A Household Model of Cockroach Infestation and Its Effects on Atopic Asthma Symptoms

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Abstract

Asthma is a chronic respiratory condition which affects 25 million people in the United States. According to the Center for Disease Control and Prevention (CDC) asthma is a significant health and economic concern, and also causes 270 deaths per month. Cockroaches are among the most common indoor pests, with its allergen being present in 63% of U.S. households. Improper extermination of cockroaches and the associated allergens has been shown to increase the occurrence of atopic asthma, a type of asthma triggered by the exposure to allergens. In this work, a household model was developed to study the dynamics of cockroach infestation in a neighborhood of houses with individuals sensitized to the cockroach allergen. The impact of extermination and removal of allergens in a household with recurrent atopic asthma was evaluated. Equilibria for the system with and without the influx or migration of cockroaches are determined, including equilibria in which both cockroaches and asthma are present. The average number of secondary infestations that can be produced by the presence of a single infestation in a population of households without cockroaches and asthma was calculated. Numerical simulations on the model and sensitivity analysis on the basic reproductive number were used to examine the impact of key parameter values. Numerical backward bifurcations for a set of parameters were obtained and the results showed that it is more effective to prevent infestation of cockroaches, rather to attempt to remove cockroaches once they have infested a house. A mathematical study of cockroach infestations and their effect on atopic asthma has not been done. Therefore, this model will assist in educating the general public about the importance of pest control and its relationship with asthma.

1. Introduction

Different regions of the world face a common problem: the infestation of cockroaches. Not only is the associated filth an issue, but also the harmful effects on the immune system. It is well known that the cockroach is a vector of intestinal diseases, such as diarrhea, dysentery, typhoid fever and cholera. However not much is known about how they can be a trigger for the development of allergies and respiratory diseases, and how the control of its population can help decrease the incidence of diseases like rhinitis and asthma.

1.1. Allergies

In the past century the prevalence of allergic diseases has increased [1]. Food and respiratory allergies are now one of the most common chronic conditions in the world population. It has been estimated that about 400 million people suffer from allergic diseases (i.e. rhinitis) and 250 million from food allergies [2].

An allergic reaction is developed when the immune system mistakes one substance that is harmless to the body, with an unwanted invader and starts producing the antibodies that will lead to the characteristic inflammation, skin rash, sneezing, among other symptoms common to allergic reactions. This substance is called an allergen, and although it may vary from individual to individual, pollen, dust, food, insect stings and mold are the most frequent form of allergens [3]. Allergic diseases can be shared between individuals due to genetic factors, as members of the same family may be sensitized to a certain group of allergens and eventually generate the same kind of allergies. Several of these allergic diseases often show themselves during childhood and the continuous exposure to allergens and the subsequent development of allergic reactions can trigger respiratory diseases such as asthma [4].

1.2. Asthma due to Allergies

It is estimated that asthma affects 300 million people worldwide; and by 2025 the number would increase to 400 million [4]. This chronic condition annually takes the life of approximately 250,000 people, many of which are avoidable with proper treatment and care [5]. Genetic and environmental factors are critical in the process of development of this condition. Atopic asthma is the result of an inherited predisposition to produce specific IgE antibodies that activate the immune system reactions [5].

Nearly 30% of children with atopic dermatitis develop asthma, and nearly 66% develop allergic sensitization as well as symptoms of allergic rhinitis [4]. Individuals with this condition present a chronic inflammation in the lower airways that in the proximity of common allergens results in variable airflow obstruction, causing recurrent episodes of coughing, wheezing, breathlessness, and chest tightness [4]. Environmental risk factors like outdoor and indoor pollution in urban areas are contributing to this risk. There is an evident growth in the prevalence of asthma especially in inner-city children [6].

Particles as those in house dust become more important due to their role as a cause of asthma. The concentration of particles in the indoor air of the home and its composition may vary with time, geographic location and life style of the inhabitants of a household [7]. Dust particles can include human and animal skin fragments,as well as, allergens including pollen and those produced by mites and cockroaches [8].

1.3. Cockroach and its allergens

The levels of cockroach allergen in homes have been studied for years as this is one of the most common risk factors for allergic sensitization and asthma morbidity. The results from the Third National Health and Nutrition Examination Survey (NHANES III) estimate that 26.1% of the population in U.S. presents allergic sensitization to the allergens of the German cockroach [9]. Depending on the species, cockroaches can be found outdoors or living very closely with the human population. An adult female German cockroach can produce 35 eggs each month, therefore once a cockroach is in a household it is vital to get rid of them quickly in order to prevent an infestation [10]. Cockroaches have been reported to be associated with asthma in many regions of the world because constant exposure to cockroach allergens may lead to recurrent wheezing and asthma. In other words, cockroach infestation in housing is an important public health problem.

Exposure has been reported to be among the most important risk factors in asthma morbidity and mortality for children from low-income families living in inner cities. For example, there is high incidence of cockroach sensitivity in children from large cities in the United States such as New York [11, 12]. Strategies for decreasing environmental exposure to cockroach allergen in inner–city homes have been investigated. The results suggest that a sustained decrease in cockroach allergen levels is difficult to accomplish, even after successful extermination of cockroach populations.[12]

In a national survey of 831 U.S. homes, 13% had a concentration higher than 2.0 U/g of the cockroach allergen Bla g 1, which is a concentration related with the prevalence of allergic and asthmatic symptoms [11]. Children with a positive skin test response to cockroach increase rapidly as the intensity of exposure to Bla g 1 increase and some studies propose the value of 8.0 U/g as disease-induction threshold [13, 14].

Currently, there is no proven method of reducing cockroach allergen in infested homes. Although it is known that actual methods like pesticides can be employed to exterminate the cockroaches successfully, it is not clear that household allergen exposure will be reduced as a result [15]. Bla g 1 and Bla g 2 are the major cockroach allergens associated with the German cockroach and the highest concentrations are found in their secretions and fecal material. It is believed that successful reduction of cockroach allergen is also linked to the reduction of cockroach–associated asthma morbidity [16].

There are no mathematical studies related to the cockroach infestations and their effect on atopic asthma. Therefore, the goal of this research is to develop a household mathematical model that would allow us to investigate how extermination and allergen removal of *Blattella germanica* (German Cockroach) prevents the recurrence of atopic asthma symptoms in a household. The results from mathematical analysis, numerical simulations and sensitivity analysis will help us understand this relationship between cockroach allergens and asthma symptoms.

2. Methods

2.1. Household model

To understand the impact of the presence of cockroaches on the prevalence of asthma symptoms in a neighborhood, we consider a mathematical model with a constant population with household as the epidemiological unit. Because the mechanisms by which one develops asthma are not yet fully understood, we assume that all households within the population contain at least one individual that possesses allergic sensitization to cockroach allergens and has already been diagnosed with atopic asthma. For the simplicity of our model, we also assume that individuals occupying a household in our population do not relocate nor do additional families immigrate into the neighborhood. Thus, we do not consider new constructions or destructions of households in our population.

The model consists of four compartments (listed in Table 1): susceptible ($S(t)$), asymptomatic infested ($A(t)$), symptomatic infested ($I(t)$) and cleaned ($C(t)$) households, all at time t. The susceptible households do not contain cockroaches or cockroach allergens, but also, no individuals within the home show asthmatic symptoms. Once a household becomes infested with cockroaches, it enters the asymptomatic infested compartment since that household is now able to spread the infestation to other homes; however, the individuals within the house have not yet developed asthma symptoms. Upon infestation of cockroaches, that home begins to accumulate cockroach allergens. In 1997, Rosenstreich et al associated an allergen threshold (Bla g 1 $>$ 8 U/g) with greater asthma morbidity among children with asthma who are sensitized to the cockroach allergen [17]. Due to the results of this study, we further assumed that once a household reaches this threshold (8 U/g), at least one individual within the home will develop asthma symptoms and that household will change its status to a symptomatic infested household; that is, with asthma. Afterwards, professional extermination of the cockroaches will convert that household's status to cleaned where it can either become reinfested with cockroaches or the cockroach allergens are decreased to a level below the asthma morbidity threshold. The latter option can be achieved by ridding the home of the allergens through professional cleaning or by simply waiting for the allergens to dissipate naturally. Both options, we assume, will eliminate the presence of asthma symptoms and change the status of that household back to susceptible. Figure 1 gives a compartmental diagram representation of our model.

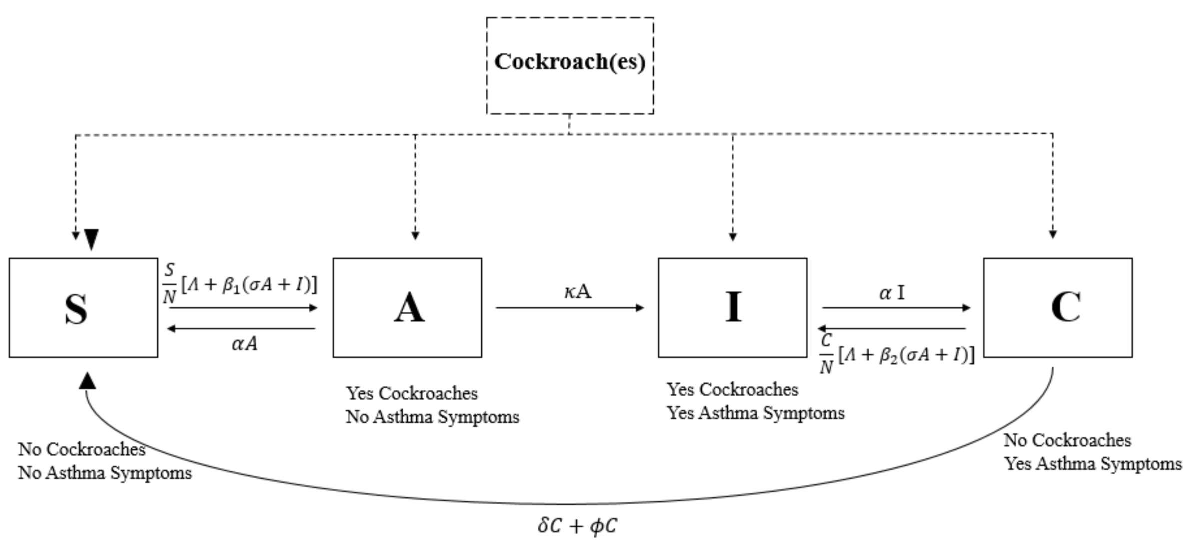


Figure 1. Schematic diagram for the infestation stages with cockroaches, including compartments for susceptible (S), asymptomatic infested (A), infested and asthmatic (I) and Cleaned (C).

Because we are not considering new construction or destruction of houses in this model, the population of households will remain constant. Thus, the total population at time t of our model is represented by $N_0 = S(t) + A(t) + I(t) + C(t)$.

A susceptible home changes its status by becoming infested with cockroaches, which could either happen by cockroaches migrating in from outside of the neighborhood and selecting a susceptible house at a rate ($\frac{S\Lambda}{N}$), or by cockroaches coming in from other infested households at a rate $\left(\frac{S}{N}\right)\beta_1(\sigma A + I)$, where β_1 represents the migration rate and σ accounts for the reduced number of cockroaches in asymptomatic infested homes compared to symptomatic infested homes. Once a household becomes infested, the cockroaches can be exterminated right away before symptoms are present in the household, which would happen at a rate α, and return the status of the household to susceptible. On the other hand, if they opt to not exterminate right away, this would lead to the eventual appearance of symptoms at a rate κ, where $\frac{1}{\kappa}$ is defined to be the time that it takes for a home to build up enough allergens to cross the asthma morbidity threshold. Symptomatic infested households become cleaned houses once professional extermination takes place, at a rate α. Finally, homes in the cleaned compartment either become reinfested with cockroaches, or the allergens are completely eradicated. Reinfestation will occur when cockroaches migrate from outside of the neighborhood and select a cleaned home at a rate $\left(\frac{C\Lambda}{N}\right)$. Additionaly, reinfestation occurs at a rate $\frac{C\beta_2(\sigma A+I)}{N}$ if the infestation comes from other infected households, that is where β_2 is the migration rate of cockroaches from houses that still have some presence of the allergen; thus, we assume $\beta_2 > \beta_1$. This assumption is made because cockroaches are usually attracted to places where there is already a presence of cockroach allergens [16]. The eradication of allergens can occur from the professional removal of allergens, at a rate δ, or from simply waiting for the allergens to dissipate with time, at a rate ϕ. The following system of non-linear ordinary differential equations represent the dynamics of the population of households in our model and a summary of the parameter definitions is given in Table 2.

$$\frac{dS}{dt} = -\frac{S}{N}[\Lambda + \beta_1(\sigma A + I)] + \alpha A + C(\delta + \phi), \tag{1a}$$

$$\frac{dA}{dt} = -\kappa A - \alpha A + \frac{S}{N}[\Lambda + \beta_1(\sigma A + I)], \tag{1b}$$

$$\frac{dI}{dt} = -\alpha I + \kappa A + \frac{C}{N}[\Lambda + \beta_2(\sigma A + I)], \tag{1c}$$

$$\frac{dC}{dt} = -(\delta + \phi)C - \frac{C}{N}[\Lambda + \beta_2(\sigma A + I)] + \alpha I, \tag{1d}$$

where $N(t) = S(t) + A(t) + I(t) + C(t)$.

