A logistic delay differential equation model for Chagas disease with interrupted spraying schedules

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(Received 23 August 2010; final version received 7 May 2011)

This work studies a mathematical model for the dynamics of Chagas disease, a parasitic disease that affects humans and domestic mammals throughout rural areas in Central and South America. It presents a modified version of the model found in Spagnuolo et al. [A model for Chagas disease with controlled spraying, J. Biol. Dyn. 5 (2011), pp. 299–317] with a delayed logistic growth term, which captures an overshoot, beyond the vector carrying capacity, in the total vector population when the blood meal supply is large. It studies the steady states of the system in the case of constant coefficients without spraying, and the analysis shows that for given-averaged parameters, the endemic equilibrium is stable and attracting. The numerical simulations of the model dynamics with time-dependent coefficients are shown when interruptions in the annual insecticide spraying cycles are taken into account. Simulations show that when there are spraying schedule interruptions, spraying may become ineffective when the blood meal supply is large.

Keywords: Chagas disease; spraying with insecticides; epidemic dynamics; delay logistic model; numerical simulations; steady states; nonlinear dynamical system

AMS Subject Classification: 34A12; 92B05; 34A34

1. Introduction

Chagas disease, which is responsible for significant morbidity and mortality throughout much of Latin America, is caused by the parasite Trypanosoma cruzi. It leads to organ deformity and early death in one-third of the 8–10 million individuals infected [13,19]. The primary domestic vector responsible for the spread of T. cruzi is Triatoma infestans, a species of reduviids. Current control measures responsible for decreasing Chagas disease include improving the quality of housing and health care, and treatment of homes with insecticide spraying [20]. Because of toxicity and questionable efficacy of the current drug treatments during the chronic stages of the disease and the lack of an effective vaccine, controlling the transmission of Chagas disease remains largely based on controlling vectors by insecticide spraying and on blood-bank screening [9,17,18,20].

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ISSN 1751-3758 print/ISSN 1751-3766 online
© 2012 Taylor & Francis
http://dx.doi.org/10.1080/17513758.2011.587896
http://www.tandfonline.com
Spraying with pyrethroid insecticides has been the method used to control the vector population. This has proven effective in retarding the spread of the disease and in some cases nearly eliminating the domestic insects.

To provide a mathematical tool for studying seasonal spraying schedules, a model for the dynamics of the disease was developed in [21], where the emphasis was on modelling and simulating the effects of annual spraying and the impact of the blood meal supply on the disease dynamics in representative villages.

In this paper, we continue the research in [21] with a different equation for the vectors and, as a result, a new term in the equation for infected vectors. In [21], the total number of vectors was modelled with a Nicholson’s blowflies type of growth rate with periodic coefficients and delays. In this work, we model the growth of the total number of vectors using a delayed logistic term with periodic coefficients. This model depends on the carrying capacity parameter, which is the maximum number of vectors in a village. The carrying capacity parameter is more convenient to use, since it seems easier to estimate than the growth parameter used in [21]. In the latter model, the growth term depends on a parameter that represents the number of vectors in a household at which the growth is maximal, and so seems much more difficult to measure. In the model presented here, the rate equation for the vectors contains a delay, related to the egg hatching period, which allows the number of vectors to overshoot, beyond the carrying capacity. The model without a delay cannot predict an overshoot in the vector population. We have also introduced a term in the vector equation that increases the mortality of vectors due to overpopulation beyond the carrying capacity. The coefficient for this term is a (new) parameter in the model. Hence, the growth rate and mortality are both functions of the carrying capacity.

The model consists of four nonlinear differential equations for the dynamics of disease transmission. The system of equations predicts the total number of vectors, infected vectors, infected humans, and infected domestic animals (dogs). In the model, most of the coefficients are assumed to be periodic in time, taking into account the dependence of the system on the seasons. We study the steady states of the system and analyse their stability only in the case when the coefficients in the model system are all constant, with their yearly average values, and without spraying.

In the numerical simulations, we use seasonally dependent coefficients and investigate the effects of interruptions in the annual insecticide spraying schedule.

The model is presented in Section 2. A detailed description of the model as well as biological references can be found in [21]. The steady states for the model, in the case of constant coefficients and no spraying, are described in Section 3 and their stability is analysed. In particular, it is found that the endemic steady state is stable and attracting. The numerical simulation results for interruptions in the annual spraying schedules and the dependence of its effectiveness on the blood meal supply, along with graphical illustrations, are presented in Section 4. The paper concludes with a discussion in Section 5.

As a contribution to research on Chagas disease, access to the computer program (used in [21]) is freely available via an internet interface [22]. It provides the interested researcher with a tool to examine the mathematical model outcome with user input parameters. We point out that the model has not been validated and its use is only intended to help gain insight into the dynamics of the disease.

2. The model

In this section, we present a new version of a model for Chagas disease dynamics. Information on the pertinent biological processes can be found in [8]. The full details of the model assumptions can be found in [21]. The model represents the overall dynamics of the populations of vectors,
infected vectors, infected humans, and infected domestic mammals, referred to as ‘dogs’ in our model. In a rural village, there are also non-mammals that are blood meal sources for the vectors, but that do not become infected with \( T. cruzi \). They are referred to as ‘chickens’ in our model. The goal of this model is to provide a tool to further study disease control. We begin with a model that reasonably replicates the known dynamics, then we study the effects of certain parameters.

We note that the model has not been validated and therefore should be used only for a qualitative study of the disease dynamics.

We consider a rural village in South America and describe the dynamics using differential equations, which means that we deal with a relatively large population. Numerical simulations indicate that the model gives reasonable results when applied to a rural village with 400 humans. As in [21], it is assumed that there is a vector population (triatomines – \( T. infestans \)) that is not killed by insecticide spraying, because the vectors just had a blood meal and hide in the deep cracks of the houses. Therefore, they do not come in contact with the insecticide while it is active. The parameters used in the model, such as the various probability factors for infection, as well as others, are given in Table 1 along with their references.

We model some of the disease dynamics in a representative village. The number of humans in the village is \( N \), the number of domestic animals that can become infected is \( D \), and the number that cannot become infected is \( C \). Each of \( N, D, \) and \( C \) is taken as a constant in our model for the sake of simplicity. We denote by \( V = V(t) \) the number of carrier insects living in the village houses at time \( t \), the number of infected insects by \( V_i = V_i(t) \), the number of infected humans by \( N_i = N_i(t) \), and the number of infected dogs by \( D_i = D_i(t) \). Each non-infected population, excluding \( C \), is assumed to be susceptible.

