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Stability Analysis for the Equilibria of a Monkeypox Model

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ABSTRACT
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Monkeypox virus was first identified in 1958 and has since been an ongoing problem in Central and Western Africa. Although the smallpox vaccine provides partial immunity against monkeypox, the number of cases has greatly increased since the eradication of smallpox made its vaccination unnecessary. Although studied by epidemiologists, monkeypox has not been thoroughly studied by mathematicians to the extent of other serious diseases. Currently, to our knowledge, only three mathematical models of monkeypox have been proposed and studied. We present the first of these models, which is related to the second, and discuss the global and local asymptotic stability of its equilibrium points. We prove the global asymptotic stability of the endemic equilibrium which has been previously incomplete. We expand this model to include a situation where the contact rate is a function of time and not simply a constant and then consider an expansion of the model with more than two populations. Then we present the results of numerical simulations for the original model and the modified models. Finally, we propose a basic network model, discuss the limitations of this model in its current form, and propose modifications for future study.

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For every person who wanted to learn.

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1 Preliminaries

In this work we seek to understand mathematical models of monkeypox. We primarily explore a system of differential equations representing both interacting human and animal populations. We build off of previously completed work and prove the global asymptotic stability of the endemic equilibrium. This is an important step in accurately modeling monkeypox and is needed if the model is to reflect reports on the disease by epidemiologists. We will propose extensions to the model and test them analytically and numerically.

1.1 Introduction

In 1958, the monkeypox virus was isolated for the first time from infected monkeys – resulting in the name – and the first human case was identified in 1970 in the Democratic Republic of Congo (DRC) during the eradication of smallpox [10, 11, 14, 31, 66]. Monkeypox presents very similarly to smallpox and is mostly found in Central and Western Africa [14, 47, 51]. While monkeypox has a lower mortality rate than smallpox at an estimated 9-12%, cases have increased 20-fold in recent years compared to past decades [10, 14, 17, 31, 44, 47, 66]. In the Bokungu Health Zone of the DRC, there were 17 cases reported in 2011 and 13 cases reported in 2012 [47]. However, during the second half of 2013 there was at least a 6-fold increase in monkeypox in this health zone [47].

Hosts of the monkeypox virus include prairie dogs, tree squirrels, chimpanzees, and baboons, but there is not currently a complete list of hosts. Since monkeypox infects both humans and animals, it is generally considered impossible to eradicate [11, 14, 17, 31, 43, 48, 49, 66].

Humans become infected with the monkeypox virus when they come into direct contact with infected animals or people. It is also believed that the virus can be transmitted through respiration as well. The incubation period is approximately 7-17 days. Symptoms are initially similar to those of the flu and include fever, muscle aches, headache, and fatigue. The lymph nodes become enlarged, a

rash develops, and vesicles or "pocks" appear all over the body, including on the palms of the hands and soles of the feet. These vesicles then form scabs before they drop off [14, 26, 48, 51, 64, 66].

In the last decade there has been a noticeable increase in monkeypox correlated to the decrease in herd immunity to smallpox. There is no vaccine currently available for monkeypox. The smallpox vaccine provides approximately 85% immunity against monkeypox and, although the vaccine can provide cross-protective immunity against monkeypox lasting decades after vaccination, only about 25% of the populations with endemic monkeypox infection are currently vaccinated against smallpox. There are also concerns about a new mass vaccination campaign given the prevalence of HIV/AIDS in those areas affected by monkeypox [26, 28, 38, 40, 43, 49, 51].

After smallpox was declared eradicated in 1977, the World Health Organization continued active surveillance of monkeypox from 1981 to 1986. Later surveillance of monkeypox from 2006-2007 looked at current incidence rates and those recorded in the 1980s. Rimoin et. al. compared "the most intense surveillance in the 1980s (Kole in the Sankuru District and Bumba health zone in the neighboring Equateur province) to zones with similarly intense efforts, comparable population demographics, and ecological characteristics (Kole, Tshudi Loto, and Lomela health zones) in 2006 and 2007. For these zones, the average annual incidence increased from 0.48 per 10,000 to 11.25 per 10,000 population" [51]. Although many people become infected through contact with infected animals, human-to-human transmission chains up to seven individuals long consisting of 42 apparent cases have been identified. Until recently, it was thought that human-to-human transmission chains were rarely, if ever, longer than two. In addition to waning herd immunity provided through the smallpox vaccine, poverty and civil war have left people to hunt for food in areas where monkeypox is endemic throughout animal populations [28, 29, 30, 47, 48, 51, 53, 64].

1.2 Outline of Chapters and Results

In Chapter 2 of this work, we discuss a previously proposed mathematical model of monkeypox from [4]. We will discuss how the model is set up and attempt to follow their work to show the global asymptotic stability of the equilibria under certain assumptions. We show that the desired result does not necessarily follow and hence the need for a new approach. Chapter 2 also presents some results needed for later proofs.

The main result of this dissertation is presented in Chapter 3. There we will prove the existence of the endemic equilibrium regardless of whether or not certain assumptions from Chapter 2 are true. We will also prove the global asymptotic stability of the endemic equilibrium. This proof was previously incomplete. This is an important result for modeling monkeypox with a system of differential equations. Knowing that the endemic equilibrium is globally asymptotically stable for the model suggests that, as long as there is monkeypox infection in the animal population, there will be infection in the human population. We end the chapter with an extension of our main result.

Chapter 4 presents numerical results for simulations of the models presented in the previous chapters. We also show numerical results for simulations on more complicated versions of these models – e.g. when there are more than two populations and when one constant parameter is changed to a function of time.

In Chapter 5 we briefly outline a network model of monkeypox. We show some preliminary results when running simulations of this model and discuss why this model does not give us the results expected based on epidemiological data. We also propose some adjustments for future work and highlight the information needed to make these adjustments.

Proposed future work is given in Chapter 6.

2 Current Monkeypox Models

Currently, only three mathematical models of monkeypox can be found in the literature. The first is an SIR model by Bhunu and Mushayabasa, the second is an expansion on this model to include co-infection of monkeypox and HIV by Bhunu, Mushayabasa and Hyman, and the third was only recently published by Emeka et. al [4, 5, 20]. Since the second is an extension of the first, we wished to understand the first and then expand on this model in a different way than was done before. During this process, we found that some results in [4] were not proven while others were proven under certain assumptions. We will complete these proofs and show that result still holds even if we use more more general assumptions.

2.1 Description of the Model

The model examined in this section was first proposed in [4] and the work in this chapter extends the work of that paper. This model considers a population of humans divided into susceptible, infected and recovered individuals, denoted S_h, I_h and R_h, respectively, and a population of animals divided into susceptible, infected and recovered individuals, denoted S_a, I_a and R_a, respectively. The total human population is given as $N_h(t) = S_h(t) + I_h(t) + R_h(t)$ and the total animal population is given as $N_a(t) = S_a(t) + I_a(t) + R_a(t)$. Susceptible humans are recruited through migration and birth at the rate Λ_h and susceptible animals are recruited at a rate of Λ_a. Let d_a, d_h be the death rates by monkeypox for the animals and humans, respectively, μ_a, μ_h be the natural death rates for the animals and humans, respectively, and ρ_a, ρ_h be the recovery rates with permanent immunity for the animals and humans, respectively. It is assumed that the impact of hunting on the animals by humans is negligible and can be ignored. Further, we assume that animals cannot become infected by humans since the vast majority of animal and human contact is when animals are hunted and eaten. Disease transmission is modeled using standard incidence, assuming a constant (density-

independent) contact rate both within and across the two populations resulting in infection rates

$$f_a\left(S_a, I_a, R_a\right) = \frac{\beta_{a_1} I_a}{N_a} S_a, \text{ and } f_h\left(S_a, I_a, R_a, S_h, I_h, R_h\right) = \left(\frac{\beta_{a_2} I_a}{N_a} + \frac{\beta_h I_h}{N_h}\right) S_h,$$

where β_{a_1}, β_{a_2} and β_h are the effective contact rates within the animal population, between the animal population and human population, and in the human population, respectively. We assume that $\Lambda_a, \Lambda_h, \mu_a, \mu_h, \rho_a, \rho_h$ are positive, while $d_a, d_h, \beta_{a_1}, \beta_{a_2}$ and β_h are non-negative parameters.

Thus we have the following system of non-linear differential equations (2.1a)-(2.1f)

$$\frac{dS_a}{dt} = \Lambda_a - \mu_a S_a - \frac{\beta_{a_1} I_a}{N_a} S_a, \tag{2.1a}$$

$$\frac{dI_a}{dt} = \frac{\beta_{a_1} I_a}{N_a} S_a - \left(\mu_a + \rho_a + d_a\right) I_a, \tag{2.1b}$$

$$\frac{dR_a}{dt} = \rho_a I_a - \mu_a R_a, \tag{2.1c}$$

$$\frac{dS_h}{dt} = \Lambda_h - \mu_h S_h - \left(\frac{\beta_{a_2} I_a}{N_a} + \frac{\beta_h I_h}{N_h}\right) S_h, \tag{2.1d}$$

$$\frac{dI_h}{dt} = \left(\frac{\beta_{a_2} I_a}{N_a} + \frac{\beta_h I_h}{N_h}\right) S_h - \left(\mu_h + \rho_h + d_h\right) I_h, \tag{2.1e}$$

$$\frac{dR_h}{dt} = \rho_h I_h - \mu_h R_h. \tag{2.1f}$$

Since

$$\frac{dN_a}{dt} = \Lambda_a - \mu_a N_a - d_a I_a \text{ and } \frac{dN_h}{dt} = \Lambda_h - \mu_h N_h - d_h I_h,$$

the set $\Omega = \Omega_a \times \Omega_h$, where

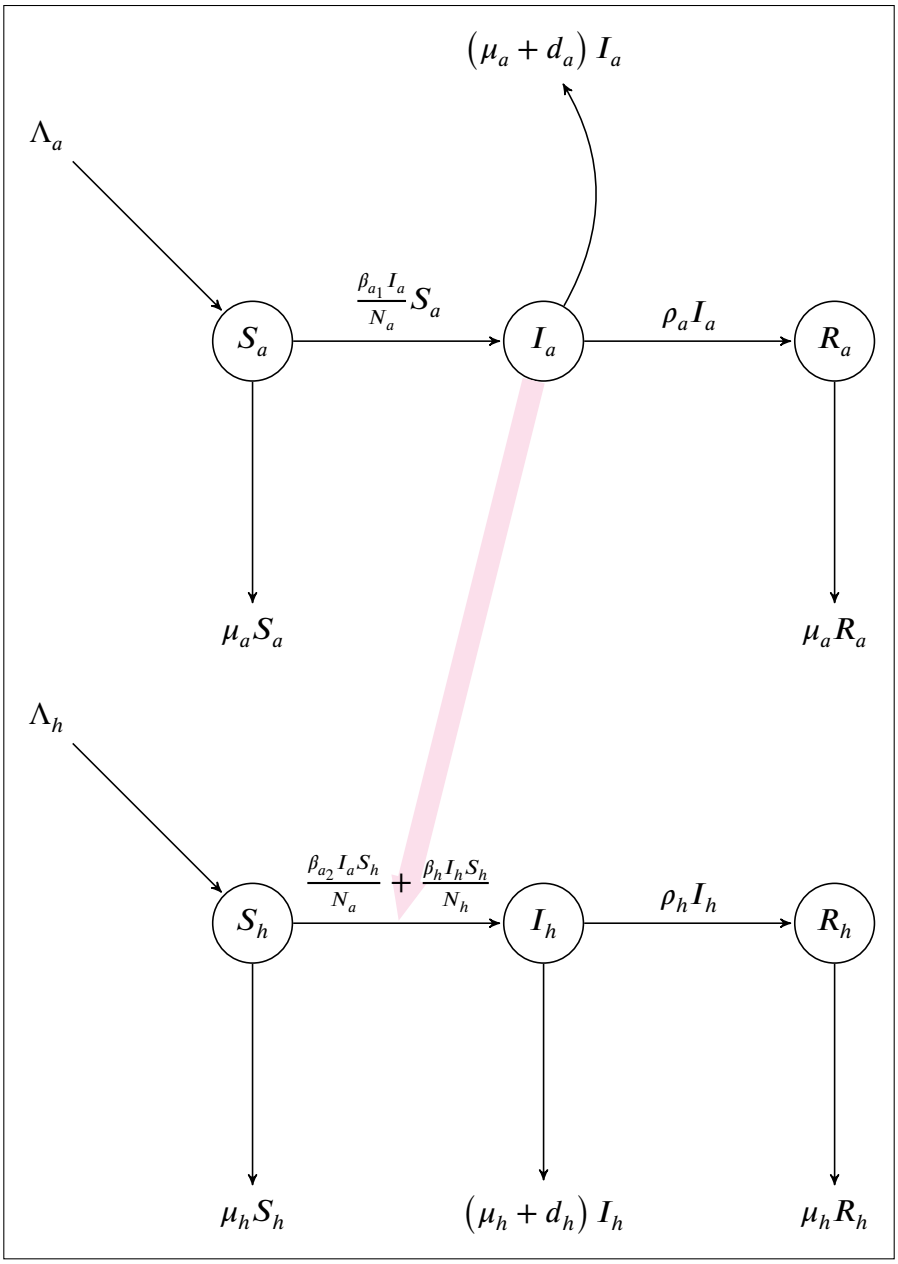

Figure 2.1: The structure of the model in the system (2.1a)-(2.1f) of differential equations

$$\Omega_a = \left\{ \left(S_a, I_a, R_a\right) \in \mathbb{R}^3_+ \,:\, S_a \geq 0, I_a \geq 0, R_a \geq 0, S_a + I_a + R_a \leq \frac{\Lambda_a}{\mu_a} \right\}$$

and

$$\Omega_h = \left\{ \left(S_h, I_h, R_h\right) \in \mathbb{R}^3_+ \,:\, S_h \geq 0, I_h \geq 0, R_h \geq 0, S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h} \right\},$$

is positively invariant under the dynamics of (2.1a)-(2.1f), and solutions with initial conditions in Ω exist globally [4, 37].

