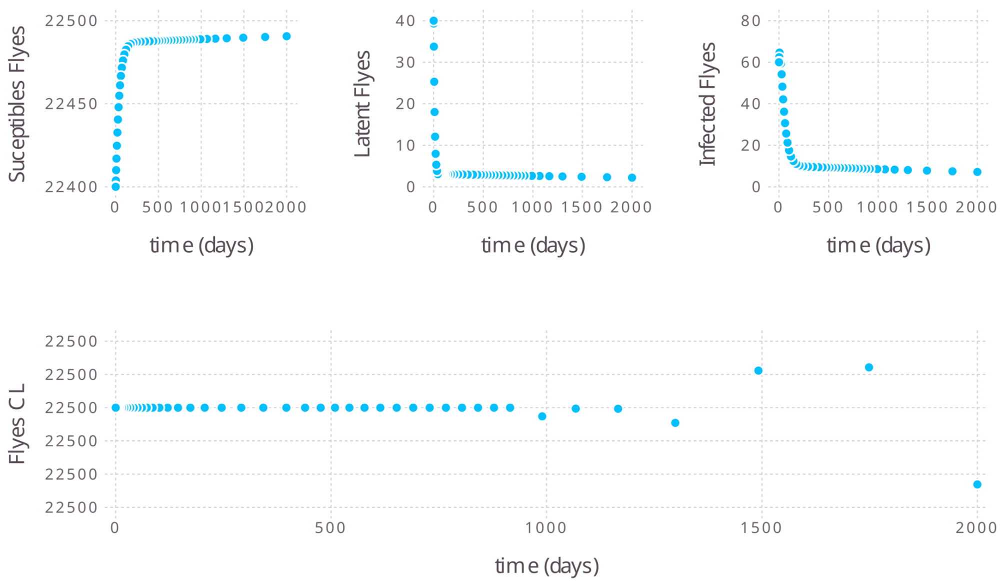

Figure 1: Solution with parameters according to $R_0 < 1$.

(i)

(ii)

(iii)

$\square$

5. Discussion

6. Numerical Results

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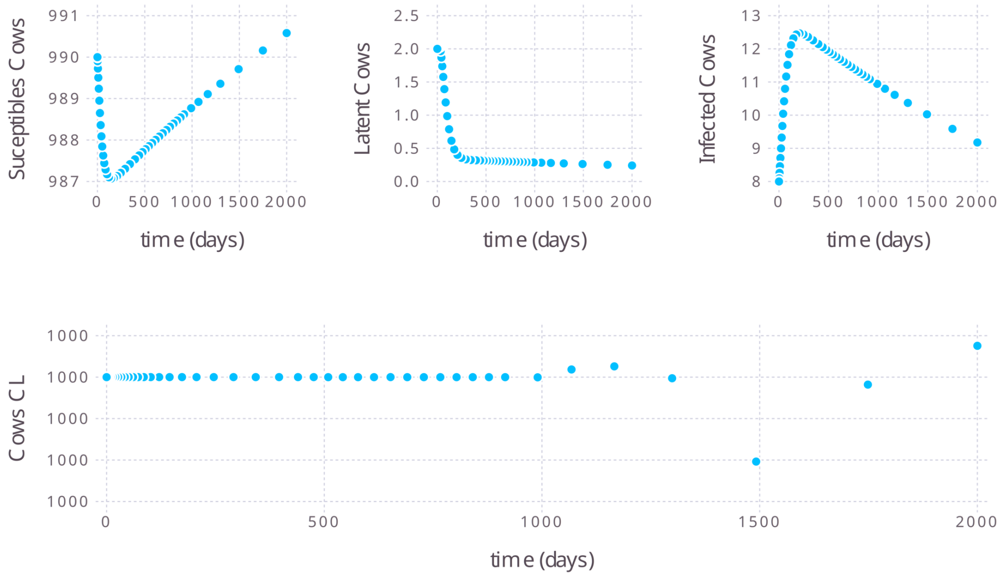

Figure 2: Solution with parameters according to $R_0 < 1$

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