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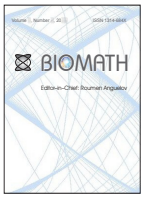

A Model for the Transmission of Chagas Disease with Random Inputs

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***Abstract*—In this work we study and simulate a model for the dynamics of Chagas disease that includes randomness in some of the system coefficients. The disease, caused by the parasite *T. cruzi*, affects 8-10 million humans throughout rural areas in the Americas. A basic model for the disease dynamics, which consists of four nonlinear differential equations for the populations of the vectors, infected vectors, humans, and domestic animals was developed in Spagnuolo et al., (2009). Here, the model is modified by using a logistic term with two delays for vector population growth and extended to include random coefficients, reflecting the uncertainty in the determination of their values. The existence of the unique local solution for the model as a stochastic process is established. Numerical simulations are performed to conduct sensitivity analysis on seven of the model parameters. Variations in two of the model parameters lead to significant changes in the number of infected humans and infected domestic mammals, indicating that these parameters need to be accurately obtained.**

***Keywords*-Chagas disease, random coefficient, epidemic dynamics, nonlinear dynamical system, sensitivity analysis**

I. 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 many of the 8-10 million individuals infected [2], [20], [29]. While the rate of early death is quite variable between countries, the average proportion of infected people that show cardiopathy is approximately 23%, [20]. Vectorial transmission of *T. cruzi* takes place through various species of insects of the subfamily *Triatominae* (family *Reduviidae*) of which *Triatoma infestans* is one of the dominant vectorial species. The control of Chagas disease transmission remains largely based on vector population control by spraying with insecticides, and on blood-bank screening [13], [24], [27], [30]. This has proven effective in limiting the spread of the disease, and in some cases eliminating the domestic insects. However, there are parts of Latin America where the disease seems to be uncontrollable, such as the Bolivian

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Chaco region [26]. Moreover, there is growing concern in the USA, Europe, and other parts of the world with the possible spread of the disease brought by infected immigrants [28], [34].

Since insecticide spraying is essential in controlling the disease, there is considerable interest in optimizing the spraying schedules so as to make them as effective as possible in decreasing the domestic insect population. A basic model for the disease transmission dynamics that includes the effects of insecticide spraying was constructed and investigated in [31], and related issues were studied in [7], [9], [32]. Several applied Chagas disease transmission models have been developed, such as a deterministic model [11], a stochastic Markovian model [35], as well as a specific mathematical model to optimize spatio-temporal strategies to control the Chagas disease vectors [18]. Other models for Chagas disease can be found in [1], [12], [21] and the references therein.

The basic model in [31] consists of a delay-differential equation for the vector population and three nonlinear differential equations for the growth of the total numbers of infected vectors, humans, and domestic mammals. Here, we build on the research in [32], where a modified model with a delayed logistic term in the vector equation was presented, analyzed, and issues related to spraying schedules were numerically simulated. In this work we also modify the delay-differential equation for the vector population growth by using two delays. Indeed, we make a distinction between the development time delay and the time lag for the population to sense the carrying capacity of the habitat.

In view of the considerable difficulties in measuring or estimating many of the model parameters, we conduct sensitivity analysis on seven of them. The following seven parameters are chosen: (i) the vector mortality rate due to insecticide spraying, (ii) the day of the year when insecticide spraying is applied, (iii) the vector natural mortality rate, (iv) the vector-to-human parasite transmission probability, (v) the vector's preference for biting people or animals and the number of animals, (vi) the vector egg development time, and (vii) the time lag in vector population sensing or responding to the carrying capacity. The first five are largely unknown and seem to affect the prevalence of infection in humans and domestic mammals. The latter two are chosen because they appear as delays in the equation for the vector population and could fundamentally alter the vector dynamics. The sensitivity analysis identifies which of these seven parameters substantially change infection outcomes and thus need to be estimated with high precision.

To perform the sensitivity analysis, for each of the seven parameters we construct the appropriate probability space and use a uniform random distribution. Each parameter is then varied in a thousand different computer simulations, while holding the other parameters at prescribed (baseline) values, see Table I. Interactions between the parameters are not considered in this study. The purpose here is to introduce randomness and start the sensitivity analysis of the model. The issue of the combined randomness, because of possible interaction among the coefficients, will be studied in depth in the future following the sensitivity analysis approach in [25]. The envelopes of the solutions in each case are depicted in Section V.

The existence of the unique local solution of the delay-differential equation for the total vector population is stated in Theorem 1. The existence and uniqueness of the local solution of the system of infected populations as a stochastic process is shown in Theorem 4. It follows from a more general result for systems of differential equations, Theorem 2, that is established first.

The paper is arranged as follows. Section II presents the model, following [31], [32]. The sensitivity analysis in the seven chosen parameters is described in Section III. The local existence of the unique solution of the model for each random choice of the parameters is established in Section IV. A numerical algorithm for the model was written in Mathematica and the results of simulations and their discussion are given in Section V. The conclusions of the paper are in Section VI, where

some unresolved questions are also identified.

II. The Model

We use an enhancement of the model for the dynamics of Chagas disease constructed in [32]. Information on the pertinent biological processes involved in the spread of the disease can be found in [11], a comprehensive summary in [19], and full details of the model and the assumptions that underlie it in [31]. The model represents the overall disease transmission dynamics, in a representative village, of the total populations of vectors (triatomines) (V), humans (N), domestic mammals– 'dogs,' (D), and chickens (C). The latter act as sources of blood-meals, but cannot become infected. For the sake of simplicity, the number of humans N, dogs D, and chickens C in the village are considered constant through time. However, C is allowed to be a different constant in different simulations, as specified below. For V, N, and D, we denote by subscript i the number of infected individuals, and the non-infected populations are assumed to be susceptible.

The *Mathematical model for Chagas disease* (a modified version of the models in [31], [32]) is as follows:

Find the functions $\{V, V_i, N_i, D_i\} : [0, T] \to \mathbb{R}^4_+$ such that:

$$\frac{dV}{dt} = r(t-\tau_1)V(t-\tau_1)\left(1-\frac{V(t-\tau_2)}{K}\right) - d_m V - d_{sp}(V-V_{min})_+, \quad \text{(II.1)}$$

$$\frac{dV_i}{dt} = b(V-V_i)\left(p_{NV}N_i + p_{DV}d_f D_i\right) - d_m V_i - d_{sp}\left(1-\frac{V_{min}}{V}\right)_+ V_i, \quad \text{(II.2)}$$

$$\frac{dN_i}{dt} = \alpha_N\left(N-N_i\right)V_i - \gamma_{N_i}N_i, \quad \text{(II.3)}$$

$$\frac{dD_i}{dt} = \alpha_D(D-D_i)V_i - \gamma_{D_i}D_i, \quad \text{(II.4)}$$

$$V_i(0) = V_{i0},\ N_i(0) = N_{i0},\ D_i(0) = D_{i0}, \quad \text{(II.5)}$$

$$V(t) = V_0(t), \qquad -\tau \le t \le 0. \quad \text{(II.6)}$$

Here, $\mathbb{R}^4_+ = \{\boldsymbol{x} = (x_1, x_2, x_3, x_4) \in \mathbb{R}^4 : 0 \le x_j,\ j = 1, \ldots, 4\}$, $\tau = \max\{\tau_1, \tau_2\}$, and we omitted the dependence of the functions on t, except in the terms with delays.

We note a change of notation from that used in [31], [32] in order to conform to the usual notation in the field of population dynamics: we use d_{sp} as the death rate due to insecticide spraying.

Equation (II.1) describes the daily rate of change of the total vector population. We use, following [33], the delayed logistic term in the growth rate of vectors to account for the natural vector carrying capacity K that effectively limits the number of domestic vectors that can live in the village (equivalently, in each house). The growth rate depends on the following: the natural death rate of triatomines, $d_m = d_m(t)$; the fecundity rate, $r = r(t)$, which is affected by a time lag (τ_1) of the hatching of eggs and the time lag (τ_2) in the population reacting to the carrying capacity K (see [33]); and the mortality rate due to insecticide spraying, $d_{sp} = d_{sp}(t)$. We note that here we use two delays or time lags, while in the previous works we used only one.

