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The steady states of a mathematical model for the dynamics of Chagas disease, developed by Spagnuolo et al., are studied and numerically simulated. The model consists of a system of four nonlinear ordinary differential equations for the total number of domestic carrier insects, and the infected insects, infected humans, and infected domestic animals. The equation for the vector dynamics has a growth rate of the blowfly type with a delay. In the parameter range of interest, the model has two unstable disease-free equilibria and a globally asymptotically stable (GAS) endemic equilibrium. Numerical simulations, based on the fourth-order Adams–Bashforth predictor corrector scheme for ODEs, depict the various cases.

1. Introduction

Chagas disease is wide spread in rural parts of South and Central America, where an estimated 10 million people are infected [Bilate and Cunha-Neto 2008; Cohen and Gürtler 2001; Schofield et al. 2006], and a search on the World Health Organization (WHO) web site yielded 1460 results. A summary of the state of the disease can be found at [WHO 2010]. Cases of the disease were also reported in Mexico and even a few in Southern California. The disease is transmitted by the insect *Triatoma infestans*, known as the "kissing bug", which bites the victim and then defecates around the bite wound. The parasites that cause the disease, *Trypanosoma cruzi*, which are in the bug's feces, enter the wound and spread throughout the body. The disease causes significant morbidity and eventually death, and there is no cure for the disease, after its initial stage. Currently the main way to control the spread of the disease is by insecticide spraying.

A mathematical model for the dynamics of the disease was developed in [Spagnuolo et al. 2011], where the main interest was to understand the disease spread

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and how to control it by using insecticide spraying. The model consists of four nonlinear ordinary differential equations (ODEs), describing the evolution of the total numbers of the insects or vectors and of the infected vectors, infected humans, and infected household mammals, which for the sake of simplicity we call dogs. It is of the MSEIR type, but with only S (susceptibles) and I (infectives) components for the insects, humans, and dogs. The model describes a typical rural village with humans, dogs, chickens, and the vectors. Although chickens cannot be infected nor are they carriers of Chagas disease, they are a blood source for the vectors, so they contribute essentially to the disease dynamics. We refer to [Spagnuolo et al. 2011] for a detailed description of the disease and the assumptions that underlie the model. An extensive literature can be found there, in [Coffield et al. 2010], and the references therein.

This work concentrates on the steady states of the model of Spagnuolo et al. and studies their stability. The time-dependent model coefficients, with their yearly oscillations are replaced by their yearly averages. Thus, the seasonal changes in the relevant system parameters are not included here. However, they were taken into account in [Coffield et al. 2010; Spagnuolo et al. 2011].

The interest in this work lies in understanding the mathematical structure of the model without spraying, and with time-independent coefficients.

We note that a somewhat different model was studied in [Spagnuolo et al. 2012; Coffield et al. 2010], where the analysis of the steady states can be found, too. There, the growth rate in the equation for the vectors was a logistic term with delay, while in [Spagnuolo et al. 2011] and here, the so-called "blowflies" term with a delay is used ([Nicholson 1954]; see also [Wei and Li 2005] and references therein).

In addition to the stability analysis of the steady states, Section 3, we present a scheme for the numerical solutions of the model and depict two sets of simulations, Section 4. The results depict the monotone ways the system approaches the endemic steady state.

2. The model

We briefly describe the mathematical model for Chagas disease developed in [Spagnuolo et al. 2011]. It describes the population dynamics of the total numbers of: vectors (bugs), infected vectors, infected humans, and infected domestic animals (dogs) in a representative village in South America. The model was used to study the effects of periodic insecticide spraying for the control of the disease. In this work we are interested in the stability of its disease-free and endemic equilibria, so we omit the terms related to insecticide spraying.

The populations are assumed to be large enough to be governed by differential equations. The total populations of humans (N), dogs (D), and chickens (C)

are assumed to remain constant over time. We denote by V = V(t) the number of carrier insects living in the houses at time t; the number of infective insects by $V_i = V_i(t)$, the number of infective humans by $N_i = N_i(t)$, and the number of infective dogs by $D_i = D_i(t)$. Each non-infected population, excluding C, is assumed to be susceptible. The rate coefficients $d_h = d_h(t)$, $d_m = d_m(t)$ and $b_i = b_i(t)$ are assumed to be periodic, with period of one year.