Table 1. State Variables of Household Model

Variable	Definition
$S(t)$	Number of households free of cockroaches and allergens at time t
$A(t)$	Number of households infested with cockroaches but symptoms of asthma are not yet present at time t
$I(t)$	Number of households infested with cockroaches and symptoms of asthma at time t
$C(t)$	Number of houses without cockroaches but allergens and symptoms still present at time t

Table 2. Parameter Definitions of Household Model

Parameter	Definition	Unit
Λ	Influx rate of cockroaches from outside neighborhoods	$households \cdot months^{-1}$
β_1	Rate of cockroach infestation/ migration to susceptible houses from outside the neighborhood	$months^{-1}$
β_2	Rate of cockroach reinfestation/ migration to cleaned houses	$months^{-1}$
σ	Reduction infestation factor for asymptomatic infested houses	$dimensionless$
α	Extermination rate	$months^{-1}$
δ	Allergen removal rate	$months^{-1}$
ϕ	Rate of natural removal of allergen	$months^{-1}$
κ	Cockroach reproduction rate	$months^{-1}$

3. Mathematical Analysis of the Household Model

In order to analyze the household model, we will consider different cases for the infestation of cockroaches in a household. First of all, we will analyze the case when there is no migration of cockroaches from the other neighborhoods ($\Lambda = 0$) but there is movement of cockroaches from other households within the neighborhood. We are considering cockroaches within a neighborhood and then numerically analyze the case where there is no migration of cockroaches from the other neighborhoods ($\Lambda \neq 0$).

3.1. No Migration of Cockroaches from Other Neighborhood ($\Lambda = 0$)

Cockroach Free Equilibrium and Derivation of R_0

In this case ($\Lambda = 0$), the equations of System (1) become:

$$\frac{dS}{dt} = -\frac{S}{N}[\beta_1(\sigma A + I)] + \alpha A + C(\delta + \phi), \tag{2a}$$

$$\frac{dA}{dt} = -\kappa A - \alpha A + \frac{S}{N}[\beta_1(\sigma A + I)], \tag{2b}$$

$$\frac{dI}{dt} = -\alpha I + \kappa A + \frac{C}{N}[\beta_2(\sigma A + I)], \tag{2c}$$

$$\frac{dC}{dt} = -(\delta + \phi)C - \frac{C}{N}[\beta_2(\sigma A + I)] + \alpha I, \tag{2d}$$

$$\text{and } N(t) = S(t) + A(t) + I(t) + C(t). \tag{2e}$$

The rate of change of the total amount of household in the neighborhood is given by:

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dA}{dt} + \frac{dI}{dt} + \frac{dC}{dt} = 0$$

Since $\frac{dN}{dt} = 0$, the total population of households is constant for all time t which is consistent with our assumption that

$$N(t) \equiv N_0 \in \mathbb{R}^+.$$

Since the total population is constant, it suffices to only consider a system of three equations where $S(t) = N_0 - (A + I + C)(t)$. By making this substitution and letting $\mu = \delta + \phi$, the simplified system of equations becomes:

$$\frac{dA}{dt} = -\kappa A - \alpha A + \left(\frac{N_0 - (A + I + C)}{N_0}\right)\beta_1(\sigma A + I), \tag{3a}$$

$$\frac{dI}{dt} = -\alpha I + \kappa A + \frac{C\beta_2(\sigma A + I)}{N_0}, \tag{3b}$$

$$\frac{dC}{dt} = -\mu C - \frac{C\beta_2(\sigma A + I)}{N_0} + \alpha I. \tag{3c}$$

Setting the equations of System (3) equal to zero, we calculate the cockroach free equilibrium (CFE) given by:

$$CFE : (S^*, A^*, I^*, C^*) = (N_0, 0, 0, 0).$$

For the local stability of cockroach free equilibrium, we must show that all the eigenvalues of the Jacobian matrix evaluated at the CFE have negative real parts.

The eigenvalues of the Jacobian matrix evaluated at the CFE is given by (for Jacobian matrix see Appendix A1)

$$J_{(0,0,0)} = \begin{bmatrix} \beta\sigma - (\alpha + \kappa) & \beta & 0 \\ \kappa & -\alpha & 0 \\ 0 & \alpha & -\mu \end{bmatrix}.$$

The characteristic equation of the matrix $J_{(0,0,0)}$ is as follows:

$$(-\lambda - \mu)\left(\lambda^2 + \lambda(2\alpha + \kappa - \beta\sigma) + \alpha^2 + \alpha\kappa - \beta\kappa + -\alpha\beta\sigma\right) = 0.$$

Therefore, the eigenvalues of CFE are given by:

$\lambda_1 = -\mu < 0,$ and $\lambda_{2,3} = \frac{1}{2}\left[(2\alpha + \kappa - \beta\sigma) \pm \sqrt{4\beta\kappa + (\kappa - \beta\sigma)^2}\right]$. Since all parameters are assumed to be positive, $\lambda_1 = -\mu$ is a negative eigenvalue.

We note that the discriminant is always positive. Therefore, both eigenvalues λ_2 and λ_3 are real for all values of the parameters. To further investigate the sign of the eigenvalues, we let:

$$E = 2\alpha + \kappa - \beta\sigma \quad \text{and} \quad F = \alpha(\alpha + \kappa) - \alpha\beta\sigma - \beta\kappa,$$

then

$$\lambda_{2,3} = \frac{1}{2}\left(-E \pm \sqrt{E^2 - 4F}\right).$$

If $E > 0$ and $F > 0$, then $\sqrt{E^2 - 4F} < E$ and the negativity of $\lambda_{2,3}$ is guaranteed.

Thus,

$$F > 0 \iff \alpha(\alpha + \kappa) > \alpha\beta\sigma + \beta\kappa \iff \frac{\beta(\alpha\sigma + \kappa)}{\alpha(\alpha + \kappa)} < 1.$$

Hence, we define

$$R_0 = \frac{\beta(\alpha\sigma + \kappa)}{\alpha(\alpha + \kappa)} = \frac{\beta\sigma}{\alpha + \kappa} + \frac{\beta}{\alpha}\left(\frac{\kappa}{\alpha + \kappa}\right).$$

Let,

$$R_0^A = \frac{\beta\sigma}{\alpha+\kappa} \quad \text{and} \quad R_0^I = \frac{\beta}{\alpha}\left(\frac{\kappa}{\alpha+\kappa}\right) \tag{4}$$

then R_0 becomes

$$R_0 = R_0^A + R_0^I.$$

On the other hand $E > 0$ is provided if

$$2\alpha + \kappa - \beta\sigma > 0 \iff \frac{\beta\sigma}{\alpha+\kappa} < 1 + \frac{\alpha}{\alpha+\kappa},$$

that is by Equation (4),

$$\iff R_0^A < 1 + \frac{\alpha}{\alpha+\kappa},$$

Which is true since $R_0^A < 1$. Therefore,

$$F > 0 \quad \text{and} \quad E > 0 \iff R_0 < 1,$$

which means both eigenvalues λ_2 and λ_3 are negative.
All the eigenvalues of the $J_{(0,0,0)}$ are real and negative, thus the cockroach free equilibrium (CFE) is locally asymptotically stable. We summarize the result in the following theorem.

Theorem 1. *If $R_0 = R_0^A + R_0^I < 1$, then the CFE is locally asymptotically stable.*

3.1.1 Interpretation of R_0

The basic reproductive number for our model, R_0, is defined to be the average number of secondary cockroach infestations produced by a single infested household in a completely susceptible neighborhood.
The basic reproductive number, R_0, for our model is given by the expression:

$$R_0 = \frac{\beta(\kappa+\alpha\sigma)}{\alpha(\alpha+\kappa)}$$

Thus, R_0 is the sum of two basic reproductive numbers; R_0^A, which is the number of new houses with cockroaches produced by the migration of cockroaches from those households that do not show any asthma symptoms and R_0^I which represents the contribution to R_0 by those households with the presence of both cockroaches and asthma symptoms. Thus, R_0 can be represented as

$$R_0 = R_0^A + R_0^I = \frac{\beta\sigma}{\alpha+\kappa} + \frac{\beta\kappa}{\alpha(\alpha+\kappa)} = \frac{\beta\sigma}{\alpha+\kappa} + \frac{\beta}{\alpha}\left(\frac{\kappa}{\alpha+\kappa}\right);$$

R_0^A is equal to the product of the reduced infestation rate ($\beta\sigma$) of asymptomatic households multiplied by the average time that these households spend with both the presence of cockroaches and the absence of asthma symptoms $\left(\frac{1}{\alpha+\kappa}\right)$. On the other hand, R_0^I is equal to the product of the infestation rate (β) of symptomatic households multiplied by the proportion of asymptomatic homes

that move on to become symptomatic $\left(\frac{\kappa}{\alpha+\kappa}\right)$ and the average time that household shows asthma symptoms and remains infested.
To further study the model, we will evaluate the endemic equilibrium at two different cases. The first case will be in the absence of both cockroach migration from outside of the neighborhood and cockroach migration into cleaned households ($\Lambda = 0, \beta_2 = 0$), that is assuming that once a household is clean, it can not right away get re-infested. For the second case, we consider the migration of cockroaches into cleaned homes from other households in the neighborhood (A and I) while continuing to ignore migration of cockroaches from outside ($\Lambda = 0, \beta_2 \neq 0$).

3.2. No Migration of Cockroaches from Other Neighborhood and no Re-infestation of Cockroaches ($\Lambda = 0$ and $\beta_2 = 0$).

The assumptions $\Lambda = 0$ and $\beta_2 = 0$ lead to the special case of the household model. Biologically, $\Lambda = 0$ implies that there is no influx of outside cockroaches into susceptible or clean houses. The term $\beta_2 = 0$ means that there is no migration of cockroaches from other houses to a cleaned house. In other words, once a household with asthma symptoms gets the extermination of cockroaches (at a rate α) the house is assumed to be cockroach free, and without the possibility of re-infestation.
In this case, the model becomes

$$\frac{dA}{dt} = -\kappa A - \alpha A + \frac{N-(A+I+C)}{N_0}\beta(\sigma A + I), \tag{5a}$$

$$\frac{dI}{dt} = -\alpha I + \kappa A, \tag{5b}$$

$$\frac{dC}{dt} = -\mu C + \alpha I, \tag{5c}$$

$$\text{where } S(t) = N_0 - (A(t) + I(t) + C(t)). \tag{5d}$$

By setting the right hand side of the equations of System (5) equal to zero, we found the cockroaches and asthma equilibrium E^*, which in terms of R_0 is given by:

$$E^* = \left(\frac{N_0}{R_0}, \frac{N_0\alpha\mu}{\kappa\mu+\alpha\mu+\kappa\alpha}\left(1-\frac{1}{R_0}\right), \frac{N_0\kappa\mu}{\kappa\mu+\alpha\mu+\kappa\alpha}\left(1-\frac{1}{R_0}\right), \frac{N_0\kappa\alpha}{\kappa\mu+\alpha\mu+\kappa\alpha}\left(1-\frac{1}{R_0}\right)\right). \tag{6}$$

That is, E^* exists provided that $R_0 > 1$.

Cockroaches and Asthma Equilibrium and Stability

Routh-Hurwith critterion was used to show the stability of cockroaches and asthma equilibrium (E^*)(Appendix A.2 for details)
Thus, the endemic equilibrium is locally stable if $R_0 > 1$.

Theorem 2. *If $R_0 = R_0^A + R_0^I > 1$, then there exists an endemic equilibrium and it is locally asymptotically stable.*

3.3. No Migration of Cockroaches from Other Neighborhoods with Reinfestation of Cockroaches: ($\Lambda = 0$ and $\beta_2 \neq 0$)

In this case, the assumption that $\Lambda = 0$, $\beta_2 \neq 0$, and $\mu = \delta + \phi$ signifies continued absence of the migration of cockroaches from outside the neighborhood. However, the possibility of a household being reinfested after extermination is now being considered.