The model assumes that a subpopulation of insects V_{min} survives spraying [14], [15], and the mortality due to spraying is modeled by the term $d_{sp}(t)(V(t) - V_{min})_+$, where $(f)_+$ denotes the positive part of f, $(f)_-$ represents the negative part, and $f = (f)_+ - (f)_-$. Including the positive part guarantees that the spray does not kill all the vectors in a house.

Equation (II.1) is a delay-differential equation with two delays and is not coupled to the other equations, so it can be solved independently.

The coupled system of equations (II.2)-(II.4) for $V_i(t), N_i(t)$, and $D_i(t)$, $(0 < t \le T)$ has to be solved simultaneously. Here, p_{NV} and p_{DV} denote the probabilities of a vector becoming infected by one bite on an infected human or an infected dog, respectively. The mortality rates of infected humans and infected dogs are denoted by γ_{N_i} and γ_{D_i}, respectively, while $N - N_i$ and $D - D_i$ are the susceptible human and dog populations, respectively. We let $\alpha_N = bp_{VN}$ and $\alpha_D =$

$bd_f p_{VD}$, be the infection rates of susceptible humans and susceptible dogs, respectively. Here, following [31], $b = b(t)$ is the insect biting rate, p_{VN} is the probability that a susceptible human becomes infected from one infected bite, p_{VD} is the probability that a susceptible dog becomes infected from one infected bite, and d_f is the biting preference factor used to represent the vectors' preference for dogs relative to humans. The vector preference for humans is set to 1 and $d_f > 1$ since *T. infestans* prefer to bite dogs, [16]. Similarly, c_f is the vector preference factor for biting chickens.

The initial populations, when the process starts (conveniently chosen as $t = 0$), are given in (II.5) and (II.6). We next add randomness to the model.

III. The model with randomness

Our main interest is to study the effects of variability in seven of the model parameters. Therefore, we apply sensitivity analysis to the following parameters:

(i) The mortality rate due to insecticide spraying d_{sp}
(ii) The day insecticide spraying is applied t_1
(iii) The natural mortality rate d_m
(iv) The parasite transmission probability p_{VN}
(v) The weighted blood supply factor b_{supp}
(vi) The egg development time τ_1
(vii) The delay in responding to the carrying capacity τ_2

For the sake of completeness, we also simulate the case when the two delays are equal in order to compare to the simulations in [32] and to see the effects of two delays.

The sensitivity analysis is performed for each parameter separately, and we do not consider the possible interactions among the parameters.

To describe the use of randomness, we use a probability space $(\Omega, \mathcal{F}, P)$, where Ω is the sample space, $\mathcal{F}$ is a σ-algebra, and P is the probability function. In each case we let $\mathcal{F}$ be the usual Borel σ-algebra of open sets in Ω, and we choose P to be the uniform probability in each sample space.

We now describe each random parameter in turn, with its sample space, which we denote by Ω_j, where $j = i, ii, \ldots vii$ is the index of the case.

(i) The randomness in the vector death rate from spraying, $d_{sp}(t)$, can occur for many reasons, including the weather (wind, temperature), and different house structures, spraying equipment, and chemicals used. Although, as expected, when the spray is so effective that it kills all the vectors that come in contact with it, there is almost no sensitivity to $d_{sp}(t)$. However, when the death rate is much smaller, representing an insecticide that is not effective or a population of vectors that developed partial resistance to the insecticide, it is found that there is considerable variation in the solutions.

The death rate function without randomness is $d_{sp}(t) = d_{max}\overline{d}$, where $\overline{d}(t; t_1, t_2)$ ([10], [31], [32]) is

$$\overline{d}(t; t_1, t_2) = \begin{cases} 2.5415(e^{-\lambda(t-t_1)^2} - e^{-1/2}) & \\ & \text{if } t_1 \le t \le t_2, \\ 0 & \text{otherwise.} \end{cases}$$

Here, since we choose the first day of the year to be the first day of Fall, the first day of spraying is chosen as $t_1 = 212.5$, which is the 30.5th day of Spring, $t_2 = 303.75$ is the last day for which the spray is still effective, as its potency lasted about 91.25 days, and $\lambda = 6 \cdot 10^{-5}$. Clearly, in different locations the active duration of different insecticides will be different. In the baseline case $d_{max} = 1$, which essentially represents death of the vector upon contact with the insecticide. To study the sensitivity of the model to d_{sp}, we choose $d_{max} = 0.1$, which represents a weaker insecticide or the acquired resistance of the vectors to the spray chemical. We choose the sample space as

$$\Omega_i = (-0.1,\ 0.2). \tag{III.1}$$

Then, the random death rate due to spraying is

$$d_{sp}(t, \omega) = (d_{max} + \omega)\overline{d}(t; t_1, t_2), \tag{III.2}$$

and the choice of Ω_i guarantees that $d_{sp}(t, \omega) > 0$, for all $t \in [0, T]$.

(ii) The first day of spraying t_1 in $\overline{d}(t; t_1, t_2)$ is chosen as a random parameter since the spraying

in different villages in a region is administered on different days. In some locations the spraying is done in Spring, so we choose t_1 to be in the Spring. To make the simulations more realistic, we allow t_1 to be different each year, out of $\widehat{N}$ years, and choose $\overline{t}_1 = 212.5$ to be the day in the middle of Spring and then $\overline{t}_2 = 303.75$. The sample space is chosen to be

$$\Omega_{ii} = (-35.5,\ 35.5)^{\widehat{N}}. \tag{III.3}$$

Then, each $\omega \in \Omega_{ii}$ is an $\widehat{N}$-tuple $\omega = (\omega_1, \omega_2, \ldots, \omega_{\widehat{N}})$, and the starting day of spraying in year κ is $t_{1\kappa} = \overline{t}_1 + \omega_\kappa$. Thus, the death rate due to spraying is $d_{sp}(t; \overline{t}_1 + \omega_\kappa, \overline{t}_2 + \omega_\kappa)$, $\kappa = 1, \ldots, \widehat{N}$. The choice of Ω_{ii} guarantees that the first day of spraying $t_{1\kappa}$ in each year is in Spring.

(iii) The inclusion of randomness in the triatomine natural mortality rate $d_m(t)$ is mainly motivated by the lack of basic field data. We denote the natural death rate function without randomness by $\overline{d}_m(t)$, and assume it is periodic with a period of one year. The following seasonal death rate function, taken from [10] where more details can be found, is used in this work:

$$\overline{d}_m(t) = \begin{cases} 0.0025 \ + \ \frac{(0.0075-0.0025)t}{136} \\ \qquad \text{if } \ 0 \le \text{Mod}(t, 365) \le 136, \\ 0.0075 \ + \ \frac{(0.0001-0.0075)(t-136)}{(222-136)} \\ \qquad \text{if } \ 136 \le \text{Mod}(t, 365) \le 222, \\ 0.0001 \ + \ \frac{(0.0025-0.0001)(t-222)}{(365-222)} \\ \qquad \text{if } \ 222 \le \text{Mod}(t, 365) < 365. \end{cases} \tag{III.4}$$

The sample space is chosen as

$$\Omega_{iii} = (-0.0001, 0.003). \tag{III.5}$$

The natural death rate with randomness for $\omega \in \Omega_{iii}$ is given by

$$d_m(t, \omega) = \overline{d}_m(t) + \omega, \tag{III.6}$$

and the choice of Ω_{iii} guarantees that $d_m(t, \omega) > 0$, for all $t \in [0, T]$.

(iv) The randomness in the disease transmission probability p_{VN} arises from lack of direct field data, however, indirect estimates can be found in [22]. We denote the infection probability from an infected vector to a susceptible person without randomness by $\overline{p}_{VN}$, and assume that it is constant. In [31] the baseline value $\overline{p}_{VN} = 8 \cdot 10^{-5}$ was used, but the estimates in [22] indicate that the range is $9 \cdot 10^{-4} - 1.2 \cdot 10^{-3}$ is more realistic. Therefore, we set $\overline{p}_{VN} = 0.001$ and choose the sample space as

$$\Omega_{iv} = (-0.0001,\ 0.0002). \tag{III.7}$$

The combined biting and infection rate with randomness is given by

$$\alpha_N(t, \omega) = b(t)(\overline{p}_{VN} + \omega), \tag{III.8}$$

where $\omega \in \Omega_{iv}$, b is the biting function, described in Sect. 5. The choice of Ω_{iv} guarantees that $\alpha_N(t, \omega) > 0$, for all $t \in [0, T]$.

