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A Susceptible, Infected, Recovered Chagas Disease Model with Multiple Households Analyzed in Parallel

Undergraduate Honors College Thesis

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Abstract

Chagas Disease impacts millions of people in South and Central America and yet it remains a mostly unheard of disease outside its area of influence. The Center of Disease Control refers to Chagas Disease as one of the primary "neglected" diseases of the world (CDC, 2013). This parasitic disease is spread primarily through the feces of blood sucking insects of the Triatominae subfamily, also known as "kissing bugs". When the insect drops its feces, a vertebrate host can transfer the parasite, *Trypanosoma cruzi* (*T. cruzi*), into the bloodstream, i.e. via the eyes, mouth, or open wounds, and become infected. In this honors thesis, a susceptible, infected and removed/resistant (SIR) model of disease transmission at the household level was developed. The model is replicated and parameterized with geospatial survey data for all households within a town. In addition, a logistic regression analysis was performed on all the household survey data collected in Guayabo and Chiquimula, Guatemala to identify parameters of importance (p<0.10) to infested houses (i.e. the presence of insects collected in a household and the presence of insect evidence within a household). Eventually the individual household models will be linked for the purpose of modeling the disease transmission between houses at the town scale. The latter will enable better insect and disease control mitigation strategies.

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1. Introduction

1.1 Motivation

Chagas disease currently infects 8 to 15 million people in Latin America with 28 million more at risk for contracting the disease (Barbu et al. 2010). Approximately 41,000 people become infected each year by a protozoan parasite called *Trypanosoma cruzi* (Barbu et al. 2010). The disease also accounts for approximately 12,500 deaths per year (Barbu et al. 2010). Chagas disease is mainly located in Central and South America; but with increased immigration, it has been showing up in the southern parts of North America (Rassi et al. 2010). This research will provide a detailed susceptible, infected and removed/resistant (SIR) household model of Chagas disease and parameterize the household model for the eventual scale up to the "town level", where it can be used to better understand disease outbreaks and optimize disease control strategies.

The vector responsible for the spread of the disease is mainly a group of blood sucking insects from the triatominae subfamily. This family of insects is capable of hosting the *T. cruzi* parasite. These insects are active mainly at night when many vertebrate hosts (humans and vertebrate animals) are sleeping. The parasite of *T. cruzi* is spread through the feces of the insect, which gets into the host's blood system through the body's openings. For example, it can enter a person's bloodstream when they scratch an insect bite, through open wounds in the feet, or from a person using parasite-laden hands on the mucous membrane of their mouth or eyes. The parasite reproduces in the blood stream, among other organs, and will remain in a body for life if not treated (Rassi et al. 2010).

When in a human host, the parasite replicates potentially causing both immediate and future complications. The immediate complications (acute Chagas disease) include a prolonged fever, malaise, and enlargement of the liver, spleen and lymph nodes. These symptoms are enough to kill many human infants infected with the disease, but it is not as lethal to adults. Sometimes symptoms of chronic Chagas disease appear 10-20 years later, and may result in the premature death of older individuals. These deaths are mostly from cardiac problems such as arrhythmia. There is no known vaccine or preventative medicine for Chagas disease (Rassi et al. 2010).

1.2 Literature Review

Rassi et al., (2010) provide a nice introduction to the significance of Chagas disease. The article describes the history of Chagas disease, how the disease is spread, the impacts of the disease in the body and the treatments available for symptoms and the parasite.

Insects from the triatominae subfamily play a large role in the spread of Chagas disease; and understanding the basic foraging techniques of the individual insects is key to understanding how the disease spreads. Hassel and Southwood (1978) compiled an article on the common foraging strategies of different insects. Their work revealed several factors that may be important in modeling, including odor, carbon dioxide output, host heat output, and the defensive nature of vertebrate hosts.

Inaba and Sekine (2004) developed mathematical models for the number of secondary infections in a completely susceptible population, defined as R_o. By definition, if R_o is less than one, then the disease will die off, while if R_o is greater than one, then the disease will spread until it reaches equilibrium. They conclude it is important to control and limit contact between the vector population and infected individuals.

An insect's niche or living area is important for modeling the vectors of insect-borne diseases. Drake et al. (2006) created a model using a learning algorithm to determine where niches would/could be located. The model accomplished this by analyzing multiple variables and their importance to insect niches. They determined that with variables specific to a vector's wellbeing, for example an important variable for mosquitoes would be a stationary body of water, an accurate location of insect niches could be modeled in an area.

Magori et al. (2009) created a mosquito model that included breeding grounds and genetics of a population. This model also includes how the distribution of mosquitoes changes between houses in a location. Breeding grounds, inter-house dispersion, and genetics are important modeling features for Chagas disease.

Slimi et al. (2009) created a spatial-temporal model of Chagas disease and showed the importance of modeling the dispersion of the disease. They concluded that the forest insect population, insect movement between locations, and re-infestation are needed to create an accurate model. A spatial distribution model of Triatominae was also developed by Hernandez et al. (2013) on a regional scale to create an accurate representation of Triatominae regional densities using macro-environmental data. Climate, geological data, topography and land cover maps were used to predict the distribution of Triatominae.

Barbu et al. (2010) created a model using the departure rates of *T. dimidiata* to find the spread of the insect through a town. They had three different locations of effect in their model, forest, domicile and the peridomicile (the area around the domicile). As might be expected, the domicle and peridomicile where found to be the most responsible for the number of insects within a home.

There is a genetic difference between Triatominae within the house ("domestic") and in the forest, ("wild" or sylvatic). Lardeux (2013) created a model to determine how likely it was for wild *T. infestans* to invade a domicile and concluded that it was unlikely for a wild *T. infestans* to start a colony in a house, if there was a colony already there.

Buitrago et al. (2013) conducted a study where they analyzed bloodmeals taken from *T. infestans* in Bolivia. They determined that the sylvatic (forest dwelling) *T. infestans* had taken human bloodmeals and therefore still expose people to *T. cruzi*. Porcasi et al. (2006) reported on the aftermath of an insecticide application in Argentina. The conclusion was that the application of insecticide was effective in towns away from the surrounding forest but had little to no effect when applied to houses on the outskirts of town and in rural areas. They also identified three variables that correlated highly with high and low infestation: average night temperature, maximum day temperature and vegetation index.

Re-infestation is always a problem with a vector-borne disease; Dohna et al. (2007) conducted insect re-infestation surveys after a community-wide insecticide spraying and found a correlation to high insect counts before sprayings to insect counts after spraying. A study by Depickere et al. (2012) performed in the Apolo region of Bolivia found a large number of Triatominae remained in the region after 5 years of chemical control. Throughout this time period, many individuals would still complain about insect bites. Despickere et al. (2012) determined that the housing quality impacted the effect of the chemical control, and was correlated with re-infestation.

Environmental factors are important to insect population distribution. Black et al. (2007) conducted a study in Ecuador that showed the quality of the house (e.g., type of construction material and conditions of walls) and piles of objects around the house were related to a higher

level of *T. cruzi* infection. Cecere et al. (2003) researched the effect of housing quality on the population capacity of *T. infestans* and found that better quality houses (i.e. houses with plastered walls and non-grass roofs) had considerably fewer insects. Houses with plaster also had significantly fewer insects than houses without plaster. Housing quality is important in insect population control. Saunders et al. (2012) conducted a survey on risk variables for infestation and found that many housing quality parameters (i.e. cracks in the walls, adobe walls, clutter around perdomicile, and free range animals) were correlated highly with infestation.

Kelly and Thompson (2000) created a model that examined the change in distribution of hosts with insect density. They concluded that host preference (human vs. animal) is an important model feature, as an insect's host preference does not remain constant. Torres-Montero et al. (2012) collected data about the insects' location and host preferences. The data identified a seasonal increase in insects during the trimester from April to June, a slight difference in male to female ratio, and that most insects had only one blood source in their body.

Gurtler et al. (1997) performed a field study of host preference in Northwest Argentina. The goal of the study was to see how animals around the household impacted the bloodmeals of *T. infestans*. Insect feeding relationships between hosts consisting of dogs, cats, chickens and humans were identified. Gurtler et al. (2009) conducted a laboratory test to determine the host preferences of *T. infestans* at different densites involving cats, dogs and chickens, all common hosts for T. infestans. The experiment found that dogs were the favored host, then chickens, followed by cats. They also showed a shift in favored hosts depending on the density of insects. Cruz-Pacheco et al. (2012) created a Chagas disease model examining the infection among humans, vectors and animals. They concluded that removing the insects and keeping animals out of the house are the best ways to fight the disease.