The system of equations produced by making these assumptions is as follows:

$$\frac{dS}{dt} = -\frac{S}{N_0}\left[\beta_1(\sigma A + I)\right] + \alpha A + \mu C, \tag{7a}$$

$$\frac{dA}{dt} = -\kappa A - \alpha A + \frac{S}{N_0}\left[\beta_1(\sigma A + I)\right], \tag{7b}$$

$$\frac{dI}{dt} = -\alpha I + \kappa A + \frac{C}{N_0}\left[\beta_2(\sigma A + I)\right], \tag{7c}$$

$$\frac{dC}{dt} = -\mu C + \alpha I - \frac{C}{N_0}\left[\beta_2(\sigma A + I)\right]. \tag{7d}$$

By setting the right hand side of all equations in the System (7) equal to zero, we were able to find the same CFE and R_0, as well as an equationa of equilibria points in terms of A, that is:

$$S(A^*) = \frac{N_0(\kappa+\alpha)}{\beta_1\left(\sigma + \frac{\kappa(\mu N + \beta_2\sigma A^*)}{\mu\alpha N - \kappa\beta_2 A^*}\right)}, I(A^*) = \frac{A^*\kappa(\mu N_0 + \beta_2\sigma A^*)}{\mu\alpha N_0 - \beta_2\kappa A^*} \text{ and } C(A^*) = \frac{\kappa}{\mu}A^*. \tag{8}$$

Rewriting $S(A^*)$ in terms of R_0 gives:

$$S(A^*) = \frac{N_0(\kappa+\alpha)}{\beta_1\left(\sigma + \frac{\kappa(\mu N + \beta_2\sigma A^*)}{\mu\alpha N - \kappa\beta_2 A^*}\right)} = \frac{1}{R_0}\left(N_0 - \frac{\beta_2\kappa}{\mu\alpha}\right)A^*. \tag{9}$$

Thus, $S(A^*)$ exists as long as,

$$N_0 > \frac{\beta_2\kappa}{\mu\alpha}.$$

Using the fact that our population is constant and substituting Equations (8) and (9) in

$$0 = N_0 - S(A^*) - A^* - I(A^*) - C(A^*),$$

we get a quadratic polynomial in terms of A^*,

$$0 = N_0 - \left(\frac{N_0}{R_0} - \frac{\beta_2\kappa}{R_0\mu\alpha}A^*\right) - A^* - \left(\frac{\mu\kappa N_0 A^* + \kappa\beta_2\sigma(A^*)^2}{\mu\alpha N_0 - \kappa\beta_2 A^*}\right) - \left(\frac{\kappa}{\mu}A^*\right)$$

Solving for A^* gives

$$\begin{aligned} 0 &= [-\kappa^2\beta_2^2 - R_0\alpha(\kappa + \mu(1-\sigma))](A^*)^2 - [N_0\alpha\mu(R_0-1)\kappa\beta_2 - \beta_2\kappa + (\kappa+\mu)\alpha R_0 + R_0\mu\kappa]A^* \\ &+ (R_0-1)\mu^2\alpha^2 N^2. \end{aligned} \tag{10}$$

Setting $\tau_1 = -\kappa^2\beta_2^2 - R_0\alpha(\kappa+\mu(1-\sigma))$, $\tau_2 = -N_0\alpha\mu(R_0-1)\kappa\beta_2 + \beta_2\kappa - (\kappa+\mu)\alpha R_0 - R_0\mu\kappa$, and $\tau_3 = (R_0-1)\mu^2\alpha^2N^2$ gives

$$f(A) = \tau_1 A^2 + \tau_2 A + \tau_3.$$

See Appendix A3 for a detailed calculation of Equation (10).
Solutions of $f(A) = 0$ will provide the cockroaches and asthma symptoms equilibrium for the case $\Lambda = 0$ and $\beta_2 \neq 0$. Since it is difficult to study the solution of $f(A^*) = 0$ analytically we will do it numerically for the relative parameter values found in the literature (see Table 3 for parameter estimation).

Endemic Equilibrium and Stability

The equation $f(A) = 0$ will provide either one or two roots of A^*, which implies there might be a bifurcation.
In particular, if we solve for the roots of the polynomial in Equation (10) for a given set of the parameter values:

$$\alpha = 0.736, \beta 1 = 0.89, \beta 2 = 2, \kappa = \frac{1}{0.6}, \mu = \frac{1}{6} + \frac{1}{8}, \sigma = \frac{1}{13}, \text{ and } N_0 = 100,$$

which gives two numerical values for $A^*_{1,2} = \{1.93121, 4.52833\}$. After using these values to solve $S^*, I^*,$ and C^*, we get $E^*_j = \left\{S^*_j, A^*_j, I^*_j, C_j\right\}$ for $j = 1, 2$ gives

$$E^*_1 = \{85.8043, 1.93121, 5.99582, 11.0355\} \tag{11}$$

and

$$E^*_2 = \{34.2257, 4.52832, 35.3698, 25.8762\}. \tag{12}$$

The Jacobian matrix for System (7), evaluated at the equilibrium E^*_1 results in three negative and one positive eigenvalues, which implies the equilibrium E^*_1 is numerically unstable for the parameters set. However, the Jacobian matrix for System (7), evaluated at the equilibrium E^*_2 gives all negative eigenvalues, which implies the equilibrium point E^*_2 is locally asymptotically stable.

Bifurcations

Typically, in an epidemiological model, $R_0 < 1$ guarantees that the population reaches the disease free equilibrium and when $R_0 > 1$, the disease persists. A similar scenario exists when the reinfestation of cockroaches in clean houses is not considered, $\beta_2 = 0$. That is, if $R_0 < 1$, the CFE will be locally asymptotically stable and when $R_0 > 1$ the cockroach and asthma equilibrium is born and is locally asymptotically stable. Thus, to prevent an infestation of cockroaches in a household and the possibility of symptomatic houses, it will be enough to decrease R_0 below one. However, for the case where there is reinfestation of cockroaches ($\beta_2 \neq 0$), we will show numerically that even if you decrease R_0 below one, it is not enough to get rid of cockroaches and possible asthma symptoms. This whole scenario can be explained through a backward bifurcation.

Usually, the bifurcation occurs when a small perturbation in parameter values results in either a different solution to the non-linear system or a change in the stability of the solutions. Since the polynomial in Equation 10 was not solved explicitly for A^*, we do not have analytical conditions for backward bifurcations yet. Therefore, these bifurcations are given by solving the polynomial from Equation 10

$$f(A) = \tau_1 A^2 + \tau_2 A + \tau_3$$

numerically for a given set of parameters (for Parameter values see Table (3). We were able to rewrite this polynomial in terms of I by using Equation 8 and plotting it with respect to β_1.

In this section, we will show two types of backward bifurcations related to the most sensitive parameters to R_0, which are α and β_1 (for Sensitivity analysis see Sec. 6).

Backward Supercritical Bifurcation

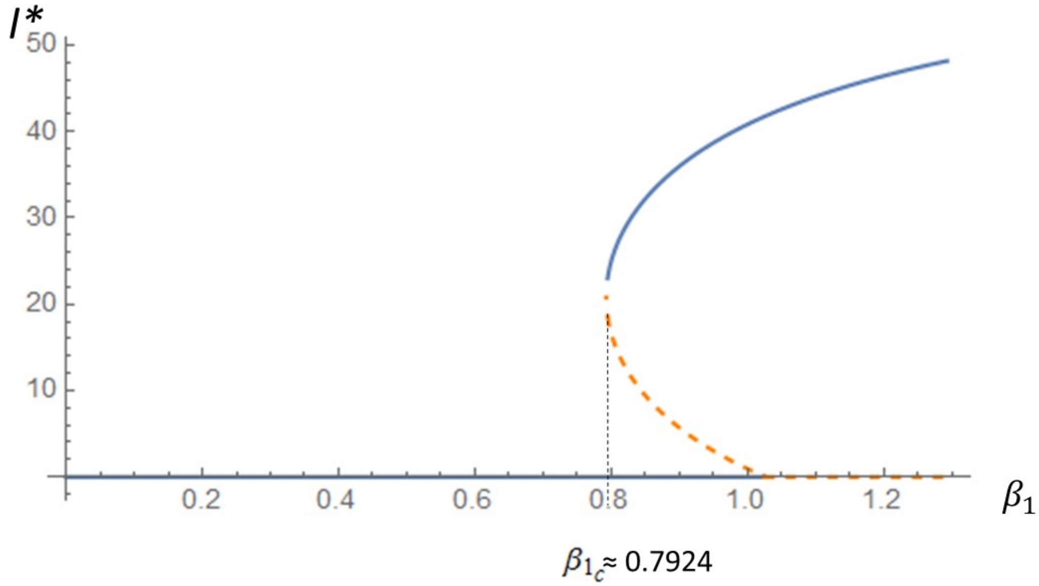


Figure 2. Supercritical backward bifurcation of I^* with respect to migration rate β_1 with parameter values: $\alpha = 0.736$, $\kappa = 1/0.6$, $\beta_2 = 2$, $\phi = 1/8$ and $\delta = 1/6$.

The backward supercritical bifurcation shown in Figure (2) represents the relationship between the infested houses (I^*) and the migration rate of cockroaches from infested to cleaned houses in the neighborhood β_1. If the migration rate is below the critical value of β_1 i.e. ($0 < \beta_1 < \beta_{1_c} \approx 0.7944$), then the number of asthmatic and infested households will always go to zero. Therefore, the cockroach free equilibrium is locally asymptotically stable for β_1 values within this range. When the migration rate of cockroaches is between the critical value of β_{1_c} and the threshold value of β_1 i.e. ($0.7944 \approx \beta_{1_c} < \beta_1 < \beta_1 \approx 1.0244$), then we need to consider two different cases depending on the initial population of infested houses (I^*). For example, when $I^* = 10$, the infested houses will not have any asthma symptoms if the migration rate is ($0.7944 \approx \beta_{1_c} < \beta_1 < \beta_1 \approx 0.8424$); however, there will be the presence of asthma symptoms if the migration rate is ($0.8424 \approx \beta_1 < \beta_1 < \beta_1 \approx 1.0244$). Finally, if the migration rate is over the threshold value of β_1 i.e. ($\beta_1 > 1.0244$), then there is a presence of asthma symptoms in a household no matter how large or small the initial population of infested houses. Additionally, there is also a presence of the hysteresis effect in this graph. That is, we need to maximize the migration rate of cockroaches in order to eventually eradicate asthma symptoms in a household.

Due to the fact that β_1 is not a parameter that is easily controlled, we will also consider the the relationship of infested houses with the extermination rate, α.

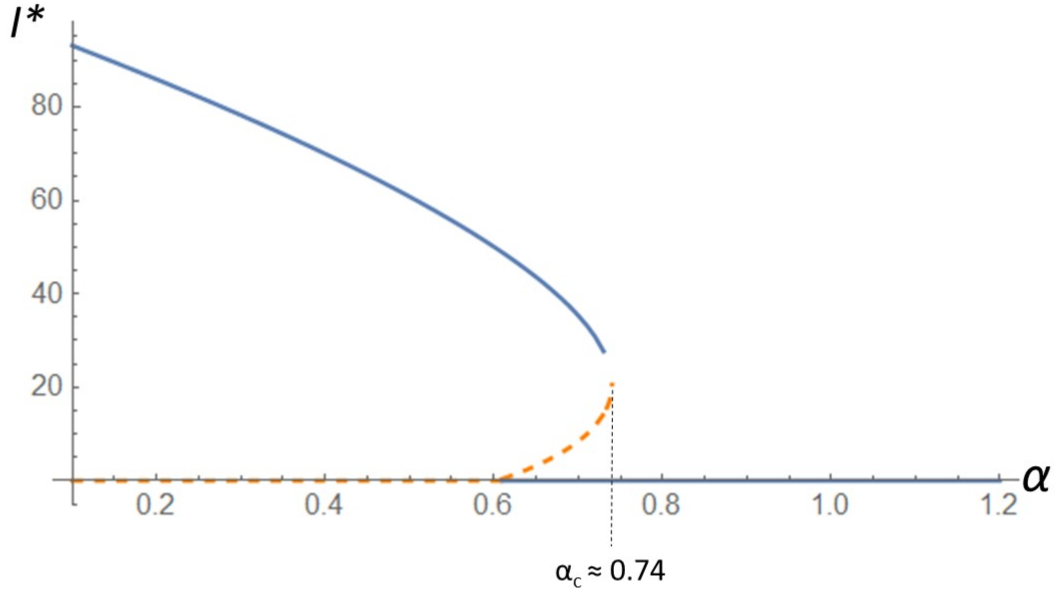


Figure 3. Subcritical backward bifurcation of I^* with respect to migration rate α with parameter values: $\beta_1 = 0.80$, $\kappa = 1/0.6$, $\beta_2 = 2$, $\phi = 1/8$ and $\delta = 1/6$.

Subcritical Backward Bifurcation

Figure 3 represents a subcritical backward bifurcation given by the relationship between infested asthmatic houses I^* and extermination rate α. If the extermination rate α is below the threshold value i.e. ($\alpha < 0.61$), then there is a presence of infestation and asthma symptoms in the house no matter how large or small the initial population of infested houses are. In this case, the extermination does not prevent a neighborhood from getting cockroaches. When the extermination rate is between the threshold value and the critical value ($0.61 \approx \alpha < \alpha < \alpha_c \approx 0.74$), two different types of scenarios can occur depending on the initial population of the infested houses. For example, if $I^* = 10$, then there are asthma symptoms if the extermination rate is ($0.61 < \alpha < 0.71$) and there are no asthma symptoms if the extermination rate is ($0.71 < \alpha < \alpha_c \approx 0.74$). In particular, the threshold value of α represents the minimum extermination rate needed to prevent the neighborhood from cockroach invasion and decreases the possibility of an household with asthma symptoms. The critical value of α is the minimum extermination rate for to save a neighborhood from cockroach infestation and decrease significantly the infested households with asthma symptoms. Finally, if the extermination rate is above the critical value ($\alpha > 0.74$), extermination is enough to get rid of the cockroaches no matter how large or small is the initial population of the infested houses.

The numerical results from backward bifurcation for a given set of parameters highlight the fact that extermination is very important in order to avoid reinfestation. In particular, with the same set of parameters used in the bifurcation, extermination every four weeks can prevent reinfestation of cockroaches and asthma symptoms. However, extermination is needed every two weeks to prevent cockroaches reinfestation; if we use a higher value for migration rate, for instance $\beta_1 \approx 5$, then, it is better to prevent infestation than getting rid of cockroaches.

