Mathematical analysis for a model to control Chagas disease: Fighting an Infection with an Infection

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Abstract

Chagas disease is a vector-borne disease that is endemic across the Americas. In this paper, we review a single strain infection model for *Trypanosoma cruzi*, the parasite that causes Chagas disease. Then we construct a two strain infection model for *Trypanosoma cruzi* and *Trypanosoma rangeli* host-vector dynamics. This creates a basis for understanding the dynamics of the competing infections. From here, we can analyze the necessary initial conditions necessary for *T. rangeli* to outcompete *T. cruzi* in a given host-vector population. Recent research has found that infection with the non-pathogenic parasite *T. rangeli* provides protection against infection from the pathogenic parasite *T. cruzi*. No research has yet been done on creating a competition between *T. cruzi* and *T. rangeli* to displace *T. cruzi*, rather than vaccinate or treat animals for the infection. Our two strain model allows us to explore this dynamic. We propose an introduction of *T. rangeli* into host populations endemic with *T. cruzi*. This briefly creates in infection wave of *T. rangeli*, but the single introduction of the *T. rangeli* is insufficient to create a break in the *T. cruzi* infection wave. Multiple introductions of *T. rangeli* under ideal conditions can significantly reduce *T. cruzi* infection, but this effect stops if reintroductions of *T. rangeli* are stopped. Introduction of *T. rangeli* into at risk populations can reduce the invasion rate of *T. cruzi*.

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1 Introduction

Chagas disease is a vector borne disease that is endemic across the Americas. It is caused by the parasite, *Trypanosoma cruzi*. While some researchers are unsure whether a viable vaccine will be produced soon for *T. cruzi*, this may not be necessary. [3, 4] Recent research has found that if animals are infected with the non-pathogenic parasite *T. rangeli* before infection with *T. cruzi*, which causes Chagas disease, the rate of infection with *T. cruzi* drops significantly. [4, 15] Introducing *T. rangeli* can create a break in the *T. cruzi* infection cycle between vectors and hosts. No studies have yet been done to explore the possibility of infecting sylvatic populations with *T. rangeli* to displace *T. cruzi* from its niche.

Partial infection of sylvatic raccoon and vector populations with nonpathogenic *Trypanosoma rangeli* can be used to reduce the prevalence of *Trypanosoma cruzi* infections, the pathogenic parasite that causes Chagas disease. In order to create a full break in the infection wave of *T. cruzi*, other mitigation methods need to be coupled with the introduction of *T. rangeli* infection. We explore the option of insecticide sprays coupled with the introduction of *T. rangeli* into host populations.

Raccoons have been shown to have 60% infection rate in Louisiana, though fewer than 30 total human infections have been found across the entire United States since 1890. [17] The rate of new infections found in the United States has increased in recent years, with better screening methods and reporting. Therefore, to mitigate Chagas disease in the United States in humans, it is important to focus on sylvatic populations like raccoons for intervention measures.

We examine a proposed mitigation program that uses the nonpathogenic parasite *T. rangeli* to displace pathogenic parasite *T. cruzi* from its niche in the ecosystem. We create a mathematical model to test this program idea, analyzing first a single strain *T. cruzi* model and then a competing two strain model with *T. cruzi* and *T. rangeli* infection.

We found that a single introduction of *T. rangeli* into host populations alone is insufficient to create a permanent break in the *T. cruzi* infection. While multiple reintroductions of *T. rangeli* into host populations can drive down the endemic equilibrium of *T. cruzi* infections, this is not a permanent solution. Once periodic introductions of *T. rangeli* stop, the population returns to its original endemic state. To summarize, *T. rangeli* in most scenarios is eventually outcompeted by *T. cruzi*.

Our results show that a single introduction and even multiple reintroductions of *T. rangeli* into an endemic *T. cruzi* host-vector population is insufficient as a mitigation method. However, introduction of *T. rangeli* into populations that have yet to be invaded by *T. cruzi* can provide protective effects and slow the rate of invasion. In other words, in populations at risk of becoming infected with *T. cruzi*, infection with *T. rangeli* can significantly delay the successful invasion of *T. cruzi* into this at risk population.

In this paper, we first review the background of Chagas disease and the single strain host-vector

model. Then we construct a competing two strain model and analyze the reproduction numbers of this model. Simulations, run in Matlab for the single strain and competing strains models, are followed by a summary of our findings and discussion of future works.

2 Background

American trypanosomiasis, more commonly known as Chagas disease, is a chronic, systemic infection caused by the parasite *T. cruzi*. [3, 24] Though it wasn't discovered until 1909 by Carlos Chagas, Chagas disease existed in human populations as early as 9,000 years ago. While it was originally confined to the poorer regions of South and Central America, the disease has become widely spread throughout the Americas, from Northern Argentina to the Southeastern United States. Today at least 8 million people are infected in all endemic areas across the Americas. [5, 17] Immigration from Latin America has made Chagas a growing health issue in Canada and the United States, as well as many parts of Europe and the western Pacific. The most common destination for Latin American immigrants is the U.S., where there are an estimated 300,000 individuals are infected with *T. cruzi*. [3] Despite this, there have been fewer than 30 locally acquired incidences (new cases) of Chagas transmission reported in the U.S., the most recent of which being in Louisiana in 2006. [10, 17]

2.1 The Vector and Hosts

Triatomine bugs are the main vector for *T. cruzi*. Although more than 130 species of triatomine bugs have been identified, not all are competent vectors of *T. cruzi*. [5] These vectors in turn infect more than 150 domestic animals and wild mammals, through transmission from bites by triatomine bugs. In the United States, triatomine vectors are found in 28 states, with 11 species present, 8 of which have been associated with human bites. [5, 8, 24] The most common hosts in the U.S. include opossums, raccoons, armadillos and dogs.

Triatomine bugs have five nymphal and one adult stage of both sexes, all of which can harbor the parasite, and the probability the bug is infected increases with the number of blood meals it has taken. [24] The total duration of the life cycle of the triatomine bug from egg to adult varies from 4 to 24 months, depending on the environment and species. Adults differ from nymphal stages in that they have fully developed wings and genitalia, therefore models of triatomine development often summarize the lifecycle to just three stages: egg, nymph, and adult.

Triatomines live in both forested and dry areas of the Americas, with adults preferring to live in the burrows and nests of wild animals, leading to high infection rates in these populations. [1] Many triatomine species have adapted to live near homes in domestic settings where they feed on livestock, pets, and humans. The probability of infection of humans increases when triatomines colonize homes. However, the probability of this in the U.S. is extremely rare, with only one notable

exception in 2006 where a Louisiana home was found to harbor triatomine colonies. Otherwise, only adult vectors enter homes to infect humans. [5] Transmission of parasite from vector to human hosts occur when the bug defecates after a blood meal. The timing and placement of defecation after feeding are crucial in determining the risk of transmission via fecal contamination of the host bite site. U.S. species of triatomines in general exhibit greater delays between feeding and defecation, which, coupled with low domestic colonization rates, greatly reduces risk of infection from vector to host. [5]

This has not prevented high infection rates in sylvatic wildlife populations. Raccoons, a favorite host of *T. cruzi* in the Southern U.S., and other wildlife boast an infection rate of 30-50% as of 2011. [3]

2.2 The Parasite and Progression of the Disease

T. cruzi, the protozoa responsible for Chagas disease, has a complex life cycle, with developmental stages within vectors and hosts. The parasite enters hosts when vectors take a blood meal and defecate. When fecal matter comes into contact with the bite site, the parasite enters the host. [3] When an infected host in turn gets bitten by a vector, the vector becomes infected with *T. cruzi*. Within this cycle, *T. cruzi* undergoes multiple developmental stages. This paper will assume, for simplification, that the infection cycle is limited to the adult stages of the triatomine bug.

While most transmission happens through blood meals, there are many transmission pathways. Parasite transmission can occur due to vector transmission from bites, vertical transmission from mother to child, blood transfusion, and oral transmission from ingestion of infected food. Risk of infection differs for all these different modes of transmission. Oral transmission is rare compared to vector transmission from bug bites, which is the most common transmission of infection. [24]

The progression of the disease is initially very quick. The acute phase of *T. cruzi* infection lasts for 4 to 8 weeks and the chronic phase lasts for the host's lifespan. The acute phase is accompanied with fever, muscle pains, anorexia, and other non-severe symptoms, with symptoms appearing 1 to 2 weeks after exposure with infected triatomines. [3] An anti-parasitic drug, such as benznidazole or nifurtimox, can cure the acute infection and prevent development of the chronic phase of the disease, though currently neither drug has FDA approval in the U.S. [5, 21, 23] Once the chronic phase of Chagas disease develops in an individual, the cure rate using anti-parasitic drugs drops from 50-80% in acute phase individuals to 20-60% in chronic phase individuals. [24] Most people remain asymptomatic throughout their lives, but they can still transmit the parasite and are at risk for further complications if their immune system becomes compromised. Because Chagas is largely asymptomatic, many cases go undiagnosed. [3, 5, 17] After years of progression into the chronic phase of the disease, 30-40% of people develop heart diseases such as abnormal rhythms, heart failure, and an increased risk of sudden death, as well as gastrointestinal problems, such as severe constipation and difficulty swallowing. [1, 3, 14] These symptoms usually develop about 10

to 30 years after the initial infection.

2.3 Issues in the United States

While the U.S. has a far lower incidence rate than South America, concerns remain because little to no programs exist for the prevention, control, and management of *T. cruzi* infection and Chagas disease. There is severely limited knowledge of *T. cruzi* transmission pathways in the U.S., almost no screening of at risk women (who might present modes of vertical transmission), and concerns regarding transmission through blood and organ donation. [5] Local transmission risk of the parasite is highly dependent on the factors influencing vector and sylvatic host distribution, which are currently not well understood in the United States. Improved knowledge in these areas could better inform control programs, screening programs, and diagnostic programs in the U.S.