1.3 Overall goals and specific aims

The overall goal of the project is to develop a household-scale SIR model and replicate and parameterize each household model within a town, such that they can be run in parallel. Figure 1 shows an example town with each household having its own individually parameterized SIR model. Each household will be supplied with data about animal populations and house conditions; and then the model will simulate infestation. Currently there are no connections between households, but each household will run in parallel during a single simulation. These individual household models will eventually be linked together to create a town-scale model of Chagas Disease that can be calibrated using real household-scale field measurements. The significance of this research is to begin the process of taking a household-scaled SIR systems model of Chagas disease and upscaling it to a town setting for the purpose of optimizing disease control strategies. This research has the following specific aims:

1) to develop the individual household SIR model,

2) to replicate and parameterize it for multiple households, and

3) perform a logistic regression analysis on survey variables to determine the significance and importance of variables with respect to house insect infestation.

Figure 1: An example of how the individual SIR household models operating in parallel.

1.4 Model Considerations

The model was designed to supply infestation data to a multitude of households and have the ability to simulate the impact of spray-infested houses. The house insecticide-spraying feature requires that the model include a temporal component and house component. Houses cannot be sprayed all at once in practice; nor are they sprayed continuously, and the model needs to be able to represent this temporal pattern. The time component allows numerical differentiation to be applied to equations that track population, mainly vectors, and vertebrate host infection. These equations are difficult and impractical to solve analytically; numerical solution of differential equations allows for a reliable approximation.

2. Methodology and Software

The following sections are very programming intensive and are included to describe in detail how the model works. The first of the methodology sections describes the reasons for modifying the modeling framework of Cohen and Gürtler (2001), while the other subsections are used to provide details of the code developed in this thesis.

2.1 Motivation for modifying the model

The code written by Cohen and Gürtler (2001) is a very useful starting point. However the overall goal for my code is to predict future infestation of insects and infected individuals in multiple households over time. In order to accomplish this, a conceptual change needed to be applied to the code of Cohen and Gürtler (2001). The most important being the inclusion of a time-step feature. This means that the output will be dynamic and will not reach steady state, unless given a large enough runtime. Time steps will allow for different features to interact and impact the system. It was also necessary to include an insecticide feature. Insecticides are used to combat Chagas disease by targeting the triatominae population.

Another important feature is the individual household models be run in parallel. This allows different types of houses to be analyzed at the same time, which is necessary before up-scaling the model to a town scale. Features of the code have been created to import and interpret town survey results collected by graduate students under the guidance of our collaborator Dr. Carlota Monroy at the University of Guatemala. Also through discussion it was decided to have a house quality parameter capable of impacting the insect cappacity limit for an individual household. The surveys rated households on a three-part scale: A, B, and C with C being the worst housing condition. The overall purpose of this code is to model multiple household infestations simultaneously over time.

2.2 Software and Data

To create the SIR household model of Chagas disease variables from field surveys were stored in Excel and then imported into MATLAB 2013b, created by MathWorks. The latter is a programming language based on C++ and uses matrices for computations and data storage. The survey data collected for the towns were also statistically analyzed for variable significance using JMP11 software, created by SAS.

Field survey data include:

1. geographic (e.g., Lat/Long of Houses, Points of Interest (e.g., roads, streams), elevation, climate),

2. demographic (e.g., number of inhabitants, employment, education number and type of animals), and

3. house characteristics (e.g., age of house, presence of electricity, house condition, house building materials, house hygiene, presence of chicken coops).

2.3 The original code

As a starting point, the MATLAB code from Cohen and Gürtler (2001) was analyzed. They designed a deterministic empirical model of the number of vectors in a household to simulate Chagas Disease. The main goal of the model was to estimate the level of infestation at the household level. The model has a user-specified number of animals, initial percentage of dogs infected by Chagas disease, initial percentage of humans infected by Chagas Disease, insect biting frequency, feeding frequency and the chance of transmission. Numbers of animals can be input in a range so that a variety of households can be evaluated in a single simulation.

The main script contains three functions named **model5**, **iterate5**, and **chidogtable5**. **Chidogtable5** calls both **model5** and **iterate5** to produce a multitude of figures. **Model5** is the part of the code that evaluates the change of infection over time. It uses two-season distinction (i.e. summer and spring) because in the summer the chickens are assumed to be moved outdoors, while in the spring chickens are kept inside and are a blood source for household insects. The code transforms the blood sources into a human equivalence of the total blood sources. For example, one chicken is equivalent to having 3 humans in a household. Equation 1 shows how human equivalence was calculated. The model does this to represent how animals get bitten at different frequencies, and more importantly, how they impact the insect population. **Model5** then uses equivalence to calculate a static seasonal insect population. The number of infected insects per season is then calculated. This is used to estimate the number of infected humans within a household. Seasonal blood meals are also estimated for humans, chickens and dogs during this process and passed into the **chidogtable5**.

Equation 1: Human Equivalences

$$\text{ppleqs} = H + R_c * C + R_d * D + R_o * O$$

ppleqs = Human Equivalence
H = Number of Humans
C = Number of Chickens
O = Number of Other animals
R_c, R_d, R_o = Number of humans equivalent to another animal (humans/animal)

Sample Calculation:
Given: H = 4, C = 2, D = 2, O = 1, $R_c = R_d = R_o = 3$
ppleqs = 4 + 3*2 + 3*2 + 1*3
ppleqs = 19

The purpose of **iterate5** is to continually evaluate the function **model5** until the change in model output has reached a steady state solution for the given initial conditions. It does this using

a while loop that runs until a user-specified tolerance has been reached. **iterate5** then passes the output into the **chidogtable5** to create multiple graphics of the results.

The function **chidogtable5** analyzes the data acquired from **iterate5** and **model5**. The output data from **model5** generates 11 figures that provide visuals of the sensitivity analysis for a varying number of dogs, chickens and humans. The graphical outputs include the fraction of insects biting humans and the percent of blood meals that would be attained from a species.

2.4 Overview of new code

The MATLAB code (Appendix J) is capable of analyzing multiple households given data acquired from town surveys. The survey information provides the initial conditions for households and specifies animal populations and house quality. It should be noted that parameters requiring further research to calibrate the model include infection rates of insects and animals within households, insect biting frequencies and blood source preference.

The code is written as a mixture of deterministic and stochastic principles. Insect upper limit is currently evaluated stochastically, once insect upper limit is selected the code runs deterministically (i.e. if houses are given the same upper insect limit and initial conditions the code will arrive at the same result). The main goal is to analyze multiple households using a time-dependent SIR model that includes an insecticide feature to model how spraying impacts disease. The user specifies transmissivity of the disease, spraying times, and which houses are sprayed. The code is split into 5 main functions with some important sub-functions within each.

2.4.1 Main Driver

This driver calls all the other functions and analyzes Chagas disease through a town with selected field survey information. The first four functions are used to acquire all of the data

needed within the model. The fifth function analyzes the data over time and stores the information acquired at each time step.

2.4.2 Constantinput

The **Constantinput** function specifies biting frequency, human equivalences, disease transmissivity, runtime and fractions of insects that bite per time step. The information is then passed out into main program.

2.4.3 Megadatainfo

Megadatainfo is used to acquire all the data from the surveys and convert it into a useful form. The passing in of survey data was implemented as one function so a user could easily replace the data from surveys with example household information. the data that would normally be acquired from this with example households. This is useful for two reasons, one if a user would like to test specific houses they may exclude this function and provide only the information they needed for testing. Reason two is that should a different survey be used, then this function could be replaced by a function that turns that survey information into useful data. **Megadatainfo** asks the user to choose the file containing the text-formatted version of the survey information. The function then passes this information into the function **numerify**, explained below in section 2.4.4 **Megadatainfo** also calls **housequality** to obtain a house quality number for each house based on the survey information. This function also estimates a value of insect population. During household surveys the amount of infestation is determined by the number of insects collected within a given amount of search time. It was assumed that this would be about a tenth of the total amount of 4th and 5th Instars based on field results from our collaborators (C. Monvy personal communication).