4. Parameter Estimation

From the literature we were able to obtain estimated values for parameters: $\alpha, \beta_1, \beta_2, \gamma, \kappa$, Λ, σ, and ϕ. Rabito et. al. [18] determined that it takes a little over two months for a home to be completely free of cockroaches after extermination , thus the extermination rate (α) was set to $\frac{1}{2}$month^{-1}. Our rate for δ was taken from a study by Eggleston et. al. in which they determined that allergen levels will decrease by 95% with a sustained allergen removal of 6 months, thus, δ was set to $\frac{1}{6}$month^{-1}.

The parameter κ was found by combining information from multiple sources. Since κ is defined to be the rate at which asymptomatic infested households become an asthma symptomatic household, it was necessary for us to find the length of time that it takes for a house to build up 8 U/g of allergen after the entrance of one cockroach. We began by assuming the cockroach that entered the home was a mated female. Therefore, within 17 days of entering the home, the nymphs would emerge from her ootheca. According to Cornwell [10], on average, 24 nymphs will hatch from each ootheca and reach adulthood, so by assuming that 50% are female, we find that each female will produce 12 other females. Furthermore, from a study by Gore et al [19], we found that each female German cockroach will excrete approximately 1037.5 U of Bla g 1 in her feces each day. Joining this information with the assumption that female nymphs produce the same amount of allergens as female adults, the reproduction rate of *Blatella germanica*, the average amount of dust in a home per square foot, and the average square footage of a home, led us to the conclusion that $\kappa = \frac{1}{0.6}$month^{-1}. From this conclusion, we determined that households in the asymptomatic infested class will typically only have 1 cockroach, while those in the symptomatic infested class will have at least 13. From this, we determined that the reduction factor of A, σ, is equal to $\frac{1}{13}$.

From Cornwell's book [10], *The Cockroach Vol.1*, it was found that German cockroaches are 83% more likely to harbor in places where a scent was left from another cockroach. Therefore, the migration rate to a cleaned house (β_2) is greater than the migration rate into a susceptible house (β_2) because of the presence of the cockroach allergen. However, because an exact rate cannot be found, the values for β_1 and β_2 will be varied assuming $\beta_2 > \beta_1$. This assumption is made because cockroaches are usually attracted to places where there is already a presence of cockroach allergens [16]. For similar reasons, the value for the influx rate of cockroaches from outside the neighborhood (Λ) will also be varied. Table 3 contains a summary of estimated values for all parameters.

5. Numerical simulations

Since the most relevant factor for the prevalence of asthma in a household is related to the influx of cockroaches, we are interested in how various types of influx of cockroaches, namely from outside and within the neighborhood, result in different behavior. When the influx of cockroaches from outside and inside the neighborhood is changed, we observe how the number of households that have an infestation also changes. This is important in order to develop strategies that reduce the incidence of asthma symptoms triggered by cockroach allergens. Numerical simulations were

Table 3. Table of estimated values for all parameters

Parameter	Definition	Estimated Value	Reference
Λ	Influx rate of cockroaches from outside neighborhoods	Varied	-
β_1	Migration rate to susceptible houses	Varied	[10]
β_2	Migration rate to cleaned houses	Varied	[10]
σ	Reduction factor for asymptomatic infested homes	$\frac{1}{13}$	-
α	Extermination rate	$\frac{1}{2}\frac{1}{months}$	[18]
δ	Allergen removal rate	$\frac{1}{6}\frac{1}{months}$	[15]
ϕ	Rate of households waiting for allergen to dissipate	$\frac{1}{8}\frac{1}{months}$	[18]
κ	Cockroach reproduction rate	$\frac{1}{0.6}\frac{1}{months}$	[10], [19]

made for the different cases studied in section 3 using the parameters estimated in Table 3.

Figure 4 shows how the population in each compartment of our model behaves under three different scenarios, where the value of R_0 for the 3 cases is greater than 1 ($R_0 = 1.574$) as result of the numerical values of the estimated parameters.

The first scenario was established with the conditions where there is no introduction of cockroaches from other neighborhoods ($\Lambda = 0$) and the houses are not re–infested by cockroaches once they are cleaned ($\beta_2 = 0$) (Figure 4 (a)). The second case which can be seen in the Figure 4(b), considers re–infestation ($\beta_2 \neq 0$). And finally in the third scenario, the migration of cockroaches from other neighborhood was taken into account ($\Lambda \neq 0$) along with the re–infestation of clean households ($\beta_2 \neq 0$).

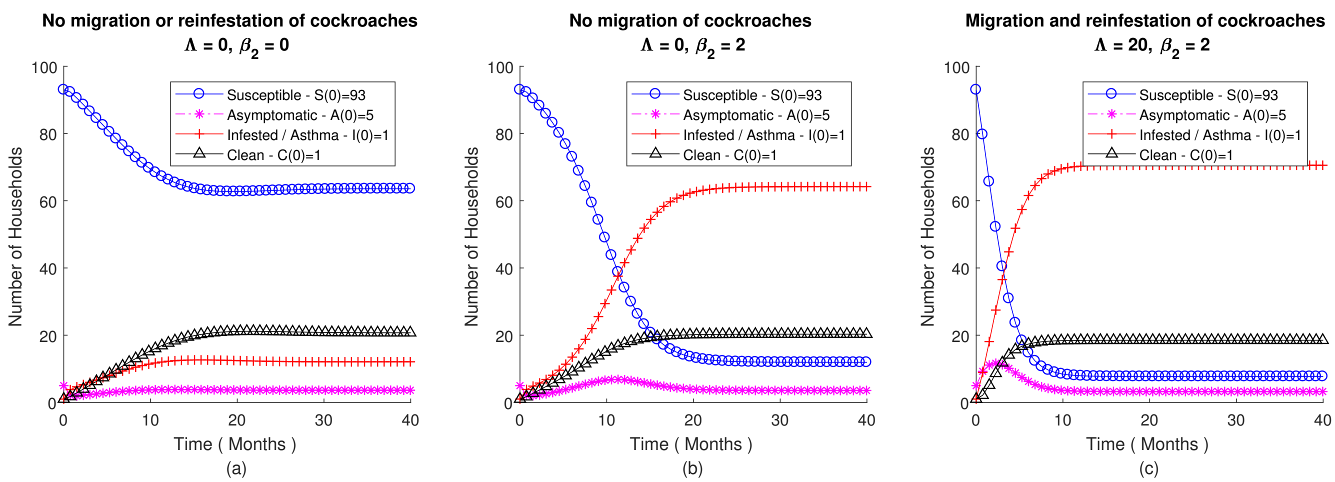


Figure 4. From left to right, Case I, Case II and Case III.

In case I (Figure 4 (a)), the population of households reached the equilibrium after approximately 15 months, in which as the value of R_0 suggested, we could see an infested symptomatic equilibria.

The results for the second scenario (Figure 4 (b)) show that the asymptomatic population grows until the 12 month, where there is also an intersection of the susceptible and infested populations. This is a critical point after which the number of infested houses exceeds the number of susceptible houses. The equilibrium of the system happens approximately after 20 months with $S^* = 11.98$, $A^* = 3.56$, $I^* = 64.16$ and $C^* = 20.3$.

Adding the cockroach migration parameter (in this case, $\Lambda = 20$) has the effect of accelerating the process of achieving equilibria, as shown in the Figure 4 (c). When $\Lambda = 0$, the equilibria is reached sooner. Additionally, the number of households in each compartment change, increasing the value of the infested asthmatic households. This switch is related to the influx of cockroaches that increase the time a household is exposed to cockroaches and consequently develop asthma symptoms.

The difference in the number of symptomatic infested households at the equilibrium in each plot of Figure 4, even where the basic reproductive number R_0 is the same for the three scenarios, can be explained due to the presence of re–infestation, β_2. This parameter generates a new threshold condition analogous to the basic reproductive number, associated with this re-infestation, which is:

$$R_{\beta_2} = \beta_2 \frac{1}{\alpha + (\delta + \phi)} \tag{13}$$

R_{β_2} is the product of β_2, re–infestation rate of the cockroaches in the clean households, and the average time a household remains clean $\left(\frac{1}{\alpha+(\delta+\phi)}\right)$. This is related to the clean households which become reinfested, which plays a role in sustaining infestations in the neighborhood.

It's expected that the equilibria when $R_0 < 1$ is free of cockroaches and asthma symptoms. But our model presents a backward bifurcation and unlike that, even when the condition is fulfilled, if the re-infestation threshold (R_{β_2}) is lower than one, there still exist the case when the numbers of households in the equilibrium show an infestation. (See Figure 6 for a schematic diagram of this situation) In the Figure 5 (a), we decrease the value of R_0 to 0.96012 by modifying β_1 and leave the other parameters without modification to have a $R_{\beta_2} = 2.5$. The equilibria for the infested asthmatic population is closer to 54, so theres is not a a free cockroach and asthma symptoms equilibria . This implies that to prevent the prevalence of asthma symptoms related to the presences of cockroaches and its allergens is necessary not only to have a $R_0 < 1$ as in the Figure 5 (a) but R_{β_2} must also be less than one. To show this, the value of R_{β_2} was modified to 0.88, while R_0 was still less than one, by changing β_2 as is presented in Figure 5 (b).

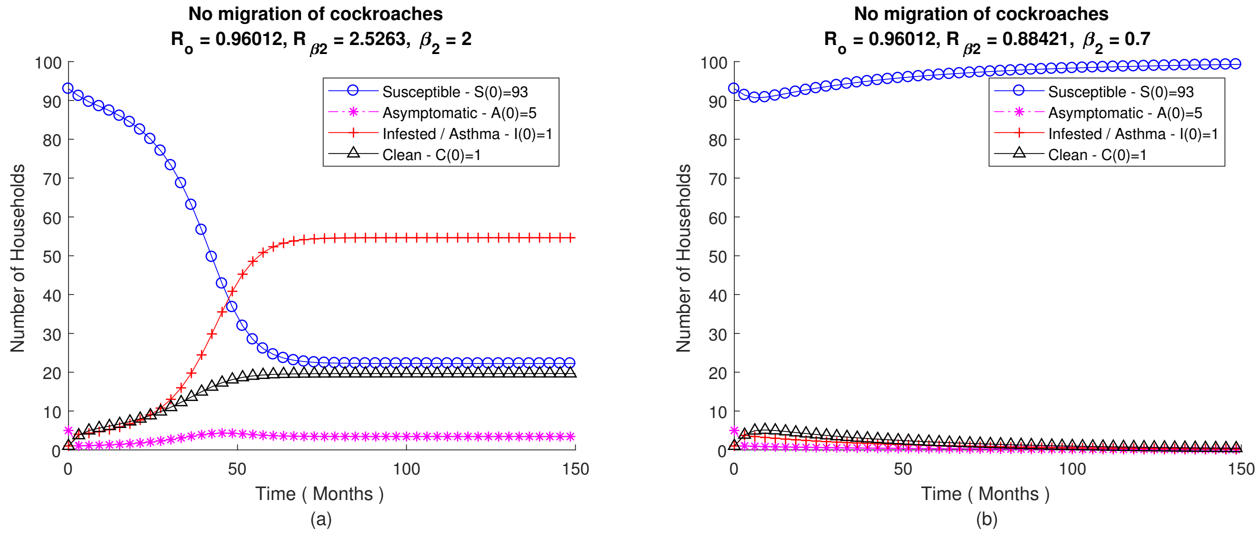


Figure 5. Effect of the change of β_2 on the equilibrium of System 1, (a) Case when $\beta_2 = 2$ and (b) Case when $\beta_2 = 0.7$

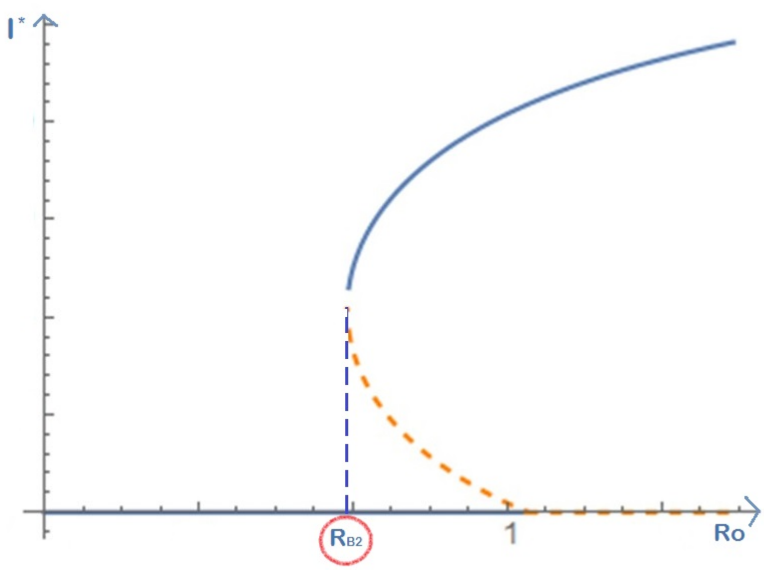


Figure 6. Graphic Sketch of the bifurcation and its relation with R_0 and R_{β_2}

Parameter values effect

In the sensitivity analysis section (Section 6) it was found that the parameters which have the most effect in the model and in R_0 are extermination (α), migration (β_1) and reproduction (κ) rates of cockroaches. In order to study how the change of α, κ and β_1 affects the recurrence of asthma symptoms in a neighborhood at the equilibrium, we calculated the equilibrium solutions for the asymptomatic infested and infested asthmatic households as α, κ and β_1 are varied.