2.4 Strategies for Control

In Latin America, the best defense against Chagas disease has been compulsory blood-bank screening. Both microscopic and serological tests are used to determine if *T. cruzi* is present in an individual. The initial phase of Chagas disease can be diagnosed by identification of the parasite in the bloodstream by microscopic examination, or even earlier using polymerase chain reaction (PCR). [18] Once the chronic stage has developed, *T. cruzi* can only be detected in tissues, not the bloodstream; therefore, it is diagnosed by the presence of *T. cruzi* specific anti-bodies. However, for conclusive evidence of chronic Chagas disease, at least two different serological tests of differing formats must be used to confirm a positive result. By detecting initial stage Chagas disease early and catching chronic stage infections, Latin American authorities can provide the necessary treatments to decrease the prevalence and incidence of Chagas disease. [18]

Prevalence of *T. cruzi* infection in Latin American countries has decreased due to vector control initiatives. [24] Traditional vector control programs focus on spraying insecticides within homes and buildings to kill domestic colonies. The goal is to interrupt the vector-human transmission cycle, as well as domestic vector-host cycles between household pets and livestock with triatomine bugs. [16, 24] Some vector control programs include the Southern Cone Initiative to Control/Eliminate Chagas Disease, the Andean Pact Initiative to Control/Eliminate Chagas Disease, and the Central America Initiative to Control/Eliminate Chagas Disease. All these programs include a preparatory phase for mapping the community, an attack phase during which spraying occurs, a surveillance phase for the detection of fecal residue from triatomines after the attack phase, and finally, an outreach phase where the community is educated on Chagas and its risks. Despite these efforts, re-infestations of homes often occur after insecticide programs. Therefore, it is important to understand how to create even more effective vector control initiatives, or think of solutions beyond vectors.

The key to the decrease in the number of cases of Chagas disease in Latin America lies in the

decrease in the incidence (new cases) of the disease (700,000 per year in 1990 versus 41,200 per year in 2006) and in the number of deaths from Chagas disease (about 50,000 per year versus 12,500 per year). Mathematical models have been used to pinpoint new areas of intervention, and to provide insight on how re-infestation occurs, the role of sylvatic hosts, and where to put resources to get the most effect.

In the United States, current mathematical models have focused on understanding sylvatic host-vector relationships because human case prevalence and incidence rates are so low. [11–13] Vector control programs do not yet exist in the U.S. for triatomine bugs for the very same reasons. Current research aims at understanding vector and sylvatic host distribution to pinpoint local health risks, since all cases of U.S. contracted Chagas disease happened in the Southern U.S., not across the whole country.

Currently, researchers are exploring other more permanent methods for control. Antigen-derived vaccines are in development, using the non-pathogenic strain *T. rangeli*, which offers some protection against *T. cruzi*. [4, 15] However, these vaccines are not yet viable options. Animal trials with live *T. rangeli* infection to stimulate the production of antibodies have been found to be very successful in mice and dogs, though human trials have not begun.[4, 15] Since human rates of infection are so low in the U.S., it would be more advantageous to investigate infecting wildlife populations with *T. rangeli*, similar to how the rabies vaccine has been used in the U.S. The rabies program which has been operational since the 1970s uses a live vaccine, similar to what the proposed *T. rangeli* infection mitigation method would be. [2] Target areas of the rabies program have had significantly reduced rabies cases, therefore we hypothesize a similar vaccination program for Chagas disease might have the same positive effect.

It is important to note however that *T. rangeli*, while nonpathogenic in host animals, has been found to be pathogenic in vectors. These studies are however limited in that they only study the *Rhodnius* species, and insufficient data to say that it decreases survivability of all vectors. [20] Therefore, for this paper, we will disregard the possibly pathogenic effects of *T. rangeli* on vectors.

3 Mathematical Model

Previous Chagas models have focused on human-vector interactions, multiple host-vector interactions, and evaluating vector control programs. Mubayi et al. created a two-strain continuous-time model to understand the role the adaptations to distinct modes of transmission plays in competition between two strains of *T. cruzi*. They found that oral transmission played a key role in mediating the competition between horizontal and vertical transmission modes. [12] This model only looked at one host population at a time, and its interactions with a single vector population. The model also predicts competitive exclusion, though reports have found trace levels of multiple *T. cruzi* strains in raccoon populations. [25] Kribs et al. went on to explore the possibility of seasonality

in demographic parameters explaining the effect of coexistence. [13] Results from this study found that in the three sylvatic cycles studied, only one strain of *T. cruzi* "wins" or rather outcompetes the other strains. Therefore, seasonality alone, nor differing disease transmission pathways, cannot explain coexistence of two strains of *T. cruzi* in a population.

While this and many other studies on Chagas in the U.S. and Mexico focus on the interplay between sylvatic hosts and vectors, [7, 12, 13, 26], no research has looked at applying a competing-infection as a mitigation program for human or sylvatic populations. In this mitigation program, *T. rangeli* would be introduced to a population to provide protective effects in much the same way a vaccine does. Murray analyzed theoretical vaccination programs of rabies for foxes in England using Fisher-Kolmogorov equations. [19] He investigated a control strategy based on creating a "break" in the wave of infection in fox populations, a "break" being defined as "a region where the susceptible fox population is reduced below the critical carrying capacity and hence will not sustain a propagating epizootic wave." [19] We can apply this idea to the spread of Chagas disease in sylvatic populations, such as raccoons. The main difference is the transmission pathway, as Chagas disease is a vector-host transmission pathway versus rabies which is a host-host transmission pathway.

We create a model that examines the possible outcomes of infecting sylvatic populations in the United States with *T. rangeli* to displace *T. cruzi* infection as a form of disease control.

We create the modeling framework for modeling competing infections in host-vector diffusion systems. This will provide insight into the effectiveness of fighting an infection with an infection, given that currently there is no viable vaccine for Chagas disease. First we will review the dynamics of a singe strain infection model of just *T. cruzi* infection. Then we will expand into a two-strain competing infection model to assess how the dynamics of the system change. In the simulations, we will expand upon this framework to explore a dual program approach: both partial *T. rangeli* infection coupled with insecticide spraying to reduce the *T. cruzi* infected population of sylvatic and vector populations simultaneously.

Figure 1a shows the single strain infection model, where susceptible hosts are cross infected by *T. cruzi* infected vectors and vice versa. Similarly, Figure 1b expands to show that susceptible hosts can either be infected with *T. rangeli* or *T. cruzi*. Vectors can also become infected with *T. rangeli* or *T. cruzi*, and additionally infected vectors with *T. rangeli* can become cross-infected with *T. cruzi*. We consider this cross-infection the equivalent of only being infected with *T. cruzi* because we are only concerned about infection with the pathogenic parasite *T. cruzi*.

3.1 Single Strain Model

We will begin by defining the system and deriving the system of differential equations for the single strain infection model, shown in Figure 1a.

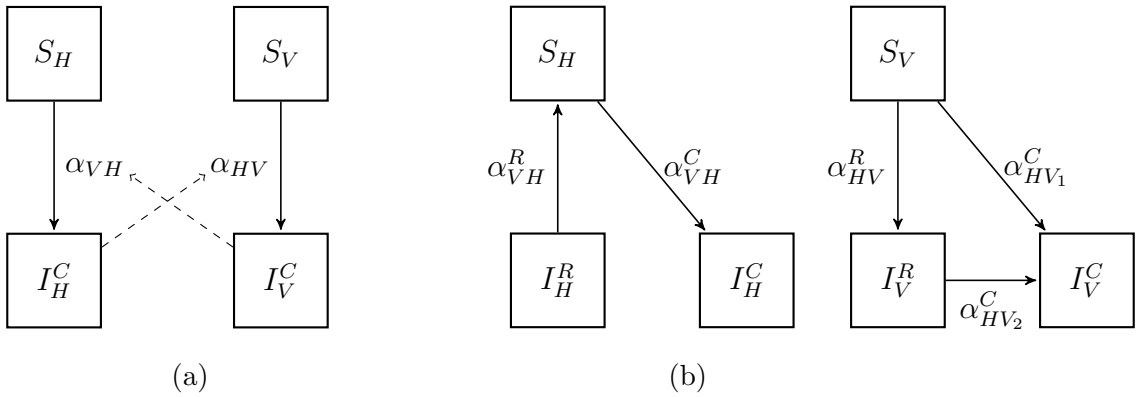


Figure 1: This figure shows a) one-strain model and b) two-strain model. (1a) This Chagas flow chart uses dotted lines to show cross infection between vectors and hosts. Solid lines are progression from susceptible to infected stage for hosts and triatomine vectors. This is a representation of how populations change states in time. Susceptible compartments are marked S_i and progress into infected compartments, marked I_i where i is a host or a vector. (1b) This Chagas flow chart is a full infection model including infection compartments for *T. rangeli* and *T. cruzi*. Susceptible compartments can now progress either into *T. rangeli* infected compartments, I_i^R or *T. cruzi* infected compartments, I_i^C.

3.1.1 Differential Equations

The general dynamics of *T. cruzi* infection begin with a susceptible host population (S_H) that gets infected by a *T. cruzi* infected vector (I_V^C) through one of the modes of transmission: eating an infected vector, being bitten by an infected vector, or consuming food contaminated by a vector. We do not consider vertical transmission in this model because transmission through this pathway is negligible. [12] These modes of contact are summarized in the contact rate, b_V. The probability of transmission of the *T. cruzi* parasite from a vector to a host through these contacts is β_{VH}^C, but this also depends on the probability that contact is with a susceptible host (P_{S_H}). The probability that a contact between a vector and a host results in transmission of *T. cruzi* is summarized by the force from infection term, α_{VH}^C.

Similarly, susceptible vectors (S_V) become infected by taking a blood meal from an infected host (I_H^C). In this case, the force from infection α_{HV}^C depends on the contact rate with the host (b_H), the probability of transmission from the host to the vector (β_{HV}^C), and the probability contact is with a susceptible vector (P_{S_V}).

All hosts die at some rate μ_H, and all vectors die at some rate μ_V. To simplify the model, we assume birth and death rates are constant such that the population of hosts and vectors does not change with time. We assume that the total population of hosts and vectors, $N_H = S_H + I_H^C$ and $N_V = S_V + I_V^C$, is constant. Then susceptibles enter the population at a rate of $\mu_H N_H$ and $\mu_V N_V$ per day to keep the population constant.