2.4.4 Numerify

This function takes the user specified survey information and converts the data into a matrix of numerical values for all of the households. This matrix is called megadata (Appendix B and C show the headers or each of the matrix columns). The survey information is initially loaded into MATlab as vectors by using **Importfile**. These vectors, consisting of both strings and numerical information, are then turned into a numerical matrix for ease of later modification. In order to convert strings to numbers, it was necessary to use a loop that analyzes each string. As a result, everything in this section that turns strings into numbers is hardcoded, and based on the two survey data sheets available. If the data in the original excel spreadsheet are entered differently (i.e. as different column heading names or varying order) then data entry errors will arise. The string input will not be recognized and therefore not entered into the correct category. To fix this data sorting error, a user will need to alter the text to match the inputted survey data. The output of this function is a matrix of values called megadata, and it contains all of the surveyed data about the houses in a town.

2.4.5 Importfile

Importfile is called within **numerify**, and transfers the survey data information into a vector format that is usable in MATLAB. This function was created by the import feature of MATLAB 2013 and separates each survey question into individual vectors. It does this because the survey data is a mix of numbers and strings and so if imported together, would be stored as a cell array. Cell arrays are ideal for holding information but are more difficult to change. These vectors of information are then passed back to **numerify,** where the string data are converted into a numerical representation.

2.4.6 Housequality

  This function takes all of the surveyed information about the house and turns the data into a house quality parameter. In reality, how each parameter will affect the overall house quality is not known. An odds ratio could be calculated for each of the survey questions to determine significant variables and their impact; this is further explained in the results section. Currently all of the surveyed information is used to create this house quality unit. To calculate the house quality, the function uses a summation of the megadata matrix per household and applies a weighting factor to the survey results. This simple summed weighting is subject to change as house quality parameters are analyzed for their overall effect on the house quality. The number of house quality parameters will likely decrease and be weighted relative to their importance. The current weights have no physical basis but are used to show variability between households. The house quality parameter is calculated and stored by household.

Equation 2: House Quality

$$HQ = \sum NSDw$$

HQ = House Quality
NSDw = Weighted Nominal Survey Data

Sample Calculation
Weight affect from poor walls 1.5; weighting from firewood next to house 0.5
HQ = 1.5 + 0.5
HQ = 2

2.4.7 Preall

  There are quite a few matrices and vectors used throughout the code that need to be pre-allocated to ensure overall program efficiency. The function **Preall** pre-allocates these matrices and assigns initial values to data. In this function, the user specifies the initial infection rates of animals and insects. These two were chosen to show variability and have no physical basis. Initial infections rates are difficult to find for ethical and practical reasons. In order to find the

infection rates, a large population needs to be sampled; or to find the rates for a household, all individuals would need to be sampled. This is not likely to happen on a town level. Also finding infection rates of the insect population is impossible because there are a large number of insects that will not be found. For this work, dogs were assumed to have the highest probability of infection followed by "other" animals (defined in equation 3) then humans and insects. An overall average infection rate could be found through laboratory testing and should be replaced when such data are acquired.

2.4.8 Stepdata

This function is used to create summary data used during the looping process. The function outputs the people equivalents, and the insect upper limit per household. It also lets the user specify spraying times, and which households will get sprayed during those times. People equivalents are calculated using three R values (i.e. R_c, R_d, and R_o. The R values represent how much more likely an animal is to be bitten compared to humans. The subscript c, d, and o refer to the animals, chickens, dogs and "other" respectively. A person equivalent is calculated by taking the total number of animals multiplied by their respective R value and totaled. A sample calculation is provided in equation 1. The R values were assumed to be three, meaning that insects are three times more likely to bite chickens, dogs and other animals over humans. The value three was obtained from Cohen and Gürtler (2001) and applied additionally to "other" animals. These values are open to debate and many laboratories have tried to obtain values for relative biting frequencies; but results are inconclusive, especially when compared to field data. It is possible that through bloodmeals measured in the field, an insect "preference" for biting an animal may be found.

Equation 3: Other Animals

$$\text{other} = \text{cats} + \text{pigs} + \text{cows} + \text{other animals}$$

Other = number of other animals
Cats = Number of cats from survey
Pigs = Number of pigs from survey
Cows = Number of cows from survey
Other animals = Number of all the other animals from survey

Sample Calculation:
Cats = 1, Pigs = 2, Cows =1, Other animals = 3
Other = 1 + 2 + 1 + 3
Other = 7

2.4.9 Blimiteq

The insect limit function takes the previously calculated house quality number and converts that into an insect upper limit carrying capacity. The house quality number is grouped into one of three categories. This system is modeled using the house "risk" survey question, where the house was rated as an A, B or C with A being the highest quality. The function then splits the house quality number and places it into one of three subcategories + or – much like the grading system. For example, a house within the A category could be further subdivided into A+, A, or A-. Once a house quality has been categorized, a normalized distribution curve is used to randomize the house quality affect. This was included to allow more overlap between categories, meaning that a house quality category that falls within the A- range has a higher chance of overlapping in their insect upper limit with a house that has a B+ rating. The purpose of the house quality affect is to allow for houses of a good quality to have a low insect limit.

Equation 4: Upper insect limit (blimit)

$$\text{Blimit} = \text{HQA} * \text{ppleqs} * \text{bbp}$$

bpp = insects that can be sustained per person
ppleqs = people equivalents
HQA = impact from house quality

16

Sample Calculation
HQA = 0.5; ppleqs = 19; bpp = 20/12
Blimit = 0.5 *19 * 20/12
Blimit = 16 insects

2.4.10 Spraydata

The **Spraydata** function allows the user to define when and which houses get sprayed with insecticide. This function first asks the user when spraying occurs and then asks to specify which houses are going to get sprayed during each of the times selected, with the default option to spray all of the houses at once.

2.4.11 Chagasvstime

The **Chagasvstime** function groups all the functions that are analyzed over time. The function stores the information used and acquired during each time step and determines when along the runtime to change seasons. This is explained in greater detail below.

2.4.12 Deathspray

Deathspray applies an insecticide affect to specified households. The initial insecticide impact kills off 100 percent of the insects and then impacts the insect upper limit carrying capacity and insect fecundity. Insecticides have a residual effect on their surroundings after application. The main impacts are: insects will be less capable of reproducing and fewer insects will be able to be supported by a household. This impact on fecundity and insect upper limit decays over time. Currently the default decay is two months after which time the initial insecticide spraying no longer impacts the insects. To simulate this, a decay feature was built into the function. This function uses an exponential decay with a lambda of one time step. After two time steps, the house returns to an insect carrying capacity and the fecundity before the spraying.

Equation 5: Incecticide Decay

$$Id = \frac{1}{e^{(sd-tsf)}}$$

Id = insecticide decay
sd = spray decay length
tfs = time from spraying

Sample Calculation:
Given: sd = 2 months, one time step is 1 month

$$Id = \frac{1}{e^2} = 0.135$$

$$Id = \frac{1}{e^1} = 0.368$$

$$Id = \frac{1}{e^0} = 1$$

Once tfs equals sd, the equation is no longer used and insecticide decay remains constant at one representing no insecticide impact.

2.4.13 dryseason

The function **dryseason** is used to calculate how the insects and other populations change over one time-step. The function initially calculates the number of infected individuals. Then it calculates the change in insect population, and given the new insect populations estimates the number of infected and non-infected bites that occur during one time-step. It then uses all the information to calculate the change of infection rate between the animals and insects and uses this information in the next time-step.

2.4.14 wetseason

The function **wetseason** currently operate in exactly the same manner as the function **dryseason**. The reason for its inclusion is to allow for a future seasonality impact. If a significant change is found relating to time of year, then this would be where it would be implemented. For

example, if insects produced more offspring during the wet-season, then fecundity would be changed within this function.

2.4.15 Figproduction

Figproduction is a "main" driver that calls the above functions. This driver uses example household information rather than surveyed data to enable figures to be more easily produced and interpreted. This driver produces 6 figures shown below in the results section of the thesis.

3. Results

Although real data exist in the form of surveys and insect bloodmeals, it should be noted again that the model has not been calibrated to real data. This means that the constants used (i.e. a dirt floor adding 1.0 to the house quality number) are not physically-based. Once the data are thoroughly analyzed, it will be possible to adjust the constants for model calibration. The results that follow show the overall picture rather than calibrated forecasts.

