

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

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],

.. vaccination? In humans?

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,

59 it might be expected that as soon as the temperature of a place of study is
60 reduced, then the levels of the infected individuals with thelazia, must reach
61 a final steady level.
62 In the mathematical side, analyse the model about stability, persistence,
63 what would happen if stochasticity gets implemented? how?

64 *1.2. Model parameters*

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

68 *1.2.1. Cattle only.*

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

79 **2. Mathematical Model**

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

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

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

After control is applied (need to find out the models we will apply) [20].

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

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where $v(t)$, $u(t)$ and $w(t)$ represent culling, treatment and fumigation, respectively. For the uncontrolled model, the basic reproductive number is given by

$$R_0 = \left(\frac{\beta_c \beta_f k_c k_f N_f^\infty}{\mu_f (\mu_c + k_c) (\mu_c + \delta_c) (\mu_f + k_f) N_c^\infty} \right)^{1/4} \tag{3}$$

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 the parameters considered in this study.

| 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 12-15 days (<i>T. Lacrymalis</i>) 28-32 days (<i>T. Gulososa</i>) | [21] [8] [8] |
| k_i^{-1} | average latency time for hosts $i = 1, 2$ | ≈ 35 days | [21] |
| μ_v^{-1} | vector average lifespan | 21-42 days | [8] |
| μ_c^{-1} | cows average lifespan | 30-60 months 1080 days | [6] [22] |

Table 1: Parameter meaning and values.

91 3. Local and global stability analysis

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

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

92 so it implies that, for a sufficiently large time, the fly and cow populations
93 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

94 reduce system 1, obtaining:

$$\begin{aligned}
\dot{L}_f &= \frac{\beta_f}{N_c^\infty} I_c (N_f^\infty - L_f - I_f) - (k_f + \mu_f) L_f \\
\dot{I}_f &= k_f L_f - \mu_f I_f \\
\dot{S}_c &= \Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \mu_c S_c + \rho (N_c^\infty - S_c - L_c - I_c) \\
\dot{L}_c &= \frac{\beta_c}{N_c^\infty} I_f S_c - (\mu_c + k_c) L_c \\
\dot{I}_c &= k_c L_c - (\mu_c + \delta) I_c
\end{aligned} \tag{4}$$

System 4 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 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

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

95 The derivative of V is as follows:

$$\begin{aligned}
\dot{V} &= a_1 \left(1 - \frac{N_c^\infty}{S_c} \right) \left[\Lambda_c - \frac{\beta_c}{N_c^\infty} I_f S_c - \mu_c S_c + \rho (N_c^\infty - S_c - L_c - I_c) \right] \\
&\quad + a_2 \left[\frac{\beta_c}{N_c^\infty} I_f S_c - (\mu_c + k_c) L_c \right] + [k_c L_c - (\mu_c + \delta) I_c] \\
&\quad + a_3 \left[\frac{\beta_f}{N_c^\infty} I_c (N_f^\infty - L_f - I_f) - (k_f + \mu_f) L_f \right] + a_4 [k_f L_f - \mu_f I_f]
\end{aligned} \tag{5}$$

Substituting the values of a_1 , a_2 , a_3 and a_4 , we simplify equation 5,

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

Replacing the expression for \mathcal{R}_0 given in (3), 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

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

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. 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

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

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

At the endemic equilibrium point, the following equalities hold

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

$$\mu_c + k_c = \frac{\beta_c \bar{S}_c \bar{I}_f}{N_c^\infty \bar{L}_c} \quad \mu_f = k_f \frac{\bar{L}_f}{\bar{I}_f} \quad \mu_c = k_c \frac{\bar{L}_c}{\bar{I}_c} \quad (6)$$

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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 6, 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. Discussion

5. Numerical Results

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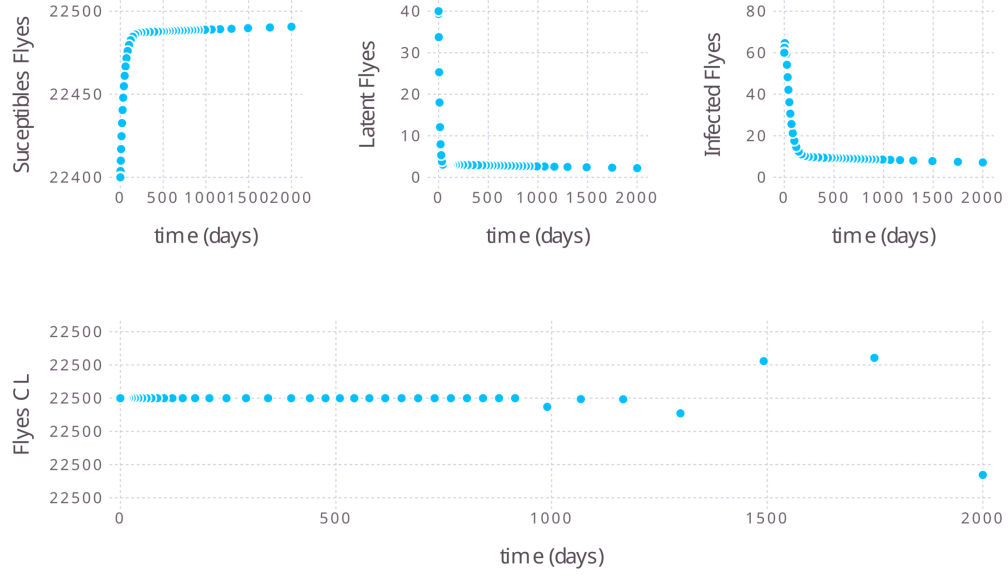


Figure 1: Solution with parameters according to $R_0 < 1$.

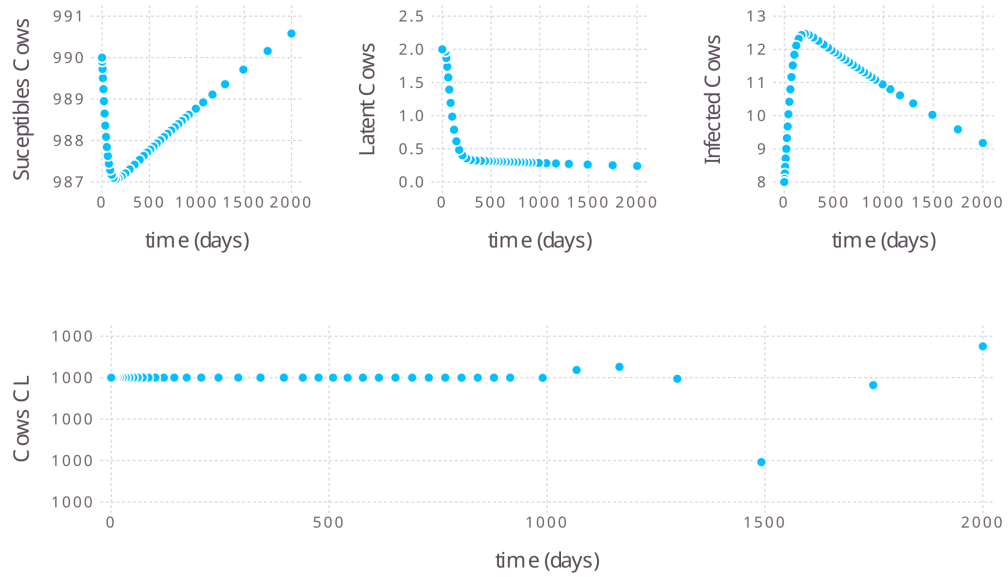


Figure 2: Solution with parameters according to $R_0 < 1$

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