2.2 Basic Reproduction Numbers

The disease free equilibrium is given as $\mathcal{E}_0 = \left(S_a^0, I_a^0, R_a^0, S_h^0, I_h^0, R_h^0\right) = \left(\frac{\Lambda_a}{\mu_a}, 0, 0, \frac{\Lambda_h}{\mu_h}, 0, 0\right)$. An analysis for this equilibrium was given in [4] and we also refer the reader to [8, 18, 19, 37, 60].

The basic reproduction number of an SIR model represents the average number of infections that will result from one infected individual. Using the method of van der Driessche and Watmough, the basic reproduction numbers of the model are $\left\{\mathcal{R}_{0_a}, \mathcal{R}_{0_h}\right\}$ where

$$\mathcal{R}_{0_a} = \frac{\beta_{a_1}}{\mu_a + \rho_a + d_a} \quad \text{and} \quad \mathcal{R}_{0_h} = \frac{\beta_h}{\mu_h + \rho_h + d_h}.$$

We find this by first defining the matrix

$$M = \begin{bmatrix} \dfrac{\beta_{a_1}}{\mu_a + \rho_a + d_a} & \dfrac{\beta_{a_2}}{\mu_h + \rho_h + d_h} \\ 0 & \dfrac{\beta_h}{\mu_h + \rho_h + d_h} \end{bmatrix}.$$

Each entry is obtained from looking at the average time a human is infected, $\left(\mu_h + \rho_h + d_h\right)^{-1}$, and the average time an animal is infected, $\left(\mu_a + \rho_a + d_a\right)^{-1}$, with the respective rates that infection is transferred from animals to animals, β_{a_1}, animals to humans, β_{a_2}, and humans to humans, β_h. Finding the eigenvalues of this matrix gives us the basic reproduction numbers. We have

$$M - \lambda I = \begin{bmatrix} \dfrac{\beta_{a_1}}{\mu_a + \rho_a + d_a} - \lambda & \dfrac{\beta_{a_2}}{\mu_h + \rho_h + d_h} \\ 0 & \dfrac{\beta_h}{\mu_h + \rho_h + d_h} - \lambda \end{bmatrix}$$

Since this matrix is upper triangular, the eigenvalues of this matrix are $\dfrac{\beta_{a_1}}{\mu_a + \rho_a + d_a}$ and $\dfrac{\beta_h}{\mu_h + \rho_h + d_h}$.

When $\mathcal{R}_{0_a} < 1$ and $\mathcal{R}_{0_h} < 1$, this equilibrium is locally asymptotically stable and unstable otherwise [4, 8]. We will discuss the global asymptotic stability of the disease-free equilibrium in the next chapter.

2.3 Endemic Equilibrium of the Animal Subsystem

We now look at what happens when there is no infection in the human population, but infection is only in the animal population. Since animals cannot get infected through humans, the spread of infection through the animal population happens independently of the dynamics of infection among humans. By assuming no infection in the human population, we hone in on the epidemic dynamics among animals. We will use the results of this section later to understand the bigger picture of how the epidemic spreads through both populations and is driven by the infection among animals.

We start with the setup provided in [4] and show that this endemic equilibrium of the animal subsystem is feasible. Suppose $\beta_{a_2} = \beta_h = 0$ so there are only animal-to-animal infections. Then $\mathcal{R}_{0_h} = 0$ and the endemic equilibrium of the animal subsystem is given as $E_a^* = \left(S_a^*, I_a^*, R_a^*\right)$. At the equilibrium point, $S_a' = I_a' = R_a' = 0$. Using the system in (2.1a)-(2.1c), we have

$$\Lambda_a = \left(\mu_a + \frac{\beta_{a_1} I_a^*}{N_a^*}\right) S_a^*, \quad \frac{\beta_{a_1} I_a^*}{N_a^*} S_a^* = \left(\mu_a + \rho_a + d_a\right) I_a^*, \quad \rho_a I_a^* = \mu_a R_a^* \tag{2.2}$$

By adding the first two equations we obtain

$$\Lambda_a + \frac{\beta_{a_1} I_a^*}{N_a^*} S_a^* = \left(\mu_a + \frac{\beta_{a_1} I_a^*}{N_a^*}\right) S_a^* + \left(\mu_a + \rho_a + d_a\right) I_a^*$$

$$\Lambda_a = \mu_a S_a^* + \left(\mu_a + \rho_a + d_a\right) I_a^*$$

$$S_a^* = \frac{\Lambda_a}{\mu_a} - \frac{\mu_a + \rho_a + d_a}{\mu_a} I_a^*. \tag{2.3}$$

Looking at the second equation above and the last equation in (2.2), we solve for N_a^* to get:

$$\Lambda_a = \mu_a S_a^* + \left(\mu_a + \rho_a + d_a\right) I_a^*$$

$$\Lambda_a = \mu_a S_a^* + \mu_a I_a^* + \mu_a R_a^* + d_a I_a^*$$

$$\Lambda_a = \mu_a N_a^* + d_a I_a^*$$

$$N_a^* = \frac{\Lambda_a - d_a I_a^*}{\mu_a}. \tag{2.4}$$

By the third equation in (2.2), we have

$$R_a^* = \frac{\rho_a}{\mu_a} I_a^*. \tag{2.5}$$

If we find I_a^* in terms of the parameters only, then we can also write S_a^*, R_a^* and N_a^* in terms of the parameters since they are given above in terms of the parameters and I_a^*. We use (2.2) and (2.3) to represent I_a^* in terms of the parameters and assume $I_a^* > 0$.

$$\frac{\beta_{a_1} I_a^*}{N_a^*} S_a^* = \left(\mu_a + \rho_a + d_a\right) I_a^*$$

$$\beta_{a_1} S_a^* = \left(\mu_a + \rho_a + d_a\right) N_a^*$$

$$\beta_{a_1}\left(\frac{\Lambda_a}{\mu_a}-\frac{\mu_a+\rho_a+d_a}{\mu_a}I_a^*\right)=\left(\mu_a+\rho_a+d_a\right)\left(\frac{\Lambda_a-d_aI_a^*}{\mu_a}\right)$$

$$\frac{\beta_{a_1}\Lambda_a}{\mu_a}-\frac{\left(\mu_a+\rho_a+d_a\right)\Lambda_a}{\mu_a}=\left(\frac{\left(\mu_a+\rho_a+d_a\right)\beta_{a_1}}{\mu_a}-\frac{d_a\left(\mu_a+\rho_a+d_a\right)}{\mu_a}\right)I_a^*$$

$$\frac{\beta_{a_1}\Lambda_a-\left(\mu_a+\rho_a+d_a\right)\Lambda_a}{\mu_a}=\left(\frac{\left(\beta_{a_1}-d_a\right)\left(\mu_a+\rho_a+d_a\right)}{\mu_a}\right)I_a^*$$

$$I_a^*=\frac{\Lambda_a\left(\beta_{a_1}-\left(\mu_a+\rho_a+d_a\right)\right)}{\mu_a}\cdot\frac{\mu_a}{\left(\beta_{a_1}-d_a\right)\left(\mu_a+\rho_a+d_a\right)}$$

$$I_a^*=\frac{\Lambda_a\left(\beta_{a_1}-\left(\mu_a+\rho_a+d_a\right)\right)}{\left(\beta_{a_1}-d_a\right)\left(\mu_a+\rho_a+d_a\right)} \tag{2.6}$$

We note that $I_a^*>0$ whenever $\mathcal{R}_{0_a}>1$ or $\beta_{a_1}<d_a$, but in the latter case the resulting S_a^* is negative. Thus the endemic equilibrium is feasible, that is, $E_a^*\in\Omega_a$, if and only if $\mathcal{R}_{0_a}>1$.

2.3.1 Stability Analysis for the Endemic Equilibrium of the Animal Subsystem

We now investigate the stability of E_a^* with the goal of proving the global asymptotic stability of the endemic equilibrium of (2.1a)-(2.1c). We start by exploring the analysis proposed in [4], which suggests a method from [33], and then we include an alternate method from [61]. The latter method is necessary because the result in [4] does not clearly follow. Once the global asymptotic stability of E_a^* is proven, we will have the result that as long as there is infection in the animal population, there will continue to be infection in the animal population regardless of what happens in the human population.

Assume that $\mathcal{R}_{0_a}>1$. Then E_a^* exists for $S_a, I_a, R_a>\varepsilon>0$. Bhunu and Mushayabasa propose the following Lyapunov function similar to that proposed by Korobeinikov in [33]. Define $g\left(S_a,I_a,R_a\right):=\dfrac{\beta_{a_1}I_aS_a}{N_a}$. This function is positive and monotonic in S_a, I_a, and R_a.

They define the following function in $\mathbb{R}^3_+$:

$$V\left(S_a, I_a, R_a\right) = \; S_a - \int_{\varepsilon}^{S_a} \frac{g\left(S_a^*, I_a^*, R_a^*\right)}{g\left(\tau, I_a^*, R_a^*\right)} d\tau + I_a - \int_{\varepsilon}^{I_a} \frac{g\left(S_a^*, I_a^*, R_a^*\right)}{g\left(S_a^*, \tau, R_a^*\right)} d\tau$$

$$+ R_a - \int_{\varepsilon}^{R_a} \frac{g\left(S_a^*, I_a^*, R_a^*\right)}{g\left(S_a^*, I_a^*, \tau\right)} d\tau. \tag{2.7}$$

This function is similar to one in [33], but must include the recovered class. Because of this, the analysis does not follow in the same way. In [4], the partial derivatives of V with respect to S_a, I_a and R_a are calculated and used to show the time derivative is negative definite and zero at equilibrium. We have

$$\frac{\partial V}{\partial S_a} = 1 - \frac{g\left(S_a^*, I_a^*, R_a^*\right)}{g\left(S_a, I_a^*, R_a^*\right)}$$

$$\frac{\partial V}{\partial S_a} = 1 - \left(\frac{\beta_{a_1} I_a^* S_a^*}{S_a^* + I_a^* + R_a^*} \cdot \frac{S_a + I_a^* + R_a^*}{\beta_{a_1} I_a^* S_a} \right)$$

$$\frac{\partial V}{\partial S_a} = 1 - \frac{S_a^*\left(S_a + I_a^* + R_a^*\right)}{S_a\left(S_a^* + I_a^* + R_a^*\right)},$$

$$\frac{\partial V}{\partial I_a} = 1 - \frac{g\left(S_a^*, I_a^*, R_a^*\right)}{g\left(S_a^*, I_a, R_a^*\right)}$$

$$\frac{\partial V}{\partial I_a} = 1 - \left(\frac{\beta_{a_1} I_a^* S_a^*}{S_a^* + I_a^* + R_a^*} \cdot \frac{S_a^* + I_a + R_a^*}{\beta_{a_1} I_a S_a^*} \right)$$

$$\frac{\partial V}{\partial I_a} = 1 - \frac{I_a^*\left(S_a^* + I_a + R_a^*\right)}{I_a\left(S_a^* + I_a^* + R_a^*\right)},$$

and

$$\frac{\partial V}{\partial R_a} = 1 - \frac{g\left(S_a^*, I_a^*, R_a^*\right)}{g\left(S_a^*, I_a^*, R_a\right)}$$

$$\frac{\partial V}{\partial R_a} = 1 - \left(\frac{\beta_{a_1} I_a^* S_a^*}{S_a^* + I_a^* + R_a^*} \cdot \frac{S_a^* + I_a^* + R_a}{\beta_{a_1} I_a^* S_a^*}\right)$$

$$\frac{\partial V}{\partial R_a} = 1 - \frac{S_a^* + I_a^* + R_a}{S_a^* + I_a^* + R_a^*}.$$

While $\frac{\partial V}{\partial S_a}$ and $\frac{\partial V}{\partial I_a}$ increase monotonically with respect to their variables, $\frac{\partial V}{\partial R_a}$ decreases monotonically with respect to its variable. In order to use [33], we need each partial derivative to be increasing monotonically with respect to its variable. Since we cannot say this, we cannot use this method.

Before abandoning the method from [33], we looked into the possibility of simply changing the signs on the last two terms of (2.7) so that

$$V\left(S_a, I_a, R_a\right) = S_a - \int_\varepsilon^{S_a} \frac{g\left(S_a^*, I_a^*, R_a^*\right)}{g\left(\tau, I_a^*, R_a^*\right)} d\tau + I_a - \int_\varepsilon^{I_a} \frac{g\left(S_a^*, I_a^*, R_a^*\right)}{g\left(S_a^*, \tau, R_a^*\right)} d\tau$$

$$- R_a + \int_\varepsilon^{R_a} \frac{g\left(S_a^*, I_a^*, R_a^*\right)}{g\left(S_a^*, I_a^*, \tau\right)} d\tau.$$

Alternatively, since the difficulty in the partial derivative comes from the fact that R_a is in the denominator of g but not the numerator, we defined g differently as $g\left(S_a, I_a, R_a\right) := \frac{\beta_{a_1} I_a S_a R_a}{N_a}$. In either case, we still cannot show that $\frac{dV}{dt}$ is negative definite following the method in [4, 33].

2.3.2 An Alternative Lyapunov Function

Despite the global asymptotic stability failing to follow clearly in the analysis in [4], the result does follow if proved in an alternative way. A Lyapunov function was proposed by Vargas De-León for a slightly more complicated version of the system in (2.1a)-(2.1c). This section follows the analysis of that system and we refer the reader to [61]. The system is given as

$$\frac{dS}{dt} = \Lambda - \frac{\beta SI}{S+I+R} - \mu S + \gamma R \tag{2.8a}$$

$$\frac{dI}{dt} = \frac{\beta SI}{S+I+R} - (\alpha + \kappa + \mu) I \tag{2.8b}$$

$$\frac{dR}{dt} = \kappa I - (\mu + \gamma) R \tag{2.8c}$$

on the positively invariant set $\Gamma = \left\{(S, I, R) \in \mathbb{R}^3_+ \,:\, N \leq \Lambda/\mu\right\}$. Notice that this system is exactly (2.1a)-(2.1c) where $\gamma = 0,\ \Lambda, \mu, \beta, \kappa > 0$, and $\alpha \geq 0$. In system (2.8a)-(2.8c), we can assume $\gamma \geq 0$. As before, we find that the basic reproduction number is $\mathcal{R}_0 = \dfrac{\beta}{\alpha + \kappa + \mu}$.