3.1 Upper Insect Limit

The Upper Insect Limit has a stochastic nature, such that houses with the same parameters could, and most likely will, end up with slightly different upper insect limits. Figure 2 shows the resulting upper insect limit for a house with the same characteristics analyzed five times. This represents the variation that occurs even if houses have the same rank (i.e. A, B or C quality houses) and same parameters (i.e. number of dogs and humans). This is important because the boundaries of the letter ranking system are not well-defined; and it is possible that a house ranked as a B will have the same number of insects as a house ranked as a C. The stochastic nature of the insect limit decreases the impact of immediately stepping into a new ranking category, in essence smoothing out the relationship between house quality and insect

limit. This system was used because one of the survey questions was a house risk level using the categories A, B, and C. Keeping the ranking system provides a variable that can be calibrated in the future.
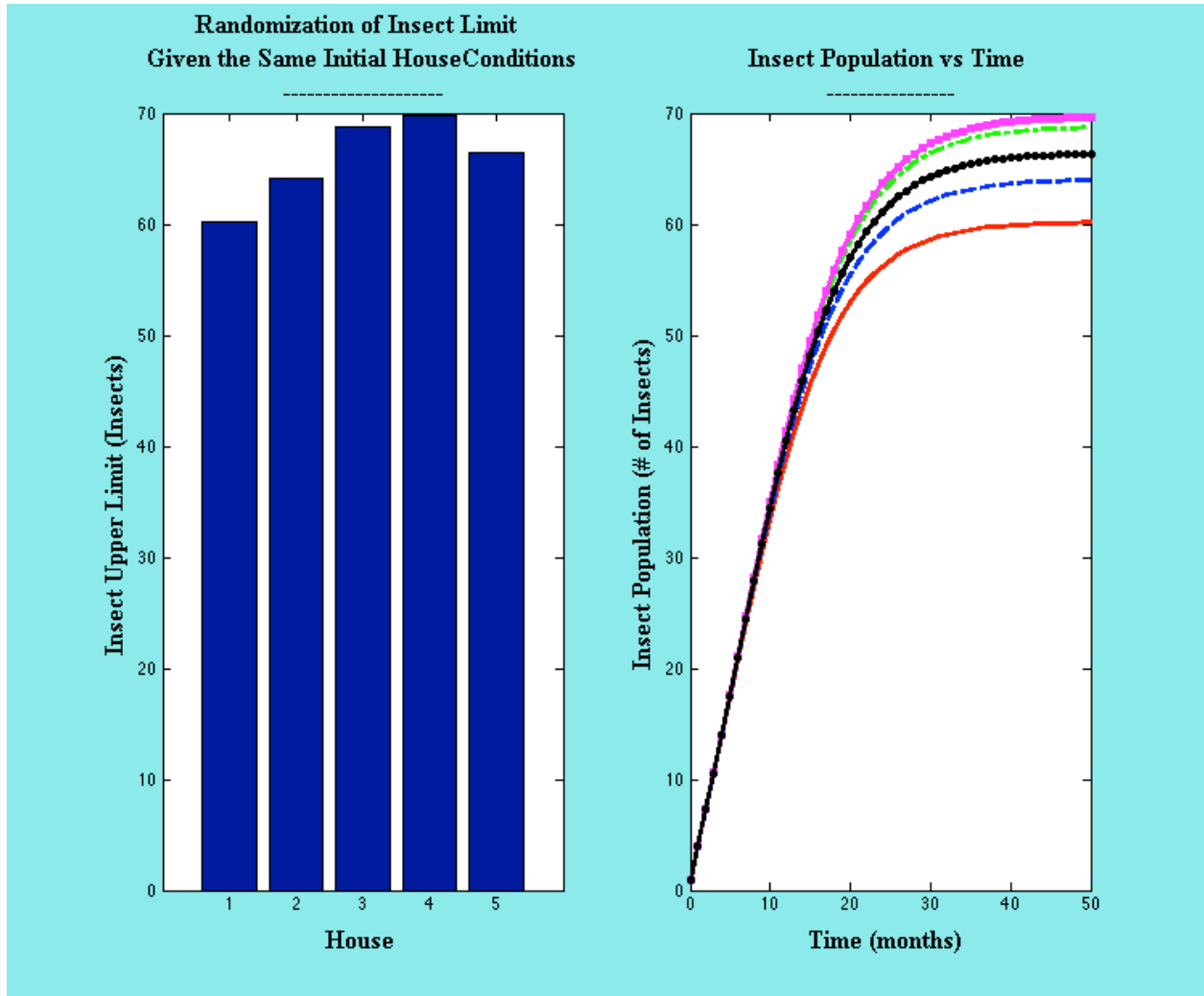

Figure 2: Upper Insect Limit given the same household conditions. The left panel shows five simulations of a household with the same parameters. Each house contained 4 humans, 1 dog, 1 cat, 1 other animal, 1 initial insect, and a house quality number of 11. The right panel of the figure shows how the Upper Insect limits impact the Insect population over time.

3.2 The Effects of Spraying

A major goal of this thesis was to show the impact that insecticide spraying would have on insect infestation. Insecticide application is often used to keep the insect population in control

when there are outbreaks. Figure 3 shows the impact of an insecticide application on houses of varying quality. Each house has the same number of humans, dogs, chickens, other animals, and initial insects but has a variety of summed weighted house quality numbers; 1, 11 and 20 respectively, corresponding to low, medium and high risk values of a household.

Figure 3 also shows the insecticide does not affect the upper insect limits of a household but does impact the population and growth rate of the insects. The only way to change the upper insect limit is by changing the house quality values. Insecticides do not improve the quality of a house, they have a shorter-term impact than any house improvement. The immediate impact of the insecticide application is an initial death of all the insects; see for example time-step 20 (Figure 3). This is expected in a real-life application, where all insects will hopefully die when a house is sprayed. The next part of the insecticide application is the "leftover" impact on the insect population resulting in decrease growth (see the solid red line of a low risk household. Immediately following the insecticide application the insect population drops to zero, which is the result of a lowered insect fecundity. What is more difficult to perceive by eye is the slight decrease in the slope of the insect population growth for the two months that the insecticide impacts a household.
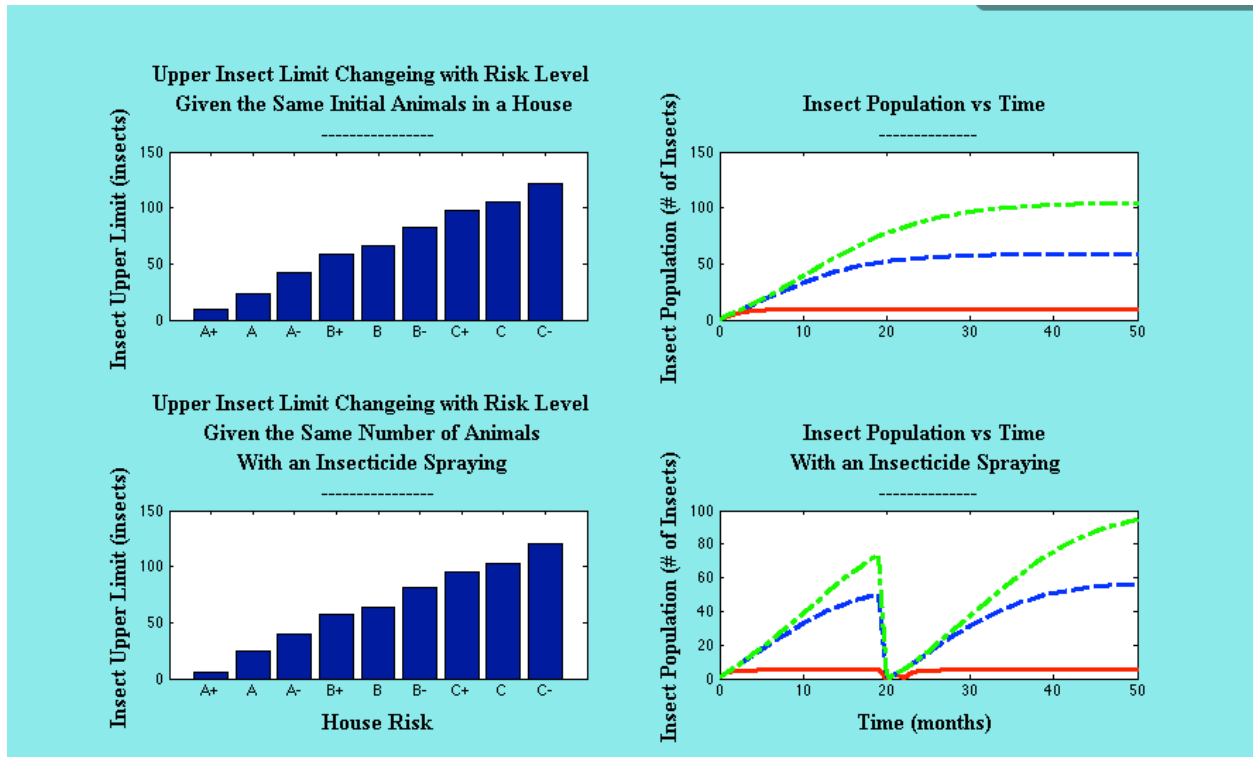
Figure 3: Impact of insecticide application on houses of varying quality. Each household contained the same parameters, except for house quality number (i.e. risk level). Each house contained 4 humans, 2 dogs, 1 cat, 1 other animal, and 1 initial insect. The house quality numbers ranged from 1 to 21 corresponding to each of the risk levels (i.e. A+ to C-). The right hand side of the figure shows the insect population for three different house risk levels. The solid red line is a Risk level of A+, the blue dashed lined is a risk level of B and the green dash dot line is a risk level of C-.