We describe the rate of change of each population per day. The changes from the model in [21] are in the equations for the total vector population and for the infected vector population. In [21], a delayed Nicolson’s blowfly-type term was used for the growth of vectors, whereas here we use a delayed logistic term to represent growth rate of the vectors; see, e.g. [1] and references therein. The former allowed us to control the maximum growth, whereas the version here allows us to take into account the natural vector carrying capacity \( K \) that effectively limits the number of domestic vectors that can sustainably live in a village. The differences in the growth terms will be discussed in more detail below. We also add a term that increases the death rate of the vectors due to overpopulation. This term has an analogue in the infected vector population equation.

The rate of change in the total vector population depends on the following parameters: the carrying capacity, \( K \), along with \( d_h, d_m, \) and \( r \). Here, the egg hatching rate \( d_h(t-\tau) \) is evaluated at time \( t-\tau \) and is a product of terms involving the fraction of the vector population that can lay eggs, the number of eggs laid by an adult female per bite, the fraction of adult females, the successful hatching of eggs after \( \tau \) days (gestation time), the total blood meal supply (in human factors), \( b_{\text{supply}} \), and the delayed seasonal biting rate per human factor per vector per day \( b(t-\tau), \tau \) days prior to hatching as well as on the natural death rate coefficients of triatomines (Table 1). By extracting seasonal data from Castanera et al. [3], we obtain the following values: the ratio of adults to the entire population of triatomines is approximately 11/365 (so we take half that number to be adult females), the ratio of eggs that survive is 0.83, and the number of \((\text{eggs/bite})/(\text{fed female})\) is 20 [3,10]. So, multiplying these numbers by the biting rate, evaluated at \( \tau \) days prior to the current time, and the blood supply, gives the form of \( d_h \):

\[
d_h(t-\tau) = \frac{11}{365} \frac{1}{2} (20)(0.83)b(t-\tau)b_{\text{supply}}.
\]  

The natural mortality rate is denoted by \( d_m = d_m(t) \). The mortality rate due to spraying with insecticides is denoted by \( r = r(t) \) and the mortality rate due to overpopulation beyond the carrying capacity is denoted by \( d_k \).
Introducing the delay in the vector equation allows the model to predict an overshoot in the number of vectors, above the carrying capacity. We discuss this in Section 4.

Thus, the rate of change in the total vector population in the village is

\[ V'(t) = d_h(t - \tau)V(t - \tau)\left(1 - \frac{1}{K}V(t - \tau)\right)_+ - r(t)(V(t) - V_{\min})_+ \]

\[ - \left(d_m(t) + d_k\left(1 - \frac{1}{K}V(t)\right)_-\right)V(t). \]

Here and below, the prime denotes the time derivative, and \((f)_+\) and \((f)_-\) denote the positive and negative parts of a function \(f = (f)_+ - (f)_-\).

In the first term, \(d_h(t - \tau)V(t - \tau)\) is the number of vectors that hatch at time \(t\) from eggs laid at time \(t - \tau\). The expression \((1 - V(t - \tau)/K)_+\) represents the fraction of the food supply that was available to the female vectors at time \(t - \tau\). This assumption says that if the vector population at time \(\tau\) days prior to the current time \(t\) was above the carrying capacity, then no eggs were laid and, indeed, when \(K < V(t - \tau)\), the first term vanishes.

The model assumes that a subpopulation of insects \(V_{\min}\) is able to survive spraying, and this is expressed by the term \(r(t)(V(t) - V_{\min})_+\). The natural death rate is \(d_m = d_m(t)\) and the death rate caused by overpopulation is described by \(d_k(1 - (1/K)V(t))_-\), which vanishes when the vector population is below the carrying capacity \((V(t) < K)\).

In the simulations, during spraying years, the spraying function is given by

\[ r(t) = \begin{cases} (e^{-\lambda(t-t_1)^2} - e^{-1/2})\bar{r}_{\max}, & \text{if } t_1 \leq t \leq t_2, \\ 0, & \text{otherwise}. \end{cases} \]

The coefficients in the simulations were chosen to be

\[ \lambda = \frac{1}{2(91.25)^2}, \quad \bar{r}_{\max} = \frac{1}{1 - e^{-1/2}}, \]

with \(t_1 = 212.5\) days and \(t_2 = 303.75\) days for a full season of spraying starting in the spring. See [15] for a reference on the duration of spraying. Note that \(r(t)\) is taken to be 0 during non-spraying years.

We now compare our vector equation to that in [21], where a Nicholson’s blowflies type of term was used. The vector rate equation there is

\[ V'(t) = d_h(t - \tau)V(t - \tau)e^{-aV(t-\tau)} - d_m(t)V(t) - r(t)(V(t) - V_{\min})_. \]

The first term on the right-hand side of Equation (3) attains its maximum when the number of vectors in the village houses at time \(t - \tau\) reaches the value of \(a^{-1}\), whereas the current model depends on the carrying capacity \(K\) of vectors in the village houses. It seems to be easier to find \(K\) experimentally, rather than to estimate \(a\). Also, the current model clearly handles the death rate differently, as described above.

Next, we consider the growth rates of the infected vectors \(V_i\), infected humans \(N_i\), and infected domestic animals \(D_i\). We denote by \(P_{NV}\) and \(P_{DV}\) the probabilities of a vector becoming infected in one bite from an infected human and an infected dog, respectively. The rate of change of infected vectors has a growth rate that is given by the following expression:

\[ b(V - V_i)(P_{NV}N_i + P_{DV}d_iD_i), \]

where \(b = b(t)\) is the same seasonal biting rate (given as bites per human factor per day per vector) that is used to define \(d_h\). We use ‘human factors’ as a measure of biting preference of the vectors.
in the following way: each human represents one human factor, each domestic animal represents
d_{f} human factors, and each non-mammal represents \( c_{f} \) human factors.

The death rate caused by spraying is as follows:

\[
r \frac{V_{i}}{V}(V - V_{\text{min}})_{+} = r \left( 1 - \frac{V_{\text{min}}}{V} \right)_{+} V_{i},
\]

where a uniform population is assumed so that the ratio of the number of infected vectors to total
number of vectors is the same inside and outside of the deep cracks in the house. We assume that
the natural death rate of the infected insects is also \( d_{m} = d_{m}(t) \), i.e. carrying the parasites does not
affect their lifespan and the term involving \( d_{k} \) is also applied to the infected vectors.