The number of households that present asthma symptoms (infested asthmatic) is reduced as the presence of cockroaches and the level of its allergen decrease because of the reduction of the

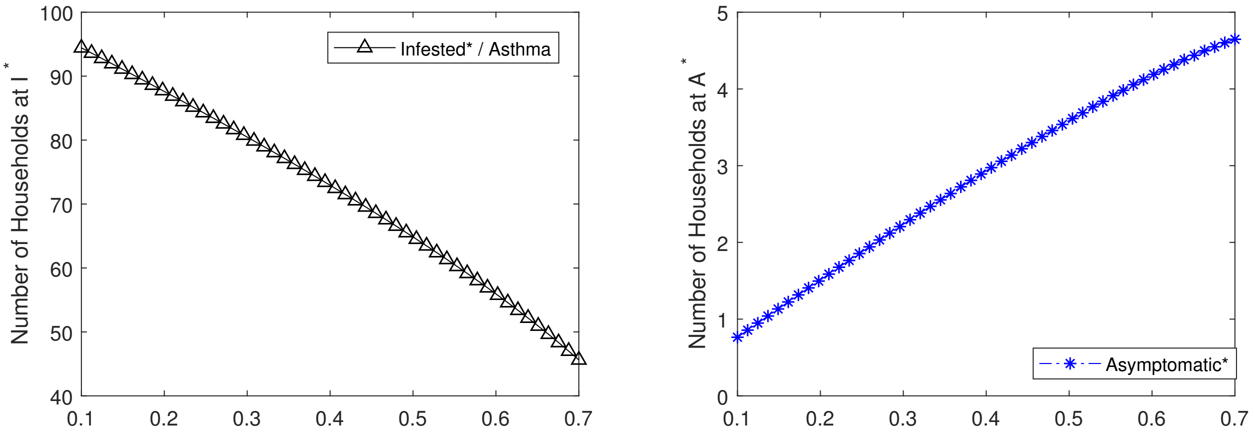


Figure 7. Effect of the change in the extermination rate α, in the asymptomatic infested (a) and infested asthmatic (b) households on their respective equilibrium values.

extermination rate (α) (Figure 7 (a)). However, as the value of the extermination rate (α) increases, the asymptomatic infested population will also increase (Figure 7 (b)). this is due to the fact that, the households spend more time as asymptomatic infested, as seen in the increase of population at the equilibria.

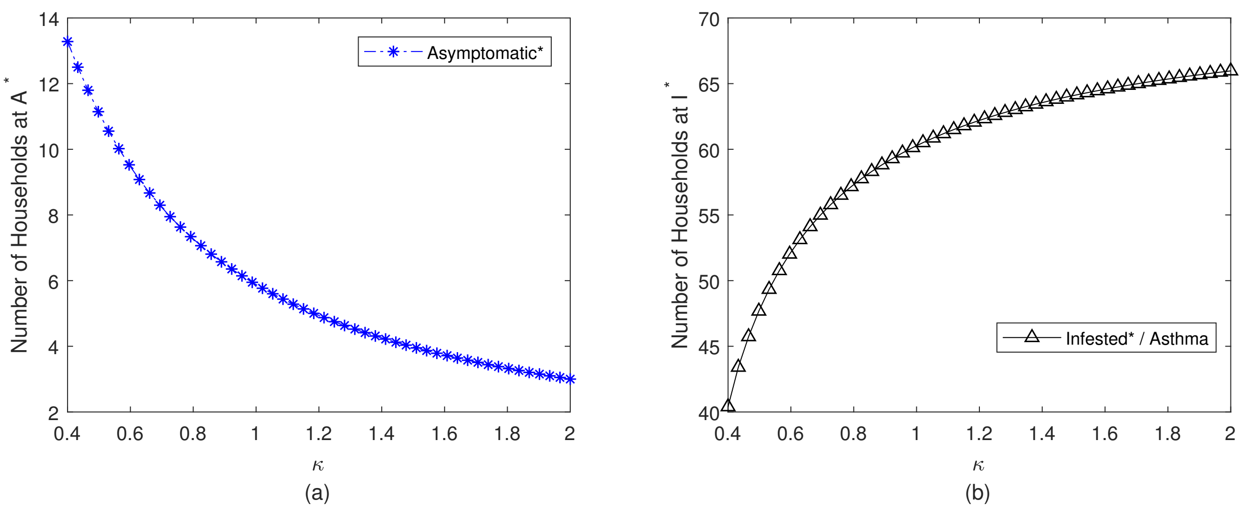


Figure 8. Effect of the change in the reproduction rate κ in the infested (a) and asthmatic infested (b) households on their values at equilibrium

Common methods that prevent infestation with cockroaches such as vacuumming frequently, removing garbage from around the home, and keeping food in places of difficult access can decrease the reproduction rate of cockroaches (κ). Otherwise, not doing these methods will increase the value of κ as this depends on availability of resources such as water and food for the cockroaches. As a result, the number of households that are asymptomatic infested at the equilibria declines (Figure 8 (a)). In other words, the rate in which the households begin to present asthmatic symptoms inside the houses, increases. Therefore the number of households that stays in infected compartment at the equilibria is higher (Figure 8 (b)), implying that the population of households shows more presence of asthmatic symptoms.

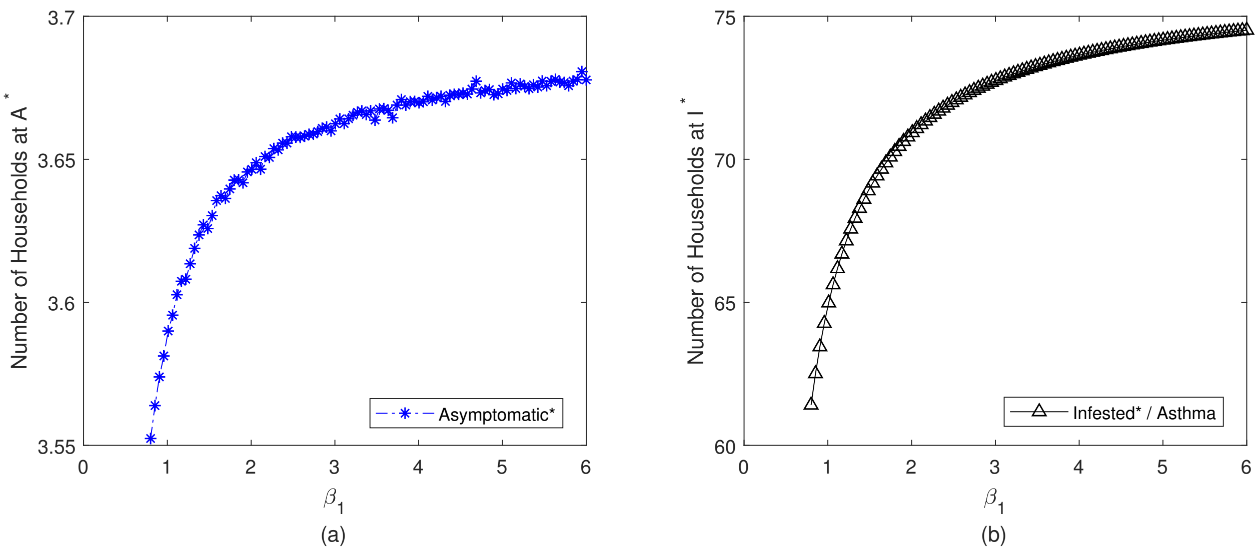


Figure 9. Effect of the parameter β_1 in the asymptomatic infested (a) and asthmatic infested (b) households.

Both the number of asymptomatic and asthmatic infested households at the equilibrium grows with the increase of the parameter β_1 (Figure 9). As a result of the constant influx of cockroaches within the neighborhood to the susceptible house, the number of households with allergen eventually will develop symptoms changes. Greater influx of cockroaches within the same neighborhood, in the equilibrium means a higher number of symptomatic households.

Backward Bifurcations

The initial conditions in the model are of great relevance to the outcome at the equilibria. Different values of initial conditions for $S(0), A(0), I(0)$ and $C(0)$, make the population of households reach two different stable equilibria for all the households, due to the bifurcation in the model. (Appendix A4).

Because of the bifurcation, it is apparent that different initial conditions can yield different behavior of the model, despite the same parameter values.

In Figure 10, is apparent that the infested population reach the equilibria of approximately 36 households when the initial conditions are $S(0) = 85, A(0) = 7, I(0) = 5$ and $C(0) = 3$: contrary to the equilibria in $I = 0$ that is reached when the initial conditions are $S(0) = 93, A(0) = 2, I(0) = 1$ and $C(0) = 3$.

6. Sensitivity Analysis

Sensitivity analysis provides insight on how parameters affect the behavior of a system. Finding the Normalized Sensitivity Indexes (NSI) aids in understanding the impact of changes in the parameters on the reproductive number. Using Forward Sensitivity Analysis (FSA) helps with the

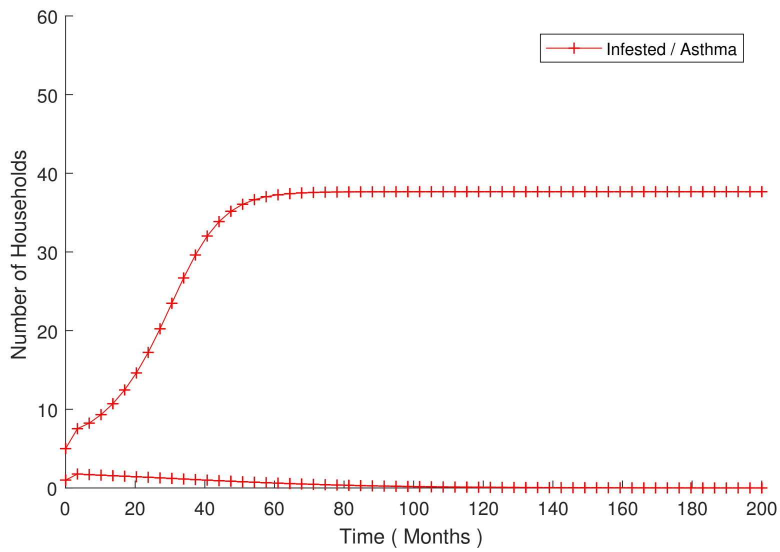


Figure 10. Example of the effect the bifurcation has in the behavior of the model.

study of how a perturbation in the parameters can cause a perturbation change to a system, in our case the model solutions with respect to time [20]. To see the effect of each parameter on the reproduction number we calculated the sensitivity indexes of R_0 with respect to the extermination rate (α), cockroach migration rate (β_1), cockroach reproductive rate (κ), and the reduction factor for asymptomatic infested households (σ).
The reproductive number is the following (Explained in section 3.1.1):

$$R_0 = \frac{\beta_1 \sigma}{\alpha + \kappa} + \frac{\beta_1 \kappa}{\alpha(\alpha + \kappa)}.$$

Let a parameter be represented as p, then the Normalized Sensitivity Index (NSI) is calculated as:

$$SI = \lim_{\delta p \to 0} \frac{\frac{\delta R_0}{R_0}}{\frac{\delta p}{p}} = \frac{p}{R_0} \frac{\partial R_0}{\partial p}.$$

To calculate the value of the sensitivity indexes (see Table 10.5 in Appendix A5) with respect to the extermination rate (α), cockroach migration rate (β_1), cockroach reproductive rate (κ), and the reduction factor for asymptomatic infested households (σ), parameter values were chosen to be $\alpha = \frac{1}{2}$, $\beta_1 = 1$, $\kappa = \frac{1}{0.6}$, $\sigma = \frac{1}{13}$ (from Table 3). The sensitivity of the model is studied with respect to the parameters, extermination rate (α) and cockroach reproductive rate (κ), in order to see the impact they have on the change of household status over time, since these are parameters values that are possible to control. See Appendix A5 to see the Forward Sensitivity Equations with respect to the extermination rate and cockroach reproductive rate.

6.1. Sensitivity Analysis of R_0

Figure 9 shows R_0 is the most sensitive to the parameter α, the extermination rate, when cockroach migration to clean households is zero ($\beta_2 = 0$). In other words, if we increase the extermination rate (α) by one percent, the reproductive number will decrease by 1.20821 percent. On the other hand, if we decrease the extermination rate (α), (i.e.,exterminating less often), by one percent, the reproductive number will increase by 1.20821 percent. By choosing the parameter with the largest magnitude in this case, the extermination rate (α), we can calculate when the reproductive number is less than 1 for there to be no infestation when cockroach migration to clean households is zero ($\beta_2 = 0$). For our given set of parameters (see Table 3) the reproductive number equals 1.574, thus a 1 percent increase in the extermination rate (α) will provide a value of R_0 = 1.541. For our given set of parameter values and the case ($\beta_2 = 0$), to make R_0 below one we should increase the extermination rate by 30% that is from, α = 0.5 to α = 0.65, this will represent a reduction of R_0 below 1. Hence, one would need to clean every month and a half in order to prevent asthma symptoms.