Figure 4 shows the impact of an insecticide application on the percent of insects infected over time. The most notable change is the sudden decrease in the percent of insects infected at time step 20. If the insect population suddenly decreases to zero, then the percent infected is expected to go to zero. The reason that the percent infected never fully reach zero is due to how the insect population grows. The model incorporates both an incoming and exporting source of insects from the peridomicile and forest. This growth dynamic causes the insect population to immediately return to three insects (an number with no physical basis but causes houses to become re-infested), which are capable of biting animals and becoming infected. An aspect worth noting is how the fraction of infection is largest for insects inside the best quality house.

This is the result of there being fewer insects to infect; so an infection of one insect, means a larger percent will become infected.

Figure 4 also shows that there is a slightly greater slope in the percent infected over time after the insecticide application. This is due to the animal population being more infected at this point than it was initially. Even though insecticides help control the insect population, if new insects enter into the system, they will rapidly become infected due to the host population's infection. The sooner the insecticide is applied, the less noticeable the change in infection rates.

Figure 4 also explores the impact of an insecticide application on the fraction of humans infected over time. The fraction of humans infected grows exponentially initially and then levels off; following the trend seen in the insect population. This trend is most pronounced immediately after the insecticide application. The plateau for fraction of infected humans occurs because the likelihood of biting an uninfected individual will decrease as the number of uninfected individuals decreases. Another trend to note is that if the insect population reaches its maximum and becomes fully infected, then the percent humans infected grows linearly. Once the insect population has reached its maximum capacity, then they will supply a constant number of bites, and infection rates will be based on the fraction of insects infected. The infection rate will still have a changing slope at this point because as more insects become infected, the faster the animals in the model will become infected. Once the insect population is 100 percent infected, the fraction of infected humans grows linearly (solid red line of Figure 4).
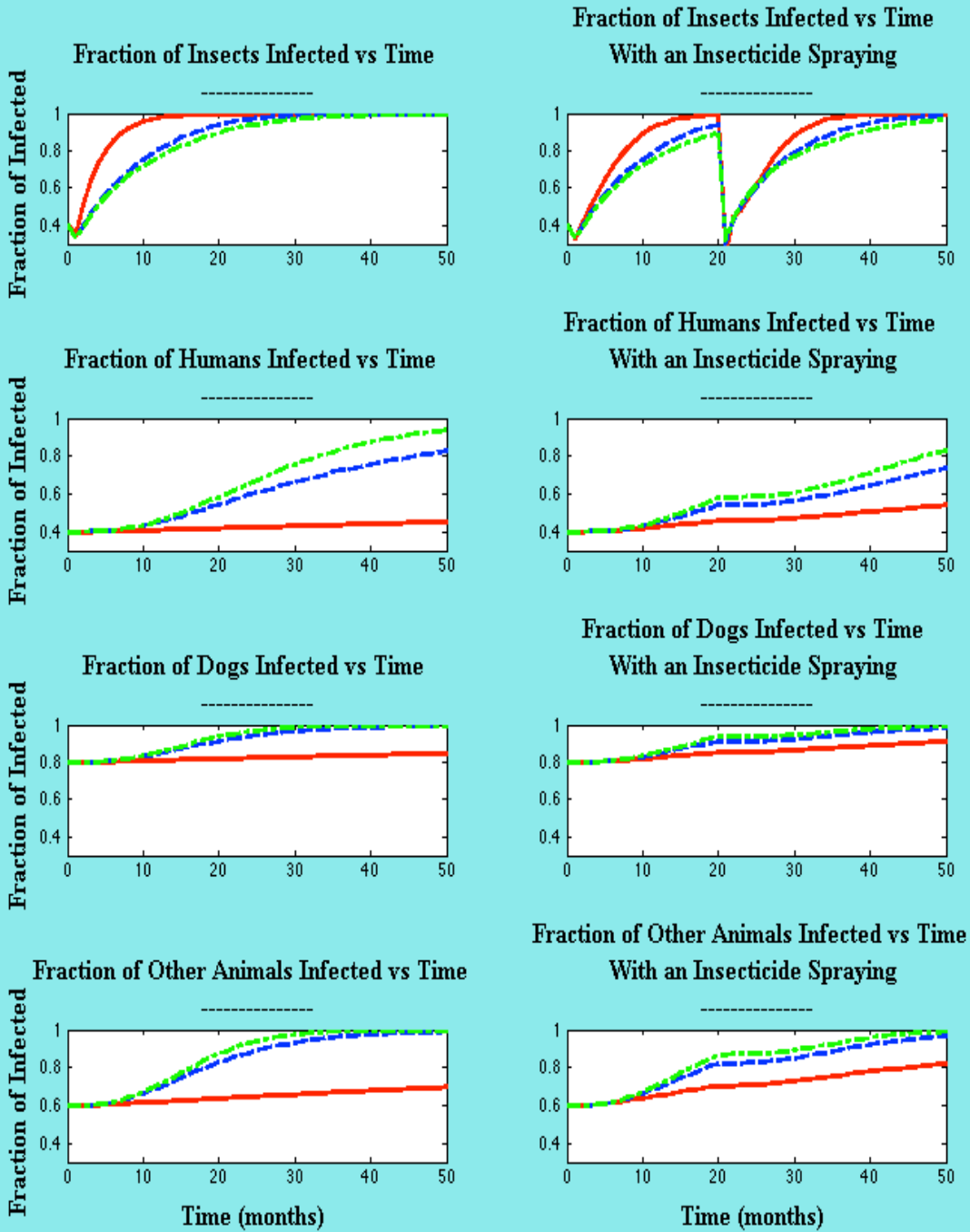
Figure 4: Impact of insecticide application on infected populations over time. The houses simulated here are the same as Figure 3. The solid red line has a Risk level of A+; the blue dashed lined has a risk level B, and the green dash-dot line has a risk level C-. The left panels of the figure represent the infection rate of populations without an insecticide application. The right panels show the infection rate of populations with an insecticide application at time step 20.

Figures 4 shows the impact of the insecticide spray on the fraction of infected dogs and other animals over time. Since the cause of infection is assumed to be the same for dogs and other animals as for humans, there is no difference in the overall trends of either figure. What is of note, however, is that the rate of infection is much higher for dogs and other animals than it is for humans. Dogs and other animals are more likely to be bitten by insects, so they are also more likely to become infected. The rate of infection for dogs and other animals are assumed to be the same in this model (i.e. defined as having the same R or insect biting preference).

3.3 Animal Sensitivity Analysis

A sensitivity analysis was performed on the household model with varying numbers of animals to examine the impact of animals on a household. This is important in determining methods for best controlling the spread of Chagas disease, as animals have a large role in the transmission of the disease.