Collecting the terms above gives the following rate equation for the infected vectors:

\[
V_{i}' = b(V - V_{i})(P_{NV}N_{i} + P_{DV}d_{f}D_{i}) - r \left( 1 - \frac{V_{\text{min}}}{V} \right)_{+} V_{i} - \left( d_{m}(t) + d_{k} \left( 1 - \frac{1}{K} V_{i} \right) \right)_{-} V_{i}.
\]

The mortality rates of infected humans and infected dogs are denoted by \( \gamma_{N_{i}} \) and \( \gamma_{D_{i}} \), respec-
tively. Therefore, the rate of change of the number of infected humans and the number of infected
dogs are given as follows:

\[
N_{i}' = b P_{VN}(N - N_{i}) V_{i} - \gamma_{N_{i}} N_{i},
\]

and

\[
D_{i}' = b d_{f} P_{VD}(D - D_{i}) V_{i} - \gamma_{D_{i}} D_{i},
\]

respectively. Here, \( P_{VN} \) and \( P_{VD} \) are the infected vector to human and infected vector to dog
transmission probabilities in one bite, respectively, and \( N - N_{i} \) and \( D - D_{i} \) are the susceptible
human and dog populations, respectively.

To complete the model, we prescribe the initial population numbers \( V_{i}(0) = V_{i0}, N_{i}(0) = N_{i0}, D_{i}(0) = D_{i0}, \) together with

\[
V(t) = V_{0}(t), \quad -\tau \leq t \leq 0,
\]

where the function \( V_{0}(t) \), due to the delay \( \tau \) in the vector equation, must be prescribed on the time
interval \( -\tau \leq t \leq 0 \).

These equations and conditions form a mathematical model for the dynamics of Chagas disease:
Find the functions \( \{V, V_{i}, N_{i}, D_{i}\} : [0, T] \rightarrow \mathbb{R}_{+}^{4} \) such that

\[
V' = d_{h}(t - \tau) V(t - \tau) \left( 1 - \frac{1}{K} V(t - \tau) \right)_{+} - r (V - V_{\text{min}})_{+}
- \left( d_{m} + d_{k} \left( 1 - \frac{1}{K} V(t) \right) \right)_{-} V,
\]

(4)

\[
V_{i}' = b(V - V_{i})(P_{NV}N_{i} + P_{DV}d_{f}D_{i}) - r \left( 1 - \frac{V_{\text{min}}}{V} \right)_{+} V_{i} - \left( d_{m} + d_{k} \left( 1 - \frac{1}{K} V_{i} \right) \right)_{-} V_{i},
\]

(5)

\[
N_{i}' = b P_{VN}(N - N_{i}) V_{i} - \gamma_{N_{i}} N_{i},
\]

(6)

\[
D_{i}' = b d_{f} P_{VD}(D - D_{i}) V_{i} - \gamma_{D_{i}} D_{i},
\]

(7)

\[
V_{i}(0) = V_{i0}, \quad N_{i}(0) = N_{i0}, \quad D_{i}(0) = D_{i0}, \quad V(t) = V_{0}(t), \quad -\tau \leq t \leq 0.
\]

(8)
Here, $\mathbb{R}^4_+ = \{(x_1, x_2, x_3, x_4) \in \mathbb{R}^4 : 0 \leq x_i, \; i = 1, \ldots, 4\}$. The coefficient functions $d_h, d_m, r,$ and $b$ are seasonal, or 1-year periodic.

Equation (4) for the total vector population is not coupled to the other equations, so it can be solved independently. Then, the coupled system of Equations (5)–(7) for $V_i(t), N_i(t),$ and $D_i(t)$, for $0 < t \leq T$, has to be solved simultaneously.

The existence and uniqueness of the solution to the model can be established in the same way as in [21]. It is based on the observation that on each bounded time interval $[0, T]$, Equation (4) leads to a positive-bounded solution $V$. This guarantees that Equations (5)–(7) yield bounded solutions on $[0, T]$, since $V_i(t), N_i(t),$ and $D_i(t)$ are bounded by $V, N,$ and $D$. If $V_i(t)$ exceeds $V$ then the term $V - V_i$ becomes negative, leading to the decrease in $V_i(t)$, and similar observations hold for the other two terms.

The study of the steady states and their stability is addressed next.

3. Steady states

The steady states of the model with constant coefficients are studied in this section. We also assume that there is no spraying, so that $r = 0$. Indeed, the interest is in the asymptotic behaviour of the system without the controls, i.e. spraying. We replace the time-dependent coefficients in the model with the average values of our seasonal biting, hatching, and mortality functions, $\bar{b}$, $\bar{d}_h$, and $\bar{d}_m$, respectively. This allows us to solve these equations for $\bar{V}$, $\bar{V}_i$, $\bar{N}_i$, and $\bar{D}_i$, the steady states of the four populations.

We first note that the equation for $\bar{V}$ is

$$0 = \bar{d}_h \bar{V} \left(1 - \frac{1}{K} \bar{V} \right) - \bar{d}_m \bar{V}.$$

It is straightforward to see that $\bar{V} \leq K$, since otherwise the first term on the right-hand side vanishes and the second term is non-positive, hence the term with $\bar{d}_k$ vanishes.

Thus, the steady states are the solutions of the system

$$0 = \bar{d}_h \bar{V} \left(1 - \frac{1}{K} \bar{V} \right) - \bar{d}_m \bar{V}, \tag{9}$$

$$0 = \bar{b}(\bar{V} - \bar{V}_i)(P_{NV} \bar{N}_i + P_{DV} d_t \bar{D}_i) - \bar{d}_m \bar{V}_i, \tag{10}$$

$$0 = \bar{b} P_{VN}(N - \bar{N}_i) \bar{V}_i - \gamma_{N} \bar{N}_i, \tag{11}$$

$$0 = \bar{b} d_t P_{VD}(D - \bar{D}_i) \bar{V}_i - \gamma_{D} \bar{D}_i. \tag{12}$$

Since Equation (9) is decoupled from Equations (10)–(12), we analyse it first. Then, we use the solutions for $\bar{V}$ in the system for the three infected populations.

3.1. Stability of total number of vectors

Equation (4) is a delay-differential equation and the stability analysis is quite involved. For the sake of brevity, we state the results here and we refer the reader to [7] for the complete steady-state stability analysis.
First, we denote by $R$ the ratio $R = \frac{\bar{d}_h}{\bar{d}_m}$ and note that when $1 < R$, the average vector growth rate exceeds the average death rate. The ratio $R$ acts as the basic stability number in problem (4) for vector population growth (see [12,23] and references therein) or as the basic reproduction number for the vector population.