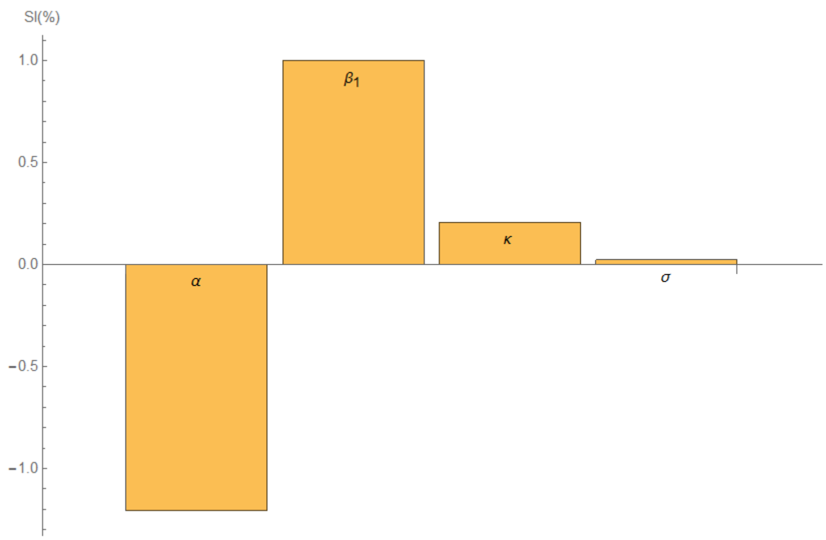
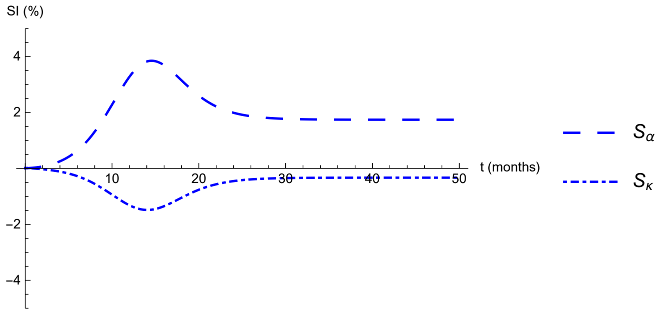
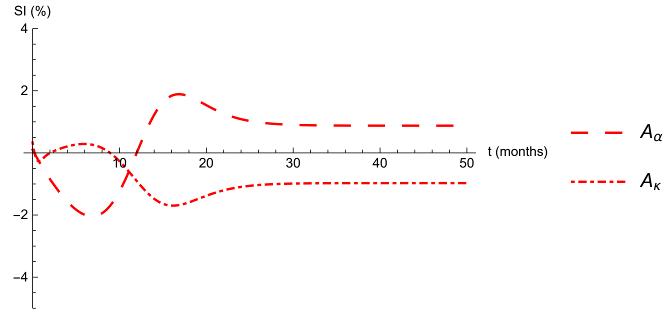


Figure 11. Sensitivity Analysis of R_0

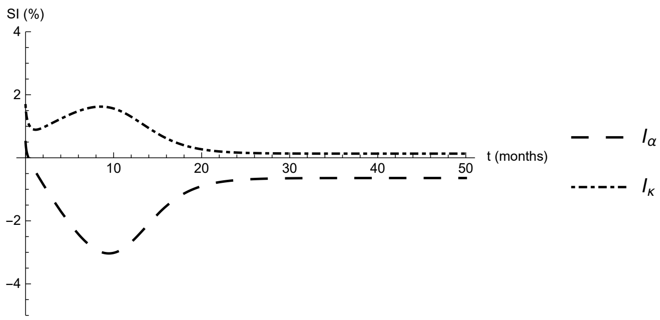
However, in the case when cockroach migration to clean households is not zero ($\beta_2 \neq 0$) it is not sufficient to say that R_0 must be less than 1 because we have a backward bifurcation that is dependent on the migration rate of cockroaches (β_1) (see Figure 2) and the extermination rate (α) (see Figure 3). Since β_1 can be written as a function of R_0 then there is a critical migration rate to susceptible households, β_c, that changes the reproductive number implicitly. For this case we have, R_{β_2} representing the threshold condition associated with re-infestation (see Equation 13). Let μ be defined as the process of getting rid of allergens by removal (δ) and by time (ϕ), $\mu = \delta + \phi$, after calculating the sensitivity index with respect to migration rate to clean households (β_2), extermination rate (α), and getting rid of allergens by removal and naturally (μ), the migration rate to clean households (β_2) is the most sensitive to changes in R_{β_2}. Furthermore, the sensitivity of R_0 is directly associated with the increase or decrease of β_1 as shown by Table 10.5. In other words, if we increase β_1 by 1 percent then R_0 will increase by 1 percent. Hence, for the case when ($\beta_2 \neq 0$), in order for no infestation to occur, the migration rate of cockroaches (β_1) must be less than the critical migration rate to susceptible households, β_c.



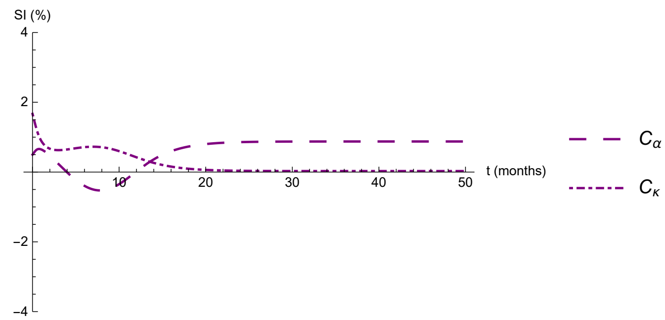
(a) Change in SI of Susceptible Households



(b) Change in SI of Asymptomatic Infested Households



(c) Change in SI of Symptomatic Infested Households



(d) Change in SI of Clean Households

Figure 12. Normalized Sensitivity Index (NSI) of susceptible, asymptomatic infested, symptomatic infested, and clean households with respect to time of the extermination rate and cockroach reproduction rate.

6.2. Sensitivity Analysis to Solutions

The sensitivity analysis of each solution was calculated using Forward Sensitivity Analysis (FSA) with respect to parameters influx rate of outside cockroaches(Λ), cockroach reproduction (κ), extermination rate (α), allergen removal rate (δ), and the reduction factor for asymptomatic infested households (σ). We do not consider the sensitivity analysis of each solution with respect to β_1, β_2, and ϕ because these parameters can not be directly controlled. After calculating the sensitivity index of each solution numerically, the only parameters that would have a large impact on all solutions is α and κ (see Appendix A5). In Figure 8 (a) the sensitivity of the susceptible households is shown with respect to the extermination rate and cockroach reproductive rate. The most impact to the susceptible households happens around 14 months, if the extermination rate (α) increases by one percent, the susceptible households will increase by about 4 percent, increasing the likelihood of staying as a susceptible household when periodical extermination is necessary. On the other hand, when we increase the cockroach reproduction rate by one percent, the susceptible households will decrease approximately 1.5 percent, increasing the possibility of changing states to an asymptomatic infested household. Long term impact on the susceptible households is similar with lower percentage change with respect to the extermination rate and cockroach reproductive rate.
In Figure 8 (b) the sensitivity of asymptomatic infested households is shown with respect to the extermination rate (α) and cockroach reproductive rate (κ). The results for this particular sensitivity index is interesting because before about 12 months, if we increase the cockroach reproductive rate by one percent the asymptomatic infested households increase about 0.4 percent. On the other hand, if we increase the extermination rate by one percent the asymptomatic infested households decreases by about 2 percent. There is an intersection at about 12 months where the impact

changes. After 12 months, if we increase the extermination rate by one percent the asymptomatic infested households increase at most about 2 percent. On the other hand, if we increase the cockroach reproductive rate by one percent the asymptomatic infested households decrease at most about 1.8 percent. This phenomena can be explained using Figure 4 (b), as susceptible households decrease, both asymptomatic and symptomatic infested household increase. However, the symptomatically infested households increase faster in between 10 and 18 months. Both intersections happen at approximately 12 months. Therefore, since moving from asymptomatic to susceptible depends on the extermination rate and moving from asymptomatic to symptomatic depends on the cockroach reproduction rate there is a time (12 months) where the impact to asymptomatic households changes.

Figure 8 (c) the sensitivity of the symptomatic infested households is shown with respect to the extermination rate and cockroach reproductive rate. The most impact to the symptomatic infested households happens around 9 months, if the extermination rate increases by 1 percent, the symptomatic infested households will decrease by about 3 percent, increasing the possibility of moving to the clean stage. On the other hand, when we increase the cockroach reproduction rate by one percent, the symptomatic infested households will increase about 1.8 percent, increasing the likelihood of staying in the symptomatic infested stage. Long term impact on the symptomatic infested households is similar with lower percentage change with respect to the extermination rate and cockroach reproductive rate.

Figure 8 (d) the sensitivity of the clean households is shown with respect to the extermination rate and cockroach reproductive rate. The most impact to the clean households happen around 8 months and after about 13 months. If the extermination rate increases by one percent, the clean households decrease by about 0.5 percent. As the extermination rate increases means that the number of infested households decrease, consequently reducing the number of clean households before 12 months. On the other hand, if the cockroach reproduction rate increases by one percent the clean households increase by about 0.7 percent. Furthermore, as the cockroach reproductive rate increase means the number of infested households increases, causing the clean households to also increase. After about 12 months, if we increase the extermination rate by one percent the clean households increase by about one percent, increasing the likelihood of staying in the clean stage. On the other hand, increasing the cockroach reproductive rate by one percent will do little to no change to the clean households.

7. Discussion

The increase in the prevalence of respiratory diseases such as asthma in the last decades has lead to the need of finding methods to prevent or control the most common triggers. Multiple studies have shown that the infestation of cockroaches may be related to the presence of asthma symptoms in both children and adults [12, 7, 15, 9]. Therefore, the reduction of exposure time to allergens produced by cockroaches may decrease the prevalence of asthma symptoms. To have a better understanding about the relationship between cockroach infestations and the occurrence of asthma symptoms, we developed a compartmental model that tracks the status of a household in response to the presence of cockroaches and cockroach allergens. In the household mathematical model developed in this work, extermination of cockroaches and the removal of allergens were considered in order to determine the impact of the presence of cockroaches in triggering asthmatic symptoms within a household. While studying this model, we considered two different cases.

First, we analyzed mathematically the case which excludes the migration of cockroaches from other neighborhoods ($\Lambda = 0$). This case is further divided into two sub cases: no re-infestation of cockroaches($\beta_2 = 0$) or re-infestation of cockroaches ($\beta_2 \neq 0$). Then, we analyzed numerically the case that includes the migration of cockroaches from other neighborhoods ($\Lambda \neq 0$) along with numerical simulations for the first case. Sensitivity analysis was also performed to determine the influence of parameters on R_0 and the household model solutions.

From the mathematical analysis of this model, we found a cockroach free equilibrium (CFE) for both sub-cases whether re–infestation exists or not when there is no migration of cockroaches from other neighborhoods. We also calculated R_0, the average number of secondary infestation that can be produced by the presence of a single infestation in a population of households without cockroaches and asthma. Moreover, CFE was known to be locally asymptotically stable for both sub-cases when $R_0 < 1$. That is, there are no cockroaches and no asthma symptoms if $R_0 < 1$. Then, we studied the first sub case $\Lambda = 0$ and $\beta_2 = 0$, where we discovered cockroaches and asthma equilibrium. This equilibrium is locally asymptotically stable if $R_0 > 1$, i.e. there will be the presence of cockroaches and asthma symptoms along with no re–infestation of cockroaches when $R_0 > 1$.

The second sub-case $\Lambda = 0$ and $\beta_2 \neq 0$ was resolved numerically as the polynomial equation 10 does not have explicit solution for A^*. As this case takes in account the re-infestation with cockroaches of the clean households, we found that for this scenario a new threshold was established as the infested population now depend not only on the value of R_0 but also R_{β_2}, a new threshold. This new re–infestation threshold (R_{β_2}) is related to how the household in the clean stage can also return to the infested symptomatic stage, because of the re–infestation. The effect of this is that even when the value of R_0 is less than 1, at equilibria the population will reach an infested condition. If $R_{\beta_2} < 1$ the free cockroach and asthma equilibria can be reached. Furthermore, we were able to show that backward bifurcation exists for a given set of parameters. Biologically, these bifurcations represent the relationship of infested houses (I^*) with the migration rate of cockroaches from one house to another in a neighborhood (β_1) or the extermination rate (α). The presence of the bifurcation generates a bi–stability of the system, and once the initial conditions are modified it's possible to reach different equilibria. This bifurcation also represents how in the real process of infestation, it's more difficult to get rid of the cockroaches than to prevent the infestation because the effort needed to return to a free cockroach equilibria is higher than the one needed to prevent the infestation.

The parameters that cause the most impact on the reproduction number and the model are the extermination rate (α) and cockroach reproductive rate (κ). We use sensitivity analysis to illustrate this behavior. The sensitivity of the reproductive number is most influenced by the increase or decrease of the extermination rate. Since we have a backward bifurcation we need to increase the extermination rate enough for our reproduction number to be less than 1. For the sensitivity analysis of the model, the extermination rate and cockroach reproductive rate influence the time and sensitivity of the solutions.