(v) The randomness in the weighted blood supply b_{supp} arises from the fact that the numbers of chickens and dogs per house vary considerably. The weighted blood supply is given by $b_{supp} = N + d_f D + c_f C$, and since N and D are constants and $d_f = 7c_f$ ([16]), the variability in the blood supply can be described by changing C and c_f. In the baseline simulations $C = 1110$ (15 chickens per house) and $c_f = 0.35$. To introduce randomness, we let the number of chickens per house be between 10 and 20 so that $C \in (740, 1480)$ and allow for variability in the vector's preference for chickens by letting $c_f \in (0.15, 0.5)$. We choose the sample space as

$$\Omega_v = (740, 1480) \times (0.15, 0.5), \tag{III.9}$$

and then for $(C, c_f) = \omega \in \Omega_v$, the random blood supply is given by

$$b_{supp}(\omega) = N + 7c_f D + c_f C. \tag{III.10}$$

The weighted blood supply affects the model by influencing the biting rate (and thus, the growth rate) of the vectors. As the blood supply increases,

more blood meals are available, and the vectors bite more frequently. The full details of how b_{supp} appears in the model are found Section V.

(vi) The randomness in the development time τ_1 is due to the natural variation in the egg laying and hatching times. We denote the time lag in hatching without randomness by $\overline{\tau_1}$, assumed to be fixed, and in the simulations we used $\overline{\tau_1} = 20$ days, [3]. Allowing for a different random development time each computer run leads us to choose the sample space as

$$\Omega_{vi} = (-10,\, 10). \tag{III.11}$$

The random development time lag τ_1 is given by

$$\tau_1(\omega) = \overline{\tau_1} + \omega, \tag{III.12}$$

where $\omega \in \Omega_{vi}$, and the choice of Ω_{vi} guarantees that $10 < \tau_1(\omega) < 30$.

(vii) The randomness in τ_2, the delay in responding to the carrying capacity, is due to a complicated mixture of behavior and physiology that results in the vectors not realizing they are reaching the limit of their environment. This delay is also influenced by natural environmental phenomena such as the weather. We denote the time lag without randomness by $\overline{\tau_2}$, and in the simulations we used $\overline{\tau_2} = 190$ days. We choose the sample space to be

$$\Omega_{vii} = (-95,\, 95) \tag{III.13}$$

and use the same random number in each run of 50 years. Then, the random delay τ_2 is given by

$$\tau_2(\omega) = \overline{\tau_2} + \omega, \tag{III.14}$$

for $\omega \in \Omega_{vii}$, and the choice of Ω_{vii} guarantees that $100 < \tau_2(\omega) < 270$ days.

In each one of the cases (i)–(vii), for each $\omega \in \Omega_l,\ l = i, \ldots, vii$, we solve (II.1)–(II.6) with the relevant random coefficient.

The unique solvability of the system, for each $\omega \in \Omega_l,\ l = i, \ldots, vii$, is discussed in the next section, together with the stochastic aspects of the problem. Numerical simulations with randomness in the seven different parameters are presented in Section V.

IV. Existence and uniqueness

This section analyzes the system (II.1)–(II.6) with randomness, cases (i)–(vii), and establishes its unique local solvability.

As was noted above, the system consists of a delay-differential equation for the vectors, (II.1), that is not coupled to the other equations, and the coupled system (II.2)-(II.4) of ordinary differential equations. Therefore, we study them separately.

We let the product probability space be

$$\Omega = \Omega_i \times \cdots \times \Omega_{vii},$$

and denote by $\mathcal{B}([0,T])$ the Borel sets on $[0,T]$ and by $\mathcal{F}$ the σ-algebra related to the probability space Ω. We use the uniform probability on Ω. Throughout the rest of this section, we consider the system (II.1)–(II.6) on $[0,T]$, where $T \leq t_*$ and

$$t_* = \inf\{t > 0 : V(t,\omega) = 0\}. \tag{IV.1}$$

We have the following result, where the assumptions on the problem data are more general than those above.

Theorem 1: Assume that $r(t), \overline{d}_m(t)$ and $d_{sp}(t)$, are nonnegative, bounded, and continuous on $[0,\infty)$, $V_0(t)$ is positive and continuous on $[-\tau,\, 0]$ with $V_0(t) < K$, and τ, d_{max}, K, and V_{min} are positive constants. Then, for each $\omega \in \Omega$ and each $0 < T \leq t_*$, the problem (II.1) and (II.6), in each one of the cases (i)–(vii), has a unique solution $V(t,\omega)$. Moreover, the function

$$(t,\omega) \to V(t,\omega)$$

is product measurable with respect to the σ-algebra $\mathcal{B}([0,T]) \times \mathcal{F}$.

Proof: The existence of a solution follows from a standard construction on successive intervals of small length. The uniqueness follows in similar fashion by considering the difference of two solutions. The solution exists on $[0,T]$ as long as it is bounded, which we show in the Appendix. Also, in the Appendix we show that the solution satisfies the measurability condition when the data is bounded on $[0,T]$. ■

In general, the existence of a global solution of the vector equation with two delays depends on the parameters in a technically detailed manner. However, we point out that our numerical simulations, which use parameter values taken from field data, exhibit well-behaved global solutions. The conditions on the parameters that ensure a globally bounded positive solution will be addressed in a different work.

We turn to the solvability of the system (II.2)–(II.5) using the solution $V(t,\omega)$ from Theorem 1.

The existence and uniqueness of the solution to (II.2)–(II.5) is based on the following general result, where $(\Omega,\mathcal{F},P)$ is a probability space, X is a topological space and $\mathcal{B}(X)$ denotes the Borel sets of X. We note that this general result has merit in and of itself.

Theorem 2: Let $\boldsymbol{f}:\mathbb{R}^n\times[0,T]\times\Omega\to\mathbb{R}^n$ satisfy the following conditions:

1) $|\boldsymbol{f}|$ is uniformly bounded by a constant M.
2) $(\boldsymbol{x},t)\to\boldsymbol{f}(\boldsymbol{x},t,\omega)$ is continuous for each $\omega\in\Omega$.
3) $(\boldsymbol{x},t,\omega)\to\boldsymbol{f}(\boldsymbol{x},t,\omega)$ is $\mathcal{B}(\mathbb{R}^n)\times\mathcal{B}([0,T])\times\mathcal{F}$ measurable (product measurable).
4) $\boldsymbol{x}(0,\omega)=\boldsymbol{x}_0(\omega)$, where $\boldsymbol{x}_0\in\mathcal{F}$, is measurable.
5) For each $\omega\in\Omega$ there exists at most one solution to the problem

$$\boldsymbol{x}'=\boldsymbol{f}(\boldsymbol{x},t,\omega),\quad \boldsymbol{x}(0)=\boldsymbol{x}_0(\omega). \quad \text{(IV.2)}$$

If $\boldsymbol{x}(t,\omega)$ denotes a solution of the initial value problem $(IV.2)$, then it is the unique solution and the function

$$\omega\to\boldsymbol{x}(t,\omega)$$

is $\mathcal{F}$ measurable, and so $\boldsymbol{x}(t)$ is a stochastic or random process, where $\boldsymbol{x}(t)(\omega)\equiv\boldsymbol{x}(t,\omega)$.