Before discussing the endemic equilibrium of (2.8a)-(2.8c) we first note that the disease-free equilibrium is globally asymptotically stable.

Theorem 2.3.1 (Vargas De-León)**.** *If $\mathcal{R}_0 \leq 1$, then the disease-free equilibrium E_0 of (2.8a)-(2.8c) is globally asymptotically stable in Γ.*

Proof. Let $U : \{(S, I, R) \in \Gamma : S > 0\} \to \mathbb{R}$ by $U(S, I, R) = \frac{1}{2} I^2$. Suppose $\mathcal{R}_0 \leq 1$. We calculate U' to obtain

$$U' = I I'$$

$$U' = I \left(\frac{\beta SI}{S+I+R} - (\alpha + \kappa + \mu) I \right)$$

$$U' = \frac{I^2}{S+I+R} \big(\beta S - (\alpha + \kappa + a\mu)(S + I + R) \big)$$

$$U' = \frac{(\alpha+\kappa+\mu)\,I^2}{S+I+R}\left(\frac{\beta S}{\alpha+\kappa+\mu} - (S+I+R)\right)$$

$$U' = -\frac{(\alpha+\kappa+\mu)\,I^2}{S+I+R}\left(S+I+R-\mathcal{R}_0 S\right)$$

$$U' = -\frac{(\alpha+\kappa+\mu)\,I^2}{S+I+R}\left(I+R+\left(1-\mathcal{R}_0\right)S\right).$$

Notice that $U' \leq 0$. If $U' = 0$ then either $I = R = 0$ with $\mathcal{R}_0 = 1$ or $I = 0$ must be true. Thus, U is a Lyapunov function on Γ and $I \to 0, R \to 0$ as $t \to \infty$. If $I = R = 0$ then by (2.8a)-(2.8c), $S \to \Lambda/\mu$. The global asymptotic stability follows by LaSalle's Invariance Principle. □

We adapt this to our particular system in (2.1a)-(2.1c) as follows:

Theorem 2.3.2. *If $\mathcal{R}_{0_a} \leq 1$ then the disease-free equilibrium $E_a^0 = \left(\Lambda_a/\mu_a, 0, 0\right)$ of (2.1a)-(2.1c) is globally asymptotically stable in Ω_a.*

Before showing the global asymptotic stability of the endemic equilibrium for the system (2.8a) - (2.8c), we must show that this equilibrium point exists. To find this endemic equilibrium point, $\mathcal{E}^* = (S^*, I^*, R^*)$, we set each equation in (2.8a)-(2.8c) to zero and find that

$$R^* = \frac{\kappa I^*}{\mu+\gamma}. \tag{2.9}$$

If we add up all three equations we get $\frac{dN}{dt} = \Lambda - \mu N^* - \alpha I^*$. Adding (2.8a) and (2.8b) at equilibrium, we get

$$\begin{aligned}
\Lambda - \frac{\beta S^* I^*}{N^*} - \mu S^* + \gamma R^* + \frac{\beta S^* I^*}{N^*} - (\alpha+\kappa+\mu)I^* &= 0 \\
\Lambda - \mu S^* + \gamma R^* - (\alpha+\kappa+\mu)I^* &= 0 \\
\Lambda + \gamma R^* - (\alpha+\kappa+\mu)I^* &= \mu S^* \\
\frac{1}{\mu}\left(\Lambda + \gamma R^* - (\alpha+\kappa+\mu)I^*\right) &= S^*.
\end{aligned} \tag{2.10}$$

Using (2.8a) and (2.8b) at equilibrium we have $\Lambda = \frac{\beta S^* I^*}{N^*} + \mu S^* - \gamma R^*$ and $\frac{\beta S^* I^*}{N^*} = (\alpha+\kappa+\mu)I^*$. Substituting the latter into the former we obtain $\Lambda = (\alpha + \kappa + \mu)I^* + \mu S^* - \gamma R^*$. Using (2.8c) at equilibrium, we obtain $\kappa I^* - \gamma R^* = \mu R^*$. Thus, we can rewrite Λ as

$$\begin{aligned}
\Lambda &= (\alpha + \kappa + \mu)I^* + \mu S^* - \gamma R^* \\
\Lambda &= \alpha I^* + \mu I^* + \mu S^* + (\kappa I^* - \gamma R^*) \\
\Lambda &= \alpha I^* + \mu I^* + \mu R^* + \mu S^* \\
\Lambda &= \alpha I^* + \mu N^*. \qquad (2.11)
\end{aligned}$$

Using (2.8b) at equilibrium again, $\frac{\beta S^* I^*}{N^*} = (\alpha+\kappa+\mu)I^*$ can be written as $\beta S^* = (\alpha+\kappa+\mu)N^*$. Using (2.11), we can write $N^* = \frac{1}{\mu}(\Lambda - \alpha I^*)$ and using this along with (2.10) then write

$$\begin{aligned}
\beta S^* &= (\alpha + \kappa + \mu)\, N^* \\
\beta\left[\frac{1}{\mu}\left(\Lambda + \gamma R^* - (\alpha + \kappa + \mu)\, I^*\right)\right] &= (\alpha + \kappa + \mu)\left(\frac{1}{\mu}\left(\Lambda - \alpha I^*\right)\right) \\
\frac{\beta\Lambda}{\mu} + \frac{\beta\gamma R^*}{\mu} - \frac{\beta(\alpha+\kappa+\mu)I^*}{\mu} &= \frac{(\alpha+\kappa+\mu)\Lambda}{\mu} - \frac{\alpha I^*(\alpha+\kappa+\mu)}{\mu} \\
\beta\Lambda - (\alpha+\kappa+\mu)\Lambda + \beta\gamma R^* &= \big(\beta(\alpha+\kappa+\mu) - \alpha(\alpha+\kappa+\mu)\big)I^*.
\end{aligned}$$

We substitute (2.9) into the above and obtain

$$\begin{aligned}
\Lambda\big(\beta - (\alpha+\kappa+\mu)\big) + \beta\gamma R^* &= \big(\beta(\alpha+\kappa+\mu) - \alpha(\alpha+\kappa+\mu)\big)I^* \\
\Lambda\big(\beta - (\alpha+\kappa+\mu)\big) + \frac{\beta\gamma\kappa I^*}{\mu+\gamma} &= \big(\beta(\alpha+\kappa+\mu) - \alpha(\alpha+\kappa+\mu)\big)I^* \\
\Lambda\big(\beta - (\alpha+\kappa+\mu)\big) &= \left(\beta(\alpha+\kappa+\mu) - \alpha(\alpha+\kappa+\mu) - \frac{\beta\gamma\kappa}{\mu+\gamma}\right)I^*
\end{aligned}$$

$$I^* = \frac{\Lambda\big(\beta - (\alpha+\kappa+\mu)\big)}{\left(\beta(\alpha+\kappa+\mu) - \alpha(\alpha+\kappa+\mu) - \dfrac{\beta\gamma\kappa}{\mu+\gamma}\right)}$$

$$I^* = \frac{\Lambda(\mu+\gamma)\big(\beta - (\alpha+\kappa+\mu)\big)}{\beta(\mu+\gamma)(\alpha+\kappa+\mu) - \alpha(\mu+\gamma)(\alpha+\kappa+\mu) - \beta\gamma\kappa}$$

$$I^* = \frac{\dfrac{\Lambda(\mu+\gamma)\beta}{(\alpha+\kappa+\mu)} - \dfrac{\Lambda(\mu+\gamma)(\alpha+\kappa+\mu)}{(\alpha+\kappa+\mu)}}{\dfrac{\beta(\mu+\gamma)(\alpha+\kappa+\mu)}{(\alpha+\kappa+\mu)} - \dfrac{\alpha(\mu+\gamma)(\alpha+\kappa+\mu)}{(\alpha+\kappa+\mu)} - \dfrac{\beta\gamma\kappa}{(\alpha+\kappa+\mu)}}$$

$$I^* = \frac{\dfrac{\beta\Lambda(\mu+\gamma)}{(\alpha+\kappa+\mu)} - \Lambda(\mu+\gamma)}{\dfrac{\beta(\mu+\gamma)(\alpha+\kappa+\mu)}{(\alpha+\kappa+\mu)} - \alpha(\mu+\gamma) - \dfrac{\beta\gamma\kappa}{(\alpha+\kappa+\mu)}}$$

$$I^* = \frac{\Lambda(\mu+\gamma)\big(\mathcal{R}_0 - 1\big)}{\mathcal{R}_0(\mu+\gamma)(\alpha+\kappa+\mu) - \alpha(\mu+\gamma) - \mathcal{R}_0\gamma\kappa}$$

$$I^* = \frac{\Lambda(\mu+\gamma)\big(\mathcal{R}_0 - 1\big)}{\mathcal{R}_0(\mu\alpha+\mu\kappa+\mu^2+\gamma\alpha+\gamma\kappa+\gamma\mu) - (\alpha\mu+\alpha\gamma) - \mathcal{R}_0\gamma\kappa}$$

$$I^* = \frac{\Lambda(\mu+\gamma)\big(\mathcal{R}_0 - 1\big)}{\mathcal{R}_0(\mu\kappa+\mu^2+\gamma\mu) + \mathcal{R}_0(\mu\alpha+\gamma\alpha) - (\alpha\mu+\alpha\gamma)}$$

$$I^* = \frac{\Lambda(\mu+\gamma)\big(\mathcal{R}_0 - 1\big)}{\mathcal{R}_0\mu(\kappa+\mu+\gamma) + \alpha(\gamma+\mu)\big(\mathcal{R}_0 - 1\big)}. \tag{2.12}$$

Since the equations for S^* and R^* given in (2.10) and (2.9) are in terms of the parameters and I^* and we have just expressed I^* in terms of only the parameters, we have found the equilibrium point. Explicitly finding these, we have

$$R^* = \frac{\kappa I^*}{\mu+\gamma}$$

$$R^* = \frac{\kappa\Lambda(\gamma+\mu)\big(\mathcal{R}_0 - 1\big)}{(\mu+\gamma)\big[\mathcal{R}_0\mu(\kappa+\mu+\gamma) + \alpha(\gamma+\mu)\big(\mathcal{R}_0 - 1\big)\big]}$$

$$R^* = \frac{\kappa\Lambda\big(\mathcal{R}_0 - 1\big)}{\mathcal{R}_0\mu(\kappa + \mu + \gamma) + \alpha(\gamma + \mu)\big(\mathcal{R}_0 - 1\big)}. \tag{2.13}$$

We can write S^* more simply than in (2.10) using $N^* = \frac{1}{\mu}(\Lambda - \alpha I^*)$ and $\beta S^* = (\alpha + \kappa + \mu)N^*$ from before to get

$$\begin{aligned}
\beta S^* &= (\alpha + \kappa + \mu)N^* \\
S^* &= \frac{(\alpha + \kappa + \mu)(\Lambda - \alpha I^*)}{\beta\mu} \\
S^* &= \frac{\Lambda - \alpha I^*}{\mathcal{R}_0\mu} \\
S^* &= \frac{\Lambda}{\mathcal{R}_0\mu} - \frac{\alpha}{\mathcal{R}_0\mu}\left(\frac{\Lambda(\mu + \gamma)\big(\mathcal{R}_0 - 1\big)}{\mathcal{R}_0\mu(\kappa + \mu + \gamma) + \alpha(\gamma + \mu)\big(\mathcal{R}_0 - 1\big)}\right) \\
S^* &= \frac{\Lambda}{\mathcal{R}_0\mu} - \frac{\Lambda}{\mathcal{R}_0\mu}\left(\frac{\alpha(\mu + \gamma)\big(\mathcal{R}_0 - 1\big)}{\mathcal{R}_0\mu(\kappa + \mu + \gamma) + \alpha(\gamma + \mu)\big(\mathcal{R}_0 - 1\big)}\right) \\
S^* &= \frac{\Lambda}{\mathcal{R}_0\mu}\left(1 - \frac{\alpha(\mu + \gamma)\big(\mathcal{R}_0 - 1\big)}{\mathcal{R}_0\mu(\kappa + \mu + \gamma) + \alpha(\gamma + \mu)\big(\mathcal{R}_0 - 1\big)}\right) \\
S^* &= \frac{\Lambda}{\mathcal{R}_0\mu}\left(\frac{\mathcal{R}_0\mu(\kappa + \mu + \gamma) + \alpha(\gamma + \mu)\big(\mathcal{R}_0 - 1\big) - \alpha(\mu + \gamma)\big(\mathcal{R}_0 - 1\big)}{\mathcal{R}_0\mu(\kappa + \mu + \gamma) + \alpha(\gamma + \mu)\big(\mathcal{R}_0 - 1\big)}\right) \\
S^* &= \frac{\Lambda}{\mathcal{R}_0\mu}\left(\frac{\mathcal{R}_0\mu(\kappa + \mu + \gamma)}{\mathcal{R}_0\mu(\kappa + \mu + \gamma) + \alpha(\gamma + \mu)\big(\mathcal{R}_0 - 1\big)}\right) \\
S^* &= \frac{\Lambda(\kappa + \mu + \gamma)}{\mathcal{R}_0\mu(\kappa + \mu + \gamma) + \alpha(\gamma + \mu)\big(\mathcal{R}_0 - 1\big)}.
\end{aligned} \tag{2.14}$$

Thus, we have the existence of the equilibrium point, $\mathcal{E}^* = (S^*, I^*, R^*)$, for (2.8a)-(2.8c), and another possible form for E_a^* when $\gamma = 0$.