It is straightforward to see that when $R \leq 1$, Equation (9) has only one non-negative solution, the trivial solution $\bar{V} = 0$. When $1 < R$, there are two non-negative steady states: the trivial one, $\bar{V} = 0$, and $\bar{V} = K_R$, which is a fraction of the carrying capacity $K$,

$$\bar{V} = K_R = K \left( 1 - \frac{1}{R} \right).$$

The following stability result and its proof can be found in [7]. The proof is straightforward, though technical, and lies beyond the scope of this work.

**Theorem 3.1** If $0 < R < 1$, then the vector-free steady state, $\bar{V} = 0$, is locally asymptotically stable. If $R > 1$, then $\bar{V} = 0$ is unstable. Furthermore, when $R > 1$, the positive equilibrium $\bar{V} = K_R$ is

1. locally asymptotically stable when $R \in (1, 2 - \sec \theta_0)$,
2. unstable when $R > 2 - \sec \theta_0$,

where $\theta_0 \in (\pi/2, \pi)$ satisfies

$$-\theta_0 \cot \theta_0 = \bar{d}_m \tau.$$  

As a practical matter, $-\sec \theta_0 = (1/\bar{d}_m \tau)(\theta_0/\sin \theta_0)$, and, on $(\pi/2, \pi)$, $(1/\bar{d}_m \tau)(\theta/\sin \theta) \geq (1/\bar{d}_m \tau)(\pi/2)$, while $-\sec \theta \geq 1$. So, if

$$1 < R < 2 + M,$$

where $M = \max\{1, (1/\bar{d}_m \tau)(\pi/2)\}$, then $\bar{V} = K_R$ is locally asymptotically stable. Furthermore, when $R > 2$, the condition

$$\bar{d}_h \tau < \frac{\pi}{2},$$

gives local asymptotic stability for $\bar{V} = K_R$ since $R - 2 < -\sec \theta_0$ is equivalent to

$$\bar{d}_h \tau \left( \frac{R - 2}{R} \right) < \frac{\theta_0}{\sin \theta_0},$$

and $\theta/\sin \theta > \pi/2$ for $\theta \in (\pi/2, \pi)$.

We use the terms ‘asymptotically stable’ and ‘stable and attracting’ interchangeably.

### 3.2. Stability of the steady states of the infected populations

The non-negative steady states of systems (10)–(12) are as follows.

When $R \leq 1$, there is only one steady state, the disease-free state, $(\bar{V}_i, \bar{N}_i, \bar{D}_i) = (0, 0, 0)$ together with $\bar{V} = 0$, and it is stable and attracting, since the infected populations die out together
with the vector population. Indeed, in this case the Jacobian matrix at \((0,0,0)\) is
\[
\mathbf{A} = \begin{pmatrix}
-\bar{d}_m & 0 & 0 \\
\bar{b} P_V N & -\gamma_N & 0 \\
\bar{b} d_f P_V D & 0 & -\gamma_D \\
\end{pmatrix}.
\]

The eigenvalues are \(\lambda_1 = -\bar{d}_m\), \(\lambda_2 = -\gamma_N\), and \(\lambda_3 = -\gamma_D\), and, therefore, the disease-free steady state is stable and attracting.

We turn to the more interesting case when \(R > 1\). When, \(\bar{V} = 0\), it follows that \(\bar{V} = \bar{N} = \bar{D} = 0\). When, \(\bar{V} = K_R\), we now show that there exists a disease-free steady state and unique positive endemic steady state. Substituting \(\bar{V}_i = K_R\) in Equation (13) into Equations (10)–(12) gives the system
\[
\begin{align*}
0 &= \bar{b}(K_R - \bar{V}_i)(P_{NV}\bar{N}_i + P_{DVd_f}\bar{D}_i) - \bar{d}_m\bar{V}_i, \\
0 &= \alpha(N - \bar{N}_i)\bar{V}_i - \gamma_N\bar{N}_i, \\
0 &= \beta(D - \bar{D}_i)\bar{V}_i - \gamma_D\bar{D}_i,
\end{align*}
\]
where
\[
\alpha = \bar{b} P_V N, \quad \beta = \bar{b} d_f P_V D.
\]

We note that the equilibrium values of \(N_i\) and \(D_i\) are given by
\[
\bar{N}_i = \frac{\alpha N \bar{V}_i}{\gamma_N + \alpha \bar{V}_i}, \quad \bar{D}_i = \frac{\beta D \bar{V}_i}{\gamma_D + \beta \bar{V}_i}.
\]

Note that \(N_i \in [0, N)\) and \(D_i \in [0, D)\), since \(\gamma_N, \gamma_D > 0\). Thus, one needs only to solve for \(\bar{V}_i\). To this end, we substitute the expressions in Equation (21) for \(\bar{N}_i\) and \(\bar{D}_i\) into Equations (18), and simplify to get
\[
\bar{V}_i p(\bar{V}_i) = \bar{V}_i q(\bar{V}_i),
\]
where
\[
\begin{align*}
p(x) &= \bar{d}_m(\gamma_N + \alpha x)(\gamma_D + \beta x), \\
q(x) &= \bar{b}(K_R - x)(\Theta + \Lambda x),
\end{align*}
\]
and
\[
\begin{align*}
\Theta &= (\alpha \gamma_D) P_{NV} N + (\beta \gamma_N) P_{DVd_f} D, \\
\Lambda &= \alpha \beta (P_{NV} N + P_{DVd_f} D).
\end{align*}
\]

Note that \(\Theta, \Lambda > 0\).

The solution \(\bar{V}_i = 0\) of Equation (22) leads to \(\bar{N}_i = \bar{D}_i = 0\), by Equations (21), giving the disease-free steady-state solution. So, the only other solutions for \(\bar{V}_i\) in Equations (21) satisfy \(p(\bar{V}_i) = q(\bar{V}_i)\). Now, the graph of the quadratic \(p(x)\) on the left-hand side of Equation (22) is a parabola opening upward with the two negative real roots \(-\gamma_N/\alpha\) and \(-\gamma_D/\beta\). Also, the graph of the quadratic \(q(x)\) on the right-hand side of Equation (22) is a parabola opening downward with
one positive root $K_R$ and one negative root $-\Theta/\Lambda$. We now point out the following inequality:

$$\frac{\min\{\alpha\gamma D_i, \beta\gamma N_i\}}{\alpha\beta} \leq \frac{\Theta}{\Lambda} \leq \frac{\max\{\alpha\gamma D_i, \beta\gamma N_i\}}{\alpha\beta},$$

giving

$$\min\left\{\frac{\gamma D_i}{\beta}, \frac{\gamma N_i}{\alpha}\right\} \leq \frac{\Theta}{\Lambda} \leq \max\left\{\frac{\gamma D_i}{\beta}, \frac{\gamma N_i}{\alpha}\right\}.$$  