Proof: We consider approximate problems used to obtain solutions via the Peano Theorem. To that end, we introduce the delay operator

$$D_h\boldsymbol{x}(t,\omega)\equiv\begin{cases}\boldsymbol{x}(t-h,\omega) & \text{if } t>h,\\ \boldsymbol{x}_0(\omega) & \text{if } t\le h,\end{cases}$$

and let

$$\boldsymbol{x}_h(t,\omega)\equiv\boldsymbol{x}_0(\omega)+\int_0^t\boldsymbol{f}(s,D_h\boldsymbol{x}_h(s,\omega),\omega)\,ds. \quad \text{(IV.3)}$$

Then the function $\boldsymbol{x}_h$ is $\mathcal{B}([0,T])\times\mathcal{F}$ measurable. Indeed, let $I_{[a,b]}$ be the indicator function of the interval $[a,b]$, i.e., $I_{[a,b]}(s)=1$ if $s\in[a,b]$ and $I_{[a,b]}(s)=0$ otherwise, then for $t\le h$,

$$\boldsymbol{x}_h(t,\omega)\equiv\boldsymbol{x}_0(\omega)+\int_0^T I_{[0,t]}(s)\,\boldsymbol{f}(s,\boldsymbol{x}_0(\omega),\omega)\,ds. \quad \text{(IV.4)}$$

Let now $\{s_i^m\}_{i=1}^{2^m}$ be a uniform partition of $[0,h]$ and consider the finite sum

$$\sum_{k=0}^{2^m-1}\boldsymbol{f}(s_k^m,\boldsymbol{x}_0(\omega))\,I_{[s_k^m\wedge t,s_{k+1}^m\wedge t)}(s),$$

where $s_{k+1}^m\wedge t\equiv min(s_{k+1}^m,t)$, which is an approximation of the integrand in (IV.4) that converges pointwise for each $(s,\omega)\in[0,T]\times\Omega$. Then, the integrals of these integrands satisfy

$$x_m(t,\omega)\equiv\sum_{k=0}^{2^m-1}f(s_k^m,x_0(\omega))\left(s_{k+1}^m\wedge t-s_k^m\wedge t\right)$$

and each function $\boldsymbol{x}_m(t,\omega)$ is measurable in $\mathcal{B}([0,T])\times\mathcal{F}$. By the dominated convergence theorem, and the boundedness of $\boldsymbol{f}$, it follows that $\boldsymbol{x}_h(t,\omega)$ in (IV.3) is the pointwise limit of the sequence of functions $\boldsymbol{x}_m$, which are product measurable and this shows that $I_{[0,h)}(t)\,\boldsymbol{x}_h(t,\omega)$ is also product measurable, and the function is continuous in t, for $0\le t<h$.

We now use the expression (IV.3) for $\boldsymbol{x}_h$ on the interval $[h,2h)$ and similar arguments and obtain that

$$(t,\omega)\to I_{[h,2h)}(t)\,\boldsymbol{x}_h(t,\omega)$$

is also product measurable. Continuing this step by step way over the intervals $[(k-1)h,kh]$, for

$1 \leq k \leq 2^m$, establishes that $(t,\omega) \to \boldsymbol{x}_h(t,\omega)$ is product measurable as claimed for $0 \leq t \leq T$.

Next, we pass to the limit $h_m \to 0$ and show that for each ω there exists a unique solution $t \to \boldsymbol{x}(t,\omega)$ to the problem

$$\boldsymbol{x}(t,\omega) = \boldsymbol{x}_0(\omega) + \int_0^t \boldsymbol{f}(s, \boldsymbol{x}(s,\omega))\, ds, \quad \text{(IV.5)}$$

that is the uniform limit of $\boldsymbol{x}_{h_m}(t,\omega)$ on $[0,T]$ as $m \to \infty$. The important observation here is that a single sequence $\{h_m\}$ works for all the ωs at once.

The functions $t \to \boldsymbol{x}_{h_m}(t,\omega)$ are equicontinuous and uniformly bounded, independently of h_m, and therefore, by the Arzela-Ascoli theorem there exists a further subsequence which converges uniformly on $[0,T]$ to a function $\boldsymbol{x}(t,\omega)$. Then, using the uniform continuity of $\boldsymbol{f}$ on a compact set including all values of $\boldsymbol{x}_{h_m}(t,\omega)$, we can pass to the limit in (IV.3) and obtain the existence of a solution to (IV.5). By assumption (*5*) this solution is unique and, therefore, the original sequence converges to this limit. Otherwise, there would exist a subsequence which does not converge to $\boldsymbol{x}(t,\omega)$ and then a further subsequence would converge to another solution which would contradict the uniqueness assumption. Since this does not depend on which ω is being considered, the existence and uniqueness part of the theorem follows.

Finally, it follows from the proof that $(t,\omega) \to \boldsymbol{x}(t,\omega)$ is $\mathcal{B}([0,T]) \times \mathcal{F}$ measurable and so $\boldsymbol{x}(t)$ is a stochastic process. ■

We note that by replacing $\boldsymbol{f}$ with a suitably truncated function, we obtain the following corollary.

Corollary 3: Let the assumptions of Theorem 2 hold, with the exception of (1) so that $\boldsymbol{f}$ is not necessarily uniformly bounded, but there exists a bound on all local solutions (IV.5). Then, the conclusions of Theorem 2 hold.

We apply the general result above to the system (II.2)–(II.5) with randomness. Since V is known on $[0,T]$, the other equations can be considered for a known V, which is product measurable. Also, as we show in the Appendix, V is uniformly bounded in ω on $[0,T]$.

Now, we observe that $0 \leq V_i < V$, $0 \leq N_i < N$, and $0 \leq D_i < D$. Thus, the equations for V_i, N_i and D_i satisfy the assumptions of Corollary 3 and we obtain the following existence and uniqueness theorem.

Theorem 4: Let $V(t,\omega)$ denote the unique solution in Theorem 1. Then, under the above assumptions, for each $0 < T \leq t_*$, there exists a unique solution $(V_i(t,\omega), N_i(t,\omega), D_i(t,\omega))$ on $[0,T]$ to the initial value problem of (II.2)–(II.5) with randomness in the coefficients, and it has the property that each of these functions is $\mathcal{B}([0,T]) \times \mathcal{F}$ measurable.

V. Numerical algorithm and simulations

A computer code was written in the software package Mathematica [36] to numerically solve the system. The approximate solutions were generated using the internal numerical differential equations solver "NDSolve," which uses adaptive step size procedures. In addition, for the sake of completeness, another set of solutions was generated in Mathematica using Adams predictor-corrector methods, yielding identical results.

All the figures below show the evolution of the vectors $V(t)$–top left, infected vectors $V_i(t)$–top right, infected humans $N_i(t)$–bottom left, and infected dogs $D_i(t)$–bottom right. In the baseline case we use the data from Table I, and in all simulations insecticide spraying begins in year 25. This is chosen so that the system settles into periodic oscillations before we activate the spraying term. In each one of the cases (i)-(vii) with randomness, we run 1000 simulations for 50 years, so 25 years are with spraying. In each figure, the shaded area is the envelope that indicates the ranges of the intervals between the highest and the lowest simulation result at each timestep. We note that the upper and lower curves of the envelopes are not solutions of the system. These envelopes, if the model describes the real process reasonably well, should contain most of the observed field information. The Gaussian and skewed distributions produce very close results to those of the

uniform distribution, so we do not include them in this report.

A. The data functions and coefficients

The vector population growth coefficient function is given by

$$r(t) = \frac{1073}{3 \cdot 20000} \cdot 20 \cdot 0.831 \cdot b_{supp} \cdot b(t), \quad \text{(V.1)}$$

where the weighted blood supply b_{supp} is given in the table and the biting rate function, taken from [8], is

$$b(t) = \frac{B(t)}{400 + 100d_f + 100c_f}. \quad \text{(V.2)}$$

Here, $B(t)$ is a periodic function, with a period of 365 days, given by

$$B(t) = \begin{cases} \frac{(-\frac{15}{365})}{91.25}t + \frac{15}{365} \\ \qquad \text{if } 0 \le \text{Mod}(t, 365) \le 91.25, \\ \frac{(\frac{30}{365})}{228.1 - 182.5}(t - 182.5) \\ \qquad \text{if } 182.5 \le \text{Mod}(t, 365) \le 228.1, \\ \frac{(\frac{7}{365} - \frac{30}{365})}{273.75 - 228.1}(t - 228.1) + \frac{30}{365} \\ \qquad \text{if } 228.1 \le \text{Mod}(t, 365) \le 273.75, \\ \frac{(\frac{15}{365} - \frac{7}{365})}{365 - 273.75}(t - 365) + \frac{15}{365} \\ \qquad \text{if } 273.75 \le \text{Mod}(t, 365) < 365. \end{cases}$$

B. The baseline case without randomness

We first present in Fig. 1 the results of numerical simulations without randomness. Then, we compare the simulation results with randomness to the baseline case. The sharp decrease in the number of vectors and infected vectors after the beginning of insecticide spraying in year 25 is noticeable. In Fig. 1, in addition to the depiction of the graphs based on daily values of the simulations (grey), we also present a linear interpolation of the values of the populations on a specific day (red). This provides better insight into what would be observed by someone who visits the village on that day each year.