Theorem 2.3.3 (Vargas De-León)**.** *Suppose $\mathcal{R}_0 > 1$ and $2\gamma + \mu \geq \alpha$. Then the unique endemic equilibrium $\mathcal{E}^* = (S^*, I^*, R^*)$ is globally asymptotically stable in the interior of Γ.*

Proof. Consider the Lyapunov function $\tilde{V}$ given in:

$$\tilde{V} = \left((S - S^*) + (I - I^*) + (R - R^*) - (S^* + I^* + R^*) \ln \frac{(S + I + R)}{(S^* + I^* + R^*)} \right)$$
$$+ \frac{(\alpha + 2\mu)(S^* + I^* + R^*)}{\beta (I^* + R^*)} \left(I - I^* - I^* \ln \frac{I}{I^*} \right) + \frac{(\alpha + 2\mu)}{2\kappa} \left(1 + \frac{S^*}{I^* + R^*} \right) \frac{(R - R^*)^2}{S + I + R}.$$

Then $\tilde{V}$ is C^1 in the interior of the positively invariant set $\Gamma = \left\{ (S, I, R) \in \mathbb{R}^3_+ : N \leq \Lambda/\mu \right\}$, $\mathcal{E}^*$ is the global minimum of $\tilde{V}$ on Γ, and $\tilde{V}(S^*, I^*, R^*) = 0$.

Computing the time derivative of $\tilde{V}$ along solutions of (2.8a)-(2.8c), we have

$$\frac{d\tilde{V}}{dt} = S'(t) + I'(t) + R'(t) - (S^* + I^* + R^*) \left(\frac{S'(t) + I'(t) + R'(t)}{S^* + I^* + R^*} \cdot \frac{S^* + I^* + R^*}{S + I + R} \right)$$
$$+ \frac{(\alpha + 2\mu)(S^* + I^* + R^*)}{\beta (I^* + R^*)} \left(I'(t) - I^* \left(\frac{I'(t)}{I^*} \cdot \frac{I^*}{I} \right) \right)$$
$$+ \frac{(\alpha + 2\mu)}{2\kappa} \left(1 + \frac{S^*}{I^* + R^*} \right) \left[\frac{2(R - R^*) R'(t)}{S + I + R} - \frac{(R - R^*)^2}{(S + I + R)^2} \cdot \left(S'(t) + I'(t) + R'(t) \right) \right]$$

$$\frac{d\tilde{V}}{dt} = \left(S'(t) + I'(t) + R'(t) \right) \left(1 - \frac{(S^* + I^* + R^*)}{S + I + R} \right) + \frac{(\alpha + 2\mu)(S^* + I^* + R^*)}{\beta (I^* + R^*)} \left(\frac{I - I^*}{I} \right) I'(t)$$
$$+ \frac{(\alpha + 2\mu)}{2\kappa} \left(1 + \frac{S^*}{I^* + R^*} \right) \left[\frac{2(R - R^*) R'(t)}{S + I + R} - \frac{(R - R^*)^2 \left(S'(t) + I'(t) + R'(t) \right)}{(S + I + R)^2} \right]$$

$$\frac{d\tilde{V}}{dt} = \left(S'(t) + I'(t) + R'(t) \right) \left(\frac{(S + I + R) - (S^* + I^* + R^*)}{S + I + R} \right)$$
$$+ \frac{(\alpha + 2\mu)(S^* + I^* + R^*)}{\beta (I^* + R^*)} \left(\frac{I - I^*}{I} \right) I'(t)$$

$$+\frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{2\,(R-R^*)\,R'(t)}{S+I+R}\right)$$

$$-\frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)^2\,N'(t)}{(S+I+R)^2}\right)$$

$$\frac{d\tilde{V}}{dt}=\left(\frac{(S-S^*)+(I-I^*)+(R-R^*)}{S+I+R}\right)\Big(S'(t)+I'(t)+R'(t)\Big)$$

$$+\frac{(\alpha+2\mu)\,(S^*+I^*+R^*)}{\beta\,(I^*+R^*)}\left(\frac{I-I^*}{I}\right)I'(t)$$

$$+\frac{(\alpha+2\mu)}{\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{R-R^*}{S+I+R}\right)R'(t)$$

$$-\frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)^2N'(t)}{(S+I+R)^2}\right).$$

Using the ODE system in (2.8a)-(2.8c) and recalling that $N'(t)=\Lambda-\mu(S+I+R)-\alpha I$, we obtain

$$\frac{d\tilde{V}}{dt}=\left(\frac{(S-S^*)+(I-I^*)+(R-R^*)}{S+I+R}\right)\Big(\Lambda-\mu(S+I+R)-\alpha I\Big)$$

$$+\frac{(\alpha+2\mu)(S^*+I^*+R^*)}{\beta(I^*+R^*)}\left(\frac{I-I^*}{I}\right)\left(\frac{\beta IS}{S+I+R}-(\alpha+\kappa+\mu)I\right)$$

$$+\frac{(\alpha+2\mu)}{\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{R-R^*}{S+I+R}\right)\Big(\kappa I-(\mu+\gamma)R\Big)$$

$$-\frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\Big(N'(t)\Big).$$

Since $\Lambda = \mu(S^* + I^* + R^*) + \alpha I^*$ and $\dfrac{\beta S^*}{S^* + I^* + R^*} = \alpha + \kappa + \mu$ at equilibrium we have

$$\frac{d\tilde{V}}{dt} = \left(\frac{(S - S^*) + (I - I^*) + (R - R^*)}{S + I + R}\right)\Big(\mu(S^* + I^* + R^*) + \alpha I^* - \mu(S + I + R) - \alpha I)\Big)$$

$$+ \frac{(\alpha + 2\mu)(S^* + I^* + R^*)}{\beta(I^* + R^*)}(I - I^*)\left(\frac{\beta S}{S + I + R} - (\alpha + \kappa + \mu)\right)$$

$$+ \frac{(\alpha + 2\mu)}{\kappa}\left(1 + \frac{S^*}{I^* + R^*}\right)\left(\frac{R - R^*}{S + I + R}\right)\big(\kappa I - (\mu + \gamma)R\big)$$

$$- \frac{(\alpha + 2\mu)}{2\kappa}\left(1 + \frac{S^*}{I^* + R^*}\right)\left(\frac{(R - R^*)}{(S + I + R)}\right)^2\big(N'(t)\big)$$

$$\frac{d\tilde{V}}{dt} = \left(\frac{(S - S^*) + (I - I^*) + (R - R^*)}{S + I + R}\right)\Big(\mu(S^* + I^* + R^*) + \alpha I^* - \mu(S + I + R) - \alpha I)\Big)$$

$$+ \frac{(\alpha + 2\mu)(S^* + I^* + R^*)}{\beta(I^* + R^*)}(I - I^*)\left(\frac{\beta S}{S + I + R} - \frac{\beta S^*}{S^* + I^* + R^*}\right)$$

$$+ \frac{(\alpha + 2\mu)}{\kappa}\left(1 + \frac{S^*}{I^* + R^*}\right)\left(\frac{R - R^*}{S + I + R}\right)\big(\kappa I - (\mu + \gamma)R\big)$$

$$- \frac{(\alpha + 2\mu)}{2\kappa}\left(1 + \frac{S^*}{I^* + R^*}\right)\left(\frac{(R - R^*)}{(S + I + R)}\right)^2\big(N'(t)\big)$$

$$\frac{d\tilde{V}}{dt} = \left(\frac{(S - S^*) + (I - I^*) + (R - R^*)}{S + I + R}\right)\Big(\mu(S^* + I^* + R^*) + \alpha I^* - \mu(S + I + R) - \alpha I)\Big)$$

$$+ \frac{(\alpha + 2\mu)(S^* + I^* + R^*)}{(I^* + R^*)}(I - I^*)\left(\frac{S}{S + I + R} - \frac{S^*}{S^* + I^* + R^*}\right)$$

$$+ \frac{(\alpha + 2\mu)}{\kappa}\left(1 + \frac{S^*}{I^* + R^*}\right)\left(\frac{R - R^*}{S + I + R}\right)\big(\kappa I - (\mu + \gamma)R\big)$$

$$- \frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\big(N'(t)\big). \tag{2.15}$$

Simplifying the first term in equation (2.15) we have

$$\left(\frac{(S-S^*)+(I-I^*)+(R-R^*)}{S+I+R}\right)\big(\mu(S^*+I^*+R^*)+\alpha I^*-\mu(S+I+R)-\alpha I\big)$$

$$=\frac{\big((S-S^*)+(I-I^*)+(R-R^*)\big)\big((-\mu)\big((S-S^*)+(I-I^*)+(R-R^*)\big)-\alpha(I-I^*)\big)}{S+I+R}$$

$$=\left(\frac{1}{S+I+R}\right)\Big(-\mu\big[(S-S^*)^2+(S-S^*)(I-I^*)+(S-S^*)(R-R^*)+(S-S^*)(I-I^*)$$

$$+(I-I^*)^2+(I-I^*)(R-R^*)+(S-S^*)(R-R^*)+(I-I^*)(R-R^*)+(R-R^*)^2\big]$$

$$-\alpha(S-S^*)(I^*-I)-\alpha(I-I^*)^2-\alpha(I-I^*)(R-R^*)\Big)$$

$$=\frac{-\mu\big((S-S^*)+(R-R^*)\big)^2}{S+I+R}-\frac{(\alpha+\mu)(I-I^*)^2}{S+I+R}-\frac{(\alpha+2\mu)(S-S^*)(I-I^*)}{S+I+R} \tag{2.16}$$

$$-\frac{(\alpha+2\mu)(I-I^*)(R-R^*)}{S+I+R}.$$

From the system in (2.8a)-(2.8c) we have $(\mu+\gamma)R^*-\kappa I^*=0$, so we can insert this into the third line of equation (2.15). Using this and (2.16) we have

$$\frac{d\tilde{V}}{dt}=\frac{-\mu\big((S-S^*)+(R-R^*)\big)^2}{S+I+R}-\frac{(\alpha+\mu)(I-I^*)^2}{S+I+R}$$

$$-\frac{(\alpha+2\mu)(S-S^*)(I-I^*)}{S+I+R}-\frac{(\alpha+2\mu)(I-I^*)(R-R^*)}{S+I+R}$$

$$+\frac{(\alpha+2\mu)(S^*+I^*+R^*)}{(I^*+R^*)}(I-I^*)\left(\frac{S}{S+I+R}-\frac{S^*}{S^*+I^*+R^*}\right)$$

$$+\frac{(\alpha+2\mu)}{\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{R-R^*}{S+I+R}\right)\big(\kappa I-(\mu+\gamma)R+(\mu+\gamma)R^*-\kappa I^*\big)$$

$$-\frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\big(N'(t)\big)$$

$$\frac{d\tilde{V}}{dt}=\frac{-\mu\big((S-S^*)+(R-R^*)\big)^2}{S+I+R}-\frac{(\alpha+\mu)(I-I^*)^2}{S+I+R}$$

$$-\frac{(\alpha+2\mu)(S-S^*)(I-I^*)}{S+I+R}-\frac{(\alpha+2\mu)(I-I^*)(R-R^*)}{S+I+R}$$

$$+\frac{(\alpha+2\mu)(S^*+I^*+R^*)}{(I^*+R^*)}(I-I^*)\left(\frac{S}{S+I+R}-\frac{S^*}{S^*+I^*+R^*}\right)$$

$$+\frac{(\alpha+2\mu)}{\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{R-R^*}{S+I+R}\right)\big(\kappa(I-I^*)-(\mu+\gamma)(R-R^*)\big)$$

$$-\frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\big(N'(t)\big).$$

Notice that we can rewrite $\dfrac{S}{S+I+R}-\dfrac{S^*}{S^*+I^*+R^*}$ in the following way:

$$\frac{S}{S+I+R}-\frac{S^*}{S^*+I^*+R^*}=\frac{S(S^*+I^*+R^*)-S^*(S+I+R)}{(S^*+I^*+R^*)(S+I+R)}$$

$$=\frac{SI^*+SR^*-S^*I-S^*R}{(S^*+I^*+R^*)(S+I+R)}$$

$$=\frac{SI^*+SR^*-S^*I-S^*R+S^*I^*-S^*I^*+S^*R^*-S^*R^*}{(S^*+I^*+R^*)(S+I+R)}$$

$$=\frac{(I^*+R^*)(S-S^*)-S^*(I-I^*)-S^*(R-R^*)}{(S^*+I^*+R^*)(S+I+R)}.$$

Then we can rearrange (2.15) as

$$\frac{d\tilde{V}}{dt} = \frac{-\mu\big((S-S^*)+(R-R^*)\big)^2}{S+I+R} - \frac{(\alpha+\mu)(I-I^*)^2}{S+I+R}$$

$$- \frac{(\alpha+2\mu)(S-S^*)(I-I^*)}{S+I+R} - \frac{(\alpha+2\mu)(I-I^*)(R-R^*)}{S+I+R}$$

$$+ \left[\frac{(\alpha+2\mu)(S^*+I^*+R^*)}{(I^*+R^*)}(I-I^*)\cdot\right.$$

$$\left.\left(\frac{(I^*+R^*)(S-S^*) - S^*(I-I^*) - S^*(R-R^*)}{(S^*+I^*+R^*)(S+I+R)}\right)\right]$$

$$+ \frac{(\alpha+2\mu)}{\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{\kappa(I-I^*)(R-R^*)}{S+I+R} - \frac{(\mu+\gamma)(R-R^*)^2}{S+I+R}\right)$$

$$- \frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\big(N'(t)\big)$$

$$\frac{d\tilde{V}}{dt} = \frac{-\mu\big((S-S^*)+(R-R^*)\big)^2}{S+I+R} - \frac{(\alpha+\mu)(I-I^*)^2}{S+I+R}$$

$$- \frac{(\alpha+2\mu)(S-S^*)(I-I^*)}{S+I+R} - \frac{(\alpha+2\mu)(I-I^*)(R-R^*)}{S+I+R}$$

$$+ \frac{(\alpha+2\mu)(I-I^*)(S-S^*)}{(S+I+R)} - \frac{(\alpha+2\mu)(S^*)(I-I^*)^2}{(S+I+R)(I^*+R^*)}$$

$$- \frac{(\alpha+2\mu)(I-I^*)(S^*)(R-R^*)}{(S+I+R)(I^*+R^*)}$$

$$+ (\alpha+2\mu)\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(I-I^*)(R-R^*)}{S+I+R}\right)$$

$$- \frac{(\alpha+2\mu)}{\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(\mu+\gamma)(R-R^*)^2}{S+I+R}\right)$$