In order to analyze the impact of different animals, the people equivalents and percent insects infected were analyzed for each household. The people equivalents of a household were analyzed because this produces constant answers (unlike the upper insect limit, which possesses a random variable) and is directly related to the insect population. The fraction of insects infected was analyzed at the 50th time step to show the overall impact of animals on the rate of infection within a household. Despite being just one potentially infected vertebrate, insects are directly related to the number of vertebrate animals that become infected. Two vertebrates were analyzed at a time, while holding all other household variables constant.

Figure 5 shows the effect of chickens and dogs within a household. Chickens and dogs are common in households and the relationship between the two will be helpful in determining a general "feel" for how houses should respond in terms of insect population and infection.

The people equivalents of a household is greatest when there are the greatest number of chickens and dogs in a house. This is expected, as a greater number of vertebrates leads to a larger host population. The results are symmetric because dogs and chickens have the same people equivalence (i.e. three people per one animal). If a different relationship for dogs or chickens is selected, then the people equivalents will not be symmetric.

The right side of Figure 5 shows the fraction of insects infected at time step 50. Note: An increase in the number of chickens decreases the percent of infected insects for a household, while an increase in dogs increases the fraction of infected insects for a household. This relationship occurs because chickens do not have the ability to become infected, so they help support insect population, but will not provide a source of infection for the insects. Dogs on the other hand have a very large initial percent infected; so if an insect bites a dog, there is a much higher chance that it will become infected. As a cautionary note, a decrease in the fraction of infected insects does not necessarily imply an overall decrease in infection, as more animals will increase the number of insects in a particular house.
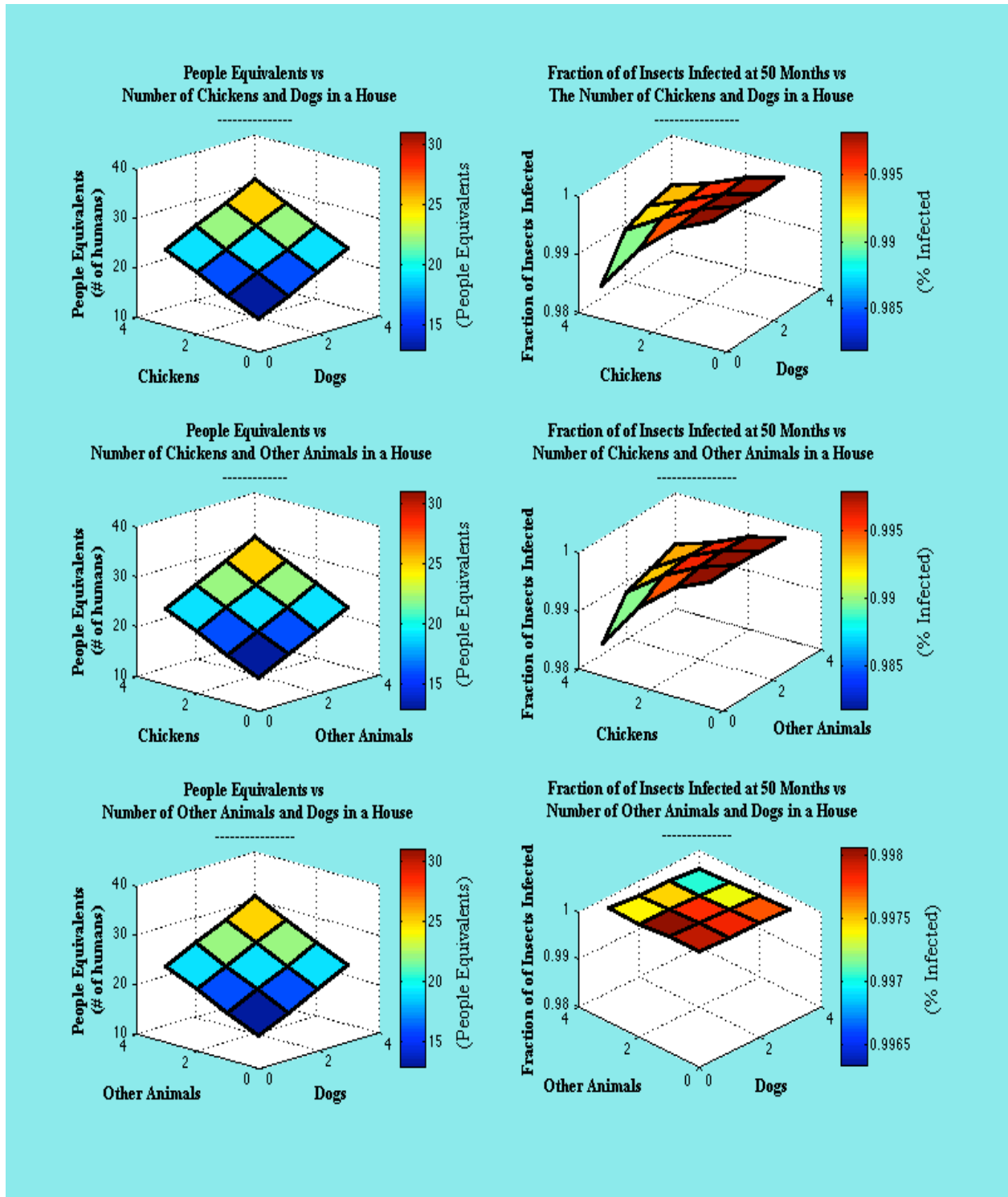
Figure 5: Sensitivity analysis of the different animals inside of a household. Parameters for each household are held constant except for the two animals being analyzed. The household has 4 humans, 1 initial insect, a house quality number of 20 and 1 for whichever animal is not being analyzed. The two animals being analyzed are varied between 1 and 4. The left panels display the people equivalence of a household for the sensitivity analysis. The right panels display the fraction of insects infected at the 50th time step for each sensitivity analysis.

Figure 5 also shows the sensitivity analysis done between chickens and other animals. The people equivalents of a household with varying numbers of chickens and other animals, look similar to the people equivalence of the chicken and dog analysis (i.e. in this case, they are identical). The people equivalence of other animals is the same as the people equivalence of chickens and dogs. Meaning that an increase in any type of animal will have the same impact on the insect population. This was chosen because of the current uncertainty in how frequently different animals become bit.

This looks similar to analysis done for chickens and other animals, with slightly different values. The reason for the similarities is due to the fact that chickens still provide no infection source to the insects, while the other animals do. This means that an increase in the number of chickens in a household will decrease the percent of infected insects, while an increase in the number of other animals will increase the percent of insects infected.

The sensitivity analysis between dogs and other animals has a similar result for people equivalence as the other two analyses, which occurs because each animal has the same number of human equivalences.

In this analysis, both sets of animals are harbors of infection, so it is less clear how the fraction of infected insects would respond to an increase in either species. Figure 5 shows the percent of infected insects remains close to 100 percent, with a slight decrease in fraction of infected insects, when other animals are added to a household. Other animals have an initial infection lower than that of dogs, and so adding an extra other animal would slightly decrease the chance for an insect's bite to cause infection.

An interesting trend appears in the data; the more animals in a household the lower the fraction of infected insects. Increasing the number of animals in a household increases the insect

population. Approximately the same number of insects become infected each time step; but since the population is so much larger, the unit impact of an insect infection is less important on the fraction of insects infected.