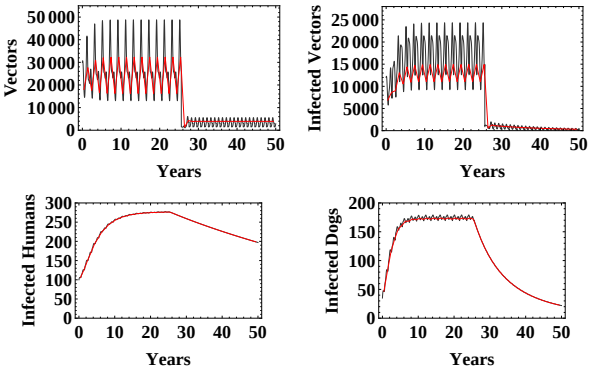

Fig. 1. System behavior in the baseline case without variability.

It is seen that the number of infected humans is large, approaching almost 95% at the peak (before spraying starts), and about 200 in year 50. The slower decline in infected humans relative to infected dogs once insecticide spraying starts is due to the longer life span of humans, sixty years for an infected human versus eight years for an infected dog. The sharp decrease in the vector population is caused by the choice of a very effective insecticide. We say more on this issue in the following subsection. More detailed simulations and analysis can be found in [10].

We note that whereas the difference between the detailed simulation results and what would be seen by an observer who visits the village once a year is very small for infected humans and dogs, it is substantial for the vectors and infected vectors.

We note that in the absence of spraying, the vector population oscillates below and above the carrying capacity. Finally, with these values of the parameters, especially τ_1 and τ_2, we see that the oscillations exhibit a 2-year cycle. These numerical observations warrant additional mathematical study of the model as well as additional field studies.

C. Variability in the spraying mortality rate d_{sp}

Since the original motivation for the model was to investigate spraying schedules (cf. [31]), we

begin with the results of the numerical simulations with random mortality rate due to spraying $d_{sp}(t)$. It was found in the simulations that when the insecticide is very effective, killing all the vectors in the house except those in the cracks, then there was very little variability in the results. Therefore, the value of d_{sp} is not important, as long as the spray kills all the available vectors upon contact. Thus, we do not depict the case with randomness in a very effective insecticide. We note that the variations were only in the height of the function $d_{sp}(t)$ and not its shape.

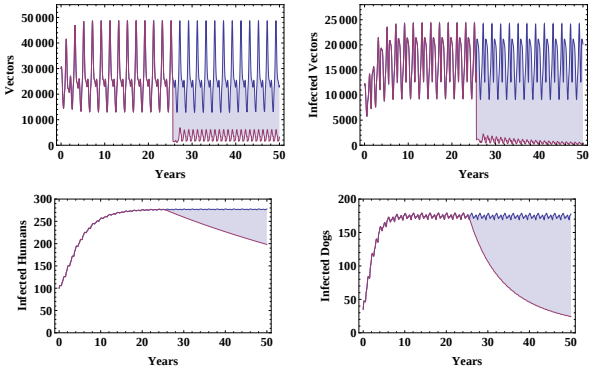

Fig. 2. Case (i): Model variability with 90% reduction of the insecticide effectiveness.

However, the vectors may become less sensitive to the chemical, develop resistance, or the weather conditions may reduce the effectiveness of the insecticide. So we run simulations of case (i) with a spray that is 10% as effective (i.e., $d_{max} = 0.1$). These simulation results are depicted in Fig. 2. It is seen that the variability in the vectors, infected vectors, and infected dogs is very large, while the variability in the infected humans is moderate. The variation in the human infections is about 80 over a period of 25 years of spraying, which in a village of 296 humans is quite significant. Indeed, at year 50 the ratio of the variability due to randomness to the infected humans is about $80/296 \approx 27\%$. In part, the effects are moderate because of the longevity of humans and our assumption of a constant human population. The effects on the domestic animals, 'dogs,' are marked, as the variation at year 50 is about $145/215 = 67\%$. This is

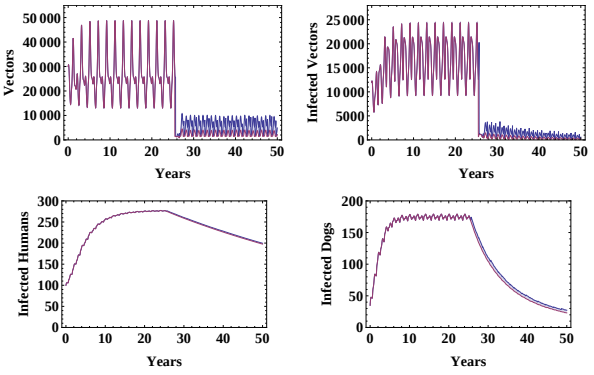

Fig. 3. Case (ii): Model behavior with variability in t_1.

similarly due in part to their shorter lifespan. We conclude that whereas in the case of very effective spray there is very little variability and the exact value of d_{sp} is not so important. On the other hand, when the insecticide is not very effective the system is sensitive to the spraying death rate. Clearly, having effective spraying is very important to reduce the variability. This raises the concern of the vectors developing resistance to the insecticide, which we discuss in Section VI.

D. Variability in the day of spraying application, t_1

In the simulations in [10], [31], [32] the first day of the year, day 1, was chosen as the first day of Fall in the southern hemisphere. Then, the first day of spraying was set as $t_1 = 212.5$, the 30.5th day of Spring. However, the day of insecticide spraying varies considerably, as explained above.

The results of the numerical simulations with random t_1 are shown in Fig. 3. It is seen that while the randomness, with $\omega \in \Omega_{ii}$, affects the vectors and the infected vectors mildly, it has a very small effect on the infected humans and dogs. It is likely that this insensitivity to t_1 is due, in part, to our choice to restrict it to Spring. If this restriction is correct, then any day in Spring is a good day for spraying. More information from field studies is needed to determine if the model needs to be modified or if the randomness interval for t_1 should be enlarged.

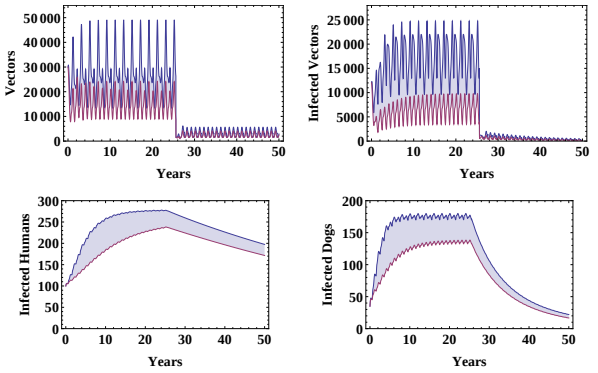

Fig. 4. Case (iii): Model behavior with variability in $d_m(t)$.

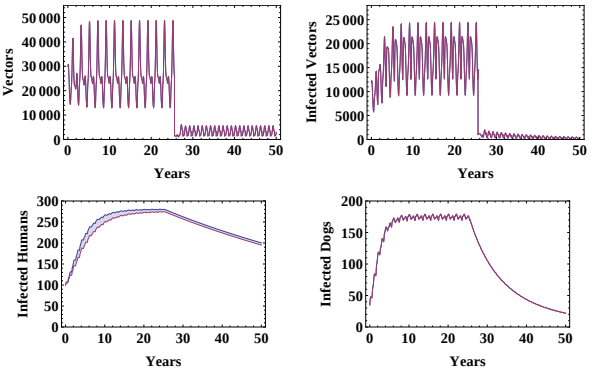

Fig. 5. Case (iv): Model behavior with variability in p_{VN}.

E. Variability in the mortality rate d_m

The numerical simulations of the model with random natural mortality rate $d_m(t)$ are shown in Fig. 4. It is seen that randomness, with $\omega \in \Omega_{iii}$, has substantial effects on the vector and infected vector populations, while having moderate effects on the infected human and dog populations. Indeed, the variation in infected humans in year 50 is about $30/296 = 10\%$, and in dogs is about $5/215 = 2\%$. We note that this variability in both populations is lower than the variability before spraying near year 25.