$$- \frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\left(N'(t)\right)$$

$$\frac{d\tilde{V}}{dt} = \frac{-\mu\left((S-S^*)+(R-R^*)\right)^2}{S+I+R} - \left(\alpha+\mu+\frac{S^*(\alpha+2\mu)}{I^*+R^*}\right)\frac{(I-I^*)^2}{S+I+R}$$

$$- \frac{(\alpha+2\mu)(\mu+\gamma)}{\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)^2}{S+I+R}\right)$$

$$- \frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\left(N'(t)\right)$$

$$- \frac{(\alpha+2\mu)(S-S^*)(I-I^*)}{S+I+R} - \frac{(\alpha+2\mu)(I-I^*)(R-R^*)}{S+I+R}$$

$$+ \frac{(\alpha+2\mu)(I-I^*)(S-S^*)}{(S+I+R)} - \frac{(\alpha+2\mu)(I-I^*)(S^*)(R-R^*)}{(S+I+R)(I^*+R^*)}$$

$$+ (\alpha+2\mu)\left(\frac{(I-I^*)(R-R^*)}{S+I+R}\right) + (\alpha+2\mu)\left(\frac{S^*(I-I^*)(R-R^*)}{(I^*+R^*)(S+I+R)}\right)$$

$$\frac{d\tilde{V}}{dt} = \frac{-\mu\left((S-S^*)+(R-R^*)\right)^2}{S+I+R} - \left(\alpha+\mu+\frac{S^*(\alpha+2\mu)}{I^*+R^*}\right)\frac{(I-I^*)^2}{S+I+R}$$

$$- \frac{(\alpha+2\mu)(\mu+\gamma)}{\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)^2}{S+I+R}\right)$$

$$- \frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\left(N'(t)\right)$$

$$\frac{d\tilde{V}}{dt} = \frac{-\mu\left((S-S^*)+(R-R^*)\right)^2}{S+I+R} - \left(\alpha+\mu+\frac{S^*(\alpha+2\mu)}{I^*+R^*}\right)\frac{(I-I^*)^2}{S+I+R}$$

$$- \frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\left(2(S+I+R)(\mu+\gamma)+N'(t)\right)$$

$$\frac{d\tilde{V}}{dt} = \frac{-\mu\big((S-S^*)+(R-R^*)\big)^2}{S+I+R} - \left(\alpha+\mu+\frac{S^*(\alpha+2\mu)}{I^*+R^*}\right)\frac{(I-I^*)^2}{S+I+R}$$

$$- \left[\frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2 \cdot \right.$$

$$\left.\big(2(S+I+R)(\mu+\gamma)+\Lambda-\mu(S+I+R)-\alpha I\big)\right]$$

$$\frac{d\tilde{V}}{dt} = \frac{-\mu\big((S-S^*)+(R-R^*)\big)^2}{S+I+R} - \left(\alpha+\mu+\frac{S^*(\alpha+2\mu)}{I^*+R^*}\right)\frac{(I-I^*)^2}{S+I+R}$$

$$- \left[\frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2 \cdot \right.$$

$$\left.\big(2\mu S+2\mu I+2\mu R+2\gamma(S+I+R)+\Lambda-\mu S-\mu I-\mu R-\alpha I\big)\right]$$

$$\frac{d\tilde{V}}{dt} = \frac{-\mu\big((S-S^*)+(R-R^*)\big)^2}{S+I+R} - \left(\alpha+\mu+\frac{S^*(\alpha+2\mu)}{I^*+R^*}\right)\frac{(I-I^*)^2}{S+I+R}$$

$$- \frac{(\alpha+2\mu)}{2\kappa}\left(1+\frac{S^*}{I^*+R^*}\right)\left(\frac{(R-R^*)}{(S+I+R)}\right)^2\big((\mu+2\gamma)(S+R)+\Lambda+(\mu+2\gamma-\alpha)I\big).$$

Thus, $\tilde{V}'$ is negative definite if $2\gamma+\mu \geq \alpha$ and $\tilde{V}' = 0$ only when $S = S^*$, $I = I^*$, and $R = R^*$ [61]. By LaSalle's invariance principle, it follows that $\mathcal{E}^*$ is globally asymptotically stable on $\mathring{\Gamma}$, hence E_a^* is globally asymptotically stable on $\mathring{\Omega}_a$ and we have established the existence of the endemic equilibrium of the animal subsystem. □

We adapt this theorem for our own case, when $\gamma = 0$, and will refer to it later.

Theorem 2.3.4. *Assume that $\mu_a \geq d_a$ and $\mathcal{R}_{0_a} > 1$, then the unique endemic equilibrium E_a^* of (2.1a)-(2.1c) is globally asymptotically stable in the interior of Ω_a.*

2.4 Co-existence Endemic Equilibrium

In this section we present the incomplete results from [4] to highlight the need for a new method of analysis proposed in the next chapter. We now look at the most complicated scenario for (2.1a)-(2.1f). This co-existence endemic equilibrium occurs when there is animal-to-animal infection, animal-to-human infection and human-to-human infection. This is the most important scenario because we want to understand the dynamics of monkeypox in both animal and human populations. We note that if $\beta_{a_2} = 0$ the human subsystem is exactly the same as the animal subsystem and becomes independent of the animal subsystem, so similar results follow as were presented in the previous section.

The co-existence endemic equilibrium point is given as $\mathcal{E}_1 = \left(E_a^*, E_h^*\right)$. The components of $\mathcal{E}_1$ related to the animal population are the same as in (2.3), (2.5), and (2.6) because infection in the animal population is independent of any infection in the human population. We find the components related to the human subsystem by setting the equations (2.1d)-(2.1f) equal to zero to obtain

$$\Lambda_h = \left(\mu_h + \frac{\beta_{a_2} I_a^*}{N_a^*} + \frac{\beta_h I_h^*}{N_h^*}\right) S_h^*, \quad \frac{\beta_{a_2} I_a^*}{N_a^*} + \frac{\beta_h I_h^*}{N_h^*} S_h^* = \left(\mu_h + \rho_h + d_h\right) I_h^*, \quad \rho_h I_h^* = \mu_h R_h^*. \tag{2.17}$$

As before, we try to express S_h^* and R_h^* in terms of the parameters and I_h^*. If we can then show that I_h^* is positive, then the components of E_h^* are positive and the endemic equilibrium point $\mathcal{E}_1$ exists. Using the first two equations from (2.17), we see that

$$\Lambda_h = \mu_h S_h^* + \frac{\beta_{a_2} I_a^*}{N_a^*} + \frac{\beta_h I_h^*}{N_h^*} S_h^*$$

$$\Lambda_h = \mu_h S_h^* + \left(\mu_h + \rho_h + d_h\right) I_h^*$$

$$S_h^* = \frac{\Lambda_h}{\mu_h} - \frac{\left(\mu_h + \rho_h + d_h\right)}{\mu_h} I_h^*. \tag{2.18}$$

Clearly, by the third equation of (2.17),

$$R_h^* = \frac{\rho_h}{\mu_h} I_h^*. \tag{2.19}$$

Next, we solve for N_h^* in a similar way to the previous case using (2.19).

$$\begin{aligned}
\Lambda_h &= \mu_h S_h^* + \left(\mu_h + \rho_h + d_h\right) I_h^* \\
\Lambda_h &= \mu_h S_h^* + \mu_h I_h^* + \rho_h I_h^* + d_h I_h^* \\
\Lambda_h &= \mu_h S_h^* + \mu_h I_h^* + \mu_h R_h^* + d_h I_h^* \\
\Lambda_h &= \mu_h N_h^* + d_h I_h^* \\
\implies N_h^* &= \frac{\Lambda_h - d_h I_h^*}{\mu_h}
\end{aligned} \tag{2.20}$$

For simplicity, let $m_h := \mu_h + \rho_h + d_h$ and $x^* := \dfrac{\beta_{a_2} I_a^*}{\mu_h N_a^*}$. Using (2.18), (2.20), and the second equation in (2.17) we have

$$\begin{aligned}
\frac{\beta_{a_2} I_a^*}{N_a^*} + \frac{\beta_h I_h^*}{N_h^*} S_h^* &= m_h I_h^* \\
\left(\frac{\beta_{a_2} I_a^*}{N_a^*} + \frac{\beta_h I_h^*}{N_h^*}\right)\left(\frac{\Lambda_h - m_h I_h^*}{\mu_h}\right) &= m_h I_h^* \\
\left(x^* \mu_h + \frac{\beta_h I_h^*}{N_h^*}\right)\left(\frac{\Lambda_h - m_h I_h^*}{\mu_h}\right) &= m_h I_h^* \\
\left[x^* \mu_h + \beta_h I_h^* \left(\frac{\mu_h}{\Lambda_h - d_h I_h^*}\right)\right]\left(\frac{\Lambda_h - m_h I_h^*}{\mu_h}\right) &= m_h I_h^* \\
\left(\frac{\Lambda_h - d_h I_h^*}{\mu_h}\right)\left[x^* \mu_h + \beta_h I_h^* \left(\frac{\mu_h}{\Lambda_h - d_h I_h^*}\right)\right]\left(\frac{\Lambda_h - m_h I_h^*}{\mu_h}\right) &= m_h I_h^* \left(\frac{\Lambda_h - d_h I_h^*}{\mu_h}\right)
\end{aligned}$$

$$\left(x^*\left(\Lambda_h - d_h I_h^*\right) + \beta_h I_h^*\right)\left(\frac{\Lambda_h - m_h I_h^*}{\mu_h}\right) = m_h I_h^*\left(\frac{\Lambda_h - d_h I_h^*}{\mu_h}\right)$$

$$\left(I_h^*\left(\beta_h - d_h x^*\right) + \Lambda_h x^*\right)\left(\frac{\Lambda_h - m_h I_h^*}{\mu_h}\right) - m_h I_h^*\left(\frac{\Lambda_h - d_h I_h^*}{\mu_h}\right) = 0.$$

By expanding, we can write the above equation as a quadratic in terms of I_h^*.

$$\frac{I_h^*\beta_h\Lambda_h}{\mu_h} - \frac{I_h^* d_h x^*\Lambda_h}{\mu_h} - \frac{\left(I_h^*\right)^2 m_h\beta_h}{\mu_h} + \frac{\left(I_h^*\right)^2 m_h d_h x^*}{\mu_h} + \frac{\Lambda_h^2 x^*}{\mu_h}$$

$$-\frac{\Lambda_h x^* m_h I_h^*}{\mu_h} - \frac{m_h I_h^*\Lambda_h}{\mu_h} + \frac{m_h d_h\left(I_h^*\right)^2}{\mu_h} = 0$$

$$\left(I_h^*\right)^2\left(m_h d_h + m_h d_h x^* - m_h\beta_h\right) + I_h^*\left(\beta_h\Lambda_h - d_h x^*\Lambda_h - \Lambda_h x^* m_h - m_h\Lambda_h\right) + \Lambda_h^2 x^* = 0$$

$$\left(I_h^*\right)^2\left(d_h + d_h x^* - \beta_h\right) + I_h^*\left(\frac{\beta_h\Lambda_h}{m_h} - \frac{d_h x^*\Lambda_h}{m_h} - \Lambda_h x^* - \Lambda_h\right) + \frac{\Lambda_h^2 x^*}{m_h} = 0$$

$$\left(I_h^*\right)^2\left(d_h(1+x^*) - \beta_h\right) + I_h^*\Lambda_h\left(\frac{\beta_h}{m_h} - \frac{d_h x^*}{m_h} - (1+x^*)\right) + \frac{\Lambda_h^2 x^*}{m_h} = 0$$

$$\left(I_h^*\right)^2\left(\beta_h - d_h(1+x^*)\right) + I_h^*\Lambda_h\left((1+x^*) - \frac{\beta_h - d_h x^*}{m_h}\right) - \frac{\Lambda_h^2 x^*}{m_h} = 0 \quad (2.21)$$

If we impose the extra condition that $\beta_h > d_h(1+x^*)$, then (2.21) is concave in I_h^*. When $I_h^* = 0$ then (2.21) is simply $-\dfrac{\Lambda_h^2 x^*}{m_h} < 0$ and so this function crosses the vertical axis below the origin. Thus, this function has a single positive root and $I_h^* > 0$ so that $R_h^* > 0$ is clear. We just need to show that $S_h^* = \dfrac{\Lambda_h}{\mu_h} - \dfrac{\mu_h + \rho_h + d_h}{\mu_h} I_h^* > 0$.

This is where the analysis in [4] ends when it comes to showing the existence of $\mathcal{E}_1$. In a our own analysis in the next chapter, we will show that $\mathcal{E}_1$ exists regardless of whether or not $\beta_h > d_h\,(1+x^*)$ is true. In the meantime, we continue to examine the work done in [4].