8. Conclusion

Cockroach allergens are one of the main triggers for atopic asthma symptoms. A household model was used to investigate how extermination and allergen removal can reduce the recurrence of these symptoms. The results of mathematical analysis, numerical simulations, and sensitivity analysis imply that it is more effective to prevent infestation than to attempt to remove cockroaches once they have infested a house. For example, an increase of extermination rate by 30% may decrease the recurrence of atopic asthma symptoms in a household when reinfestation is not possible for a given set of parameter values found in the literature. When considering reinfestation, it may not be enough to increase the extermination rate; but we must also consider increasing the rate of allergen removal because it is possible for reinfestations to sustain the prevalence of cockroaches in the neighborhood. For future work, it may be important to consider households of different socio-economic statuses because the problem of cockroach infestations greatly affect the lower-income households, which may not be able to easily afford the more effective treatments of both cockroach infestations and asthma symptoms. Moreover, the real problem with cockroach infestation lies in preventing the complete extermination of cockroaches and its allergens. There is currently no effective treatment of this problem. Addressing the early stages of infestation may have a bigger impact in reducing the prevalence of atopic asthma symptoms.

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10. Appendix

10.1. Appendix A1

Following is the Jacobian matrix for the System (3) :

$$J = \begin{bmatrix} -(\alpha+\kappa) + \beta_1\sigma(1 - \frac{A+I+C}{N_0}) - \frac{\beta_1(I+\sigma A)}{N_0} & \beta_1(1 - \frac{A+I+C}{N_0}) - \frac{\beta_1(I+\sigma A)}{N_0} & -\frac{\beta_1(I+\sigma A)}{N_0} \\ \kappa + \frac{C\beta_2\sigma}{N_0} & -\alpha + \frac{C\beta_2}{N_0} & \frac{\beta_2(I+\sigma A)}{N_0} \\ -\frac{C\beta_2\sigma}{N_0} & \alpha - \frac{C\beta_2}{N_0} & -\mu - \frac{\beta_2(I+\sigma A)}{N_0} \end{bmatrix}$$

10.2. Appendix A2

The stability of the cockroach and asthma equilibrium will be shown by the Routh-Hurwitz Criterion. Following is the Jacobian matrix evaluated at E^*:

$$J_{(E^*)} = \begin{bmatrix} \frac{\beta\sigma}{R_0} - \frac{\alpha\mu(\alpha+\kappa)}{\kappa\mu+\alpha\mu+\kappa\alpha}(R_0-1) - (\alpha+\kappa) & \frac{\beta}{R_0} - \frac{\alpha\mu(\alpha+\kappa)}{\kappa\mu+\alpha\mu+\kappa\alpha}(R_0-1) & -\frac{\alpha\mu(\alpha+\kappa)}{\kappa\mu+\alpha\mu+\kappa\alpha}(R_0-1) \\ \kappa & -\alpha & 0 \\ 0 & \alpha & -\mu \end{bmatrix}.$$

Let

$$A = \frac{\alpha\mu(R_0-1)}{\kappa\mu+\alpha\mu+\kappa\alpha} > 0 \text{ iff } R_0 > 1, \tag{14}$$

then, the Jacobian matrix $J_{(E^*)}$ can be reduce to:

$$J_{(E^*)} = \begin{bmatrix} -(\alpha+\kappa)\left[\frac{\kappa}{\alpha\sigma+\kappa} + A\right] & (\alpha+\kappa)\left[\frac{\alpha}{\alpha\sigma+\kappa} - A\right] & -(\alpha+\kappa)A \\ \kappa & -\alpha & 0 \\ 0 & \alpha & -\mu \end{bmatrix}.$$

The characteristic polynomial of $J_{(E^*)}$ will be given by solving:

$$0 = (J_{(E^*)} - \lambda I).$$

Recall, E^* will be locally asymptotically stable if all eigenvalues (λ) of the characteristic polynomial have negative real part. In this case, the characteristic polynomial is given by:

$$\lambda^3 + a_2\lambda_2 + a_1\lambda + a_0 = 0$$

where

$$\begin{aligned}
a_2 &= (\alpha+\mu) + (\alpha+\kappa)\left[\frac{\kappa}{\alpha\sigma+\kappa} + A\right];\\
a_1 &= (\alpha+\kappa)(\alpha+\mu)\left[\frac{\kappa}{\alpha\sigma+\kappa} + A\right] + \alpha\mu - \kappa(\alpha+\kappa)\left[\frac{\alpha}{\alpha\sigma+\kappa} - A\right];\\
\text{and }\ a_0 &= \alpha\mu(\alpha+\kappa)\left[\frac{\kappa}{\alpha\sigma+\kappa} + A\right] + \alpha\kappa(\alpha+\kappa)A - \kappa\mu(\alpha+\kappa)\left[\frac{\alpha}{\alpha\sigma+\kappa} - A\right].
\end{aligned}$$

Therefore, E^* will be locally asymptotically stable if $a_0 > 0, a_2 > 0$ and $a_2a_1 > a_0$ (Routh - Hurwitz Criterion). The values of a_0, a_1 and a_2 can be further simplified as:

$$a_2 = \frac{1}{\alpha\sigma+\kappa}\left\{(\alpha+\mu)(\alpha\sigma+\kappa) + (\alpha+\kappa)\left[\kappa + A(\alpha\sigma+\kappa)\right]\right\} > 0 \text{ iff } (R_0 > 1); \tag{15}$$

$$a_1 = \frac{1}{\alpha\sigma+\kappa}\left\{\alpha\mu(\alpha\sigma+\kappa) + (\alpha+\kappa)\left[\kappa\mu + (\alpha\sigma+\kappa)(\alpha+\kappa+\mu)A\right]\right\} > 0 \text{ iff } (R_0 > 1); \tag{16}$$

$$\text{and }\ a_0 = \alpha\mu(\alpha+\kappa)(R_0 - 1) > 0 \text{ iff } (R_0 > 1). \tag{17}$$

Notice that, a_0 and a_2 are positive iff $R_0 > 1$, thus if

$$a_2a_1 > a_0 \iff a_2a_1 - a_0 > 0, \tag{18}$$

then the local stability of E^* is guaranteed. Substituting the equations 15, 16, and 17 we can further simplify equation 18 and rewrite as:

$$\begin{aligned}
a_2a_1 - a_0 = {} & (\alpha+\kappa)(\alpha^2+\mu\alpha+\mu^2)A + \frac{(\alpha+\mu)}{\alpha\sigma+\kappa}\left[\alpha\mu(\alpha\sigma+\kappa) + \kappa\mu(\alpha+\kappa)\right]\\
& + \left\{\frac{\kappa(\alpha+\kappa)}{\alpha\sigma+\kappa}(\alpha+\kappa)A\right\}\left\{\alpha\mu(\alpha\sigma+\kappa) + \frac{\kappa\mu(\alpha+\kappa)}{\alpha\sigma+\kappa}\kappa\mu(\alpha+\kappa) + (\alpha+\kappa)(\alpha+\kappa+\mu)A\right\}\\
& > 0
\end{aligned} \tag{19}$$

By Routh Hurwitz Criterion, all the eigenvalues for the characteristic equation are negative or have negative real part since $a_0 > 0, a_2 > 0$ and $a_2a_1 > a_0$.

10.3. Appendix A3

In this appendix, the calculations to obtain E^* where re- infestation is possible ($\lambda = 0, \beta 2 \neq 0$) are shown. By solving System 2 in terms of A, we obtain:

$$S(A) = \frac{N_0(\kappa+\alpha)}{\beta_1\left(\sigma + \frac{\kappa(\mu N_0 + \beta_2\sigma A)}{\mu\alpha N_0 - \kappa\beta_2 A}\right)}, I(A) = \frac{A\kappa(\mu N_0 + \beta_2\sigma A)}{\mu\alpha N_0 - \beta_2\kappa A} \quad \text{and} \quad C(A) = \frac{\kappa}{\mu}A$$

Rewriting $S(A)$ in terms of R_0 gives:

$$S(A) = \frac{N_0(\kappa+\alpha)}{\beta_1\left(\sigma + \frac{\kappa(\mu N_0 + \beta_2\sigma A)}{\mu\alpha N_0 - \kappa\beta_2 A}\right)} = \frac{1}{R_0}\left(N_0 - \frac{\beta_2\kappa}{\mu\alpha}\right)A \tag{20}$$

$$0 = N_0 - (S + A + I + C)$$

Substituting in our equations for $S(A), I(A)$, and $C(A)$ gives

$$0 = N_0 - \frac{N_0}{R_0} + \frac{\beta_2 \kappa A}{R_0 \mu \alpha} - A - \frac{\mu N_0 \kappa A + \kappa \beta_2 \sigma A^2}{\mu \alpha N_0 - \kappa \beta_2 A} - \frac{\kappa}{\mu} A$$

By setting $\mu \alpha N_0 - \kappa \beta_2 A = L$, we obtain:

$$\begin{aligned}
0 &= N_0 R_0 \mu \alpha L - N_0 \mu \alpha L + \beta_2 \kappa L A - R_0 \mu \alpha L A - R_0 \mu \alpha (\mu N_0 \kappa A + \kappa \beta_2 \sigma A^2) - \kappa R_0 \alpha L A \\
0 &= N_0 \mu \alpha L (R_0 - 1) + \beta_2 \kappa L A - R_0 \alpha L A (\mu + \kappa) - R_0 \mu \alpha \kappa A (\mu N_0 + \beta_2 \sigma A)
\end{aligned}$$

Simplifying each section of the above equation gives

$$\begin{aligned}
N_0 \mu \alpha L (R_0 - 1) &= N_0 \mu \alpha (\mu \alpha N_0 - \kappa \beta_2 A)(R_0 - 1) \\
&= (R_0 - 1)(\mu^2 \alpha^2 N_0^2 - \kappa \beta_2 N_0 \mu \alpha A) \\
&= (R_0 - 1) \mu^2 \alpha^2 N_0^2 - (R_0 - 1) \kappa \beta_2 N_0 \mu \alpha A
\end{aligned}$$

$$\begin{aligned}
\beta_2 \kappa L A &= \beta_2 \kappa (\mu \alpha N_0 - \kappa \beta_2 A) A \\
&= \mu \alpha N_0 \beta_2 \kappa A - \kappa^2 \beta_2^2 A^2
\end{aligned}$$

$$\begin{aligned}
-R_0 \alpha L A (\mu + \kappa) &= -R_0 \alpha (\mu \alpha N_0 - \kappa \beta_2 A) A (\kappa + \mu) \\
&= [-\mu \alpha^2 N_0 R_0 A + \kappa \beta_2 R_0 \alpha A^2](\kappa + \mu) \\
&= -(\kappa + \mu) \mu \alpha^2 N_0 R_0 A + (\kappa + \mu) \kappa \beta_2 R_0 \alpha A^2
\end{aligned}$$

$$-R_0 \mu \alpha \kappa A (\mu N_0 + \beta_2 \sigma A) = -R_0 \mu^2 \alpha \kappa N_0 A - R_0 \mu \alpha \kappa \beta_2 \sigma A^2$$

Plugging the simplified expressions back in to the original equation gives

$$\begin{aligned}
0 &= (R_0 - 1) \mu^2 \alpha^2 N_0^2 - (R_0 - 1) \kappa \beta_2 N_0 \mu \alpha A + \mu \alpha N_0 \beta_2 \kappa A - \kappa^2 \beta_2^2 A^2 - (\kappa + \mu) \mu \alpha^2 N_0 R_0 A \\
&\quad + (\kappa + \mu) \kappa \beta_2 R_0 \alpha A^2 - R_0 \mu^2 \alpha \kappa N_0 A - R_0 \mu \alpha \kappa \beta_2 \sigma A^2 \\
0 &= [-\kappa^2 \beta_2^2 + (\kappa + \mu) \kappa \beta_2 R_0 \alpha - R_0 \mu \alpha \kappa \beta_2 \sigma] A^2 \\
&\quad + [-(R_0 - 1) \kappa \beta_2 N_0 \mu \alpha + \mu \alpha N_0 \beta_2 \kappa - (\kappa + \mu) \mu \alpha^2 N_0 R_0 - R_0 \mu^2 \alpha \kappa N_0] A \\
&\quad + [(R_0 - 1) \mu^2 \alpha^2 N_0^2] \\
0 &= \kappa \beta_2 [-\kappa \beta_2 + (\kappa + \mu) R_0 \alpha - R_0 \mu \alpha \sigma] A^2 \\
&\quad - N_0 \alpha \mu [(R_0 - 1) \kappa \beta_2 - \beta_2 \kappa + (\kappa + \mu) \alpha R_0 - R_0 \mu \kappa] A \\
&\quad + [(R_0 - 1) \mu^2 \alpha^2 N_0^2]
\end{aligned}$$

The final polynomial in terms of A then becomes

$$0 = -\kappa\beta_2[\kappa\beta_2 - R_0\alpha(\kappa+\mu(1-\sigma))]A^2 - N_0\alpha\mu[(R_0-1)\kappa\beta_2 - \beta_2\kappa + (\kappa+\mu)\alpha R_0 - R_0\mu\kappa]A + [(R_0-1)\mu^2\alpha^2 N_0^2]$$

By setting

$$\begin{aligned}
\tau_1 &= -\kappa\beta_2[\kappa\beta_2 - R_0\alpha(\kappa+\mu(1-\sigma))] \\
\tau_2 &= -N_0\alpha\mu[(R_0-1)\kappa\beta_2 - \beta_2\kappa + (\kappa+\mu)\alpha R_0 - R_0\mu\kappa] \\
\tau_3 &= [(R_0-1)\mu^2\alpha^2 N_0^2]
\end{aligned}$$