F. Variability in disease transmission probability p_{VN}

The numerical simulation results with random transmission probability p_{VN} are shown in Fig. 5. We see that the randomness, with $\omega \in \Omega_{iv}$, mildly affects the number of infected humans, but has almost no effect on the other populations. We conclude that the model does not depend on this parameter and a precise value is not necessary, unless the sample space Ω_{iv} is too small.

G. Variability in the blood supply factor b_{supp}

Next, we run numerical simulations with random variability in the weighted blood supply factor b_{supp}. The results are depicted in Fig. 6. It is seen that there is considerable variability caused by this parameter in the number of vectors, infected vectors and infected dogs. However, the variability in the numbers of infected humans is quite small, so it is not clear how accurate the value of b_{supp} needs to be. If the concern is only for humans, a not very accurate value is sufficient. But, if one wants to have good insight into the whole process, a more accurate value is needed.

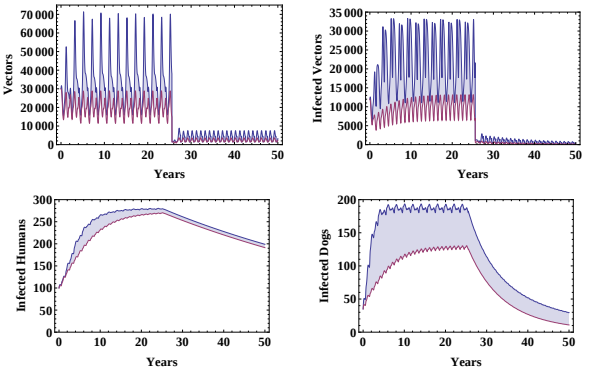

Fig. 6. Case (v): Model behavior with variability in the blood supply b_{supp}.

H. Variability in the development time τ_1

The results of the numerical simulations with random development time τ_1 are shown in Fig. 7. The randomness, with $\omega \in \Omega_{vi}$, has very little effect on any of the four populations. We conclude that the model is not sensitive to the development time with our choice of the sample space Ω_{vi}, which seems reasonable.

I. Variability in the time lag τ_2

The numerical simulation results with random time delay in responding to the carrying capacity,

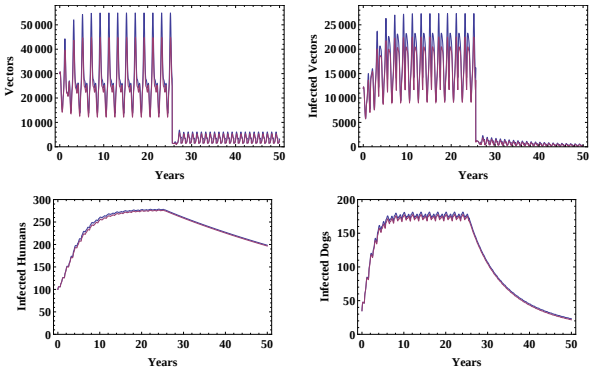

Fig. 7. Case (vi): Model behavior with variability in τ_1.

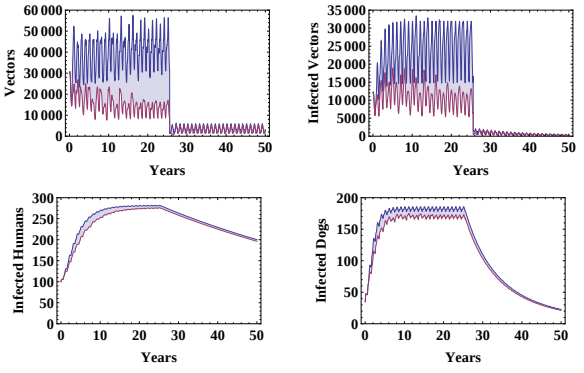

Fig. 8. Case (vii): Model behavior with variability in τ_2.

τ_2, are shown in Fig. 8. We see that the randomness, with $\omega \in \Omega_{vii}$, has a sizable effect on the vectors and infected vectors, but a very small effect on the infected humans and dogs. We conclude that only the vector part of the model depends on τ_2. Moreover, our choice of the sample space Ω_{vii} is reasonable and therefore a precise value of τ_2 is likely not necessary if the interest is in using the model to predict human or dog infections. On the other hand, as noted above, if the overall process is of interest, a reasonable value of τ_2 has to be determined, preferably from field data.

We note here that by changing the delay τ_2 there is numerical evidence that the type of vector oscillations changed. We discuss this point below as it warrants further mathematical and numerical investigation.

J. Variability in the time delay with $\tau_1 = \tau_2$

For the sake of completeness, we run simulations of the case when $\tau_1 = \tau_2$, which was studied in [32]. The sample space was chosen to be the same as in Case (vi), centered about $\tau_1 = 20$, in order to be comparable to [32] where the time delay is 20 days.

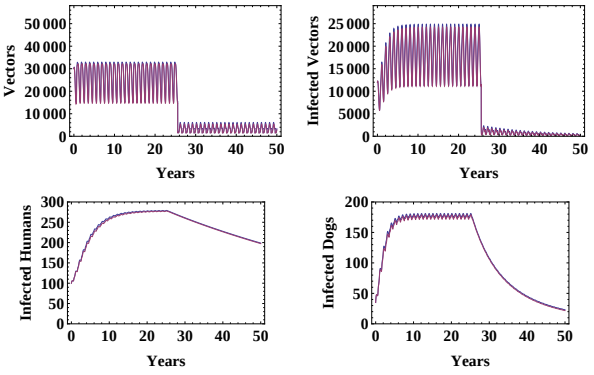

Fig. 9. Model behavior with $\tau_1 = \tau_2$.

The results are depicted in Fig. 9. It is seen that there is a big change in the dynamics of the vector population as compared to Fig. 7 and 8 as the maximum number of vectors is much lower. Also, the variability due to randomness is insignificant in all four of the populations. Additionally, when there are two delays, the main difference is the emergence of a two-year cycle that changes the nature of the yearly oscillations. Therefore, the use of two delays requires further study as the details of the dynamics are qualitatively different.

VI. Conclusions

This work studies an extension of the model for the spread of Chagas disease, developed in [31], [32], by considering a two-delay equation for the vectors, and allowing randomness in seven system parameters. The study of the model sensitivity is motivated by the simple observation that most of the model parameters are difficult or even impossible to obtain experimentally. So the knowledge of the parameters for which the model is not sensitive allows the use of good estimates of their values without distorting the solutions. On the other hand, those parameters to which the model

is very sensitive must be found or estimated with higher accuracy, entailing much more effort.

The existence of the unique local solution of the model for each choice of the parameters was established, as well as the fact that for each random parameter the solution $\boldsymbol{x}(t,\omega)$ is a stochastic or random process. The result, Theorem 2, is very general and can be used in the sensitivity studies of many related types of models.

The sensitivity analysis was done by running 1000 numerical simulations of the system dynamics over 50 years for each of the seven chosen parameter, randomly chosen from the appropriate sample space while holding all other parameters at their baseline values. It was found that the model is sensitive to the natural mortality rate d_m and insecticide spraying d_{sp} when it is only 10% as effective.

The model is moderately sensitive to the weighted blood supply factor $b_{supp} = N + c_d D + c_f D$ and the time delay in responding to the carrying capacity, τ_2. In the b_{supp} case there was considerable sensitivity for the vectors, infected vectors and dogs, while in the case of τ_2 there was considerable sensitivity for the vectors and infected vectors only. The insensitivity of the human population is due, in part, to the longevity of the human life-span (even with the disease).

Within the parameter ranges of the appropriate sample spaces, the model seems to be insensitive to the values of the mortality rate due to insecticide spraying d_{sp} (with 100% effectiveness), the developmental delay τ_1, the day of spraying application t_1, and the disease transmission probability p_{VN}. The latter is somewhat surprising and further study is needed to clarify the reasons.

The numerical simulations show that the system is insensitive to the values of d_{sp} when the insecticide is very effective and kills all the vectors, except those in the cracks (V_{min}). However, the simulations with a death rate due to spraying at 10% effectiveness show considerable system sensitivity. This highlights the importance of insecticide resistance. If the effectiveness of the insecticide is reduced, the death rate would decrease and the model would become more sensitive to this parameter. The issues of deterioration of the spray or the vectors developing resistance are real concerns in the field and warrant additional study.