2.4.1 Previously Proposed Stability Analysis for the Co-existence Endemic Equilibrium

Bhunu and Mushayabasa suggest using the following function, referring to it as a Lyapunov function, to prove the global asymptotic stability of the co-existence endemic equilibrium for (2.1a)-(2.1f):

$$\begin{aligned} W =&\left(S_a - S_a^* \ln S_a\right) + \left(I_a - I_a^* \ln I_a\right) + \left(R_a - R_a^* \ln R_a\right) \\ &+ \left(S_h - S_h^* \ln S_h\right) + \left(I_h - I_h^* \ln I_h\right) + \left(R_h - R_h^* \ln R_h\right). \end{aligned}$$

They suggest following the method of McCluskey [4, 42]. No details on this calculation are included in [4] and this function is not necessarily positive definite in the above form. Instead, let $A, B, C, D, E > 0$ be constants and consider a Lyapunov function of the form suggested by McCluskey and similar to one used by Korobeinikov and Maini in [34]:

$$\begin{aligned} \tilde{W} =&A\left(S_a - S_a^* - S_a^* \ln \frac{S_a}{S_a^*} \right) + B\left(I_a - I_a^* - I_a^* \ln \frac{I_a}{I_a^*} \right) + C\left(R_a - R_a^* - R_a^* \ln \frac{R_a}{R_a^*} \right) \\ &+ \left(S_h - S_h^* - S_h^* \ln \frac{S_h}{S_h^*} \right) + D\left(I_h - I_h^* - I_h^* \ln \frac{I_h}{I_h^*} \right) + E\left(R_h - R_h^* - R_h^* \ln \frac{R_h}{R_h^*} \right). \end{aligned}$$

Using the method of McCluskey, we will find that it is not clear that $\tilde{W}$ is a Lyapunov function. First, calculate the derivative of $\tilde{W}$ with respect to time to obtain

$$\begin{aligned} \tilde{W}'(t) =&AS_a'(t) - AS_a^*\left(\frac{S_a'(t)}{S_a(t)} \right) + BI_a'(t) - BI_a^*\left(\frac{I_a'(t)}{I_a(t)} \right) + CR_a'(t) - CR_a^*\left(\frac{R_a'(t)}{R_a(t)} \right) \\ &+ S_h'(t) - S_h^*\left(\frac{S_h'(t)}{S_h(t)} \right) + DI_h'(t) - DI_h^*\left(\frac{I_h'(t)}{I_h(t)} \right) + ER_h'(t) - ER_h^*\left(\frac{R_h'(t)}{R_h(t)} \right) \end{aligned}$$

$$\tilde{W}' = AS_a'\left(1 - \frac{S_a^*}{S_a}\right) + BI_a'\left(1 - \frac{I_a^*}{I_a}\right) + CR_a'\left(1 - \frac{R_a^*}{R_a}\right) + S_h'\left(1 - \frac{S_h^*}{S_h}\right)$$

$$+ DI_h'\left(1 - \frac{I_h^*}{I_h}\right) + ER_h'\left(1 - \frac{R_h^*}{R_h}\right)$$

$$\tilde{W}' = A\frac{S_a'}{S_a}\left(S_a - S_a^*\right) + B\frac{I_a'}{I_a}\left(I_a - I_a^*\right) + C\frac{R_a'}{R_a}\left(R_a - R_a^*\right) + \frac{S_h'}{S_h}\left(S_h - S_h^*\right)$$

$$+ D\frac{I_h'}{I_h}\left(I_h - I_h^*\right) + E\frac{R_h'}{R_h}\left(R_h - R_h^*\right).$$

For simplicity, define $\zeta_a := \frac{\beta_{a_1} I_a}{N_a}$, $\zeta_a^* := \frac{\beta_{a_1} I_a^*}{N_a^*}$, $\zeta_h := \frac{\beta_{a_2} I_a}{N_a} + \frac{\beta_h I_h}{N_h}$, and $\zeta_h^* := \frac{\beta_{a_2} I_a^*}{N_a^*} + \frac{\beta_h I_h^*}{N_h^*}$. Using the system in (2.1a)-(2.1f), we have

$$\tilde{W}' = A\left(\frac{\Lambda_a - \left(\mu_a + \zeta_a\right) S_a}{S_a}\left(S_a - S_a^*\right)\right) + B\left(\frac{\left(\zeta_a S_a - \left(\mu_a + \rho_a + d_a\right) I_a\right)}{I_a}\left(I_a - I_a^*\right)\right)$$

$$+ C\left(\frac{\left(\rho_a I_a - \mu_a R_a\right)}{R_a}\left(R_a - R_a^*\right)\right) + \frac{\Lambda_h - \left(\mu_h + \zeta_h\right) S_h}{S_h}\left(S_h - S_h^*\right) +$$

$$D\left(\frac{\left(\zeta_h S_h - \left(\mu_h + \rho_h + d_h\right) I_h\right)}{I_h}\left(I_h - I_h^*\right)\right) + E\left(\frac{\left(\rho_h I_h - \mu_h R_h\right)}{R_h}\left(R_h - R_h^*\right)\right).$$

Using the fact that $\Lambda_a = \left(\mu_a + \zeta_a^*\right) S_a^*$ and $\Lambda_h = \left(\mu_h + \zeta_h^*\right) S_h^*$, we obtain

$$\tilde{W}' = \left(\frac{A\left(\mu_a + \zeta_a^*\right) S_a^*}{S_a} - \frac{A\left(\mu_a + \zeta_a\right) S_a}{S_a}\right)\left(S_a - S_a^*\right)$$

$$+ \left(\frac{B\zeta_a S_a}{I_a} - \frac{B\left(\mu_a + \rho_a + d_a\right) I_a}{I_a}\right)\left(I_a - I_a^*\right) + \left(\frac{C\rho_a I_a}{R_a} - \frac{C\mu_a R_a}{R_a}\right)\left(R_a - R_a^*\right)$$

$$+ \left(\frac{\left(\mu_h + \zeta_h^*\right) S_h^*}{S_h} - \frac{\left(\mu_h + \zeta_h\right) S_h}{S_h}\right)\left(S_h - S_h^*\right)$$

$$+\left(\frac{D\zeta_h S_h}{I_h}-\frac{D\left(\mu_h+\rho_h+d_h\right)I_h}{I_h}\right)\left(I_h-I_h^*\right)+\left(\frac{E\rho_h I_h}{R_h}-\frac{E\mu_h R_h}{R_h}\right)\left(R_h-R_h^*\right)$$

$$\tilde{W}' = -\frac{A\mu_a\left(S_a-S_a^*\right)^2}{S_a}-\frac{A\left(\zeta_a S_a-\zeta_a^* S_a^*\right)\left(S_a-S_a^*\right)}{S_a}$$

$$+\left(\frac{B\zeta_a S_a}{I_a}-B\left(\mu_a+\rho_a+d_a\right)\right)\left(I_a-I_a^*\right)+\left(\frac{C\rho_a I_a}{R_a}-\frac{C\mu_a R_a}{R_a}\right)\left(R_a-R_a^*\right)$$

$$-\frac{\mu_h\left(S_h-S_h^*\right)^2}{S_h}-\frac{\left(\zeta_h S_h-\zeta_h^* S_h^*\right)\left(S_h-S_h^*\right)}{S_h}$$

$$+\left(\frac{D\zeta_h S_h}{I_h}-D\left(\mu_h+\rho_h+d_h\right)\right)\left(I_h-I_h^*\right)$$

$$+\left(\frac{E\rho_h I_h}{R_h}-\frac{E\mu_h R_h}{R_h}\right)\left(R_h-R_h^*\right).$$

Notice that $\tilde{W}'$ is of the form

$$\tilde{W}' = -\frac{A\mu_a\left(S_a-S_a^*\right)^2}{S_a}-\frac{\mu_h\left(S_h-S_h^*\right)^2}{S_h}+g\left(S_a,I_a,R_a,S_h,I_h,R_h\right).$$

We wish to show that g is negative definite away from the equilibrium point $\mathcal{E}_1$ and $g=0$ at $\mathcal{E}_1$. If this is true, then $\tilde{W}'$ is negative definite except at the equilibrium where it is zero.

Since $\zeta_a=\frac{\beta_{a_1}I_a}{N_a}$ and $\zeta_h=\frac{\beta_{a_2}I_a}{N_a}+\frac{\beta_h I_h}{N_h}$. Then $\tilde{W}'$ can be rearranged and rewritten as

$$\tilde{W}' = -\frac{A\mu_a\left(S_a-S_a^*\right)^2}{S_a}-\frac{\mu_h\left(S_h-S_h^*\right)^2}{S_h}-\frac{A\left(\zeta_a S_a-\zeta_a^* S_a^*\right)\left(S_a-S_a^*\right)}{S_a}$$

$$+\left(\frac{B\zeta_a S_a}{I_a}-\left(\mu_a+\rho_a+d_a\right)\right)\left(I_a-I_a^*\right)+\left(\frac{C\rho_a I_a}{R_a}-\frac{C\mu_a R_a}{R_a}\right)\left(R_a-R_a^*\right)$$

$$-\frac{\left(\zeta_h S_h-\zeta_h^* S_h^*\right)\left(S_h-S_h^*\right)}{S_h}+\left(\frac{D\zeta_h S_h}{I_h}-D\left(\mu_h+\rho_h+d_h\right)\right)\left(I_h-I_h^*\right)$$

$$+\left(\frac{E\rho_h I_h}{R_h}-\frac{E\mu_h R_h}{R_h}\right)\left(R_h-R_h^*\right)$$

$$\tilde{W}'=-\frac{A\mu_a\left(S_a-S_a^*\right)^2}{S_a}-\frac{\mu_h\left(S_h-S_h^*\right)^2}{S_h}-\frac{A}{S_a}\left(\frac{\beta_{a_1} I_a S_a}{N_a}-\frac{\beta_{a_1} I_a^* S_a^*}{N_a^*}\right)\left(S_a-S_a^*\right)$$

$$+\frac{B\beta_{a_1} S_a}{N_a}\left(I_a-I_a^*\right)-B\left(\mu_a+\rho_a+d_a\right)\left(I_a-I_a^*\right)+\frac{C\rho_a I_a}{R_a}\left(R_a-R_a^*\right)$$

$$-C\mu_a\left(R_a-R_a^*\right)-\left[\left(\frac{\beta_{a_2} I_a}{N_a}+\frac{\beta_h I_h}{N_h}\right)\frac{S_h}{S_h}-\left(\frac{\beta_{a_2} I_a^*}{N_a^*}+\frac{\beta_h I_h^*}{N_h^*}\right)\frac{S_h^*}{S_h}\right]\left(S_h-S_h^*\right)$$

$$+D\left(\frac{\beta_{a_2} I_a}{N_a}+\frac{\beta_h I_h}{N_h}\right)\frac{S_h}{I_h}\left(I_h-I_h^*\right)-D\left(\mu_h+\rho_h+d_h\right)\left(I_h-I_h^*\right)$$

$$+\frac{E\rho_h I_h}{R_h}\left(R_h-R_h^*\right)-E\mu_h\left(R_h-R_h^*\right),$$

so that

$$g\left(S_a,I_a,R_a,S_h,I_h,R_h\right)=-\frac{A}{S_a}\left(\frac{\beta_{a_1} I_a S_a}{N_a}-\frac{\beta_{a_1} I_a^* S_a^*}{N_a^*}\right)\left(S_a-S_a^*\right)+\frac{B\beta_{a_1} S_a}{N_a}\left(I_a-I_a^*\right)$$

$$-B\left(\mu_a+\rho_a+d_a\right)\left(I_a-I_a^*\right)+\frac{C\rho_a I_a}{R_a}\left(R_a-R_a^*\right)$$

$$-C\mu_a\left(R_a-R_a^*\right)$$

$$
\begin{aligned}
&- \left[\left(\frac{\beta_{a_2} I_a}{N_a} + \frac{\beta_h I_h}{N_h}\right)\frac{S_h}{S_h} - \left(\frac{\beta_{a_2} I_a^*}{N_a^*} + \frac{\beta_h I_h^*}{N_h^*}\right)\frac{S_h^*}{S_h}\right]\left(S_h - S_h^*\right) \\
&+ D\left(\frac{\beta_{a_2} I_a}{N_a} + \frac{\beta_h I_h}{N_h}\right)\frac{S_h}{I_h}\left(I_h - I_h^*\right) \\
&- D\left(\mu_h + \rho_h + d_h\right)\left(I_h - I_h^*\right) + \frac{E\rho_h I_h}{R_h}\left(R_h - R_h^*\right) \\
&- E\mu_h\left(R_h - R_h^*\right).
\end{aligned}
$$

In order to show this is negative definite except at the equilibrium point, we rewrite this function so that all variables are in a ratio to their respective element of the equilibrium point – e.g., S_a will only be included in the function in the form $\frac{S_a}{S_a^*}$ or $\frac{S_a^*}{S_a}$. We accomplish this by factoring out constants and distributing terms where necessary. For simplicity, and so we can see that g is not obviously negative definite, we write g so that each term has the same sign. Then we have

$$
\begin{aligned}
g = &- \frac{A\beta_{a_1} I_a S_a^*}{N_a}\left(\frac{S_a}{S_a^*} - 1\right) - \frac{A\beta_{a_1} I_a^* S_a^*}{N_a^*}\left(\frac{S_a^*}{S_a} - 1\right) - \frac{B\beta_{a_1} S_a I_a}{N_a}\left(\frac{I_a^*}{I_a} - 1\right) \\
&- B\left(\mu_a + \rho_a + d_a\right) I_a^*\left(\frac{I_a}{I_a^*} - 1\right) - C\rho_a I_a\left(\frac{R_a^*}{R_a} - 1\right) - C\mu_a R_a^*\left(\frac{R_a}{R_a^*} - 1\right) \\
&- \left(S_h - S_h^*\right)\left[\left(\frac{\beta_{a_2} I_a S_h}{N_a S_h} + \frac{\beta_h I_h S_h}{N_h S_h}\right) - \left(\frac{\beta_{a_2} I_a^* S_h^*}{N_a^* S_h} + \frac{\beta_h I_h^* S_h^*}{N_h^* S_h}\right)\right] \\
&- \frac{D\beta_{a_2} I_a S_h}{N_a}\left(\frac{I_h^*}{I_h} - 1\right) - \frac{D\beta_h S_h I_h}{N_h}\left(\frac{I_h^*}{I_h} - 1\right) - D\left(\mu_h + \rho_h + d_h\right) I_h^*\left(\frac{I_h}{I_h^*} - 1\right) \\
&- E\rho_h I_h\left(\frac{R_h^*}{R_h} - 1\right) - E\mu_h R_h^*\left(\frac{R_h}{R_h^*} - 1\right)
\end{aligned}
$$