3.4 Spray, Recovery and House Improvements

It is important to examine the household insect population household with respect to mitigating the spread of the disease. There are many mitigation strategies; however, the most common is applying insecticide to a house. Another option is to spray the house in combination with house quality improvements. The house quality could be improved by improving the condition of the floors, walls, or roofs. Figure 6 shows the result of three different control strategies. All three options have the same house parameters. The first scenario (solid red line of Figure 6) has a spraying that occurs at the 20th time step and then a "do nothing" strategy. The second option (the dashed blue line of Figure 6) has spraying at the 20th time step, again at the 30th time step, and then "do nothing". The third option (the dash dotted green line of Figure 6) has spraying at time step 20, followed by a spray and house quality improvement at time step 30. The first scenario shows that if the insecticide applications are not kept up, the insect population will recover to full strength within a fifteen year time frame. With the repeated insecticide treatments of the second scenario, insect populations can be kept at a manageable level. The third scenario, however, shows that combined spraying techniques and household improvements have a much longer impact on the reduction of the insect population.
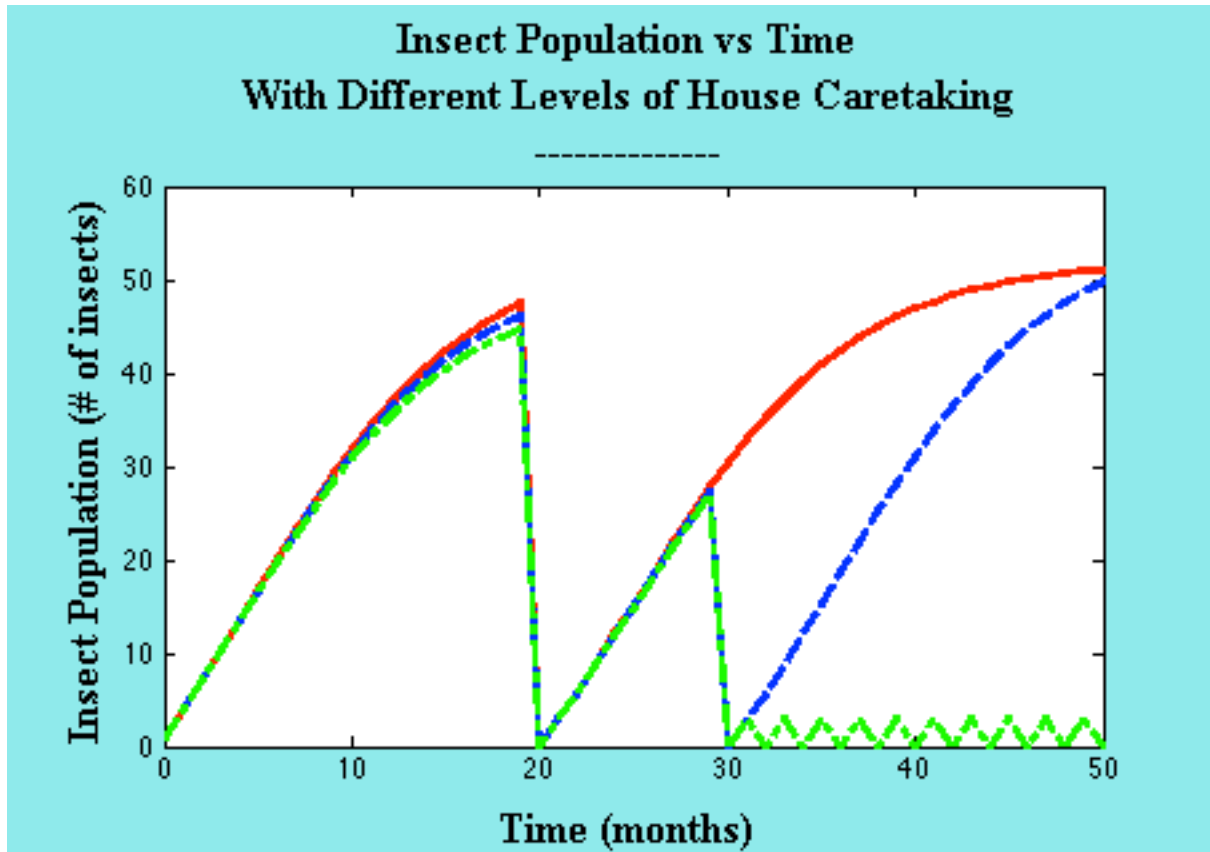
Figure 6: Insect population with three different house treatment plans. All three simulations have the same initial conditions. Each simulation contains a household with 4 humans, 1 dog, 1 cat, 1 other animal, 1 initial insect and a house quality number of 11. Scenario 1, the solid red line, represents a household with an insecticide application at the 20th time step. Scenario 2, the dashed blue line, represents a household with an insecticide application at the 20th and 30th time step. The third scenario, the dash dot green line, represents a household with an insecticide application at the 20th and 30th time step and a improvement in house quality number at the 30th time step.

Figure 7 shows the impact on the percent of creatures infected over time. The top left panel of Figure 7 shows the fraction of insects infected. After each insecticide application, there is a sharp decrease in percent insects infected. If there are no insects, then the infestation will be zero. The reason the model simulation does not go to zero is that the insect population has a default number of insects (i.e. three) that come from outside of the household boundary resulting in insects within the house. The third scenario has the greatest percent of insects infected because, as was the case with Figure 4, so few insects are available for infection greatly

increasing the unit impact of each infected insect. The other three panels of Figure 7 look very similar, yet vary in slope because they all work under the same principles. Each is directly related to the number of insects, the number of bites, and the fraction of infected insects, it would make sense that they all behave similarly. As noted earlier, the fraction of infected animals initially grows exponentially with the insect population, and then levels off as it approaches one. In the third scenario (i.e. one that includes the house quality improvement) the rate of the fraction of infected animals quickly approaches a straight line, which is a result of the insect population approaching its growing capacity and reaching 100 percent infection.
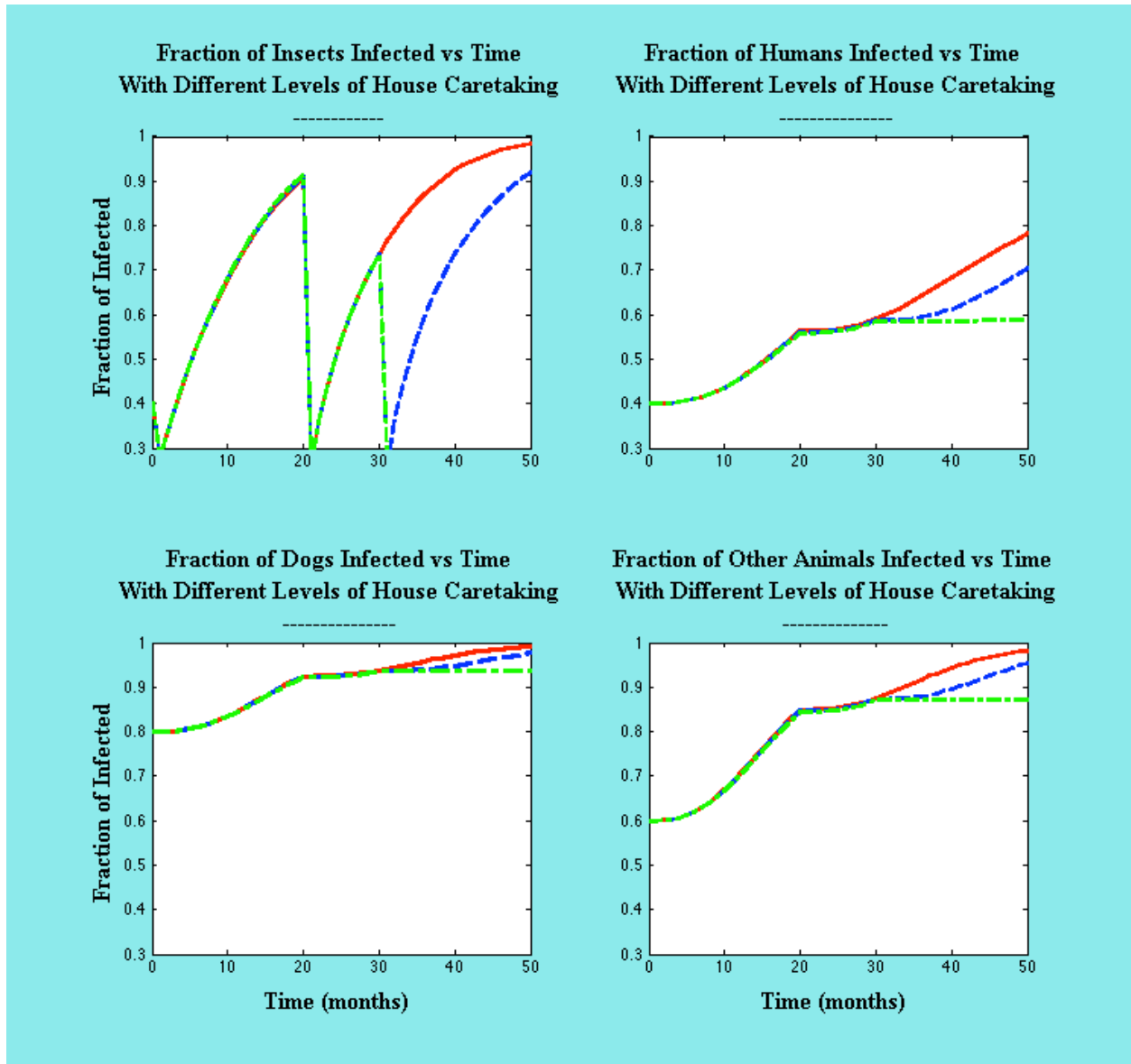
Figure 7: Impact of the three different house treatment plans on the population infection rates. Scenario 1, the solid red line, represents a household with an insecticide application at the 20th time step. Scenario 2, the dashed blue line, represents a household with an insecticide application at the 20th and 30th time step. The third scenario, the dash dot green line, represents a household with an insecticide application at the 20th and 30th time step and a improvement in house quality number at the 30th time step.