Another conclusion is that even very large variability in the vector and infected vector populations does not automatically translate into large variability in the infected humans and domestic animals.

This study raises questions that warrant further study. In addition to those mentioned above, we note the following. There is a need for a deeper analysis of the vector equation, especially to establish the global boundedness and positivity of the solutions with two delays. There is numerical indication of a two-cycle baseline solution, i.e., the system repeats each oscillation every two years. This seems to be related to the chosen values of the delays τ_1 and τ_2, since when τ_2 is allowed to change this two-cycle solution changes, Fig. 7. This is a topic of interest and a mathematical investigation is warranted. This may lead to a deeper study of the effects of the two delays on the system. In addition, we note that in several cases the numerical simulations show the vector population oscillating below and above the carrying capacity. Also, it is of mathematical interest to establish the existence of periodic solutions as seen in the numerical results.

This work opens a way to study related models and to allow the field research to put more effort into the determination of those parameters to which the model is sensitive. Finally, we plan to run more simulations with the other parameters, some joint combinations, and also other versions of the model.

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APPENDIX

We first present a short proof of the boundedness of the vector population $V(t,\omega)$ for $\omega \in \Omega$ and $t \in [0,T]$, where $T \leq t_* \equiv \inf\{t>0 : V(t,\omega)=0\}$. We note that $t_* > 0$, and in fact, $t_* > \tau_* \equiv \min\{\tau_1,\tau_2\}$. To see this we recall that the equation for V is

$$V' = r(t-\tau_1)V(t-\tau_1)\left(1-\frac{V(t-\tau_2)}{K}\right) - d_m V - d_{sp}(V-V_{min})_+. \quad \text{(A.1)}$$

Since $V(t_*)=0$ and $V'(t_*)\leq 0$, we see from equation (A.1) that either $V(t_*-\tau_1)\leq 0$ or $V(t_*-\tau_2)\geq K$. But $0<V_0(t)<K$ for $t\in[-\tau,0]$, and thus $t_*>\tau_*$.

Now, because V is positive on $[0,T]$, it suffices to bound V from above. We will use induction by bounding the solution on successive intervals of length τ_*. Recall that $V_0(t)$ is bounded and positive on $[-\tau,0]$, and thus, there exists a constant B_{-1} such that $0<V_0(t)<B_{-1}$ for all $t\in[-\tau_*,0]$. Now, in the inductive step we assume that $0<V(t)<B_j$, for every $t\in[j\tau_*,(j+1)\tau_*]$, where $j=-1,0,1,2,\ldots,m$. Then, it follows from equation (A.1) that for all $t\in[(m+1)\tau_*,(m+2)\tau_*]$ we have

$$V'(t) < r^* B_m, \quad \text{(A.2)}$$

where, using the 365 day periodicity of r, we set

$$r^* = \sup_{\omega\in\Omega}\left\{\max_{0\leq s\leq 365}\{r(s,\omega)\}\right\}. \quad \text{(A.3)}$$

Note that r^* is finite because of how Ω is defined.

Finally, a simple integration of inequality (A.2) from $(m+1)\tau_*$ to t yields

$$V(t) < V((m+1)\tau_*) + r^* B_m \tau_*.$$

Thus, $V(t)$ is bounded above on $[(m+1)\tau_*,(m+2)\tau_*]$:

$$V(t) < B_{m+1} \equiv B_m(1+r^*\tau_*) = B_{-1}(1+r^*\tau_*)^{m+2}. \quad \text{(A.4)}$$

We note that the mathematical analysis of the problem with two delays, and particularly the issue of global positivity, is very involved and will be studied elsewhere.

We turn now to show the measurability of $V(t,\omega)$ with respect to $\omega\in\Omega$. For $t\in[-\tau,T]$ consider the functions V_δ given by

$$\begin{aligned} V_\delta(t) &= V_0(0\wedge t) \\ &+ I_{[0,\infty)}(t)\int_0^t r(s-\delta-\tau)V(s-\delta-\tau) \\ &\qquad \times (1-V(s-\delta-\tau))\,ds \\ &- I_{[0,\infty)}(t)\int_0^t d_m(s-\delta)V(s-\delta)\,ds \\ &- I_{[0,\infty)}(t)\int_0^t d_{sp}(s-\delta)(V(s-\delta)-V_{min})_+\,ds \end{aligned}$$

where $a\wedge b=\min(a,b)$. The set of functions V_δ is bounded, as was shown above, and equicontinuous, so by the Ascoli-Arzela theorem there exists a subsequence, still denoted by subscript δ, such that $V_\delta\to V$ uniformly in $C([-\tau,T])$, when $\delta\to 0$ through a sequence of values. Then, taking the limit as $\delta\to 0$ for a suitable subsequence, one obtains the following equation on $[-\tau,T]$:

$$\begin{aligned} V(t) &= V_0(0\wedge t) \\ &+ I_{[0,\infty)}(t)\int_0^t r(s-\tau)V(s-\tau) \\ &\qquad \times (1-V(s-\tau))\,ds \\ &- I_{[0,\infty)}(t)\int_0^t d_m(s)V(s)\,ds \\ &- I_{[0,\infty)}(t)\int_0^t d_{sp}(s)(V(s)-V_{min})_+\,ds. \end{aligned}$$

Thus, the fundamental theorem of calculus yields a solution to (A.1). Moreover, the right-hand side of the equation is Lipschitz continuous since V is bounded. It follows that the solution is unique and is obtained by letting $\delta\to 0$. This holds true for each $\omega\in\Omega$. This allows us to assert that the resulting solution is a measurable function of t and ω. Each V_δ is product measurable in $\mathcal{B}([0,T])\times\mathcal{F}$ from the construction. Now, we choose a sequence $\delta_n\to 0$ and use the uniqueness just discussed to argue that for each (t,ω)

$$\lim_{\delta_n\to 0} V_{\delta_n}(t,\omega) = V(t,\omega).$$

TABLE I
THE MODEL PARAMETERS AND THE BASELINE SIMULATION VALUES

Parameter	Definition	Baseline Value	Source
H	Total number of houses (houses/village)	74	Est. from [5]
V	Total number of vectors (vectors/village)	$V(0) = 30000$	This study
N	Number of humans (humans/house)	4	This study
D	Number of domestic dogs (dogs/house)	2.9	Est. from [17]
C	Number of chickens (chickens/houses)	15	Est. from [5]
V_i	Infected domestic triatomids (vectors/village)	$V_i(0) = 12000$	This study
N_i	Number of infected humans (humans/village)	$N_i(0) = 100$	This study
D_i	Number of infected dogs (dogs/village)	$D_i(0) = 35$	This study
V_{min}	Number of vectors surviving spraying (vectors/house)	20	Est. from [14], [15]
r	Egg hatching rate (1/day)	See (V.1)	[5], [17]
d_m	Natural death rate of vectors (1/day)	$\bar{d}_m$, see (III.4)	Est. from [3]
τ_1	Vector egg development time (days)	20	[3]
τ_2	Carrying capacity response delay (days)	190	This study
b	Biting rate $(\text{bites}/(\text{day} \cdot \text{human factor} \cdot \text{vector}))$	See (V.2)	Est.from [3], [4]
b_{supp}	Weighted blood supply (human factors)	$N + d_f D + c_f C$	[11]
P_{NV}	Human to vector infection probability (per bite)	0.03	[11]
P_{DV}	Dog to vector infection probability (per bite)	0.49	[11]
P_{VN}	Vector to human infection probability (per bite)	0.001	Est. from [11], [22]
P_{VD}	Vector to dog infection probability (per bite)	0.001	Est. from [11]
d_f	Human factor of one dog	2.45	[17]
c_f	Human factor of one chicken	0.35	[16], [17]
γ_{N_i}	Mortality rate of infected humans (1/day)	$\frac{0.3}{50 \cdot 365} + \frac{0.7}{76.12 \cdot 365}$	Est. from [6], [23]
γ_{D_i}	Mortality rate of infected dogs (1/day)	$\frac{1}{8 \cdot 365}$	This study, est. 8 years
K	Carrying capacity of vectors (vectors/house)	500	This study

Therefore, $(t, \omega) \to V(t, \omega)$ is also product measurable. The proof is complete.