So, the root $-\Theta/\Lambda$ of $q(x)$ lies between the two negative roots of $p(x)$ for any parameter set. Therefore, there exist two real solutions to $p(x) = q(x)$, and we can classify them as follows: there is always a negative solution; there is another negative solution if $p(0) > q(0)$; there is a zero solution if $p(0) = q(0)$; and there is a unique positive solution in $(0, K_R)$ if $p(0) < q(0)$, which is true if $\bar{m}\gamma N_i\gamma D_i < bK_R\Theta$. Therefore, there exists a unique positive solution $\tilde{V}_i$ if and only if

$$\mathcal{R}_0 = \frac{bK_R\Theta}{\bar{m}\gamma N_i\gamma D_i} > 1. \quad (27)$$

Later, we will see that $\mathcal{R}_0$, defined in Equation (27), is the basic stability number for the infected populations. The biological meaning of $\mathcal{R}_0$ is not clear.

We can also see that $\tilde{V}_i < K_R$ by considering the following form of the solution for $\tilde{V}_i$ in terms of $\tilde{N}_i$ and $\tilde{D}_i$ in Equation (20):

$$\tilde{V}_i = \frac{\bar{b}(P_{NV}\tilde{N}_i + d_f P_{DV}\tilde{D}_i)}{\bar{b}(P_{NV}\tilde{N}_i + d_f P_{DV}\tilde{D}_i) + \bar{m}K_R}.$$  

Clearly, the positive value of $\tilde{V}_i$ can be found by solving the quadratic equation $p(x) - q(x) = 0$ in a straightforward manner.

Therefore, we have shown that systems (5)–(7) have two non-negative steady states in the case that $R > 1$.

(i) The disease-free state: $\tilde{V}_i = 0$, $\tilde{N}_i = 0$, $\tilde{D}_i = 0$;

(ii) The endemic state: under condition (27), $\tilde{V}_i > 0$, $\tilde{N}_i > 0$, $\tilde{D}_i > 0$.

We now study the stability of the steady states. The Jacobian matrix of systems (18)–(20) is

$$J(K_R; \tilde{V}_i, \tilde{N}_i, \tilde{D}_i) = \begin{pmatrix} -\bar{b}(P_{NV}\tilde{N}_i + d_f P_{DV}\tilde{D}_i) - \bar{m} & \bar{b}P_{NV}(K_R - \tilde{V}_i) & \bar{b}d_f P_{DV}(K_R - \tilde{V}_i) \\ \alpha(N - \tilde{N}_i) & -\alpha \tilde{V}_i - \gamma N_i & 0 \\ \beta(D - \tilde{D}_i) & 0 & -\beta \tilde{V}_i - \gamma D_i \end{pmatrix}.$$  

For convenience, let us denote the entries of the Jacobian matrix by $(a_{ij})$, where $i, j = 1, 2, 3$. Then, the diagonal entries $a_{ii}, i = 1, 2, 3$ are all negative, and the nonzero nondiagonal entries are all positive. The characteristic equation for the eigenvalues $\lambda$ can be simplified to

$$(\lambda - a_{11})(\lambda - a_{22})(\lambda - a_{33}) = A\lambda - A_y,$$  

where $A = a_{12}a_{21} + a_{13}a_{31} > 0$ and $A_y = a_{12}a_{21}a_{33} + a_{13}a_{31}a_{22} < 0$. The cubic polynomial $Q(\lambda)$ on the left-hand side of Equation (28) has three negative roots $a_{11}, a_{22}$, and $a_{33}$. The linear equation $L(\lambda)$ on the right-hand side of Equation (28) has positive slope $A$ and one negative root $A_y/A$. Also, note that

$$\min\{a_{22}, a_{33}\} \leq \frac{A_y}{A} \leq \max\{a_{22}, a_{33}\} < 0.$$  

Therefore, the root of $L$ lies between two of the roots of the cubic $Q$, and so, there are two real negative solutions of Equation (28). Thus, the other root is also real, and it is negative if
\( L(0) < Q(0) \); it is positive if \( L(0) > Q(0) \); and, it is equal to zero if \( L(0) = Q(0) \). Thus, a steady state is stable and attracting if

\[
\mathcal{R} = \frac{L(0)}{Q(0)} = \frac{A_y}{a_{11}a_{22}a_{33}} < 1;
\]

it is stable if \( \mathcal{R} = 1 \); and, it is unstable if \( \mathcal{R} > 1 \). It is not clear if \( \mathcal{R} \) has any biological meaning.

In (i), the disease-free steady state, we have that \( A_y = -\Theta KR \bar{b} \) and \( a_{11}a_{22}a_{33} = -\bar{d}_m \gamma_N \gamma_D \), so that \( \mathcal{R} = \mathcal{R}_0 \). So, inequality (29) gives that the disease-free steady state is stable and attracting under the condition that \( \mathcal{R}_0 < 1 \).

When this condition holds, there is no positive endemic solution anyway, because inequality (27) is not satisfied. Therefore, when the endemic steady-state solution exists, which is when Equation (27) is satisfied, we have that Equation (29) is not satisfied, so that the disease-free solution is unstable.

We now investigate the stability of (ii), the unique positive endemic steady-state solution, which exists when inequality (27) is satisfied. In this case, we must have that \( \mathcal{R} < 1 \) which is equivalent to

\[
\bar{b}(K_R - \bar{V}_i) \frac{\alpha P_{NV} \bar{N} (\beta \bar{V}_i + \gamma_D)}{\bar{\Gamma} (\alpha \bar{V}_i + \gamma_N) (\beta \bar{V}_i + \gamma_D)} < 1,
\]

where

\[
\bar{N} = N - N_i \\
\bar{D} = D - D_i \\
\bar{\Gamma} = \bar{b}(P_{NV} \bar{N}_i + d_l P_{DV} \bar{D}_i) + \bar{d}_m,
\]

and \( \bar{N}, \bar{D}, \bar{\Gamma} > 0 \), in this case by Equation (21). Now, we show that inequality (30) is satisfied at our positive endemic steady state. Using the definitions in Equations (23)–(24), the term on the left-hand side of inequality (30) is strictly less than

\[
\frac{\bar{b}(K_R - \bar{V}_i) \alpha P_{NV} \bar{N} (\beta \bar{V}_i + \gamma_D) + d_i P_{DV} \beta D (\alpha \bar{V}_i + \gamma_N)}{\bar{d}_m (\alpha \bar{V}_i + \gamma_N) (\beta \bar{V}_i + \gamma_D)} = \frac{q(\bar{V}_i)}{p(\bar{V}_i)} = 1,
\]

because \( \bar{D} < D \) and \( \bar{N} < N \), and \( \bar{\Gamma} > \bar{d}_m \). Therefore, we have proven that under condition (27), there exists a unique positive endemic solution, and it is stable and attracting.