This model can be expressed as the system of ordinary differential equations (ODEs):

$$\frac{dS_H}{dt} = -\alpha_{VH}^C I_V^C + \mu_H N_H - \mu_H S_H \tag{1a}$$

$$S_H = N_H - I_H^C$$

$$\frac{dI_H^C}{dt} = \alpha_{VH}^C I_V^C - \mu_H I_H^C \tag{1b}$$

$$\frac{dS_V}{dt} = -\alpha_{HV}^C I_H^C + \mu_V N_V - \mu_V S_V \tag{1c}$$

$$S_V = N_V - I_V^C$$

$$\frac{dI_V^C}{dt} = \alpha_{HV}^C I_H^C - \mu_V I_V^C \tag{1d}$$

where α_{ij}^C represents the force from infection, or rather the rate at which an infected host infects a susceptible vector and vice versa. Each α_{ij}^C is constructed for $ij = HV$ or $ij = VH$ by the following:

$$\alpha_{ij}^C = \begin{pmatrix} \text{\# of contacts} \\ \text{from } i \text{ to } j \\ \text{per day} \end{pmatrix} \begin{pmatrix} \text{Probability of} \\ \text{transmission per} \\ \text{contact from } i \text{ to } j \end{pmatrix} \begin{pmatrix} \text{Probability} \\ \text{the contact is with} \\ \text{a susceptible } j \end{pmatrix} ,$$

$$\alpha_{ij}^C = b_i \beta_{ij}^C P_{S_j} ,$$

where b_i is the contacts from i to j, β_{ij}^C is the probability of transmission of *T. cruzi* from i to j, and $P_{S_j} = \frac{S_j}{N_j}$ is the probability that the contact is being made with a susceptible host or vector. Therefore, we define each α_{ij}^C explicitly as the following:

$$\alpha_{VH}^C = b_V \beta_{VH}^C (\frac{S_H}{N_H}) \tag{2a}$$

$$\alpha_{HV}^C = b_H \beta_{HV}^C (\frac{S_V}{N_V}) \tag{2b}$$

A summary of the variables and parameters in this system can be found in Table 1.

3.1.2 Basic reproduction Number

In this section, we will describe the basic reproduction number, how it is calculated, and how it can be interpreted.

The basic reproduction number, $\mathcal{R}_0$, is the number of secondary cases produced by a single infection in a completely susceptible population over one generation. First we will describe how the basic reproduction number is derived from the point of view of the susceptible. The basic reproduction number can be considered in its most basic state $\mathcal{R}_0^{iC} = b_i \beta_{ij}^C \tau_i$, where

Symbol	Interpretation	Units
S_H, S_V	Susceptible host, and triatomines	animals
I_H^C, I_V^C	Host and triatomine vectors infected with *T. cruzi*	animals
N_H, N_V	Total population of host and triatomine vectors	animals
μ_H, μ_V	Death and birth rate of host and triatomine vectors	day^{-1}
α_{ij}^C	Force of infection with *T. cruzi* from infected species i to j	dimensionless
β_{ij}^C	Probability of transmission per contact of *T. cruzi* from i to j	contact^{-1}
b_V	Number of bites on host per vector per day	contacts day^{-1}
b_H	Number of bites from vector per host per day	contacts day^{-1}

Table 1: Model Variables and Parameters

$$\mathcal{R}_0^{iC} = \begin{pmatrix} \text{\# of contacts} \\ \text{from } i \text{ to } j \\ \text{per day} \end{pmatrix} \begin{pmatrix} \text{Probability of} \\ \text{transmission per} \\ \text{contact from } i \text{ to } j \end{pmatrix} \begin{pmatrix} \text{Time a host or} \\ \text{vector } i \text{ is infectious} \\ \text{with } T.\ cruzi \end{pmatrix}.$$

Therefore, the basic reproduction number, $\mathcal{R}_0$, is the product of the number of contacts from an infectious species i to a susceptible species j times the probability of transmission per contact and the time that the infectious species i is infectious.

We now derive each of these factors defining $\mathcal{R}_0$. The number of contacts per vector/host per day is denoted in our model by b_i. The probability of transmission of *T. cruzi* per contact, β_{ij}^C, depends on how many contacts a host has with a vector or vice versa. Finally, we consider the time a host or vector is infectious, defined as $\tau_i = \frac{1}{\mu_i}$. Thus, τ_i is the average amount of time spent in an infected compartment of our model.

In general we can find two possible $\mathcal{R}_0$ based on the two infectious states:

$$\mathcal{R}_0^{HC} = b_V \beta_{VH}^C \tau_V \tag{3a}$$

$$\mathcal{R}_0^{VC} = b_H \beta_{HV}^C \tau_H \ . \tag{3b}$$

The $\mathcal{R}_0$ for the *T. cruzi* epidemic can be found as the square root of the product of the host and vector reproduction numbers. The square root arises because it takes two generations for infected hosts to produce new infected hosts; and similarly it takes two generations for infected vectors to produce new infected vectors. Thus, we find the following equation for $\mathcal{R}_0^C$, the basic reproduction number of *T. cruzi*:

$$\mathcal{R}_0^C = \sqrt{\mathcal{R}_0^{HC} \times \mathcal{R}_0^{VC}} \ . \tag{4a}$$

If $\mathcal{R}_0 < 1$, then on average an infected individual produces less than one new infected individual, and therefore the epidemic dies out. If $\mathcal{R}_0 > 1$, then on average an infected individual produces more than one new infected individual, and therefore the epidemic spreads [28].

Next Generation Matrix Analysis

The basic reproduction number, $\mathcal{R}_0$, measures the average number of secondary cases produced by one infected individual in a completely susceptible population [9]. We are going to derive $\mathcal{R}_0$ using the Next Generation Matrix approach.

First the system is divided into $\mathcal{F}$, a vector summarizing the rate at which all new infections in compartment i appear, and $\mathcal{V}$, a vector summarizing the rates of transfer out of compartment i and into other infected compartments $i = 1, ..., n$, where n is the number of infected compartments. We assume disease free equilibrium (DFE) because a stable equilibrium solution for the model exits at DFE [28]. Therefore, the system is: $\dot{I} = \mathcal{F} - \mathcal{V}$ where $\dot{I}$ summarizes the equations for all infected compartments. In our system with susceptible (S) and infected (I) vector and host states, $\dot{I}$ would be expressed as:

$$\dot{I} = \begin{bmatrix} \dot{I}_H^C \\ \dot{I}_V^C \end{bmatrix} .$$

If vectors $\mathcal{F}$ and $\mathcal{V}$ are greater than or equal to zero for all compartments i, then we can evaluate $\mathcal{F}$ and $\mathcal{V}$ at DFE. Now we compute the Jacobian matrices for $\mathcal{F}$ and $\mathcal{V}$ to find F and V.

$\mathbb{J}_{F_{i,j}} = \frac{\partial \mathcal{F}_i}{\partial x_j}$ where i is the compartment being evaluated where the newly infected individuals are placed, and $j = 1, \cdots, n$. The entry $\mathbb{J}_{F_{i,j}}$ is the rate at which infected individuals in compartment j produce new infections in compartment i [28].

Similarly, $\mathbb{J}_{V_{j,k}} = \frac{\partial \mathcal{V}_j}{\partial x_k}$, where j is the infected compartment being evaluated from 1 to n, and $j = 1, \cdots, n$, where n is all compartments. The entry $\mathbb{J}_{V_{j,k}}^{-1}$ is the average amount of time an individual spends in compartment j during their lifetime assuming the population remains near DFE and that there is no reinfection. [28] This entry also depends on the probability that a person enters compartment j in order to spend time in compartment j.

Therefore, the (i, k) entry of $\mathbb{J}_F\mathbb{J}_V^{-1}$ is the expected number of new infections in compartment i produced from the infected individual originally in compartment k. $\mathbb{J}_F\mathbb{J}_V^{-1}$ is the next generation matrix. $\mathcal{R}_0$ is defined as

$$\rho(\mathbb{J}_F\mathbb{J}_V^{-1}) = \mathcal{R}_0,$$

where $\rho(\mathbb{J}_F\mathbb{J}_V^{-1})$ is the spectral radius of $\mathbb{J}_F\mathbb{J}_V^{-1}$.

Next Generation Analysis: Applied to the Model

To find the next generation matrix, $\mathbb{J}_F\mathbb{J}_V^{-1}$, we begin by looking at the infected compartments of our model, namely I_H^C, and I_V^C.

We construct our model as the difference of two vectors:

$$\dot{I} = \frac{d}{dt}\begin{bmatrix} \dot{I}_H^C & \dot{I}_V^C \end{bmatrix}^T = \mathcal{F} - \mathcal{V} = \begin{bmatrix} b_V \beta_{VH}^C P_{S_H} I_V^C \\ b_H \beta_{HV}^C P_{S_V} I_H^C \end{bmatrix} - \begin{bmatrix} \mu_H I_H^C \\ \mu_V I_V^C \end{bmatrix}.$$

At disease free equilibrium, $\mathcal{F}$ becomes:

$$\begin{bmatrix} b_V \beta_{VH}^C I_V^C \\ b_H \beta_{HV}^C I_H^C \end{bmatrix}.$$

Jacobian matrix of $\mathcal{F}$ is:

$$\mathbb{J}_F = \begin{bmatrix} 0 & b_V \beta_{VH}^C \\ b_H \beta_{HV}^C & 0 \end{bmatrix}.$$

Similarly, the inverse of the Jacobian matrix of $\mathcal{V}$, can be written as:

$$\mathbb{J}_V^{-1} = \begin{bmatrix} \tau_H & 0 \\ 0 & \tau_V \end{bmatrix}.$$

Therefore, $\mathbb{J}_F \mathbb{J}_V^{-1}$ is as follows:

$$\mathbb{J}_F \mathbb{J}_V^{-1} = \begin{bmatrix} 0 & b_V \beta_{VH}^C \tau_V \\ b_H \beta_{HV}^C \tau_H & 0 \end{bmatrix}.$$

As we saw above, we can see that the basic reproduction number, $\mathcal{R}_0$ for the host and for the vector are the eigenvalues of $\mathbb{J}_F \mathbb{J}_V^{-1}$, equivalent to what we found in 3a and 3b. Given that the eigenvalues take the form $\lambda^2 = \mathcal{R}_0^{CH} \mathcal{R}_0^{CV}$, the basic reproduction number, $\mathcal{R}_0$, for *T. cruzi* is again found as the square root of the product of the host and vector reproduction numbers:

$$\mathcal{R}_0^C = \sqrt{\mathcal{R}_0^{HC} \times \mathcal{R}_0^{VC}}\,.$$

Reproduction Number from the Perspective of the Infected

As defined above, the basic reproduction number, $\mathcal{R}_0$, measures the average number of secondary cases produced by one infected individual in a completely susceptible population. [28] We can construct $\mathcal{R}_0$ heuristically through the perspective of the infected. Recall the system of equations:

$$\frac{dI_H^C}{dt} = b_V \beta^C (\frac{S_H}{N_H}) I_V^C - \mu_H I_H^C$$
$$\frac{dI_V^C}{dt} = b_H \beta^C (\frac{S_V}{N_V}) I_H^C - \mu_V I_V^C\,,$$

and the α_{ij}^C terms are defined as in Equations 2a and 2b such that the system of equations is now:

$$\frac{dI_H^C}{dt} = \alpha_{VH}^C I_V^C - \mu_H I_H^C$$
$$\frac{dI_V^C}{dt} = \alpha_{HV}^C I_H^C - \mu_V I_V^C \ .$$

By the definition of $\mathcal{R}_0$, we are only interested in time zero. At time zero, the entire population is assumed to be almost entirely susceptible due to DFE, or equivalently $S_i \cong N_i$. This assumes that the population of all other states is equal to zero. Therefore every α_{ij}^C term reduces to the following form at DFE:

$$\alpha_{ij}^C(0) = b_i \beta_{ij}^C P_{S_j}(0) = b_i \beta_{ij}^C$$

Considering how $\mathcal{R}_0$ was constructed above, $\alpha_{ij}(0)$ summarizes the first two terms: the number of bites per day and the probability of transmission per contact with state state i. To finish constructing $\mathcal{R}_0$, we need to consider τ_i, the time a host or vector spends in an infectious state, which could affect a susceptible vector or host.