The *mathematical model for Chagas disease* of Spagnuolo et al., without insecticide spraying, is this:

$$V' = d_h V(t - \tau) e^{-aV(t - \tau)} - d_m V,$$
(2-1)

$$V'_{i} = b_{i}(V - V_{i}) \left(P_{NV}N_{i} + P_{DV}d_{f}D_{i} \right) - d_{m}V_{i}, \qquad (2-2)$$

$$N'_{i} = b_{i} P_{VN} (N - N_{i}) V_{i} - \gamma_{N} N_{i}, \qquad (2-3)$$

$$D'_i = b_i d_f P_{VD} (D - D_i) V_i - \gamma_D D_i, \qquad (2-4)$$

$$V_{i}(0) = V_{i0}, \quad N_{i}(0) = N_{i0}, \quad D_{i}(0) = D_{i0},$$

$$V(t) = V_{0}(t), \quad -\tau \le t \le 0.$$
(2-5)

Equation (2-1) describes the rate of change of the total vector population. The first term on the right-hand side is similar in form to Nicholson's *blowflies model* where the growth rate at time t (days) depends on the population size at time $t - \tau$ (days) [Gurney et al. 1980; Győri and Ladas 1991; Nicholson 1954]. However, in the Nicholson model $d_{h\tau}$ is a constant, since blowflies have only two stages of development: pupae and adult. In contrast, triatomines have six distinct stages of life: five instar stages and an adult stage. The egg hatching rate $d_{h\tau} = d_{h\tau}(t)$ at time t depends on the fraction of adult females at time $t - \tau$, as well as other factors including seasonal temperatures and blood supply. In particular, the growth term attains a maximum when the number of vectors in the village houses at time $t - \tau$ reaches the value of 1/a. The natural death rate coefficient of the vectors is d_m . We note that (2-1) is decoupled from the other equations and can be solved separately.

Equation (2-2) models the rate of change of the number of infected vectors. The first term represents the rate of growth of the infectives. The factor $b_i(t) = b/b_{sup}$ is the biting rate of the vectors *b* divided by the total available blood supply $b_{sup} = N + d_f D + c_f C$, where d_f and c_f are the blood supply weights of the dogs and the chickens, respectively. The susceptible vector population is $V - V_i$, and P_{NV} and P_{DV} are the respective probabilities of a vector becoming infected from biting a human or a dog.

The rate of change in the number of infected humans, (2-3), is determined by the biting rate of infected vectors $b_i(t)V_i$ and the probability $P_{VN}(N - N_i)$ of a susceptible human catching the disease in one bite. The death rate of infective humans is $\gamma_N N_i$, where γ_N is the death rate constant, and is known to be higher than that of the susceptibles, [Rassi et al. 2009]. Equation (2-4) for infected dogs is similar, but with the addition of the factor d_f to take into account the vectors' preference to feed on dogs.

The model has time-dependent coefficients that incorporate seasonal variations in the life cycles of the vectors. The oscillatory behavior of the solutions can be found in the simulations in [Spagnuolo et al. 2011]. However, to study the steady states, which we do in the next section, we replace them with their yearly averages.

3. The steady states

We now study the steady states of the problem. To this end, we first rewrite the system using time-independent averaged coefficients. We set

$$a_1 = d_h, \quad a_3 = b_i P_{NV}, \quad a_5 = b_i P_{VN},$$

 $a_2 = d_m, \quad a_4 = b_i d_f P_{DV}, \quad a_6 = b_i d_f P_{VD},$

where we take each a_i , i = 1, ..., 6 to be the average value, over 365 days, of its corresponding function in the *baseline* simulation case studied in [Spagnuolo et al. 2011]. These system parameters are positive constants. The definitions of the various coefficients and their values used in the baseline simulation case of the model can be found in Table 1.

To simplify the presentation, we rename the dependent variables as follows: v = V, $x = V_i$, $y = N_i$, $z = D_i$.

The problem in the new notation is: Find the functions $\{v, x, y, z\}$, defined on the time interval [0, *T*], such that,

$$v' = a_1 v(t - \tau) e^{-av(t - \tau)} - a_2 v, \qquad (3-1)$$

$$x' = a_3(v - x)y + a_4(v - x)z - a_2x, \qquad (3-2)$$

$$y' = a_5 (N - y) x - \gamma_N y,$$
 (3-3)

$$z' = a_6(D-z)x - \gamma_D z,$$
 (3-4)

$$\begin{aligned} x(0) &= V_{i0}, \quad y(0) = N_{i0}, \quad z(0) = D_{i0}, \\ v(t) &= V_0(t), \quad -\tau \le t \le 0. \end{aligned}$$
(3-5)