$$
\begin{aligned}
g = &- \frac{A\beta_{a_1} I_a S_a^*}{N_a}\left(\frac{S_a}{S_a^*} - 1\right) - \frac{A\beta_{a_1} I_a^* S_a^*}{N_a^*}\left(\frac{S_a^*}{S_a} - 1\right) - \frac{B\beta_{a_1} S_a I_a}{N_a}\left(\frac{I_a^*}{I_a} - 1\right) \\
&- B\left(\mu_a + \rho_a + d_a\right) I_a^*\left(\frac{I_a}{I_a^*} - 1\right) - C\rho_a I_a\left(\frac{R_a^*}{R_a} - 1\right) - C\mu_a R_a^*\left(\frac{R_a}{R_a^*} - 1\right) \\
&- \left(S_h - S_h^*\right)\left[\frac{\beta_{a_2}}{S_h}\left(\frac{I_a S_h}{N_a} - \frac{I_a^* S_h^*}{N_a^*}\right) + \frac{\beta_h}{S_h}\left(\frac{I_h S_h}{N_h} - \frac{I_h^* S_h^*}{N_h^*}\right)\right] \\
&- \frac{D\beta_{a_2} I_a S_h}{N_a}\left(\frac{I_h^*}{I_h} - 1\right) - \frac{D\beta_h S_h I_h}{N_h}\left(\frac{I_h^*}{I_h} - 1\right) - D\left(\mu_h + \rho_h + d_h\right) I_h^*\left(\frac{I_h}{I_h^*} - 1\right) \\
&- E\rho_h I_h\left(\frac{R_h^*}{R_h} - 1\right) - E\mu_h R_h^*\left(\frac{R_h}{R_h^*} - 1\right)
\end{aligned}
$$

$$
\begin{aligned}
g = &- \frac{A\beta_{a_1} I_a^* S_a^*}{N_a^*}\left(\frac{I_a N_a^*}{I_a^* N_a}\right)\left(\frac{S_a}{S_a^*} - 1\right) - \frac{A\beta_{a_1} I_a^* S_a^*}{N_a^*}\left(\frac{S_a^*}{S_a} - 1\right) \\
&- \frac{B\beta_{a_1} S_a^* I_a^*}{N_a^*}\left(\frac{I_a S_a N_a^*}{I_a^* S_a^* N_a}\right)\left(\frac{I_a^*}{I_a} - 1\right) - B\left(\mu_a + \rho_a + d_a\right) I_a^*\left(\frac{I_a}{I_a^*} - 1\right) \\
&- C\rho_a I_a^*\left(\frac{I_a}{I_a^*}\right)\left(\frac{R_a^*}{R_a} - 1\right) - C\mu_a R_a^*\left(\frac{R_a}{R_a^*} - 1\right) \\
&- \left(1 - \frac{S_h^*}{S_h}\right)\left[\frac{\beta_{a_2} I_a^* S_h^*}{N_a^*}\left(\frac{I_a S_h N_a^*}{I_a^* S_h^* N_a} - 1\right) + \frac{\beta_h I_h^* S_h^*}{N_h^*}\left(\frac{I_h S_h N_h^*}{I_h^* S_h^* N_h} - 1\right)\right] \\
&- \frac{D\beta_{a_2} I_a^* S_h^*}{N_a^*}\left(\frac{I_a S_h N_a^*}{I_a^* S_h^* N_a}\right)\left(\frac{I_h^*}{I_h} - 1\right) - \frac{D\beta_h S_h^* I_h^*}{N_h^*}\left(\frac{S_h I_h N_h^*}{S_h^* I_h^* N_h}\right)\left(\frac{I_h^*}{I_h} - 1\right) \\
&- D\left(\mu_h + \rho_h + d_h\right) I_h^*\left(\frac{I_h}{I_h^*} - 1\right) - E\rho_h I_h^*\left(\frac{I_h}{I_h^*}\right)\left(\frac{R_h^*}{R_h} - 1\right) - E\mu_h R_h^*\left(\frac{R_h}{R_h^*} - 1\right).
\end{aligned}
$$

Notice that we can rewrite the terms with the constant A to get

$$-\frac{A\beta_{a_1} I_a^* S_a^*}{N_a^*}\left(\frac{I_a N_a^* S_a}{I_a^* N_a S_a^*} - \frac{I_a N_a^*}{I_a^* N_a} + \frac{S_a^*}{S_a} - 1\right).$$

Thus, the first three terms in g can be written as

$$-\frac{\beta_{a_1} S_a^* I_a^*}{N_a^*}\left(\frac{A I_a N_a^* S_a}{I_a^* N_a S_a^*} - \frac{A I_a N_a^*}{I_a^* N_a} + \frac{A S_a^*}{S_a} - A - \left(\frac{B I_a S_a N_a^*}{I_a^* S_a^* N_a}\right)\left(\frac{I_a^*}{I_a} - 1\right)\right)$$

$$= -\frac{\beta_{a_1} S_a^* I_a^*}{N_a^*}\left(\frac{A I_a N_a^* S_a}{I_a^* N_a S_a^*} - \frac{A I_a N_a^*}{I_a^* N_a} + \frac{A S_a^*}{S_a} - A + \frac{B S_a N_a^*}{S_a^* N_a} - \frac{B I_a S_a N_a^*}{I_a^* S_a^* N_a}\right).$$

Combining these results and reworking some more terms, results in

$$\begin{aligned}
g = &-\frac{\beta_{a_1} S_a^* I_a^*}{N_a^*}\left(\frac{A I_a N_a^* S_a}{I_a^* N_a S_a^*} - \frac{A I_a N_a^*}{I_a^* N_a} + \frac{A S_a^*}{S_a} - A + \frac{B S_a N_a^*}{S_a^* N_a} - \frac{B I_a S_a N_a^*}{I_a^* S_a^* N_a}\right) \\
&- B\left(\mu_a + \rho_a + d_a\right) I_a^*\left(\frac{I_a}{I_a^*} - 1\right) - C\rho_a I_a^*\left(\frac{I_a}{I_a^*}\right)\left(\frac{R_a^*}{R_a} - 1\right) - C\mu_a R_a^*\left(\frac{R_a}{R_a^*} - 1\right) \\
&- \left(1 - \frac{S_h^*}{S_h}\right)\left[\frac{\beta_{a_2} I_a^* S_h^*}{N_a^*}\left(\frac{I_a S_h N_a^*}{I_a^* S_h^* N_a} - 1\right) + \frac{\beta_h I_h^* S_h^*}{N_h^*}\left(\frac{I_h S_h N_h^*}{I_h^* S_h^* N_h} - 1\right)\right] \\
&- \frac{D\beta_{a_2} I_a^* S_h^*}{N_a^*}\left(\frac{I_a S_h N_a^*}{I_a^* S_h^* N_a}\right)\left(\frac{I_h^*}{I_h} - 1\right) - \frac{D\beta_h S_h^* I_h^*}{N_h^*}\left(\frac{S_h I_h N_h^*}{S_h^* I_h^* N_h}\right)\left(\frac{I_h^*}{I_h} - 1\right) \\
&- D\left(\mu_h + \rho_h + d_h\right) I_h^*\left(\frac{I_h}{I_h^*} - 1\right) - E\rho_h I_h^*\left(\frac{I_h}{I_h^*}\right)\left(\frac{R_h^*}{R_h} - 1\right) - E\mu_h R_h^*\left(\frac{R_h}{R_h^*} - 1\right)
\end{aligned}$$

$$\begin{aligned}
g = &-\frac{\beta_{a_1} S_a^* I_a^*}{N_a^*}\left(\frac{A I_a N_a^* S_a}{I_a^* N_a S_a^*} - \frac{A I_a N_a^*}{I_a^* N_a} + \frac{A S_a^*}{S_a} - A + \frac{B S_a N_a^*}{S_a^* N_a} - \frac{B I_a S_a N_a^*}{I_a^* S_a^* N_a}\right) \\
&- B\left(\mu_a + \rho_a + d_a\right) I_a^*\left(\frac{I_a}{I_a^*} - 1\right) - C\rho_a I_a^*\left(\frac{R_a^* I_a}{R_a I_a^*} - \frac{I_a}{I_a^*}\right)
\end{aligned}$$

$$- C\mu_a R_a^*\left(\frac{R_a}{R_a^*} - 1\right) - \frac{\beta_{a_2} I_a^* S_h^*}{N_a^*}\left(\frac{I_a S_h N_a^*}{I_a^* S_h^* N_a} - 1 - \frac{I_a N_a^*}{I_a^* N_a} + \frac{S_h^*}{S_h}\right)$$

$$- \frac{\beta_h I_h^* S_h^*}{N_h^*}\left(\frac{I_h S_h N_h^*}{I_h^* S_h^* N_h} - 1 - \frac{I_h N_h^*}{I_h^* N_h} + \frac{S_h^*}{S_h}\right)$$

$$- \frac{D\beta_{a_2} I_a^* S_h^*}{N_a^*}\left(\frac{I_a S_h N_a^* I_h^*}{I_a^* S_h^* N_a I_h} - \frac{I_a S_h N_a^*}{I_a^* S_h^* N_a}\right) - \frac{D\beta_h S_h^* I_h^*}{N_h^*}\left(\frac{S_h N_h^*}{S_h^* N_h} - \frac{S_h I_h N_h^*}{S_h^* I_h^* N_h}\right)$$

$$- D\left(\mu_h + \rho_h + d_h\right) I_h^*\left(\frac{I_h}{I_h^*} - 1\right) - E\rho_h I_h^*\left(\frac{R_h^* I_h}{R_h I_h^*} - \frac{I_h}{I_h^*}\right) - E\mu_h R_h^*\left(\frac{R_h}{R_h^*} - 1\right).$$

Although each term in g is being subtracted, it is still not clear whether each term subtracted is positive or negative. To help determine this, let $w = \frac{S_a}{S_a^*}$, $x = \frac{I_a}{I_a^*}$, $y = \frac{R_a}{R_a^*}$, $z = \frac{S_h}{S_h^*}$, $t = \frac{I_h}{I_h^*}$, $r = \frac{R_h}{R_h^*}$, $v = \frac{N_a}{N_a^*}$, and $u = \frac{N_h}{N_h^*}$ and rewrite g in terms of these variables. If we rearrange this function and can show that the coefficients of terms involving these variables are negative when $A, B, C, D, E > 0$, then we can continue on to show that g is negative definite except at the equilibrium point. To this end, substitute the new variables into the function to obtain

$$g = -\frac{\beta_{a_1} S_a^* I_a^*}{N_a^*}\left(\frac{Awx}{v} - \frac{Ax}{v} + \frac{A}{w} - A + \frac{Bw}{v} - \frac{Bwx}{v}\right) - B\left(\mu_a + \rho_a + d_a\right) I_a^*(x-1)$$

$$- C\rho_a I_a^*\left(\frac{x}{y} - x\right) - C\mu_a R_a^*(y-1) - \frac{\beta_{a_2} I_a^* S_h^*}{N_a^*}\left(\frac{xz}{v} - 1 - \frac{x}{v} + \frac{1}{z}\right)$$

$$- \frac{\beta_h I_h^* S_h^*}{N_h^*}\left(\frac{tz}{u} - 1 - \frac{t}{u} + \frac{1}{z}\right) - \frac{D\beta_{a_2} I_a^* S_h^*}{N_a^*}\left(\frac{xz}{tv} - \frac{xz}{v}\right) - \frac{D\beta_h S_h^* I_h^*}{N_h^*}\left(\frac{z}{u} - \frac{tz}{u}\right)$$

$$- D\left(\mu_h + \rho_h + d_h\right) I_h^*(t-1) - E\rho_h I_h^*\left(\frac{t}{r} - t\right) - E\mu_h R_h^*(r-1).$$

For simplicity, let $\alpha^* = \frac{\beta_{a_1} S_a^* I_a^*}{N_a^*}$, $\eta^* = \frac{\beta_{a_2} I_a^* S_h^*}{N_a^*}$, and $\theta^* = \frac{\beta_h I_h^* S_h^*}{N_h^*}$. Rewriting, it follows that

$$g = \alpha^* \left(\frac{(B-A)wx}{v} + \frac{Ax}{v} - \frac{A}{w} + A - \frac{Bw}{v} \right) + I_a^* \Big[- B \left(\mu_a + \rho_a + d_a \right) (x-1) + C\rho_a \Big(x - \frac{x}{y} \Big) \Big]$$

$$- C\mu_a R_a^* (y-1) + \eta^* \Big(1 - \frac{xz}{v} + \frac{x}{v} - \frac{1}{z} - \frac{Dxz}{tv} + \frac{Dxz}{v} \Big)$$

$$+ \theta^* \Big(1 - \frac{tz}{u} + \frac{t}{u} - \frac{1}{z} - \frac{Dz}{u} + \frac{Dtz}{u} \Big)$$

$$+ I_h^* \Big[- D \left(\mu_h + \rho_h + d_h \right) (t-1) + E\rho_h I_h^* \Big(t - \frac{t}{r} \Big) \Big] - E\mu_h R_h^* (r-1).$$

Next, we express g as its constants added to the variables that have more than one coefficient term each multiplied by their respective coefficients, and then subtract all other terms. Unlike the associated function in [42], we have one extra positive variable term, $\frac{\theta^* t}{u}$, and include it with the positive constants. If the coefficients of all the variables are positive, then it is possible that g is positive, so we aim to show that these coefficients are all negative. If we can do that, the next step is to show that the negative terms outweigh the positive terms, so that g itself is negative semidefinite and only zero at equilibrium.