Therefore, each $\mathcal{R}_0$ can be written as:

$$\mathcal{R}_0^{HC} = \alpha_{VH}^C(0)\tau_V \qquad = b_V \beta_{VH}^C \tau_V$$
$$\mathcal{R}_0^{VC} = \alpha_{HV}^C(0)\tau_H \qquad = b_H \beta_{HV}^C \tau_H \ .$$

Note that as before we can find $\mathcal{R}_0^C$ of the *T. cruzi* epidemic to be equivalent to:

$$\mathcal{R}_0^C = \sqrt{b_V \beta_{VH}^C \tau_V \times b_H^C \beta_{HV}^C \tau_H} \ .$$

From these calculations the $\mathcal{R}_0$ calculated from the view of the susceptible population using the Next Generation matrix technique is equivalent to the $\mathcal{R}_0$ calculated heuristically from the view of the infected population.

3.1.3 Effective Reproduction Number

At time zero, all hosts and vectors are susceptible, therefore the number of contacts made by susceptibles has no impact on the initialization of the epidemic, as shown in the calculations of $\mathcal{R}_0$. However, we want to look at $\mathcal{R}_{eff}$, the effective reproduction number, or the average number of secondary cases produced over time by one infected individual in a partially susceptible population. Note that the effective reproduction number definition does not require that we fix $t = 0$, but rather can be calculated at any point in time t.

Derivation of Effective Reproduction Number

We can calculate the effective reproduction number by looking at how we constructed $\mathcal{R}_0$ from the perspective of the infected population in Section 3.1.2.

Looking at our initial equations, $\mathcal{R}_0$ for each epidemic was calculated by looking at the following equation at time zero:

$$\mathcal{R}_0^C = \sqrt{\mathcal{R}_0^{HC} \times \mathcal{R}_0^{VC}} \qquad = \sqrt{\alpha_{VH}^C(0)\tau_V \times \alpha_{HV}^C(0)\tau_H}\ .$$

To look at how the effective reproduction number changes over time all we need to do is look at α_* as a function of time, t:

$$\begin{aligned}
\mathcal{R}_{eff}^C &= \sqrt{\alpha_{VH}^C(t)\tau_V \times \alpha_{HV}^C(t)\tau_H} \\
&= \sqrt{b_V\beta_{VH}^C\tau_V\left(\frac{S_H(t)}{N_H}\right) \times b_H\beta_{HV}^C\tau_H\left(\frac{S_V(t)}{N_V}\right)} \\
&= \sqrt{\mathcal{R}_0^{HC}\left(\frac{S_H(t)}{N_H}\right) \times \mathcal{R}_0^{VC}\left(\frac{S_V(t)}{N_V}\right)} \qquad (5a)
\end{aligned}$$

Using this equation, we can now calculate the effective reproduction number at any given point in time. The number of secondary cases produced over time is now a function of the fraction of contacts made by susceptible people in the entire population.

Endemic Equilibrium

The endemic equilibrium occurs when the the disease is globally stable and persists in the population at a replacement rate of one; this is when one current infection produces only one new infection. We can find this point in time when $\mathcal{R}_{eff} = 1$, or rather when the effective reproduction number is equal to 1. Looking at Equation 5a, we can find the following condition:

$$\mathcal{R}_{eff}^C = \sqrt{\mathcal{R}_0^{HC}\left(\frac{S_H(t)}{N_H}\right) \times \mathcal{R}_0^{VC}\left(\frac{S_V(t)}{N_V}\right)} \qquad = 1$$

Additionally, at the endemic equilibrium all derivatives are equal to zero, or rather the rate of change of all compartments is zero, because now the infection is spreading at a constant rate. This provides the following conditions:

$$\begin{bmatrix} \dot{S}_H \\ \dot{I}_H^C \\ \dot{S}_V \\ \dot{I}_V^C \end{bmatrix} = 0$$

Recall also the assumption that the populations are constant such that $N_H = S_H + I_H^C$ and $N_V = S_V + I_V^C$. Combining these conditions we find that the endemic infected populations occur

when the following conditions are met:

$$S_H^* = \frac{N_H^2}{N_H + \mathcal{R}_0^{HC} I_V^{C*} \frac{\tau_H}{\tau_V}} \tag{6a}$$

$$I_H^{C*} = \mathcal{R}_0^{HC} \left(\frac{S_H^*}{N_H} \right) \frac{\tau_H}{\tau_V} I_V^{C*} \tag{6b}$$

$$S_V^* = \frac{N_V^2}{N_V + \mathcal{R}_0^{VC} I_H^{C*} \frac{\tau_V}{\tau_H}} \tag{6c}$$

$$I_V^{C*} = \mathcal{R}_0^{VC} \left(\frac{S_V^*}{N_V} \right) \frac{\tau_V}{\tau_H} I_H^{C*} \tag{6d}$$

$$0 = \mathcal{R}_0^{HC} \left(\frac{S_V^*}{N_V} \right) \times \mathcal{R}_0^{VC} \left(\frac{S_H^*}{N_H} \right) - 1 \tag{6e}$$

where the final condition is derived from combining Conditions 6b and 6d. Note that Condition 6e is equivalent to our first condition, $\mathcal{R}_{eff} = 1$.

Using these four conditions, we can solve to find the following endemic infected equilibriums:

$$I_H^{C*} = \frac{N_H^2 N_V^2 (\mathcal{R}_0^{HC} \mathcal{R}_0^{VC} + 1)}{N_V (\mathcal{R}_0^{HC} N_H)(\mathcal{R}_0^{VC} N_V) - (\mathcal{R}_0^{VC} N_V) N_H^2 \frac{\tau_V}{\tau_H}} \tag{7a}$$

$$I_V^{C*} = \frac{N_H^2 N_V^2 (\mathcal{R}_0^{HC} \mathcal{R}_0^{VC} + 1)}{N_H (\mathcal{R}_0^{HC} N_H)(\mathcal{R}_0^{VC} N_V) - (\mathcal{R}_0^{HC} N_H) N_V^2 \frac{\tau_H}{\tau_V}} \ . \tag{7b}$$

These equations give us the number of hosts and vectors that are infected with *T. cruzi* in an endemic population.

3.2 Two Strain Model

Now we will build a model for two strains of infection.

3.2.1 Differential Equations

As before, we have a susceptible host population (S_H), but now there are two strains of infection. A susceptible host can become infected by a vector with *T. rangeli* infection (I_V^R), or a vector with *T. cruzi* infection (I_V^C). In this case, the force from infection α_{VH}^* depends on the contact rate of the vector with the host (b_V), the probability of transmission from the vector to the host (β_{VH}^*), and the probability contact is with a susceptible host (P_{S_H}). The type of infection is indicated by $* = R$ for *T. rangeli* infection and $* = C$ for *T. cruzi* infection.

Similarly, we have a susceptible vector population (S_V) which can become infected by a host with *T. rangeli* infection (I_H^R), or a host with *T. cruzi* infection (I_H^C). Again, the force from infection α_{HV}^* depends on the contact rate of the host with the vector (b_H), the probability of transmission from the host to the vector (β_{HV}^*), and the probability contact is with a susceptible vector (P_{S_V}).

For vectors, infection with *T. rangeli* provides no protection against cross-infection with *T. cruzi*. Since the protective effects of *T. rangeli* only work if the host is infected with *T. rangeli* before *T. cruzi*, we do not consider the case where a host with *T. cruzi* is infected with *T. rangeli*. Also due to the protective effects, we do not consider the case where a host with *T. rangeli* is infected with *T. cruzi*.

However, vectors with *T. rangeli* can become infected with both *T. rangeli* and *T. cruzi*. In this case, when they infect a host, there is not enough time for *T. rangeli* to provide protection from the *T. cruzi* infection. Therefore, we assume the host was only infected with *T. cruzi*. By this assumption, vectors cross-infected with *T. rangeli* and *T. cruzi* are the same as vectors only infected with *T. cruzi*. Therefore, vectors with cross-infection are a subclass contained within the I_V^C compartment.

We again assume that the total populations (N_H, N_V) are kept constant. By doing so, we can deduce the following: $N_H = S_H + I_H^C + I_H^R$ and $N_V = S_V + I_V^C + I_V^R$. This model in Fig. 1b can be expressed as the system of ordinary differential equations:

$$\frac{dS_H}{dt} = -\alpha_{VH}^R I_V^R - \alpha_{VH}^C I_V^C + \mu_H N_H - \mu_H S_H \tag{8a}$$
$$\frac{dI_H^R}{dt} = \alpha_{VH}^R I_V^R - \mu_H I_H^R \tag{8b}$$
$$\frac{dI_H^C}{dt} = \alpha_{VH}^C I_V^C - \mu_H I_H^C \tag{8c}$$
$$\frac{dS_V}{dt} = -\alpha_{HV}^R I_H^R - \alpha_{HV_1}^C I_H^C + \mu_V N_V - \mu_V S_V \tag{8d}$$
$$\frac{dI_V^R}{dt} = \alpha_{HV}^R I_H^R - \alpha_{HV_2}^C I_H^C - \mu_V I_V^R \tag{8e}$$
$$\frac{dI_V^C}{dt} = \alpha_{HV_1}^C I_H^C + \alpha_{HV_2}^C I_H^C - \mu_V I_V^C \tag{8f}$$

where the α_{ij}^*, the force from infection terms, are defined as:

$$\alpha_{VH}^R = b_V \beta_{VH}^R P_{S_H} \tag{9a}$$
$$\alpha_{VH}^C = b_V \beta_{VH}^C P_{S_H} \tag{9b}$$
$$\alpha_{HV}^R = b_H \beta_{HV}^R P_{S_V} \tag{9c}$$
$$\alpha_{HV_1}^C = b_H \beta_{HV}^C P_{S_V} \tag{9d}$$
$$\alpha_{HV_2}^C = b_H \beta_{HV}^C P_{I_V^R} \tag{9e}$$

The term α_{HV_1} is the force from infection of hosts with *T. cruzi* on susceptible vectors, and the term α_{HV_2} is the force from infection of hosts with *T. cruzi* on vectors infected with *T. rangeli* respectively.

