

# A Mathematical model for Thelaziasis

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## Abstract

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

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

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## 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 excessive lacrimation, conjunctivitis, 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 *Thelazia spp* were found. Data from slaughtered 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 presumed 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] study 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

59 reduced, then the levels of the infected individuals with thelazia, must reach  
60 a final steady level.

61 In the mathematical side, analyse the model about stability, persistence,  
62 what would happen if stochasticity gets implemented? how?

### 63 *1.2. Model parameters*

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

#### 67 *1.2.1. Cattle only.*

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

## 78 **2. Mathematical Model**

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

83 [19] we obtain the following SI vector host model for cattle and flies.

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

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

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

95 eventually the light worm burden becomes high and then a change to the  
 96 class  $I_{ch}$ . Our model in this case becomes

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

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

103 Under these hypothesis our model with applied control becomes,

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

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

106

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

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

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

### 111 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
$\Lambda_f$	Fly recruitment rate		This study
$\Lambda_c$	Cattle recruitment rate		This study
$\beta_c$	Number of successful contacts of a fly that infects a cattle host		This study
$\beta_f$	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 12-15 days ( <i>T. Lacrymalis</i> ) 28-32 days ( <i>T. Guloosa</i> )	[21] [8] [8]
$k_i^{-1}$	average latency time for hosts $i = 1, 2$	$\approx 35$ days 21-42 days	[21] [8]
$\mu_v^{-1}$	vector average lifespan	30-60 months	[6]
$\mu_c^{-1}$	cows average lifespan	1080 days	[22]

Table 1: Parameter meaning and values.

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

114 reduce system 1, obtaining:

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

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

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

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  $\Omega$ , 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

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

115 The derivative of  $V$  is as follows:

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



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

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

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

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

121 Proof: Solving the equations for the state variables, we end up with the fol-  
 122 lowing relationships

$$\begin{aligned} 123 \quad S_f &= \frac{\Lambda_f}{\left(\frac{\beta_f}{N_c^\infty} I_c + \mu_f\right)}; L_f = \left(\frac{\beta_f}{N_c^\infty (\lambda_f + \mu_f)}\right) \left(\frac{\Lambda_f}{\left(\frac{\beta_f}{N_c^\infty} I_c + \mu_f\right)}\right) I_c; \\ 124 \quad I_f &= \left(\frac{\lambda_f}{\mu_f}\right) \left(\frac{\beta_f}{N_c^\infty (\lambda_f + \mu_f)}\right) \left(\frac{\Lambda_f}{\left(\frac{\beta_f}{N_c^\infty} I_c + \mu_f\right)}\right) I_c; S_c = \frac{(\mu_c + \lambda_c)(\mu_c + \delta)(\lambda_f + \mu_f)\mu_f(N_c^\infty)^2 \left(\frac{\beta_f}{N_c^\infty} I_c + \mu_f\right)}{\lambda_c \beta_c \lambda_f \beta_f \Lambda_f}; \\ 125 \quad T_c &= \frac{\delta T_c}{\rho + \mu_c}; L_c = \frac{(\mu_c + \delta) I_c}{\lambda_c} \text{ and } I_c = \frac{A}{B} (R_0^4 - 1), \text{ with} \\ 126 \quad A &= \frac{\mu_c \mu_f^2 (\mu_c + \lambda_c)(\mu_c + \delta)(\lambda_f + \mu_f)(N_c^\infty)^2}{\lambda_c \beta_c \lambda_f \beta_f \Lambda_f} \text{ and } B = \frac{(\mu_c + \lambda_c)(\mu_c + \delta)}{\lambda_c} \left[ 1 + \frac{\mu_c (\lambda_f + \mu_f) \mu_c N_c^\infty}{\beta_c} \right] - \\ 127 \quad &\frac{\rho \delta}{\rho + \mu_c}. \end{aligned}$$

128 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,  
 129  $I_c > 0$  if and only if  $R_0 > 1$ .

130

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

134

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

Proof: Following the ideas in [23], we consider the Lyapunov function

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

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

At the endemic equilibrium point, the following equalities hold

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

$$\mu_c + k_c = \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty \bar{L}_c} \quad \mu_f = k_f \frac{\bar{L}_f}{\bar{I}_f} \quad \mu_c = k_c \frac{\bar{L}_c}{\bar{I}_c} \quad (8)$$

137

From this information, we obtain

$$\begin{aligned} \dot{V}(t) = & a_1 \left( \Lambda_f - \frac{\beta_f}{N_c^\infty} I_c S_f - \mu_f S_f \right) \left( 1 - \frac{\bar{S}_f}{S_f} \right) + a_2 \left( \frac{\beta_f}{N_c^\infty} I_c S_f - (k_f + \mu_f) L_f \right) \left( 1 - \frac{\bar{L}_f}{L_f} \right) \\ & + a_3 (k_f L_f - \mu_f I_f) \left( 1 - \frac{\bar{I}_f}{I_f} \right) + a_4 \left( \Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \mu_c S_c \right) \left( 1 - \frac{\bar{S}_c}{S_c} \right) \\ & + a_5 \left( \frac{\beta_c}{N_c^\infty} I_f S_c - (\mu_c + k_c) L_c \right) \left( 1 - \frac{\bar{L}_c}{L_c} \right) + a_6 (k_c L_c - \mu_c I_c) \left( 1 - \frac{\bar{I}_c}{I_c} \right). \end{aligned}$$