REFERENCES

[1] Barbu C, Dumonteil E, Gourbière S (2010) Evaluation of spatially targeted strategies to control non-domiciliated Triatoma dimidiata vector of Chagas disease, PLoS Neglected Tropical Diseases 4(8): e1045. Available at http://dx.doi.org/10.1371/journal.pntd.0001045

[2] Bilate AM, Cunha-Neto E (2008) *Chagas disease cardiomyopathy: current concepts of an old disease*, Rev. Inst. Med. Trop. Sao Paulo 50(2), 67–74.

[3] Castanera MB, Aparicio JP, Gurtler RE (2003) A stage-structured stochastic model of the population dynamics of Triatoma infestans, the main vector of Chagas disease, Ecol. Model. 162, 33–53.

[4] Catalá S (1991) *The biting rate of* Triatoma infestans *in Argentina*, Med. Vet. Entomol. 5(3), 325–333.

[5] Ceballos LA, Vazquez-Prokopec GM, Cecer MCe, Marcet PL, Gürtler RE (2005) *Feeding rates, nutritional status and flight dispersal potential of peridomestic populations of* Triatoma infestans *in rural northwestern Argentina*, Acta Tropica. 95, 149–159

[6] Central Intelligence Agency (2009) *The World Factbook*. Available at https://www.cia.gov/library...the-world-factbook/

[7] Clauson M, Harrison A, Shuman L, Shillor M, Spagnuolo AM (2012) *Analysis of the steady states of a mathematical model for Chagas disease,* Involve, a Journal of Mathematics 5(3), 237–246. Available at http://dx.doi.org/10.2140/involve.2012.5.237

[8] Coffield DJ Jr, Spagnuolo AM, Shillor M, Mema E, Pell B, et al. (2013) A Model for Chagas Disease with Oral and Congenital Transmission. PLoS ONE 8(6): e67267. Available at http://dx.plos.org/10.1371/journal.pone.0067267

[9] Coffield DJ Jr, Spagnuolo AM (2014) Steady State Stability Analysis of a Chagas Disease Model, Biomath 3, 1405261, 1–13.

[10] Coffield DJ Jr, Shillor M, Spagnuolo AM, Carignan AM, Corcoran A, VanLoo B, Modeling Chagas Disease with Domestic and Peridomestic Triatoma infestans in the Gran Chaco Region, to be submitted.

[11] Cohen JE, Gurtler RE (2001) *Modeling household transmission of American trypanosomiasis,* Science 293, 684–688. Available at http://www.sciencemag.org/content/293/5530/694.full

[12] Cruz-Pacheco G, Esteva L,Vargas C (2012) Control measures for Chagas disease, Math. Biosciences 237,

49–60.
[13] Garg N, Bhatia V (2005) *Current status and future prospects for a vaccine against American trypanosomiasis,* Expert Rev. Vaccines 4(6), 867–880.
[14] Gorla DE (1991) *Recovery of* Triatoma infestans *populations after insecticide application: an experimental field study*, Med. Vet. Entomol. 5, 311–324.
[15] Gorla DE, Schofield CJ (1985) *Analysis of egg mortality in experimental populations of* Triatoma infestans *under natural climatic conditions in Argentina*, Bull. Soc. Vector Ecol. 10, 107–117.
[16] Gurtler RE, Ceballos LA, Ordonez-Krasnowski P, Lanati LA, Stariolo R, et al. (2009) Strong host-feeding preferences of the vector Triatoma infestans modified by vector density: Implications for the epidemiology of Chagas disease, PLoS Negl Trop Dis 3(5): e447. Available at http://dx.doi.org/10.1371/journal.pntd.0000447
[17] Gürtler RE, Cecere MC, Lauricella MA, Cardinal MV, Kitron U, Cohen JE (2007) *Domestic dogs and cats as sources of* Trypanosoma cruzi *infection in rural northwestern Argentina*, Parasitology 134, 69–82.
[18] Levy MZ, Malaga Chavez FS, Cornejo del Carpio JG, Vilhena DA, McKenzie FE, Plotkin JB (2010) Rational Spatio-Temporal Strategies for Controlling a Chagas Disease Vector in Urban Environments, Journal of the Royal Society Interface 7, 1–10.
[19] Noireau F, Dujardin J.-P (2010) *Biology of Triatominae*, in: "American Trypanosomiasis Chagas Disease One Hundred Years of Research," Telleria J. and Tibayrenc M (eds) Elseiver, London, UK, 2010.
[20] Organizacion Panamericana de la Salud (2006) Estimacion cuantitativa de la enfermedad de Chagas en las Americas. Montevideo, Uruguay: Organizacion Panamericana de la Salud. PAHO Publishing, Washington, D.C., 1-28 [OPS/HDM/CD/425-06]. Available at http://www.bvsops.org.uy/pdf/chagas19.pdf
[21] Rabinovich JE, Himschoot P (1990) *A population-dynamics simulation model of the main vectors of Chagas' Disease transmission, Rhodnius prolixus and Triatoma infestans,* Ecological Modelling 52, 249–266.
[22] Rabinovich JE, Wisnivesky-Colli C, Solarz ND, Gurtler RE (1990) *Probability of transmission of Chagas disease by Triatoma infestans (Hemiptera: Reduviidae) in an endemic area of Santiago del Estero, Argentina*, Bulletin of the World Health Organization 68(6), 737–746. Available at http://www.ncbi.nlm.nih.gov/pmc/a...-0049.pdf
[23] Rassi A Jr, Rassi A, Marin-Neto JA (2009) *Chagas heart disease: pathophysiologic mechanisms, prognostic factors and risk stratification*, Mem. Inst. Oswaldo Cruz. 104 (Suppl 1), 152–158.
[24] Rodriques Coura J, de Castro SL (2002) *A critical review on Chagas disease chemotherapy*, Mem. Inst. Oswaldo Cruz 97(1), 3–24. Available at http://www.scielo.br/pdf/mioc/v97n1/review.pdf
[25] Saltelli A, Ratto M, Andres T, Campolongo F, Cariboni J, Gatelli D, Saisana M, Tarantola S (2008) Global Sensitivity Analysis, The Primer, John Wiley & Sons.
[26] Samuels AM, Clark EH, Galdos-Cardenas G, Wiegand RE, Ferrufino L, et al. (2013) Epidemiology of and impact of insecticide spraying on Chagas disease in communities in the Bolivian Chaco, PLoS Negl Trop Dis 7(8): e2358. Available at http://dx.doi.org/10.1371/journal.pntd.0002358
[27] Schmunis GA (1999) *Prevention of transfusional Trypanosoma cruzi infection in Latin America*, Mem. Inst. Oswaldo Cruz 94(Suppl 1), 93–101.
[28] Schmunis GA, Yadon ZE (2010) *Chagas disease: A Latin American health problem becoming a world health problem*, Acta Tropica 115(1–2), 14–21. Available at http://www.sciencedirect.com/...003623
[29] Schofield CJ, Jannin J, Salvatella R (2006) *The future of Chagas disease control,* Trends Parasit. 22, 583–588. Available at http://dx.doi.org/10.1016/j.pt.2006.09.011
[30] Silveira A, Vinhaes M (1999) Elimination of vector-borne transmission of Chagas disease, Mem. Inst. Oswaldo Cruz 94(Suppl 1), 405–411.
[31] Spagnuolo AM, Shillor M, Stryker GA (2010) A model for Chagas disease with controlled spraying, Journal of Biological Dynamics 5(4), 299–317.
[32] Spagnuolo AM, Shillor M, Kingsland L, Thatcher A, Toeniskoetter M, Wood B (2012) A logistic delay differential equation model for Chagas disease with interrupted spraying schedules. Journal of Biological Dynamics 6(2), 377–394. Available at http://dx.doi.org/10.1080/17513758.2011.587896
[33] Wangersky PJ, Cunningham WJ (1956) On time lags in equations of growth, Proc. Nat. Acad. Sciences 42, 699–702.
[34] http://www.who.int/mediacentre/factsheets/fs340/en/
[35] Wilson LS, Strosberg AM, Barrio K (2005) Cost-Effectiveness of Chagas Disease Interventions in Latin America and the Caribbean: Markov Models, American Journal of Tropical Medicine and Hygiene 73, 901–910.
[36] http://wolfram.com/