3.2.2 Basic Reproduction Number

Again the basic reproduction number for each epidemic can be calculated using Next Generation analysis or heuristic means.

Next Generation Analysis

To find the next generation matrix, $\mathbb{J}_F\mathbb{J}_V^{-1}$, we begin by looking at the infected compartments of our model, namely I_H^R, I_H^C, I_V^R, and I_V^C.

We construct our model as the difference of two vectors:

$$\frac{d}{dt}\begin{bmatrix} I_H^R & I_H^C & I_V^R & I_V^C \end{bmatrix}^T = \mathcal{F} - \mathcal{V} =$$
$$\begin{bmatrix} b_V^R\beta_{VH}^R P_{S_H} I_V^R \\ b_V^C\beta_{VH}^C P_{S_H} I_V^C \\ b_H^R\beta_{HV}^R P_{S_V} I_H^R \\ b_H^C\beta_{HV}^C (P_{S_V} + P_{I_V^R}) I_H^C \end{bmatrix} - \begin{bmatrix} \mu_H I_H^R \\ \mu_H I_H^C \\ \mu_V I_V^R + b_H^C\beta_{HV}^C \frac{I_V^R}{N_V} I_H^C \\ \mu_V I_V^C \end{bmatrix}.$$

At disease free equilibrium, $\mathcal{F} - \mathcal{V}$ becomes:

$$\begin{bmatrix} b_V^R\beta_{VH}^R I_V^R \\ b_V^C\beta_{VH}^C I_V^C \\ b_H^R\beta_{HV}^R I_H^R \\ b_H^C\beta_{HV}^C I_H^C \end{bmatrix} - \begin{bmatrix} \mu_H I_H^R \\ \mu_H I_H^C \\ \mu_V I_V^R \\ \mu_V I_V^C \end{bmatrix}.$$

Jacobian matrix of $\mathcal{F}$ is:

$$\mathbb{J}_F = \begin{bmatrix} 0 & 0 & b_V^R\beta_{VH}^R & 0 \\ 0 & 0 & 0 & b_V^C\beta_{VH}^C \\ b_H^R\beta_{HV}^R & 0 & 0 & 0 \\ 0 & 0 & b_H^C\beta_{HV}^C & 0 \end{bmatrix}.$$

Similarly, $\mathbb{J}_V^{-1}$ is derived by simple calculations to be:

$$\mathbb{J}_V^{-1} = \begin{bmatrix} \tau_H & 0 & 0 & 0 \\ 0 & \tau_H & 0 & 0 \\ 0 & 0 & \tau_V & 0 \\ 0 & 0 & 0 & \tau_V \end{bmatrix}.$$

Therefore, $\mathbb{J}_F\mathbb{J}_V^{-1}$ is as follows:

$$\mathbb{J}_F\mathbb{J}_V^{-1} = \begin{bmatrix} 0 & 0 & b_V^R\beta_{VH}^R\tau_V & 0 \\ 0 & 0 & 0 & b_V^C\beta_{VH}^C\tau_V \\ b_H^R\beta_{HV}^R\tau_H & 0 & 0 & 0 \\ 0 & b_H^C\beta_{HV}^C\tau_H & 0 & 0 \end{bmatrix}.$$

As we saw above, we can see that the basic reproduction number, $\mathcal{R}_0$ for each host-parasite combination is:

$$\mathcal{R}_0^{HR} = b_V^R \beta_{VH}^R \tau_V \tag{10a}$$
$$\mathcal{R}_0^{HC} = b_V^C \beta_{VH}^C \tau_V \tag{10b}$$
$$\mathcal{R}_0^{VR} = b_H^R \beta_{HV}^R \tau_H \tag{10c}$$
$$\mathcal{R}_0^{VC} = b_H^C \beta_{HV}^C \tau_H \ , \tag{10d}$$

and the $\mathcal{R}_0$ for each parasite, *T. rangeli*, R, and *T. cruzi*, C, can be found as the square root of the product of the host and vector reproduction numbers:

$$\mathcal{R}_0^R = \sqrt{\mathcal{R}_0^{HR} \times \mathcal{R}_0^{VR}}$$
$$\mathcal{R}_0^C = \sqrt{\mathcal{R}_0^{HC} \times \mathcal{R}_0^{VC}} \ .$$

Basic Reproduction Number: Perspective of the Infected

Here we construct $\mathcal{R}_0$ heuristically through the perspective of the infected.

Again, by the definition of $\mathcal{R}_0$, we are only interested in time zero. At time zero, the entire population is assumed to be almost entirely susceptible due to DFE. Therefore every α term to the following form at time zero:

$$\alpha_{ij}^*(0) = b_i \beta_{ij}^* P_{S_j}(0) = b_i \beta_{ij}^*$$

Considering how $\mathcal{R}_0$ was constructed above, $\alpha_{ij}^*(0)$ summarizes the first two terms: number of bites per day and the probability of transmission per contact with state state i. To finish constructing $\mathcal{R}_0$, we need to consider τ_i, the time a host spends in an infectious state, which could affect a susceptible vector, and vice versa.

Therefore, each $\mathcal{R}_0$ can be written as:

$$\begin{aligned}
\mathcal{R}_0^{HR} &= \frac{\alpha_{VH}^R(0)}{\tau_V^{-1} + \alpha_{HV2}^C(0)} && = b_V^R \beta_{VH}^R \tau_V \\
\mathcal{R}_0^{HC} &= \alpha_{VH}^C(0)\tau_V && = b_V^C \beta_{VH}^C \tau_V \\
\mathcal{R}_0^{VR} &= \alpha_{HV}^R(0)\tau_H && = b_H^R \beta_{HV}^R \tau_H \\
\mathcal{R}_0^{VC} &= (\alpha_{HV1}^C(0) + \alpha_{HV2}^C(0))\tau_H && = b_H^C \beta_{HV}^C \tau_H \ .
\end{aligned}$$

Note that as before we can find $\mathcal{R}_0^R$ of the *T. rangeli* epidemic and $\mathcal{R}_0^C$ of the *T. cruzi* epidemic to be equivalent to:

$$\mathcal{R}_0^R = \sqrt{b_V^R \beta_{VH}^R \tau_V \times b_H^R \beta_{HV}^R \tau_H}$$
$$\mathcal{R}_0^C = \sqrt{b_V^C \beta_{VH}^C \tau_V \times b_H^C \beta_{HV}^C \tau_H} \ .$$

From these calculations the $\mathcal{R}_0$ calculated from the view of the susceptible population using the Next Generation matrix technique is equivalent to the $\mathcal{R}_0$ calculated heuristically from the view of the infected population.

3.2.3 Effective Reproduction Number

As we stated in Section 3.1.3, $\mathcal{R}_{eff}$, the effective reproduction number is the average number of secondary cases produced over time by one infected individual in an initially completely susceptible population. We calculate by looking at how we constructed $\mathcal{R}_0$ from the perspective of the infected population in Section 3.1.2.

Looking at our initial equations, $\mathcal{R}_0$ for each epidemic was calculated by looking at the following equation at time zero:

$$\mathcal{R}_0^R = \sqrt{\frac{\alpha_{VH}^R(0)}{\tau_V^{-1} + \alpha_{HV2}^C(0)} \times \alpha_{HV}^R(0)\tau_H}$$
$$\mathcal{R}_0^C = \sqrt{\alpha_{VH}^C(0)\tau_V \times (\alpha_{HV1}^C(0) + \alpha_{HV2}^C(0))\tau_H} \ .$$

To look at how the effective reproduction number changes over time, all we need to do is look at α_{ij}^* as a function of time:

$$\mathcal{R}_{eff}^R = \sqrt{\frac{\alpha_{VH}^R(t)}{\tau_V^{-1} + \alpha_{HV2}^C(t)} \times \alpha_{HV}^R(t)\tau_H} \tag{11a}$$
$$\mathcal{R}_{eff}^C = \sqrt{\alpha_{VH}^C(t)\tau_V \times (\alpha_{HV1}^C(t) + \alpha_{HV2}^C(t))\tau_H} \ . \tag{11b}$$

Using this equation, we can now calculate the effective reproduction number at any given point in time. The number of secondary cases produced over time is now a function of the fraction of contacts made by susceptible people in the entire population.

Finding the Endemic Equilibrium

The endemic equilibrium occurs when the the disease is globally stable and persists in the population at a replacement rate of one current to one new infection. We can find this point in time when $\mathcal{R}_{eff}$ = 1, or rather when the effective reproduction number is equal to 1. Looking at equations 11a and 11b, we can find the following:

$$\mathcal{R}_{eff}^R = \sqrt{\mathcal{R}_0^{HR}\left(\frac{S_H(t)}{N_H}\right) \times \mathcal{R}_0^{VR}\left(\frac{S_V(t)}{N_V}\right)} = 1$$
$$\mathcal{R}_{eff}^C = \sqrt{\mathcal{R}_0^{HC}\left(\frac{S_H(t)}{N_H}\right) \times \mathcal{R}_0^{VC}\left(\frac{S_V(t)}{N_V}\right)} = 1$$

As in Section 3.1.3, we use the fact that the populations are constant and that all state changes are equal to zero to find the following additional conditions:

$$S_H^* = \frac{N_H^2}{N_H + \mathcal{R}_0^{HR} I_V^{R*} \frac{\tau_H}{\tau_V} + \mathcal{R}_0^{HC} I_V^{C*} \frac{\tau_H}{\tau_V}} \tag{12a}$$

$$I_H^{R*} = \mathcal{R}_0^{HC} \left(\frac{S_H^*}{N_H} \right) \frac{\tau_H}{\tau_V} I_V^{C*} \tag{12b}$$

$$I_H^{C*} = \mathcal{R}_0^{HC} \left(\frac{S_H^*}{N_H} \right) \frac{\tau_H}{\tau_V} I_V^{C*} \tag{12c}$$

$$S_V^* = \frac{N_V^2 - I_V^{R*} I_H^{C*} \mathcal{R}_0^{VC} \frac{\tau_V}{\tau_H}}{N_V + \frac{\mathcal{R}_0^{VR} I_H^{C*} N_V}{N_V \left(\frac{\tau_H}{\tau_V} \right) + \mathcal{R}_0^{VC} I_H^{C*}}} + \mathcal{R}_0^{VC} I_H^{C*} \frac{\tau_V}{\tau_H}} \tag{12d}$$

$$I_V^{R*} = \frac{\mathcal{R}_0^{VR} S_V^* I_H^{C*}}{N_V \frac{\tau_H}{\tau_V} + \mathcal{R}_0^{VC} I_H^{C*}} \tag{12e}$$

$$I_V^{C*} = \mathcal{R}_0^{VC} \left(\frac{S_V^* + I_V^{R*}}{N_V} \right) \frac{\tau_V}{\tau_H} I_H^{C*} \tag{12f}$$

Unfortunately, due to the cross infection terms, it is difficult to solve for an explicit expression of the endemic conditions. However, we know it exists from Figure 2a.