We summarize the above results in the following theorem.

**Theorem 3.2** Let \( \bar{V} = K_R \) with \( R > 1 \) satisfying condition (1) in Theorem 3.1. Let \( \mathcal{R}_0 \) be defined in Equation (27). If \( \mathcal{R}_0 < 1 \), then the disease-free equilibrium is the only equilibrium, and it is stable and attracting. If \( \mathcal{R}_0 > 1 \), then the disease-free equilibrium is unstable and there exists a unique positive endemic equilibrium \( (\bar{V}_i, \bar{N}_i, \bar{D}_i) \) that is stable and attracting.

We now apply the theoretical results to the steady states of the baseline case simulation. The parameters used in the system are average values of those in Table 1. The eigenvalues of the Jacobian matrix are

\[
\lambda_1 = -0.64 \times 10^{-4}, \quad \lambda_2 = -0.38 \times 10^{-3}, \quad \lambda_3 = -0.47 \times 10^{-2}.
\]

We conclude that the endemic equilibrium, given in Section 4, is stable and attracting. Here, \( \mathcal{R}_0 \approx 2.09 \).
Table 1. The model parameters, baseline simulation values, and the sources.

| Parameter | Definition | Baseline simulation value | Source |
|-----------|------------|---------------------------|--------|
| $V$       | Total number of vectors (vectors/village) | $V(0) = 23,000$ | This study$^a$ |
| $N$       | Total number of humans (humans/village) | 400 | This study$^a$ |
| $D$       | Total number of domestic dogs (dogs/village) | 100 | This study$^a$ |
| $C$       | Total number of chickens (chickens/village) | 100 | This study$^a$ |
| $H$       | Total number of houses (houses/village) | 100 | This study$^a$ |
| $V_i$     | Infected domestic triatomines (vectors/village) | $V_i(0) = 5,000$ | This study$^a$ |
| $N_i$     | Number of infected humans (humans/village) | $N_i(0) = 45$ | This study$^a$ |
| $D_i$     | Number of infected dogs (dogs/village) | $D_i(0) = 35$ | This study$^a$ |
| $V_{min}$ | Minimum number of vectors (vectors/village) | 2000 | This study$^a$ |
| $d_h$     | Egg hatching rate (1/day) | $\frac{11}{2 \cdot 360} \cdot 20 \cdot 0.83 \cdot b(t) \cdot b_{supply}$ | Figure 1, Castanera et al. [3] Gorla and Schofield [10] |
| $d_m$     | Death rate of vectors (1/day) | Seasonal piecewise linear | Estimation from Castanera et al. [3], Figure 1 |
| $d_k$     | Death rate of vectors (for $V \geq K$) (1/day) | 0.005 | This study$^a$ |
| $\tau$    | The delay factor (days) | 20 | Estimate from Castanera et al. [3] |
| $r(t)$    | The spraying rate (1/day) | Equation (2) | This study$^a$, Ramsey et al. [15] |
| $b(t)$    | Vector biting rate (bites/(day · (human factor) · (vector))) | Seasonal piecewise linear | Estimation from Castanera et al. [3] Catalá [4], Figure 1 |
| $P_{NV}$  | Human to vector infection probability (per bite) | 0.03 | Cohen and Gurtler [8] |
| $P_{DV}$  | Dog to vector infection probability (per bite) | 0.49 | Cohen and Gurtler [8] |
| $P_{VN}$  | Vector to human infection probability (per bite) | 0.00008 | Estimate from Cohen and Gurtler [8] |
| $P_{VD}$  | Vector to dog infection probability (per bite) | 0.001 | Estimate from Cohen and Gurtler [8] Rabinovich et al. [14] |
| $d_f$     | Human factor of one dog | 2.45 | Gurtler et al. [11] |
| $c_f$     | Human factor of one chicken | 4.8 | Gurtler et al. [11] |
| $\gamma_{Ni}$ | Mortality rate of infected humans (1/day) | $0.7 \cdot \frac{2 \ln 2}{76.12 \cdot 365} + 0.3 \cdot \frac{\ln 2}{25 \cdot 365}$ | Estimate from Central Intelligence Agency [5] Rassi et al. [16] |
| $\gamma_{Di}$ | Mortality rate of infected dogs (1/day) | $\frac{\ln 2}{4 \cdot 365}$ | Estimate 8 years |
| $K$       | Carrying capacity per village | 50,000 | This study$^a$ |
| $b_{supply}$ | Blood meal supply | $N + d_1 D + c_1 C$ | This study$^a$ |
| $d_1$     | First day of fall (day of year) | 0 | 20 March |
| $d_2$     | First day of winter (day of year) | 91.25 | 21 June |
| $d_3$     | First day of spring (day of year) | 182.5 | 22 September |
| $d_4$     | First day of summer (day of year) | 273.75 | 21 December |

$^a$See Section 4.
4. Simulation results

In this section, we use numerical simulations to study the effects of interruptions in the annual spraying schedule on the disease dynamics. The results of simulations without interruptions in annual spraying schedules can be found in [6,21].

Chagas disease is largely spread over rural areas that may be difficult to reach, and annual insecticide spraying can be relatively costly. Moreover, some of the regions have unstable governments or may become inaccessible for natural or other reasons. Therefore, annual spraying schedules could become interrupted. For example, a village could possibly be skipped some years. In order to understand the consequences of this scenario, we used our model to investigate the effects of interruptions in the annual spraying schedule. All simulations are shown for 100 years. We first simulated our model using the baseline parameters with 30 years of consecutive annual spraying, from year 51 until year 80 (Section 4.1). In Section 4.2, the spraying schedule is interrupted every third year. More specifically, spraying takes place on years 51 and 52 and is skipped on year 53, then it is done on years 54 and 55 and skipped on year 56, etc. The results of such spraying schedule interruptions in the baseline case (with four humans, one dog, and one chicken in each house in the village) are compared with the case in which a village has a larger blood meal supply, namely two dogs and five chickens per house, with all the other parameters set to the baseline values.