We now have

$$0 = \tau_1 A^2 + \tau_2 A + \tau_3$$

10.4. Appendix A4

Equilibria Simulation

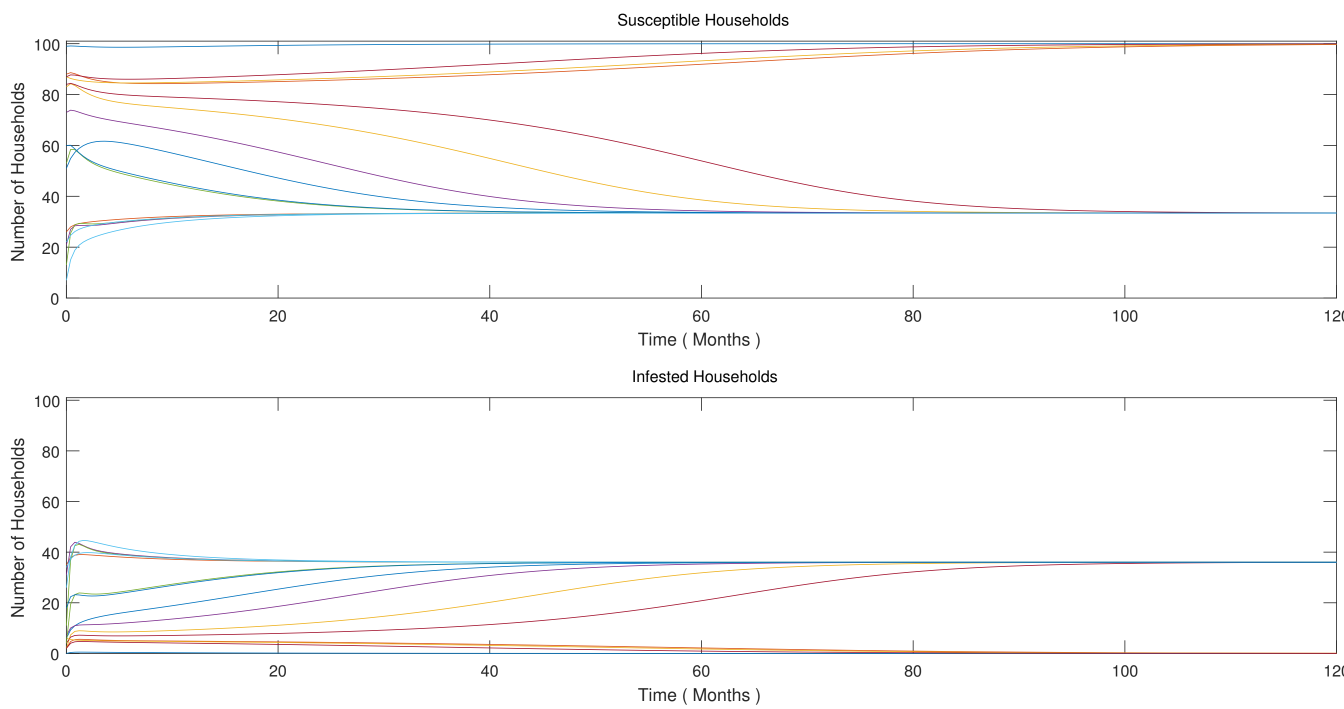

Figure 13. : Equilibria points for susceptible (S) and Infested (I) compartments

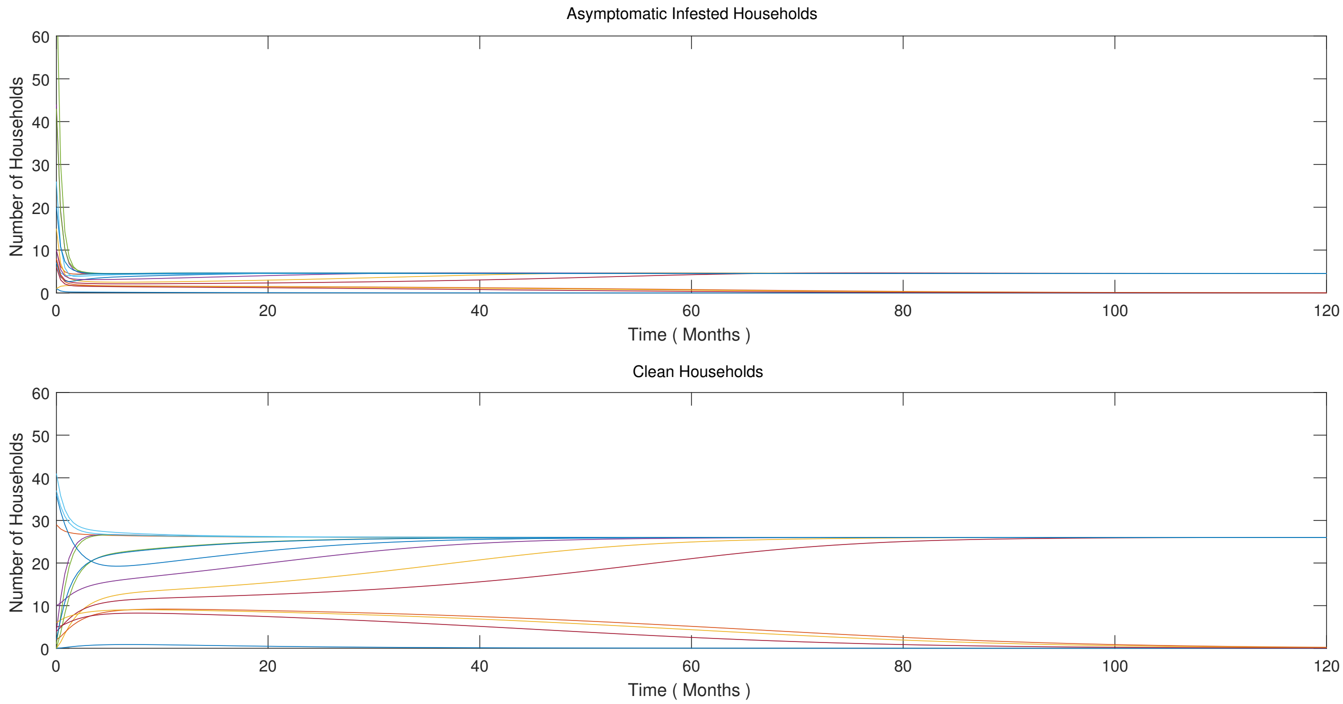

Figure 14. : Equilibria points for asymptomatic infested(A) and Cleaned (C) compartments

10.5. Appendix A5

Sensitivity Analysis

Table 4. Sensitivity Analysis

	Sensitivity Index	Value
$SI_\alpha = \frac{\alpha}{R_0}\left(\frac{\partial R_0}{\partial \alpha}\right)$	$SI_\alpha = -\frac{\alpha}{\alpha+\kappa} - \frac{\kappa}{\kappa+\alpha\sigma}$	-1.20821
$SI_\beta = \frac{\beta_1}{R_0}\left(\frac{\partial R_0}{\partial \beta_1}\right)$	$SI_\beta = 1$	$-$
$SI_\kappa = \frac{\kappa}{R_0}\left(\frac{\partial R_0}{\partial \kappa}\right)$	$SI_\kappa = \kappa(-\frac{1}{\alpha+\kappa} + \frac{1}{\kappa+\alpha\sigma})$	0.20821
$SI_\sigma = \frac{\sigma}{R_0}\left(\frac{\partial R_0}{\partial \sigma}\right)$	$SI_\sigma = \frac{\alpha\sigma}{\kappa+\alpha\sigma}$	0.02256

Table 4 shows the sensitivity index with respect to the parameters in R_0 evaluated at the values of the parameters to see which parameter will have the most effect on the reproductive number.

To calculate the sensitivity index of the solutions we first had to find the partial differential equations with respect to each controllable parameter (Λ, κ, α, δ, σ). However, after running the simulations in Mathematica we found that the extermination rate (α) and cockroach reproduction rate (κ) cause the most impact to all solutions.
Forward Sensitivity Equations (FSE) with respect to extermination rate and cockroach reproduction rate:

$$\frac{d}{dt}\left[\frac{\partial S}{\partial \alpha}\right] = -\frac{\Lambda}{N}\left(\frac{\partial S}{\partial \alpha}\right) - \frac{\sigma\beta_1}{N}\left(\frac{\partial S}{\partial \alpha}A + \frac{\partial A}{\partial \alpha}S\right) - \frac{\beta_1}{N}\left(\frac{\partial S}{\partial \alpha}I + \frac{\partial I}{\partial \alpha}S\right) + \frac{\partial A}{\partial \alpha}\alpha + A + \frac{\partial C}{\partial \alpha}\delta + \frac{\partial C}{\partial \alpha}\phi$$

$$\frac{d}{dt}\left[\frac{\partial S}{\partial \kappa}\right] = -\frac{\Lambda}{N}\left(\frac{\partial S}{\partial \kappa}\right) - \frac{\sigma\beta_1}{N}\left(\frac{\partial S}{\partial \kappa}A + \frac{\partial A}{\partial \kappa}S\right) - \frac{\beta_1}{N}\left(\frac{\partial S}{\partial \kappa}I + \frac{\partial I}{\partial \kappa}S\right) + \frac{\partial A}{\partial \kappa}\alpha + \frac{\partial C}{\partial \kappa}\delta + \frac{\partial C}{\partial \kappa}\phi$$

$$\frac{d}{dt}\left[\frac{\partial A}{\partial \alpha}\right] = -\frac{\partial A}{\partial \alpha}\kappa - \frac{\partial A}{\partial \alpha}\alpha - A + \frac{\Lambda}{N}\left(\frac{\partial S}{\partial \alpha}\right) + \frac{\sigma\beta_1}{N}\left(\frac{\partial S}{\partial \alpha}A + \frac{\partial A}{\partial \alpha}S\right) + \frac{\beta_1}{N}\left(\frac{\partial S}{\partial \alpha}I + \frac{\partial I}{\partial \alpha}S\right)$$

$$\frac{d}{dt}\left[\frac{\partial A}{\partial \kappa}\right] = -\frac{\partial A}{\partial \kappa}\kappa - A - \frac{\partial A}{\partial \kappa}\alpha + \frac{\Lambda}{N}\left(\frac{\partial S}{\partial \kappa}\right) + \frac{\sigma\beta_1}{N}\left(\frac{\partial S}{\partial \kappa}A + \frac{\partial A}{\partial \kappa}S\right) + \frac{\beta_1}{N}\left(\frac{\partial S}{\partial \kappa}I + \frac{\partial I}{\partial \kappa}S\right)$$

$$\frac{d}{dt}\left[\frac{\partial I}{\partial \alpha}\right] = -\frac{\partial I}{\partial \alpha}\alpha - I + \frac{\partial A}{\partial \alpha}\kappa + \frac{\Lambda}{N}\left(\frac{\partial C}{\partial \alpha}\right) + \frac{\sigma\beta_2}{N}\left(\frac{\partial C}{\partial \alpha}A + \frac{\partial A}{\partial \alpha}C\right) + \frac{\beta_2}{N}\left(\frac{\partial C}{\partial \alpha}I + \frac{\partial I}{\partial \alpha}C\right)$$

$$\frac{d}{dt}\left[\frac{\partial I}{\partial \kappa}\right] = -\frac{\partial I}{\partial \kappa}\alpha + \frac{\partial A}{\partial \kappa}\kappa + A + \frac{\Lambda}{N}\left(\frac{\partial C}{\partial \kappa}\right) + \frac{\sigma\beta_2}{N}\left(\frac{\partial C}{\partial \kappa}A + \frac{\partial A}{\partial \kappa}C\right) + \frac{\beta_2}{N}\left(\frac{\partial C}{\partial \kappa}I + \frac{\partial I}{\partial \kappa}C\right)$$

$$\frac{d}{dt}\left[\frac{\partial C}{\partial \alpha}\right] = -\frac{\partial C}{\partial \alpha}\delta - \frac{\partial C}{\partial \alpha}\phi - \frac{\Lambda}{N}\left(\frac{\partial C}{\partial \alpha}\right) - \frac{\sigma\beta_2}{N}\left(\frac{\partial C}{\partial \alpha}A + \frac{\partial A}{\partial \alpha}C\right) - \frac{\beta_2}{N}\left(\frac{\partial C}{\partial \alpha}I + \frac{\partial I}{\partial \alpha}C\right) + \frac{\partial I}{\partial \alpha}\alpha + I$$

$$\frac{d}{dt}\left[\frac{\partial C}{\partial \kappa}\right] = -\frac{\partial C}{\partial \kappa}\delta - \frac{\partial C}{\partial \kappa}\phi - \frac{\Lambda}{N}\left(\frac{\partial C}{\partial \kappa}\right) - \frac{\sigma\beta_2}{N}\left(\frac{\partial C}{\partial \kappa}A + \frac{\partial A}{\partial \kappa}C\right) - \frac{\beta_2}{N}\left(\frac{\partial C}{\partial \kappa}I + \frac{\partial I}{\partial \kappa}C\right) + \frac{\partial I}{\partial \kappa}\alpha$$