4 Simulation Experiments

For the simulation runs, we went to through the literature to find baseline values for our parameters using Triatoma sanguisuga as our vector and raccoons as the host animal. Table 2 is a summary of all the baseline values.

Symbol	**Interpretation**	**Baseline**	**Reference**
μ_V	Death rate of triatomine vectors	0.217	[22]
μ_H	Death rate of host (raccoons)	0.4	[29]
β_{HV}^*	Probability of transmission per host to vector	0.116	[8]
β_{VH}^*	Probability of transmission per vector to host	0.132	[8]
b_V	Number of bites on host per vector per day	7	[6]
b_H	Number of bites from vector per host per day	7	[6]

Table 2: The baseline values used for the simulation runs. We assumed that the probability of transmission of *T. rangeli* is the same as that of *T. cruzi* because there is not enough data available on this yet. The biting rates were determined such that the endemic fraction infected of *T. cruzi* vectors matched a study done in Louisiana in 2011. [6]

Based on these baseline parameters, we find that the reproduction numbers $\mathcal{R}_0^*$ are

$$\mathcal{R}_0^R = 2.6309$$
$$\mathcal{R}_0^C = 2.6109 \ .$$

First we will consider four mitigation scenarios for a single introduction of *T. rangeli* into an endemic *T. cruzi* population. Then we will consider four mitigation scenarios for multiple reintroductions of *T. rangeli* into an endemic population. Finally, we will consider the protective effects of a *T. rangeli* introduction into a population at risk of *T. cruzi* invasion, or rather a population where *T. cruzi* is not yet present.

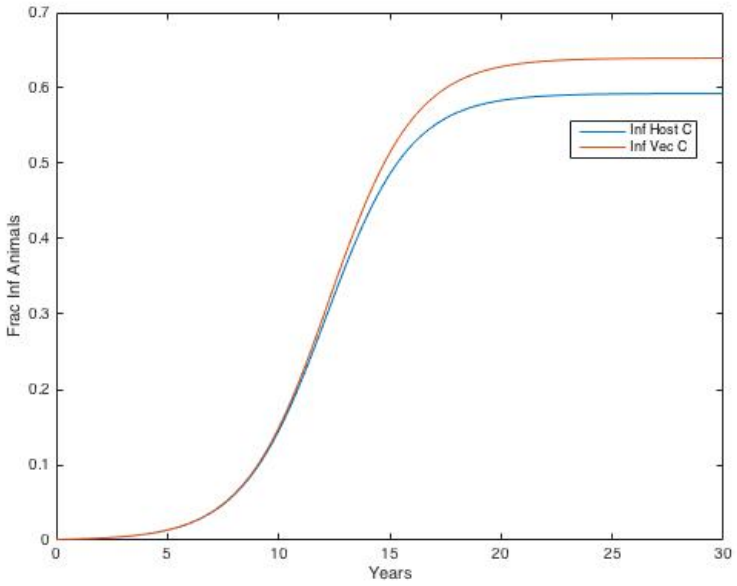
4.1 Single Introduction Mitigation Programs

Since the values of $\mathcal{R}_0^*$ are greater than 1, we know that both epidemics will initially grow. Figure 2a shows how a theoretical *T. cruzi* epidemic would grow in a population. We can see that initially, the epidemic grows exponentially until the rate of infection becomes constant. At this point, the epidemic becomes endemic. In Figure 2a, we can note that the vector and host populations reach an endemic state after approximately 20 years.

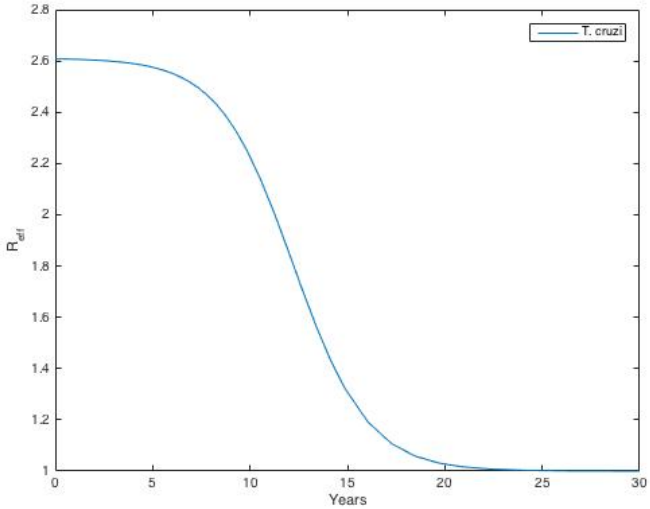
The effective reproduction number, a graph of which is shown in Figure 2b, changes over time as the epidemic grows and eventually slows. We can see that when the epidemic reaches its endemic state at time 20, the effective reproduction number reaches a constant value of 1. This is expected because now for every existing *T. cruzi* infection in the population, one new *T. cruzi* infection is expected, or rather the rate of infection is constant.

However, we are only interested in the introduction of *T. rangeli* after *T. cruzi* has reached an endemic state. So, we change the simulation to begin when the population has already reached an endemic state for *T. cruzi*. Figure 3b shows the dynamics of the *T rangeli* and *T. cruzi* epidemics when *T. rangeli* is introduced to 100% of all remaining hosts after *T. cruzi* infection is endemic in host and vector populations. Figure 4a shows the dynamics of the *T rangeli* and *T. cruzi* epidemics when *T. rangeli* is introduced to 100% of all remaining hosts and vectors after *T. cruzi* infection is endemic in host and vector populations. Figure 4b shows the dynamics of the *T rangeli* and *T. cruzi* epidemics when *T. rangeli* is introduced to 100% of all remaining hosts and vectors after *T. cruzi* infection is endemic in host and vector populations, and half of all infected *T. cruzi* vectors are killed in an insecticide scheme.

Figure 2

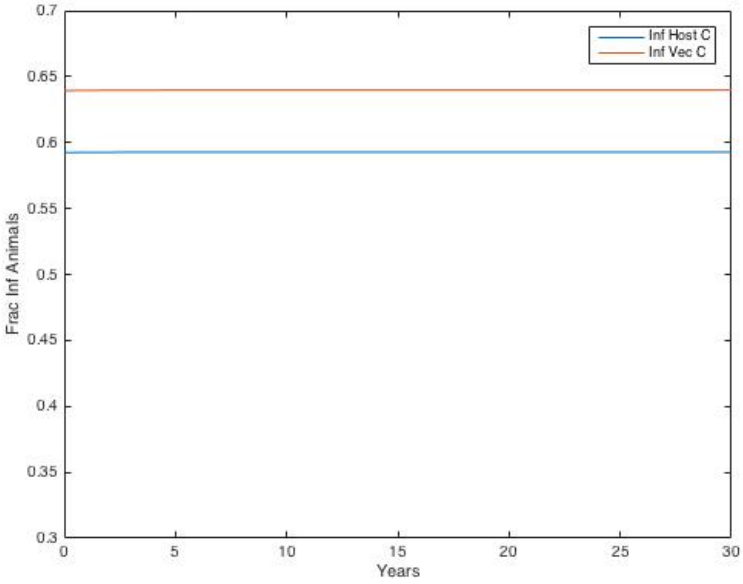


(a) The density of the infected populations with only *T. cruzi* infection when we look at the growth of the epidemic over time.

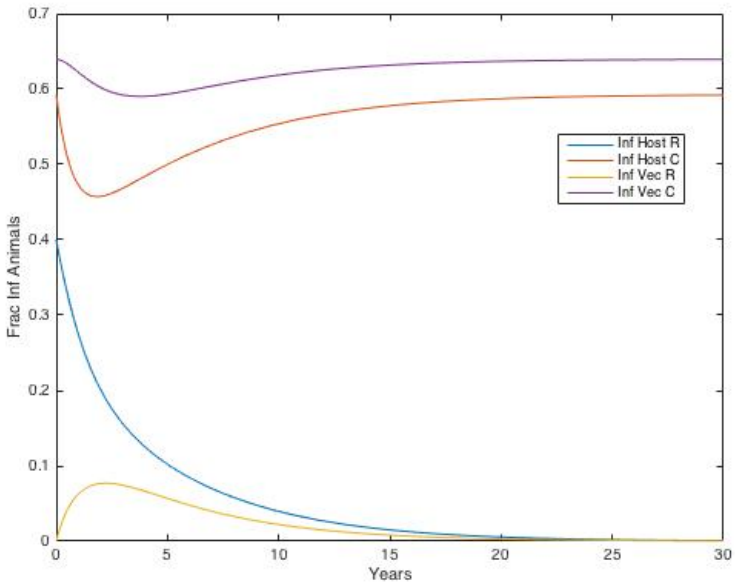


(b) Graph of how the effective reproduction number, $\mathcal{R}_{eff}$ changes over time during epidemic growth. As the epidemic reaches an endemic state, the effective reproduction number approaches 1.

Figure 3

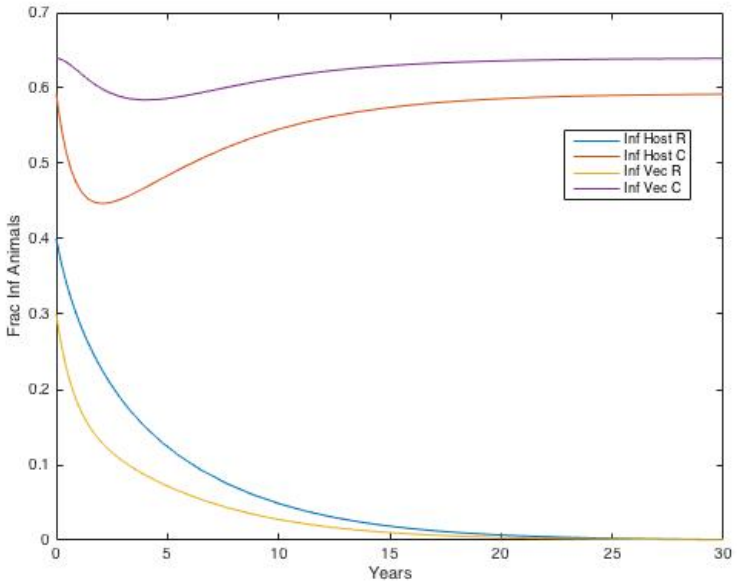


(a) The density of the infected populations with only *T. cruzi* infection.