3.5 Odds Ratios as Determined by Logistic Regression Analysis

One way to calculate the importance and significance of the survey information used in calculating the house quality and other house parameters is by performing a logistic regression.

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An odds ratio in essence shows how much more likely a piece of information is in predicting an outcome compared to another. In other words, event C is three times as likely to result in X than event A. This type of information allows one to identify the relative importance of the survey data, and can also provide information about demographics. Tables showing the full logistic regression analyses are provided in Appendix E through H.

There were two parameters used as the response or the dependent variable: the presence or absence of insects collected within a house, and the presence or absence of evidence that insects existed in a house. The first parameter was chosen because if an insect is collected from a house, then the house is likely infested. Parameter two (i.e. evidence of insects being in the home), although similar to parameter one, does not always have the same result as insects being collected within a household. As a result, the evidence of insects within a house was analyzed as a surrogate for infestation.

Initially the survey data were analyzed for variables of significance using a $p \leq 0.100$, which allowed many of the survey questions to be eliminated altogether. Appendix I shows the variables that were first identified as important using a Chi squared analysis. Next, a logistic regression was performed on the variables that showed statistical significance. The logistic regression odds ratios were performed using a $p \leq 0.05$. The odds ratio tests were completed on both the Chiquimula (n = 1140) and Guayabo (n = 302) survey data to show the difference between a large spatial data set and a subset of that data. The analysis showed more variables as being significant when using the larger (Chiquimula) data set. But also of note was that different variables were identified as significant between the two data sets, indicating that variables may be important to some towns but not others. Table 1 contains a list of variables that showed up frequently between the four odds ratio tests. The four odds ratio tests were; two on Chiquimula

(i.e. one with the presence/absence of insects collected as the dependent and one with the presence/absence of insect evidence collected) and two on Guayabo (i.e. one with the presence/absence of insects collected as the dependent and one with the presence/absence of insect evidence collected). A sample of the significant odds ratio on Chiquimula with presence/absence of insects collected as the dependent variable is shown in Table 2.

Table 1: List of the variables that showed up common between the different odds ratio tests. The left column of the table displays the variables that showed up as significant in all four of the odds ratios tests. The right column displays the variables that showed significance in three of the four odds ratios.

Variables Common To All Four Odds Ratios	Variables that show up Frequently
What Type of improvement have you done in the last 2 years	Number of people in house
Do you know some symptoms of Chagas Disease	How long Ago have you lived in the house
If you were given sand would you fix your walls	How long ago was the house constructed
Are there birds nests	Presence of animals in bedroom
Are there signs of mice	Hygenic condition of the house
Number of beds in house	Do you know T. Dimidiata
What are the predominant materials of the house walls	Can you show me which one is T dimidiata in the photo
Conditions of walls where family sleeps	Have you or someone in your family been bitten
Condition of walls for the rest of the house	Primary material of floor
Is the bedroom dark	
Presence/ Absence	
Number of bugs in	
Risk	
Have you seen T. Dimidiata in your house	

Table 2: Sample odds ratio table, Chiquimula Presence/absence of insects in house. The grayed out portion of the table represents the variables that had shown up frequently between all of the different odds ratio tests.

Variable	Category	Odds Ratio	Lower 95% Confidence Interval	Upper 95% Confidence Interval	p	Degrees of Freedom	Chi Square
What are the predominant materials of the house walls					0.0002	7	28.11
	Cinderblock vs Mud and Sticks	6.03E+06	4.94	-	0.0001		
	Cinderblock vs Adobe	5.66E+06	4.58	-	0.0001		
	Cinderblock vs Sticks Strands & Leaves	4.11E+06	2.74	-	0.0044		
Conditions of walls where family sleeps					0.0001	2	43.06
	Good Condition vs Deteriorated	5.81	2.88	13.86	0.0001		
Condition of walls for the rest of the house					0.0001	2	36.67
	Good Condition vs Deteriorated	5.20	2.58	12.42	0.0001		
Primary material of floor	-				0.0001	2	24.02
	Brick or Cement vs Earth	3.34	1.71	7.54	0.0002		
Is the bedroom dark					0.0004	2	15.90
	Yes vs No	1.76	1.16	2.73	0.0067		
Number of bugs in	unit	0.00	0.00	.	0.0001	1	977.54
Marks of bugs					0.0001	1	166.28
	Absence vs Presence	9.60	6.76	13.75	0.0001		
Number of insects outised	unit	0.60	0.34	0.87	0.0006	1	11.84
Risk					0.0001	3	47.26
	A,B	5.89	1.02	111.18	0.0466		
	A,C	21.98	4.84	388.47	0.0001		
	B,C	3.73	1.83	8.96	0.0001		

The odds ratio tests were done for the *absence of insects collected* (i.e. a given variable is more likely to result in an absence of insects than another variable). Column 2 (Category) is modified from its original naming scheme to be more understandable. The original naming scheme uses a numerical representation for variables, the conversions are shown in Appendix D. The variables associated with the question "What are the predominant materials of the house walls" shows three categorical variable comparisons to be statistically significant. However, since the odds ratios are so large and the comparisons lack an upper 95% confidence interval, then it is not conclusive as to whether these odds ratios fall in a particular confidence interval. This may be the result of a lack of power in the available survey information.

On the other hand, the odds ratios reported for the variable question "Conditions of walls where family sleeps" does have an upper and lower 95% confidence interval and these variables

show statistical significance ($p<0.0001$, Chi Squared of 43.06). For this variable, the odds of "good condition" resulting in the absence of insects is approximately 6 times more likely (with an lower and upper bound of 3 times more and 14 times more likely respectively) than the odds of "poor condition" resulting in the absence of insects ($p <0.0001$).

This analysis provides a simple way to weight survey information in order to acquire a house quality parameter and also how the evidence of insects relates to whether an insect was collected within a household. The analysis allows the user to remove variables that do not show importance, while also showing how much more likely a variable (or category) is to link to infestation than another variable (or category).

4. Conclusions and Future Work

The main accomplishments of this research were the creation of a SIR model that analyzes the insect population and infection in a household. This is important for the modeling of Chagas disease; insect populations, and the infected population will change over time. Another accomplishment of this research was the inclusion of an insecticide application. Insecticides are often used for controlling the insect population; and modeling their impact on a house is an important consideration for infestation. This model allows individual houses to be sprayed at different times. Every house may not be sprayed during a particular time step, and it is important to include the option to accurately simulate the real scenario. The main goal of this research was to create a model that allowed multiple households to be simulated in parallel during a single time step. This was done by bringing in data sets from excel to supply the initial conditions for each individual household. The model is then capable of interpreting this data and running a unique simulation for each house simultaneously for each time step.

This research provides an initial starting point for the overall modeling of insect populations and Chagas disease at the town scale. Some important next steps for model calibration will be to parameterize the variables using values from the literature. The current model is designed with the hope that research and information acquired from the ongoing insect bloodmeal laboratory analysis will be able to provide insight on more realistic values.

Another consideration to advance to a town level is to find a relationship that links transmission between individual households. This can be done in different ways. One is determining the impact of neighbors with a house reported as being infested. Once that information is identified, then a transmission rate can be created using the quality of nearby houses. Another way to potentially represent house linkages is to use spatial distance. Part of the survey data contains the GPS coordinates of each house; with this information, a function could be created that relates the impact of distance on insect transmission.

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Appendices:

****Appendices are available upon request****