The code for the numerical simulations uses the Adams–Bashforth fourth-order method and is written in gfortran. Other standard convergent numerical methods were also used for the sake of comparison, and all of them matched our results. Moreover, our results were reproducible for simulations of 1000 years. For the delay differential equation, Theorem 6.2.1 in [2, p. 156] guarantees the correctness of the numerical scheme. The simulations were run on Cent OSX with an Intel Core 2 Duo T7500 processor (2.20 GHz). A typical run of 100 years took less than 20 s. The figures were generated with Tecplot.

4.1. Baseline simulation

The simulation results for a representative village of 100 houses, each with four humans, one dog, and one chicken, are shown in Figure 2. This is the baseline case with insecticide spraying (without interruptions). The values of the parameters are given in Table 1, which, in part, can be found in [21]. It is listed here for convenience. The vector hatching rate coefficient $d_h(t)$ in the baseline case and the vector mortality rate coefficient $d_m(t)$ as well as the biting coefficient $b(t)$ are shown in Figure 1 over a 1-year period. The biting function $b(t)$ is assumed to be piecewise linear in time and has the units of bites per day per human factor per vector. It is presented in its simplest form, but is derived using estimates from [3] for the baseline simulation case and assuming that the number of bites per vector per day is directly proportional to the blood meal supply. It is depicted in Figure 1.

The seasonal behaviour is reflected in the annual oscillations of each population. Insecticide spraying begins in year 51 and is applied for 30 consecutive years, until year 80, when it stops.

The endemic steady-state values in the baseline case, studied in Section 3.2, using average values of the coefficients given in Table 1 and with $r = 0$ are

$$\bar{V} = 23,350, \quad \bar{V}_i = 5,540, \quad \bar{N}_i = 57, \quad \bar{D}_i = 38.$$

Before spraying begins, the graphs in Figure 2 depict stable population oscillations around the endemic steady-state values. Once spraying begins, in the spring in year 51, there is a considerable drop in the number of total vectors and, therefore, in the number of infected vectors. The vector population does not reach zero, because the model assumes that there is an irreducible vector
population, of $V_{\text{min}} = 20$ per house, living in the deep cracks (see [21] for details). The model predicts that annual spraying with insecticides causes a small decrease in infected humans and a rapid decrease in infected dogs. This reflects the difference in the life expectancy of infected humans and dogs.
A main observation from these results is that when spraying ceases, it takes less than 10 years for the vector population to get back to its prespraying levels, while it takes much longer for the infected vectors to reach that level. In all cases, the populations grow to their stable baseline oscillations over time. It was shown in [21] that the time period required for the populations to grow back to their original stable oscillations after spraying ceases is reduced when the blood meal supply is larger than that in the baseline case.

4.2. Interrupted spraying schedules and blood meal supply

We now study two cases when the annual schedule for insecticide spraying is interrupted. We assume that spraying is skipped every third year; that is, in years 53, 56, etc., until year 80 when spraying is stopped completely. We consider: (i) the baseline case and (ii) the case with two dogs and five chickens per house, with all other parameters set to the baseline case values.

The simulation results of case (i) with baseline parameters and interrupted spraying are depicted in Figure 3. During the interrupted spraying period, the total vector population oscillates with approximately a 3.5-fold increase from the minimum to the maximum number of vectors. Moreover, in a period of 10 consecutive years without spraying (years 80–89), it returns to its prespraying level. The decline in the infected vectors is more pronounced, the decline continues and the recovery after spraying stops is slow. The decline in infected humans is slow, while the number of infected dogs almost reaches zero.

Figure 3. Baseline simulations with interrupted spraying.
In Figure 3, the baseline case with interruptions in the spraying schedule are not much different from the consecutive annual spraying case. The recovery of the vectors when spraying ceases is similar to the uninterrupted case.

We now turn to the simulation results in case (ii) which are depicted in Figure 4, and a close-up view of the vector population is depicted in Figure 5. As shown in Figure 5, the model is able to capture an overshoot above the carrying capacity in the vector population. The overshoot is captured because of the delay in the vector equation. Such an overshoot cannot occur in a model without delay. Indeed, the uniqueness of the solution for the problem without a delay prevents the solution from becoming larger than $K$. Some numerical experiments indicate that the overshoot is important when the blood meal supply is large. The parameter $d_k$ controls how high the vector population can go over the carrying capacity. For clarity, we point out that the baseline case did not exhibit such behaviour, because the blood meal supply did not allow the vector population to grow beyond the carrying capacity.

Notice that in Figure 4, the number of vectors oscillates considerably. In each year when spraying is skipped, the total vector population peaks back into the range of its prespraying oscillation values. Therefore, the skipped spraying years have a dramatic effect on the total vector population in that the vectors recover immediately. However, the peaks seen in the infected vector population during the skipped spraying years decrease over time. But, when spraying ceases, the infected vector population quickly recovers back to its original oscillation values, reaching its stable oscillation values in approximately 5 years. A detailed view of the effects of interruptions
in spraying schedule on the infected vector population is shown in Figure 6. The infected dog population responds to this increase in the infected vector population with a recovery back to its prespraying values within approximately 7 years, while the infected human population continues towards its original prespraying oscillation values throughout the simulation time. Therefore, in case (ii) which has a much more realistic blood meal supply, the model predicts that interruptions in spraying schedules can have a profound effect on disease outcome.

5. Discussion

The paper presents a delayed logistic-type model for the dynamics of Chagas disease that consists of four nonlinear differential equations for the vector population and the populations of infected
vectors, infected humans, and infected domestic animals. The dynamics of Chagas disease are complicated and depend on many factors, and indeed, the model contains many parameters. Since the model has not been validated, it should be used only to study the qualitative dynamics of the disease. In particular, it may be useful in gaining a deeper understanding of spraying strategies, to help better control the disease.

The steady-state analysis of the model with constant coefficients and no spraying is presented and simulations of the solutions when insecticide spraying schedules are interrupted are depicted. Such interruptions could have dramatic effects on the disease outcome, especially when a large blood meal supply is present in the village houses.