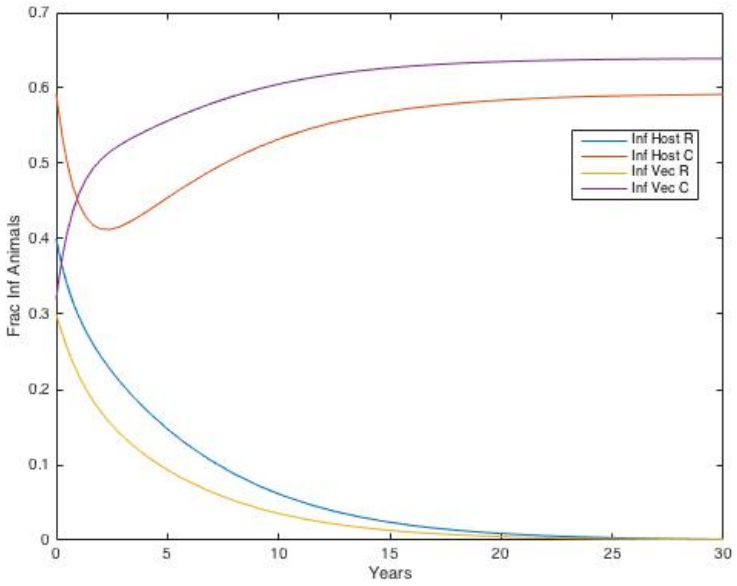


(b) The density of infected populations with both *T. cruzi* and *T. rangeli* infections. Here *T. rangeli* is introduced to 100% of all remaining hosts when *T. cruzi* is endemic.

Figure 4



(a) The density of infected populations with both *T. cruzi* and *T. rangeli* infections. Here *T. rangeli* is introduced to 100% of all remaining hosts and vectors when *T. cruzi* is endemic.



(b) The density of infected populations with both *T. cruzi* and *T. rangeli* infections. Here *T. rangeli* is introduced to 100% of all remaining hosts and vectors when *T. cruzi* is endemic, after an insecticide spraying kills half of all vectors.

4.2 Multiple Introduction Mitigation Programs

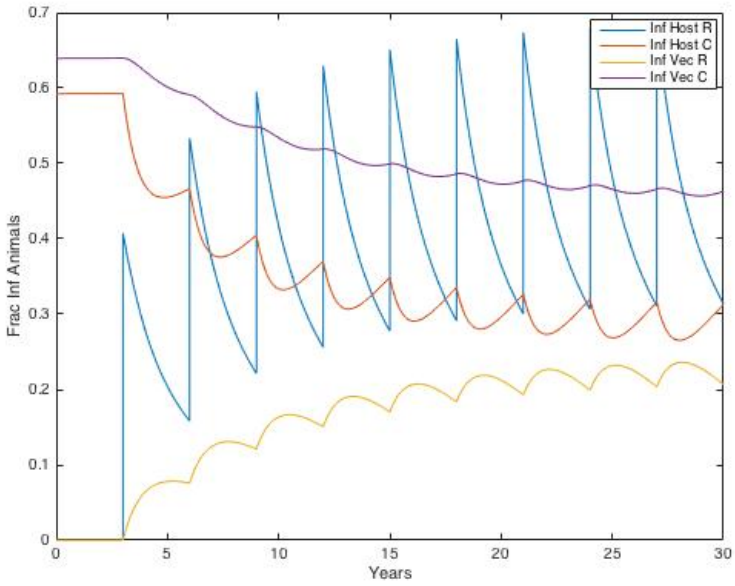
Since a single introduction of *T. rangeli* is not enough to displace *T. cruzi* permanently, we consider simulating multiple reintroductions of *T. rangeli* into the population. In the previous section, we considered infecting 100% of all remaining hosts and vectors with *T. rangli* after *T. cruzi* was already endemic in the populations. For the following simulations, we adjust this parameter considering first the ideal of infecting 100% of all remaining hosts and vectors with *T. rangeli*, but also the more realistic value of 30% of all remaining hosts and vectors. [27] For the idealized scenarios, reintroductions of *T. rangeli* are on a 3 year cycle. For the realistic scenario, reintroductions of *T. rangeli* is on a 5 year cycle, like that of the U.S. rabies program.

Figure 5a reintroduces *T. rangeli* into 100% of all remaining hosts every 3 years given that the vector and host populations begin endemic for *T. cruzi*. Figure 5b expands on this mitigation scenario to include an insecticide spray which kills half of all vectors before reintroduction of *T. rangeli* on each cycle.

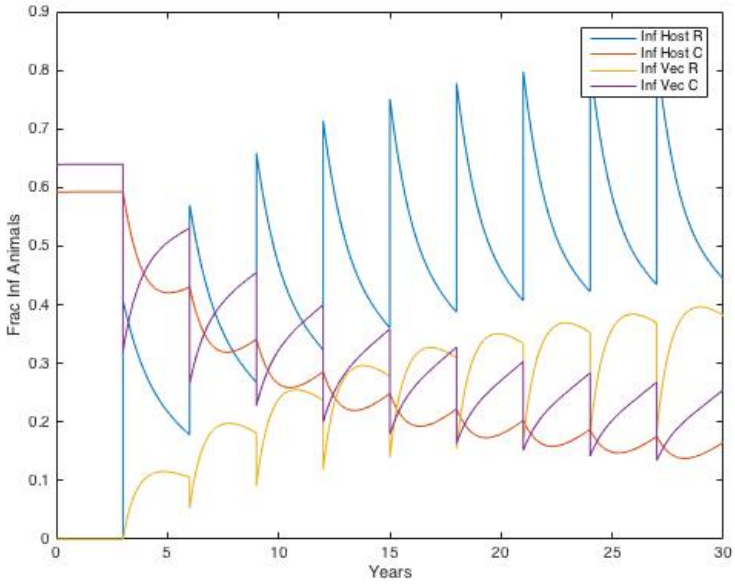
While the latter mitigation strategy appears to be successful, with the periodic endemic states of *T. cruzi* driven below the periodic endemic states of *T. rangeli*, we want to see if these endemic states hold if the mitigation program stops. Figure 6a reintroduces *T. rangeli* into 100% of all remaining hosts every 3 years after an insecticide spray which kills half of all vectors for a 21 year period, then halts the mitigation program at $t = 24$. The simulation continues to run to show how populations return to the original endemic states.

Finally, we consider a more realistic scenario were *T. rangeli* is introduced into only 30% of all remaining hosts on a 5 year cycle, more similar to that of the current rabies program. The results of this mitigation program are shown in Figure 6b.

Figure 5

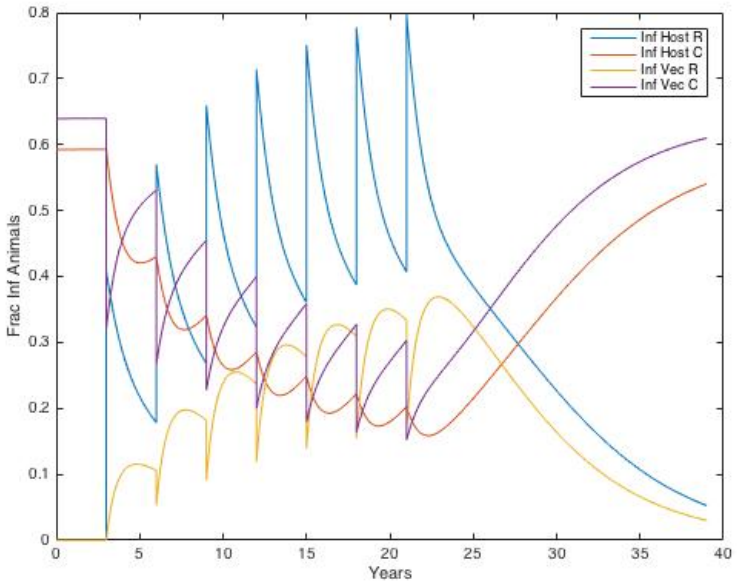


(a) The density of infected populations with both *T. cruzi* and *T. rangeli* infections. Here *T. rangeli* is reintroduced all susceptible hosts every 3 years.

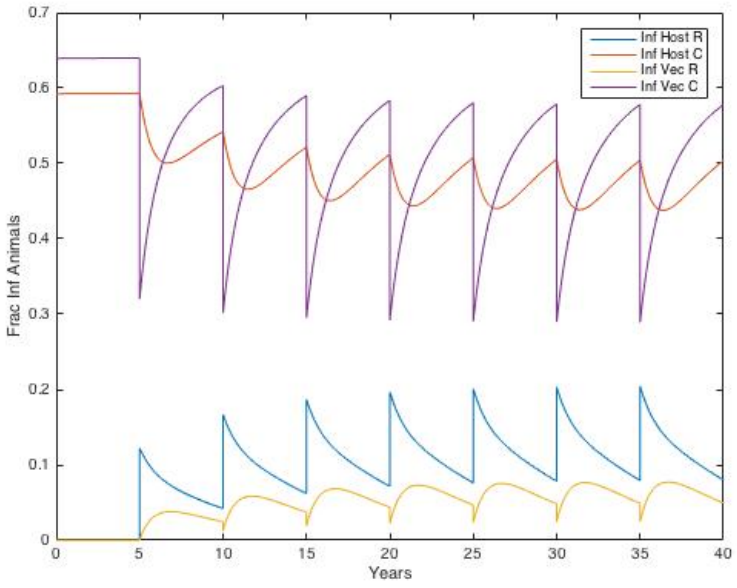


(b) The density of infected populations with both *T. cruzi* and *T. rangeli* infections. Here *T. rangeli* is reintroduced to all susceptible hosts every 3 years, after an insecticide spraying kills half of all vectors.

Figure 6



(a) The density of infected populations with both *T. cruzi* and *T. rangeli* infections. Here *T. rangeli* is reintroduced to all susceptible hosts every 3 years for a 21 year period, then halted for the remaining 15 years of the simulation.