Then, by taking the scaled variables

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

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

$$\begin{aligned} \dot{V}(t) = & -a_1 \frac{\mu_f \bar{S}_f}{s_f^*} (s_f^* - 1)^2 - a_4 \frac{\mu_c \bar{S}_c}{s_c^*} (s_c^* - 1)^2 + a_1 \frac{\beta_f \bar{S}_f \bar{I}_c}{N_c^\infty} (1 - s_f^* i_c^*) - a_1 \frac{\beta_f \bar{S}_f \bar{I}_c}{s_f^* N_c^\infty} (1 - s_f^* i_c^*) \\ & + a_2 \frac{\beta_f \bar{S}_f \bar{I}_c}{N_c^\infty} (s_f^* i_c^* - l_f^*) \left( 1 - \frac{1}{l_f^*} \right) + a_3 k_f \bar{L}_f \left( 1 - \frac{1}{i_f^*} \right) (l_f^* - i_f^*) \\ & + a_4 \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty} \left( 1 - \frac{1}{s_c^*} \right) (1 - i_f^* s_c^*) + a_5 \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty} \left( 1 - \frac{1}{l_c^*} \right) (i_f^* s_c^* - l_c^*) \\ & + a_6 k_c \bar{L}_c \left( 1 - \frac{1}{i_c^*} \right) (l_c^* - i_c^*). \end{aligned}$$

After rearranging terms we end up with

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

$$\begin{aligned}
& + \left( a_4 \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty} - a_3 k_f \bar{L}_f \right) i_f^* + \left( a_6 k_c \bar{L}_c - a_5 \frac{\beta_c \bar{I}_f \bar{S}_c}{N_c^\infty} \right) l_c^* + \left( a_1 \frac{\beta_f \bar{S}_f \bar{I}_c}{N_c^\infty} - a_6 k_c \bar{L}_c \right) i_c^* \\
& + (a_2 - a_1) \frac{\beta_f \bar{S}_f \bar{I}_c}{N_c^\infty} s_f^* i_c^* + (a_5 - a_4) \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty} i_f^* s_c^* + a_1 \frac{\beta_f \bar{S}_f \bar{I}_c}{N_c^\infty} + a_2 \frac{\beta_f \bar{S}_f \bar{I}_c}{N_c^\infty} \\
& + a_3 k_f \bar{L}_f + a_4 \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty} + a_5 \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty} + a_6 k_c \bar{L}_c - a_1 \frac{\beta_f \bar{S}_f \bar{I}_c}{N_c^\infty} \left( \frac{1}{s_f^*} \right) - a_2 \frac{\beta_f \bar{S}_f \bar{I}_c}{N_c^\infty} \left( \frac{s_f^* i_c^*}{l_f^*} \right) \\
& - a_3 k_f \bar{L}_f \left( \frac{l_f^*}{i_f^*} \right) - a_4 \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty} \left( \frac{1}{s_c^*} \right) - a_5 \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty} \left( \frac{s_c^* i_f^*}{l_c^*} \right) - a_6 k_c \bar{L}_c \left( \frac{l_c^*}{i_c^*} \right)
\end{aligned}$$

By taking the constant values as

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

, we obtain

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

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. Persistence

## 4. Optimal Controlled Model

According to [20], 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.

153 We consider this practices to obtain a optimal controlled model. Let  $w_f(t)$   
 154 denotes the race of mortality of flies due to fumigation. Denote by  $v_l(t)$  the  
 155 use of medicament treatment in cattle with light and medium worm burden  
 156 and let  $v_h(t)$  the manual removal of worms.

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

$$J(x, u) := \int_0^T A_{l_c} L_c + A_{cl} I_{cl} + A_{ch} I_{ch} + B_{wf} w_f^2 + B_{vl} v_l^2 + B_{vh} v_h^2 ds. \quad (9)$$

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

163 Then, our problem will be minimize  $J$  subject to the controlled dynamics  
 164 governed by eq. (4), that is, we want to solve the following optimization  
 165 problem.

$$\min_{u \in \mathcal{U}[0, T]} J(x, u) := \int_0^T A_{l_c} L_c + A_{cl} I_{cl} + A_{ch} I_{ch} + B_{wf} w_f^2 + B_{vl} v_l^2 + B_{vh} v_h^2 ds$$