To study the long time behavior of the system (3-1)–(3-4) [Hethcote 2000; Thieme 2003], we note that the steady states or the fixed points are the solutions of the system

$$0 = a_1 \bar{v} e^{-av} - a_2 \bar{v}, \tag{3-6}$$

$$0 = a_3(\bar{v} - \bar{x})\bar{y} + a_4(\bar{v} - \bar{x})\bar{z} - a_2\bar{x}, \qquad (3-7)$$

$$0 = a_5(N - \bar{y})\bar{x} - \gamma_N \bar{y}, \qquad (3-8)$$

$$0 = a_6 (D - \bar{z})\bar{x} - \gamma_D \bar{z}.$$
 (3-9)

| Symbol | Description | Units |
|------------|---|------------------|
| V | total number of vectors | bugs/village |
| N | total number of humans | humans/village |
| D | total number of domestic dogs | dogs/village |
| C | total number of chickens | chickens/village |
| V_i | infected domestic triatomines | bugs/village |
| Ni | number of infected humans | humans/village |
| D_i | number of infected dogs | dogs/village |
| $d_{h	au}$ | egg hatching rate | 1/day |
| d_m | death rate of bugs | 1/day |
| τ | the delay factor | days |
| b | biting rate | 1/day |
| P_{NV} | human to bug infection probability (per bite) | NA |
| P_{DV} | dog to bug infection probability (per bite) | NA |
| P_{VN} | bug to human infection probability (per bite) | NA |
| P_{VD} | bug to dog infection probability (per bite) | NA |
| d_f | human factor of one dog | NA |
| c_f | human factor of one chicken | NA |
| γ_N | mortality rate of infected humans | 1/day |
| γD | mortality rate of infected dogs | 1/day |
| a^{-1} | value of V at which growth rate the largest | bugs |

Table 1. The model variables and coefficients.

The two solutions of the steady-state equation (3-6) for v are

$$\bar{v}_0 = 0$$
 and $\bar{v}_1 = \frac{1}{a} \log \frac{a_1}{a_2}$. (3-10)

We note that since $\bar{v}_1 > 0$, (because $a_1 > a_2$ in our setting), it follows from the results in [Wei and Li 2005] that the solution $\bar{v}_0 = 0$ is unstable. Also, when $\bar{v} = \bar{v}_0 = 0$, we have that $\bar{x} = \bar{y} = \bar{z} = 0$. So, (0, 0, 0, 0) is an unstable equilibrium point of the system. This corresponds to the observation that Chagas disease is endemic in Latin America.

We turn to the steady states with a positive number \bar{v}_1 , (3-10), of total vectors. In the baseline case we have $\bar{v}_1 \approx 31$, 500. It follows from [Wei and Li 2005] that \bar{v}_1 is locally asymptotically stable. Moreover, it is found that the condition for intrinsic oscillations in Equation (2) of [Wei and Li 2005],

$$a_2\tau e^{\tau a}\left(\log\frac{a_1}{a_2}-1\right) > \frac{1}{e},$$

is not satisfied, so the delay τ does not cause any oscillations of the solution. In this case, there are two nonnegative equilibria for \bar{x} , \bar{y} , and \bar{z} . One is the disease-free equilibrium (0, 0, 0), and the other, an endemic state, is approximately (9239, 86, 51), as computed numerically, using the baseline parameters.

The Jacobian matrix evaluated at the disease-free equilibrium is

$$J(0,0,0) = \begin{bmatrix} -a_2 & a_3 \bar{v}_1 & a_4 \bar{v}_1 \\ a_5 N & -\gamma_N & 0 \\ a_6 D & 0 & -\gamma_D \end{bmatrix}.$$

This matrix has three distinct real eigenvalues, one positive and the other two negative. Therefore, (31500, 0, 0, 0) is an unstable equilibrium. In Section 4 we simulate the model in cases when the initial conditions are near (31500, 0, 0, 0).

Finally, at the endemic equilibrium ($\bar{v}_1 = 31500, 9239, 86, 51$) the Jacobian matrix at ($\bar{x}, \bar{y}, \bar{z}$) is:

$$J(\bar{x}, \bar{y}, \bar{z}) = \begin{bmatrix} -a_3 \bar{y} - a_4 \bar{z} - a_2 & a_3(\bar{v}_1 - \bar{x}) & a_4(\bar{v}_1 - \bar{x}) \\ a_5(N - \bar{y}) & -a_5 \bar{x} - \gamma_N & 0 \\ a_6(D - \bar{z}) & 0 & -a_6 \bar{x} - \gamma_D \end{bmatrix}.$$

A straightforward computation shows that J(9239, 86, 51) has three real negative eigenvalues. Therefore, the endemic steady state (31500, 9239, 86, 51) is stable and attracting, or globally asymptotically stable (GAS). It follows from the model that under these conditions, without insecticide spraying or other interventions, the disease will persist. We note that we do not make a general statement on the conditions for the endemic steady state to be GAS, only that this is so in this case.

4. Simulations

We used the fourth-order Adams–Bashforth predictor corrector method to compute the numerical approximations of the model, equations (3-1)–(3-5). Due to the delay, a small step size of $\frac{1}{100}$ of a day was chosen. We also solved the system using other numerical schemes and they all matched our results for 1000 years of simulations. Moreover, Theorem 6.2.1 in [Bellen and Zennaro 2003, p. 156], guarantees the correctness of our numerical scheme.