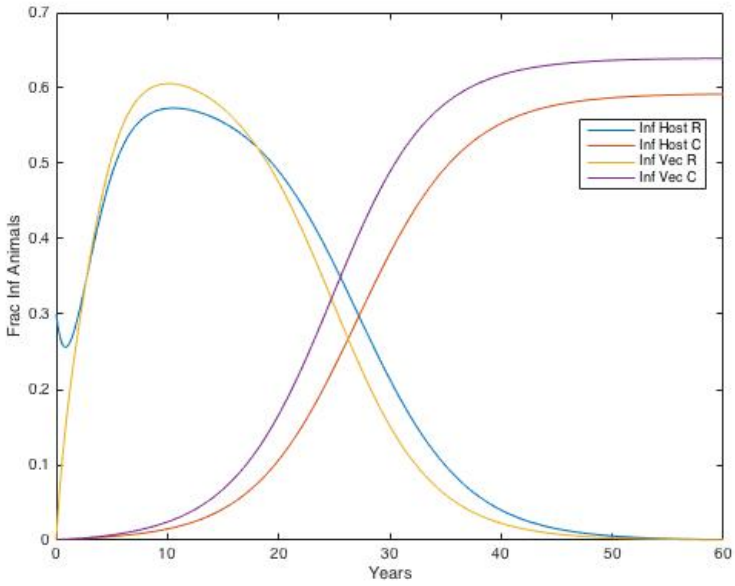


(b) The density of infected populations with both *T. cruzi* and *T. rangeli* infections. Here *T. rangeli* is reintroduced to 30% of susceptible hosts every 5 years, after an insecticide spraying kills half of all vectors.

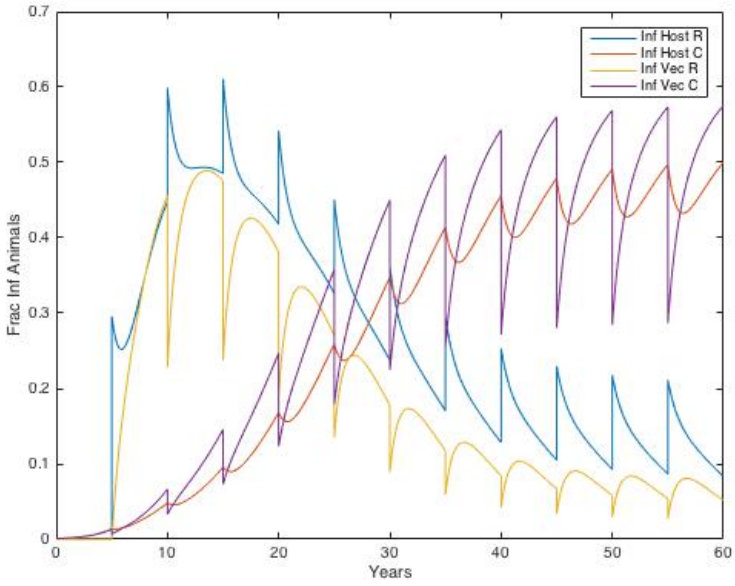
4.3 Mitigation Program for *T. cruzi* Invasion

Introduction of *T. rangeli* can also be used to deter the invasion of *T. cruzi* in at risk populations. Figure 2a depicts the invasion of *T. cruzi* into a completely susceptible population and reaches its endemic equilibrium in at time $t = 20$. In Figure 7a shows a single introduction of *T. rangeli* to 30% of all susceptible hosts after an insecticide spray in a population at risk of *T. cruzi* invasion, where now the endemic equilibrium is not reached until time $t = 40$. Similarly, Figure 7b shows multiple reintroductions of *T. rangeli* to 30% of all susceptibles hosts after insecticide sprays on a 5 year cycle. In this case, the endemic equilibrium is not reached until time $t = 50$.

Figure 7



(a) The density of infected populations with both *T. cruzi* and *T. rangeli* infections. Here *T. rangeli* is introduced once, after an insecticide spraying kills half of all vectors.



(b) The density of infected populations with both *T. cruzi* and *T. rangeli* infections. Here *T. rangeli* is reintroduced to all susceptible hosts every 3 years, after an insecticide spraying kills half of all vectors.

5 Summary and Conclusions

Currently, *T. cruzi* is endemic in wildlife populations across the Americas. We chose to run baseline parameter values for the rates of infection currently encountered in Louisiana, with Triatoma sanguisuga as the vector and raccoons as the host animal of interest. Figure 2a explored what the growth of a *T. cruzi* epidemic in raccoons and triatomines would theoretically look like before reaching an endemic state. This gave us a point of reference on what epidemic and endemic states look like in our model.

In this paper, we explored heuristically solving for the effective reproduction number, $\mathcal{R}_{eff}$, in order to better understand the dynamics of epidemic growth, as well as endemic conditions. Figure 2b showed preliminary results for the single-strain model's effective reproduction number. As we expected, the effective reproduction number approached the value of 1 as the epidemic became endemic in the population, confirming that our heuristically acquired equation appeared to be accurate.

However, *T. cruzi* is already, as we stated earlier, endemic across the Americas. Therefore, we should begin our simulations with *T. cruzi* already endemic in the populations. In Figure 3a, we simulated the current conditions where only *T. cruzi* is endemic in the population, with vectors infected at about 60%. Figure 3b simulated the first mitigation possibility: a single introduction of *T. rangeli* infection to the remaining 40% of hosts in this given population. Comparing this to Figure 3a, we see that this mitigation strategy briefly caused an interruption in the *T. cruzi* infection wave, but it was not enough to displace *T. cruzi* from its niche. *T. cruzi* infection rates in vectors and hosts returned to their original endemic state of vectors infected at about 60% and hosts infected at about 65% with *T. cruzi*.

This mitigation strategy only considered introducing *T. rangeli* to hosts in Figure 3b. Figure 4a considered the option of a single introduction of both *T. rangeli* infected hosts and vectors. While this strategy initially created a stronger interruption in the *T. cruzi* infection wave, it again was unable to sustain and change the endemic value of *T. cruzi* in the population.

Finally, for the third possible mitigation strategy, we theorize an insecticide spray which kills half of all *T. cruzi* vectors before the introduction of *T. rangeli*. We simulated the most ideal situation where again 40% of hosts and 35% of vectors become infected with *T. rangeli* in our mitigation program. This represents 100% infection of all possible susceptible hosts and vectors remaining in our population after endemic *T. cruzi* levels are reached. Figure 4b revealed that while this strategy initially decreased the population of *T. cruzi* infected vectors and hosts, again the populations returned to their initial endemic state when given enough time.

These scenarios only consider a single introduction of *T. rangeli*. The rabies vaccination program that the original mitigation program idea was based off of reintroduces the rabies vaccine every 5 years. Multiple introductions of *T. rangeli* were therefore considered by adding a periodic cycle of *T. rangeli* introductions into the endemic population.

We first considered an ideal situation where 100% of all available hosts were infected with *T. rangeli* at the beginning of each cycle, with a short cycle of 3 years. Figure 5a shows this simulation, and while the endemic state of *T. cruzi* infected hosts and vectors decreased by about half (from 60% to 30% endemic with *T. cruzi*, the *T. rangeli* epidemic was unable to outcompete the *T. cruzi* epidemic. With the addition of insecticide sprays to this scenario, Figure 5b shows that *T. rangeli* can now outcompete *T. cruzi*. While under these conditions *T. rangeli* appears to reach an endemic state above *T. cruzi*, we wanted to test whether these new endemic states would hold if the mitigation program was suddenly halted (representing loss of funding due to positive results or other external circumstances). Figure 6a illustrates that the new endemic equilibriums found under the mitigation program conditions do not sustain after the program is halted. The system eventually returns to its original endemic state.

These scenarios only consider ideal conditions. In reality, funding for such a mitigation program may be similar to the existing rabies program and only allow reintroductions of *T. rangeli* on a 5 year cycle. Studies of the vaccination rates of such programs show that only 30% of raccoons were reached by them.[27] Therefore, Figure 6b simulates reintroductions of *T. rangeli* to 30% of susceptible hosts on a 5 year cycle after insecticide sprays. While endemic states for *T. cruzi* infection is reduced from 60% to 50% in hosts, this does not represent a displacement of the parasite in the target host population.

In conclusion, extreme mitigation programs can significantly reduce the endemic population of *T. cruzi* infected hosts and vectors, but this reduced state is not permanent. If the mitigation program is halted, the populations return to their original endemic state values. Furthermore, under realistic conditions, the proposed mitigation program has little effect on reducing the endemic population of *T. cruzi* infected hosts and vectors.

Therefore, we considered the idea that the proposed mitigation program could be used to instead reduce the invasion rate of *T. cruzi* into at risk host and vector populations. Returning to the epidemic conditions, Figure 7a considers the effect of a single introduction of *T. rangeli* into 30% of a population at risk of *T. cruzi* invasion. Without introduction of *T. rangeli*, *T. cruzi* reached endemic states in host and vector populations by $t = 20$ years. After a single introduction of *T. rangeli*, *T. cruzi* did not reach endemic states in host and vector populations until $t = 40$ years. The invasion rate was halved by a single introduction of *T. rangeli* into the at risk population. Similarly, Figure 7b simulated multiple reintroductions of *T. rangeli* to slow the invasion of *T. cruzi* into the population. *T. cruzi* under these conditions was unable to reach endemic states until $t = 50$ years. Thus, introduction of *T. rangeli* into at risk populations can provide protective effects against the invasion of *T. cruzi*.

Part of the inability of *T. rangeli* to sustain in our endemic and epidemic host and vector populations may be because we assumed our population was constant, with the birth rate equalling the death rate and all births occurring only in the susceptible compartments of hosts and vectors. Since both *T. cruzi* and *T. rangeli* have the capability of being vertically transmitted, adding this

component to the model may change how long *T. rangeli* is able to sustain in the population.

But it is also important to note that we did not consider the pathogenic tendencies of *T. rangeli* in vectors, even though it is non-pathogenic in host animals. This factor may make *T. rangeli* even less competitive than *T. cruzi* and change the dynamics considered in this model.

This model also does not account for the fact that vectors and hosts are mobile with different densities across a given area. Kribs et al. looked at vector migration and its effect on the spread of *T. cruzi* when *T. cruzi* was the only form of infection. [8] For future work, we can apply the framework of the analysis done by Kribs et al. and expand it to include the competing infections of *T. rangeli* and *T. cruzi* as we have done here. Such a model would provide the framework to see if a mitigation program like the one we theorized would work with mobile vectors and hosts.

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