subject to

$$\begin{aligned} \dot{S}_f &= \Lambda_f - \frac{S_f}{N_c^\infty} \left( \beta_f I_{cl} + \tilde{\beta}_f I_{ch} \right) - (\mu_f + w_f(t)) S_f \\ \dot{L}_f &= \frac{S_f}{N_c^\infty} \left( \beta_f I_{cl} + \tilde{\beta}_f I_{ch} \right) - (k_f + \mu_f + w_f(t)) L_f \\ \dot{I}_f &= k_f L_f - (w_f(t) + \mu_f) I_f \\ \dot{S}_c &= \Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \mu_c S_c + v_h(t) I_{ch} + \rho T_c \\ \dot{L}_c &= \frac{\beta_c}{N_c^\infty} I_f S_c - (\mu_c + k_c) L_c \\ \dot{I}_{cl} &= \theta k_c L_c - \frac{\tilde{\beta}_c}{N_c^\infty} I_{cl} I_f - (\mu_c + v_l(t)) I_{cl} \\ \dot{I}_{ch} &= (1 - \theta) k_c L_c + \frac{\tilde{\beta}_c}{N_c^\infty} I_{cl} I_f - (\mu_c + v_h(t)) I_{ch} \\ \dot{T}_c &= v_l(t) I_{cl} - (\mu_c + \rho) T_c. \end{aligned} \quad (10)$$

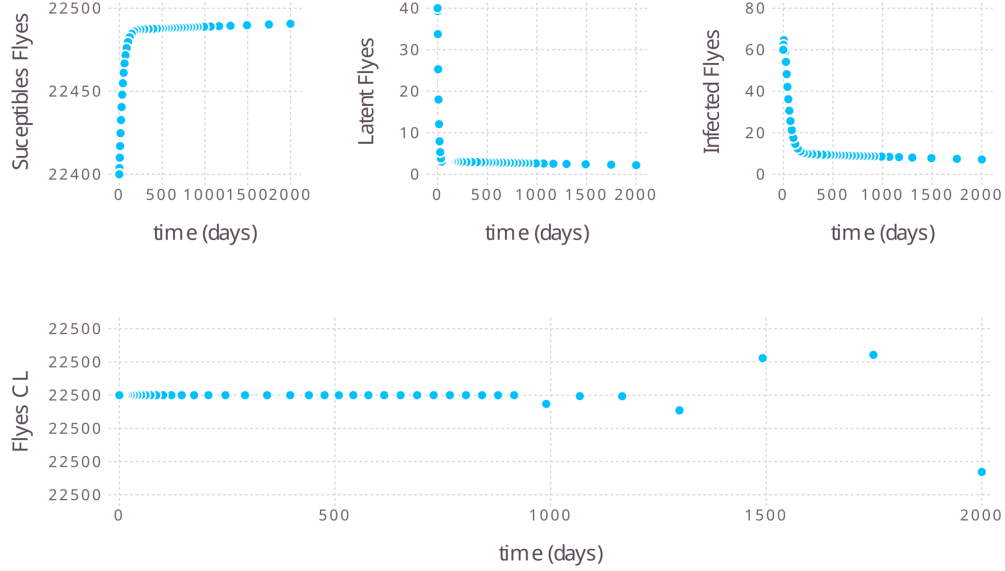


Figure 1: Solution with parameters according to  $R_0 < 1$ .

166 We solve this optimization by an indirect method. To this end first  
 167 we have to existence of a control  $u(t) := (w_f(t), v_l(t), v_h(t))^T$ , that satisfies  
 168 eq. (10). This is the statement of the following result.

## 169 5. Discussion

## 170 6. Numerical Results

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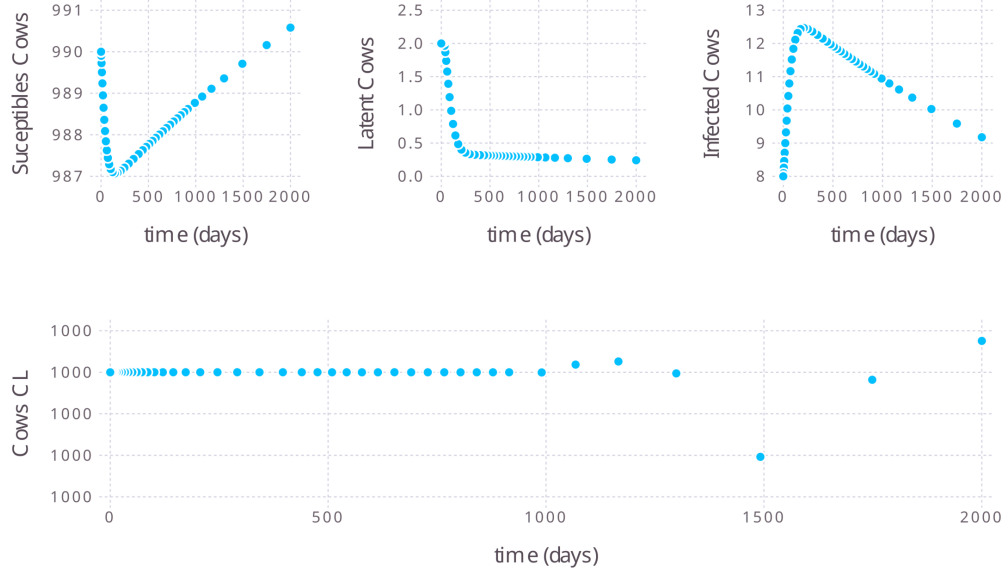


Figure 2: Solution with parameters according to  $R_0 < 1$

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