The values of the parameters (with their references) used in the simulations are provided in Table 2. These were taken from [Spagnuolo et al. 2011]. The simulations were run using gfortran on a 3.0 GHz Intel Core 2 Duo CPU with Cent OS 5. A typical simulation of 100 years with 100 time steps per day $(3.65 \times 10^6$ time steps) took approximately 300 seconds. It was found that very long runs, over a few hundred years (tens of millions of time steps) were computationally reproducible, which indicates that the solution algorithm was stable.

| Symbol | Baseline simulation value | Reference |
|----------------|---|--|
| d_f | 2.45 | [Gürtler et al. 2007] |
| c_f | 4.8 | [Gürtler et al. 2007] |
| d_m | 0.00327 | Estimate from [Castanera et al. 2003] |
| $d_{h\tau}$ | 0.00613 | Estimate from [Castanera et al. 2003; |
| | | Gorla and Schofield 1985] |
| b_i | 0.0000215 | Estimate from [Castanera et al. 2003; |
| | | Catalá 1991] |
| γ_N | $0.7\frac{2\ln 2}{76.12\cdot 365} + 0.3\frac{\ln 2}{25\cdot 365}$ | Estimate from [CIA 2009; |
| | | Rassi et al. 2009] |
| γ _D | $\frac{\ln 2}{4.365}$ | Estimated 8 years |
| C | 100 | This study |
| N | 400 | This study |
| D | 100 | This study |
| P_{NV} | 0.03 | [Cohen and Gürtler 2001] |
| P_{DV} | 0.49 | [Cohen and Gürtler 2001] |
| P_{VN} | 0.00008 | Estimate from [Cohen and Gürtler 2001] |
| P_{VD} | 0.001 | Estimate from [Cohen and Gürtler 2001] |
| a^{-1} | 50,000 | This study |

Table 2. The parameters used in the baseline case.

We now present two numerical simulations of the model, with averaged coefficients, with different initial conditions, showing the convergence of the system to the endemic steady state (\bar{v}_1 , 9239, 86, 51). The first simulation has initial conditions that are considerably smaller than the steady state and chosen as V(0) = 2, $V_i(0) = 2$, $N_i(0) = 10$, and $D_i(0) = 0$. In the second example, the initial conditions were chosen to be larger than the steady state values, and the values were V(0) = 45, 000, $V_i(0) = 10$, 000, $N_i(0) = 100$, and $D_i(0) = 100$.

The results of both simulations are depicted in Figure 1. In each figure the heavy line represents the solution of the case with small initial conditions, i.e., starting near zero, and the thin line is the solution starting above the steady state. The convergence to the steady state of the total number of vectors can be seen at upper left; that of the infected vectors at upper right; infected humans at lower left; and infected dogs at lower right. It is seen clearly that each one of the populations, in both cases, converges monotonically to the steady state.

However, we stress that this monotone approach is characteristic of the system with averaged parameters. So it provides only qualitative insight at best. In the field, the parameters are affected by seasonal changes and are time dependent. This was taken into account in [Spagnuolo et al. 2011], since spraying is done once a year.

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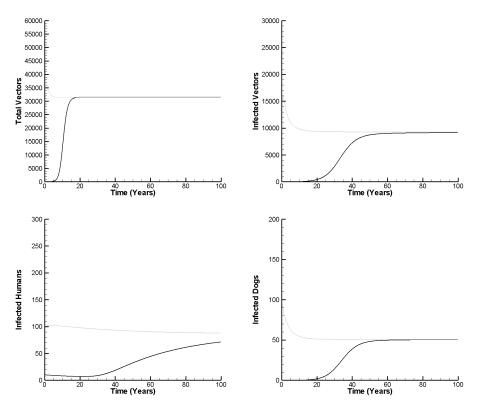


Figure 1. Convergence to the endemic state from above (thin line) and below (thick line).

5. Conclusions

A model for the dynamics of the Chagas disease, with averaged coefficients, was presented, following [Spagnuolo et al. 2012; 2011]. It consists of rate equations for the total numbers of vectors, and infected vectors, humans, and dogs (mammals). The model shows, within the conditions that seem to be observed in South America, an unstable disease-free equilibrium and a stable endemic equilibrium.

Then, our computer code was used to obtain numerical approximations of the model. In particular, we simulated the approach of the solutions to the endemic steady state. Two examples were presented, in the first one the initial conditions are below the values of the endemic equilibrium, and in the second they were above it. It was found, numerically, that the convergence to the endemic state was found to be monotone in both cases.

It may be of interest to prove that the convergence is monotone, however, the question is unresolved, yet.

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