The steady-state analysis in the case of constant coefficients and no spraying in Section 3 shows that there are two basic stability numbers $R$ and $R_0$. The first number controls the stability of the vector-free state. In particular, when $R > 1$ a nonzero stable and attracting steady state exists for the total vector population, while the vector-free state becomes unstable. The second basic stability number, $R_0$ given in Equation (27), describes the stability of the disease-free and the endemic equilibrium points in the case that $R > 1$ and the steady state for the vectors is $V = K_R > 0$. It contains all of the parameters in the model. We have shown that whenever a positive endemic equilibrium exists, which is when Equation (27) holds, it is always stable and attracting while the disease-free state is unstable in that case. If a positive equilibrium does not exist, then the disease-free state is stable and attracting in all cases. In the baseline case, the endemic steady state is stable and attracting, since $R_0 > 1$, while the disease-free steady state is unstable.

The main goal of the numerical simulations in Section 4 is to study the system dynamics when spraying schedules are interrupted. The results depend on the total blood meal supply in the houses in the village. The simulation results reveal that in the baseline case, if spraying is skipped every third year, the disease outcome is not much different from that if spraying was not skipped during those years. However, when the blood meal supply is larger (two dogs and five chickens per house), which seems more likely in some villages, interruptions in the spraying schedules cause dramatic changes in the disease outcome, making spraying during the other years almost irrelevant. This indicates that consistent spraying may be of considerable importance when the blood meal supply is large enough.

In addition to the model validation, there are a number of open issues that may be of interest. Here and in [6,21], the effects of the disease in the wildlife were not modelled. However, it is known that the existence of the disease in the wildlife makes its eradication unlikely. Therefore, the issue warrants further investigation. Moreover, it may be of interest to study the interaction of the disease in neighboring villages. It is also of interest to test insecticide resistance. Finally, an important issue for future study is the sensitivity analysis of the model to many parameters.

Acknowledgements

The authors would like to thank the reviewers for their comments, which helped to improve the manuscript. This research was partially supported by the NSF-REU Grant DMS 0649099.

References

[1] L.J.S. Allen, An Introduction to Mathematical Biology, Pearson Prentice-Hall, Upper Saddle River, NY, 2007.
[2] A. Bellen and M. Zennaro, Numerical Methods for Delay Differential Equations, Oxford Science Publications, Oxford, 2003.
[3] M.B. Castanera, J.P. Aparicio, and R.E. Gürtler, A stage-structured stochastic model of the population dynamics of Triatoma infestans, the main vector of Chagas disease, Ecol. Model. 162 (2003), pp. 33–53.
[4] S. Catalá, The biting rate of Triatoma infestans in Argentina, Med. Vet. Entomol. 5(3) (1991), pp. 325–333.
[5] Central Intelligence, The World Factbook (2009). Available at https://www.cia.gov/library/publications/the-world-factbook/geos/ar.html.
[6] M. Clauson, A. Harrison, L. Shuman, M. Shillor, and A.M. Spagnuolo, *Analysis of the steady states of a mathematical model for Chagas disease*, (2010), submitted for publication.

[7] D.J. Coffield and A.M. Spagnuolo, *Stability of steady states of vector equations in models for Chagas disease*, submitted for publication, 2010.

[8] J.E. Cohen and R.E. Gürtler, *Modeling household transmission of American trypanosomiasis*, Science 293 (2001), pp. 684–688.

[9] N. Garg and V. Bhatia, *Current status and future prospects for a vaccine against American trypanosomiasis*, Expert Rev. Vaccines 4(6) (2005), pp. 867–880.

[10] D.E. Gorla and C.J. Schofield, *Analysis of egg mortality in experimental populations of Triatoma infestans under natural climatic conditions in Argentina*, Bull. Soc. Vector Ecol. 10 (1985), pp. 107–117.

[11] R.E. Gürtler, M.C. Cecere, M.A. Lauricella, M.V. Cardinal, U. Kitron, and J.E. Cohen, *Domestic dogs and cats as sources of Trypanosoma cruzi infection in rural northwestern Argentina*, Parasitology 134 (2007), pp. 69–82.

[12] H.W. Hethcote, *The mathematics of infectious disease*, SIAM Rev. 42(4) (2000), pp. 599–653.

[13] Organizacion Panamericana de la Salud, Estimacion cuantitativa de la enfermedad de Chagas en las Americas, Organizacion Panamericana de la Salud, Montevideo, Uruguay. PAHO Publishing, Washington, DC, 2006, pp. 1–28 (OPS/HDM/CD/425-06).

[14] J. Rabinovich, N. Schweigmann, V. Yohai, and C. Wisnivesky-Colli, *Probability of Trypanosoma cruzi transmission by Triatoma infestans (Hemiptera: Reduviidae) to the opossum Didelphis albiventris (Marsupialia: Didelphidae)*, Am. J. Trop. Med. Hyg. 65(2) (2001), pp. 125–130.

[15] J.M. Ramsey, A. Cruz-Celis, L. Salgado, L. Espinosa, R. Ordonez, R. Lopez, and C.J. Schofield, *Efficacy of pyrethroid insecticides against domestic and peridomestic populations of Triatoma pallidipennis and Triatoma barberi Reduviidae: Triatominae vectors of Chagas disease in Mexico*, J. Med. Entomol. 40 (2003), pp. 912–920.

[16] A. Rassi Jr, A. Rassi, and J.A. Marin-Neto, *Chagas heart disease: Pathophysiologic mechanisms, prognostic factors and risk stratification*, Mem. Inst. Oswaldo Cruz 104(Suppl. 1) (2009), pp. 152–158.

[17] C.J. Rodrigues and S.L. Castro, *A critical review on Chagas disease chemotherapy*, Mem. Inst. Oswaldo Cruz 97(1) (2002), pp. 3–24.

[18] G.A. Schmunis, *Prevention of transfusional Trypanosoma cruzi infection in Latin America*, Mem. Inst. Oswaldo Cruz 94(Suppl. 1) (1999), pp. 93–101.

[19] C.J. Schofield, J. Jannin, and R. Salvatella, *The future of Chagas disease control*, Trends Parasitol. 22 (2006), pp. 583–588.

[20] A. Silveira and M. Vinhaes, *Elimination of vector-borne transmission of Chagas disease*, Mem. Inst. Oswaldo Cruz 94(Suppl. 1) (1999), pp. 405–411.

[21] A.M. Spagnuolo, M. Shillor, and G.A. Stryker, *A model for Chagas disease with controlled spraying*, J. Biol. Dyn. 5 (2011), pp. 299–317.

[22] A.M. Spagnuolo, M. Shillor, and G.A. Stryker, *A model for Chagas disease with controlled spraying computer simulation package* (2010). Available at http://euler.oakland.edu/chagas/.

[23] H.R. Thieme, *Mathematics in Population Biology*, Princeton University Press, Princeton, NJ, 2003.