We write g as

$$g = \Big(\alpha^* A + B I_a^* \left(\mu_a + \rho_a + d_a \right) + C\mu_a R_a^* + \eta^* + \theta^* + D I_h^* \left(\mu_h + \rho_h + d_h \right) + E\mu_h R_h^* + \frac{\theta^* t}{u} \Big)$$

$$+ \frac{x}{v} \big(\alpha^* A + \eta^* \big) + x \big(C\rho_a I_a^* - B \left(\mu_a + \rho_a + d_a \right) I_a^* \big) + \frac{xw}{v} \big((B-A)\alpha^* \big)$$

$$+ \frac{xz}{v} \big(\eta^* (D-1) \big) + t \big(E\rho_h I_h^* - D \left(\mu_h + \rho_h + d_h \right) I_h^* \big) + \frac{tz}{u} \big(\theta^* (D-1) \big)$$

$$- \Big(\frac{A}{w} + \frac{Bw}{v} + C\rho_a I_a^* \Big(\frac{x}{y} \Big) + \frac{\eta^* + \theta^*}{z} + \frac{\eta^* Dxz}{tv} + \frac{\theta^* Dz}{u} + E\rho_h \Big(\frac{t}{r} \Big) + E\mu_h R_h^* \Big).$$

Unlike the associated function obtained by McCluskey, we cannot simply set all of the coefficients of $\frac{x}{v}, x, \frac{wx}{v}, \frac{xz}{v}, t$ and $\frac{tz}{u}$ to be negative except at the equilibrium point. Since $\alpha^*, \eta^*, \theta^* > 0$ are given, I_a^*, I_h^* are fixed and $A, B, C, D, E > 0$, we see that $\alpha^* A + \eta^* > 0$ and we can include this with the positive terms. If we set the remaining coefficients – those of $x, \frac{wx}{v}, \frac{xz}{v}, t$ and $\frac{tz}{u}$ – to be negative except at the equilibrium point, we get the following:

$$(B - A)\alpha^* \leq 0 \implies 0 < B \leq A,$$

$$C\rho_a I_a^* - B\left(\mu_a + \rho_a + d_a\right) I_a^* \leq 0 \implies 0 < C \leq B\frac{\left(\mu_a + \rho_a + d_a\right)}{\rho_a},$$

$$\eta^*(D - 1) \leq 0,\ \theta^*(D - 1) \leq 0 \implies 0 < D \leq 1,$$

$$E\rho_h I_h^* - D\left(\mu_h + \rho_h + d_h\right) I_h^* \leq 0, \implies 0 < E \leq D\frac{\left(\mu_h + \rho_h + d_h\right)}{\rho_h}.$$

There is not enough information identify A, B, C, D or E explicitly as was done in [42] and so we cannot determine whether or not the negative terms outweigh the positive terms. Thus, we cannot say for certain that $\tilde{W}'$ is negative semidefinite, nor can we say that $\tilde{W}$ is positive semidefinite and zero only at the equilibrium. Hence, it is not clear that $\tilde{W}$ is a Lyapunov function following the method of McCluskey.

There are two suspected reasons why this method does not work for the system in (2.1a)-(2.1f). There are two SIR-type models in the McCluskey paper. The first is an SEIR model and the second is an SIR model with five compartments. We attempted to apply the method used in the five compartment model above since the SEIR model was too simplistic compared to our situation. The models in the McCluskey paper are only for one population, but (2.1a)-(2.1f) is a system with two interacting populations. Additionally, (2.1a)-(2.1f) includes the terms N_a and N_h and these are not included in [42]. Even if we ignore the terms N_a and N_h in (2.1a)-(2.1f) and write N_a and N_h in terms of S_a, I_a, R_a, S_h, I_h, and R_h, we still do not have enough information to explicitly identify A, B, C, D or E.

A proof of the global asymptotic stability of the co-existence endemic equilibrium is the focus of the next chapter.

3 Existence and Stability of the Co-existence Endemic Equilibrium

In this chapter we present a proof of the global asymptotic stability of the co-existence endemic equilibrium. The idea is that since we have the global asymptotic stability of the animal subsystem's endemic equilibrium and since the animal population is independent of the human population, we can essentially consider only the human subsystem (2.1d)-(2.1f) when searching for a Lyapunov function. Using a theorem from Thieme, we can essentially write the cross-infection terms in (2.1d)-(2.1f) as constants and this allows us to prove our result. (This new result was recently published in [37].)

3.1 An Asymptotically Autonomous System

Now that we know the dynamics of the disease in the animal population from the theorems in the previous chapter, we can consider how this affects disease propagation in the human population. Here our analysis diverges from what was done previously in [4] and we also refer the reader to [41]. Individuals in the human population can get infected by contact with infectious animals or infectious humans. However, we know that if $\mathcal{R}_{0_a} \leq 1$, then $I_a(t) \to 0,\ N_a(t) \to \Lambda_a/\mu_a$ as $t \to \infty$, while if $\mathcal{R}_{0_a} > 1$ and $\mu_a \geq d_a$, then $I_a(t) \to I_a^* > 0$, $N_a(t) \to N_a^* = S_a^* + I_a^* + R_a^*$ as $t \to \infty$. Thus we can think of (2.1d)-(2.1f) as a non-autonomous system

$$\frac{dS_h}{dt} = \Lambda_h - \mu_h S_h - \left(\beta_{a_2} g(t) + \frac{\beta_h I_h}{N_h}\right) S_h, \tag{3.1a}$$

$$\frac{dI_h}{dt} = \left(\beta_{a_2} g(t) + \frac{\beta_h I_h}{N_h}\right) S_h - \left(\mu_h + \rho_h + d_h\right) I_h, \tag{3.1b}$$

$$\frac{dR_h}{dt} = \rho_h I_h - \mu_h R_h, \tag{3.1c}$$

where $g(t) := \dfrac{I_a(t)}{N_a(t)}$. By Theorem 2.3.2 and Theorem 2.3.4, we have that

$$\lim_{t\to\infty} g(t) = \frac{\lim_{t\to\infty} I_a(t)}{\lim_{t\to\infty} N_a(t)} = \frac{I_a^e}{N_a^e},$$

where the limits I_a^e and N_a^e depend on $\mathcal{R}_{0_a}$ and the corresponding parameters. That is, $I_a^e = 0$ when $\mathcal{R}_{0_a} \leq 1$ and $I_a^e = I_a^*$ when $\mathcal{R}_{0_a} > 1$. Thus, (2.1d)-(2.1f) is an asymptotically autonomous system with limit system

$$\frac{dS_h}{dt} = \Lambda_h - \mu_h S_h - \left(\beta_{a_2}\frac{I_a^e}{N_a^e} + \frac{\beta_h I_h}{N_h}\right) S_h, \tag{3.2a}$$

$$\frac{dI_h}{dt} = \left(\beta_{a_2}\frac{I_a^e}{N_a^e} + \frac{\beta_h I_h}{N_h}\right) S_h - \left(\mu_h + \rho_h + d_h\right) I_h, \tag{3.2b}$$

$$\frac{dR_h}{dt} = \rho_h I_h - \mu_h R_h, \tag{3.2c}$$

and we can use the theory developed for such systems found in [9, 59] to address the stability properties of our model in all possible cases. In particular, we repeatedly make use of the following corollary applied to our systems:

Corollary 3.1.1 (Thieme)**.** *If solutions of the system (3.1a)-(3.1c) are bounded, and the equilibrium E of the limit system (3.2a)-(3.2c) is globally asymptotically stable, then any solution $\left(S_h(t), I_h(t), R_h(t)\right)$ of the system (3.1a)-(3.1c) satisfies $\left(S_h(t), I_h(t), R_h(t)\right) \to E_h$ as $t \to \infty$.*

3.2 Existence of the Endemic Equilibrium

Previously, it was only shown that the co-existence endemic equilibrium existed under the assumption that $\beta_h > d_h(1 + x^*)$. We will now prove the existence of this equilibrium without the assumed inequality and use a method similar to that in [2]. We start with the following claim:

Proposition 3.2.1. *Assume that $\mathcal{R}_{0_a} > 1$, $\beta_{a_2} > 0$, and $\mu_a \geq d_a$, so the disease in the animal pop-*

ulation tends to the endemic equilibrium E_a^*. Then (2.1d)-(2.1f) has a unique endemic equilibrium $E_h^* \in \Omega_h$, and $\mathcal{E}_1 = \left(E_a^*, E_h^*\right)$ is the unique endemic equilibrium of (2.1a)-(2.1f) in Ω.

Proof. To calculate $E_h^* = \left(S_h^*, I_h^*, R_h^*\right)$ we set the right sides of equations (2.1d)-(2.1f) equal to zero to obtain

$$\Lambda_h = \left(\mu_h + \frac{\beta_{a_2} I_a^*}{N_a^*} + \frac{\beta_h I_h^*}{N_h^*}\right) S_h^*, \tag{3.3}$$

$$\left(\frac{\beta_{a_2} I_a^*}{N_a^*} + \frac{\beta_h I_h^*}{N_h^*}\right) S_h^* = \left(\mu_h + \rho_h + d_h\right) I_h^*, \tag{3.4}$$

$$\rho_h I_h^* = \mu_h R_h^*. \tag{3.5}$$

For simplification, define

$$\xi_a^* := \frac{\beta_{a_2} I_a^*}{N_a^*}, \quad m_h := \mu_h + \rho_h + d_h, \quad \xi_h^* := \frac{\beta_h I_h^*}{N_h^*},$$

$$a := \frac{\Lambda_h \xi_a^*}{m_h}, \; b := \frac{\Lambda_h}{m_h}, \; c := \frac{\rho_h a}{\mu_h}, \; d := \frac{\rho_h b}{\mu_h}, \; e := \Lambda_h + a + c, \; f := b + d.$$

Using (3.3),

$$S_h^* = \frac{\Lambda_h}{\mu_h + \xi_a^* + \xi_h^*}. \tag{3.6}$$

From (3.4) and using (3.6),

$$I_h^* = \frac{S_h^* \left(\xi_a^* + \xi_h^*\right)}{m_h}$$

$$I_h^* = \left(\frac{\Lambda_h}{\mu_h + \xi_a^* + \xi_h^*}\right)\left(\frac{\xi_a^* + \xi_h^*}{m_h}\right)$$

$$I_h^* = \left(\frac{\Lambda_h \xi_a^*}{m_h} + \frac{\Lambda_h \xi_h^*}{m_h}\right)\left(\frac{1}{\mu_h + \xi_a^* + \xi_h^*}\right)$$

$$I_h^* = \frac{a + b\xi_h^*}{\mu_h + \xi_a^* + \xi_h^*}. \tag{3.7}$$

Clearly, by (3.5) and (3.7),

$$R_h^* = \frac{\rho_h}{\mu_h} I_h^*$$

$$R_h^* = \left(\frac{a + b\xi_h^*}{\mu_h + \xi_a^* + \xi_h^*} \right) \left(\frac{\rho_h}{\mu_h} \right)$$

$$R_h^* = \frac{c + d\xi_h^*}{\mu_h + \xi_a^* + \xi_h^*}. \tag{3.8}$$

Then it follows that

$$\frac{I_h^*}{N_h^*} = \left(\frac{a + b\xi_h^*}{\mu_h + \xi_a^* + \xi_h^*} \right) \left(\frac{\mu_h + \xi_a^* + \xi_h^*}{\Lambda_h + a + b\xi_h^* + c + d\xi_h^*} \right)$$

$$\frac{I_h^*}{N_h^*} = \frac{a + b\xi_h^*}{e + f\xi_h^*}$$

so that

$$\xi_h^* = \frac{\beta_h \left(a + b\xi_h^* \right)}{e + f\xi_h^*}. \tag{3.9}$$

Rearranging (3.9), we obtain

$$\xi_h^* \left(e + f\xi_h^* \right) = \beta_h \left(a + b\xi_h^* \right)$$

$$f\xi_h^{*2} + e\xi_h^* - a\beta_h - b\beta_h\xi_h^* = 0$$

$$f\xi_h^{*2} + \xi_h^* \left(e - b\beta_h \right) - \beta_h a = 0. \tag{3.10}$$

Since (3.10) is quadratic equation in ξ_h^*, it has one positive root. Now (3.6), (3.7), and (3.8) imply that the corresponding $E_h^* = \left(S_h^*, I_h^*, R_h^* \right)$ is feasible. □

3.3 Global Stability of the Co-existence Endemic Equilibrium

Now we prove the global asymptotic stability of the co-existence endemic equilibrium. This results in the conclusion that infection in the animal population leads to infection in the human population.

Consider the endemic equilibrium $\mathcal{E}_1 = \left(E_a^*, E_h^*\right) \in \Omega$. We prove the following theorem.

Theorem 3.3.1. *If $\mathcal{R}_{0_a} > 1, \mu_a \geq d_a$, $\beta_{a_2} > 0$, and $\mu_h \geq d_h$ then the unique endemic equilibrium $\mathcal{E}_1 = \left(E_a^*, E_h^*\right)$ of (2.1a)-(2.1f) is globally asymptotically stable in the interior of Ω.*

Proof. Since $\mathcal{R}_{0_a} > 1$ and $\mu_a \geq d_a$ Theorem 2.3.4 implies that E_a^* is a globally asymptotically stable equilibrium of (2.1a)-(2.1c) in the interior of Ω_a. Using this result, and the assumption that $\beta_{a_2} > 0$ we have that the system

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - \mu_h S_h - \left(\beta_{a_2}\frac{I_a^*}{N_a^*} + \frac{\beta_h I_h}{N_h}\right) S_h, \\
\frac{dI_h}{dt} &= \left(\beta_{a_2}\frac{I_a^*}{N_a^*} + \frac{\beta_h I_h}{N_h}\right) S_h - \left(\mu_h + \rho_h + d_h\right) I_h, \\
\frac{dR_h}{dt} &= \rho_h I_h - \mu_h R_h
\end{aligned}$$

is the asymptotic limit of system (2.1d)-(2.1f), and E_h^* is its unique equilibrium. We claim that E_h^* is a globally asymptotically stable equilibrium of (3.2a)-(3.2c).

Consider the function $L : \left\{\left(S_h, I_h, R_h\right) \in \Omega_h : S_h > 0, I_h > 0, R_h > 0\right\} \to \mathbb{R}$ given by

$$\begin{aligned}
L =& N_h - N_h^* - N_h^* \ln\left(\frac{N_h}{N_h^*}\right) + \frac{N_h^*\left(d_h + 2\mu_h\right)}{\beta_h\left(I_h^* + R_h^*\right)}\left[I_h - I_h^* - I_h^* \ln\left(\frac{I_h}{I_h^*}\right)\right] \\
&+ \frac{\left(d_h + 2\mu_h\right)}{2\rho_h}\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\left(\frac{\left(R_h - R_h^*\right)^2}{N_h}\right) + A\left(N_h - N_h^*\right)^2 + B\left(R_h - R_h^*\right)^2,
\end{aligned}$$

where $A, B > 0$ are yet to be determined. $L \in C^1\left(\Omega_h\right)$, $L\left(S_h^*, I_h^*, R_h^*\right) = 0$ and L is positive

definite except at E_h^* where $L = 0$. Calculating the derivative of L along solutions of (3.2a)-(3.2c) we have

$$
\begin{aligned}
L' = &\left(N_h'\right)\left(\frac{N_h - N_h^*}{N_h}\right) + \frac{N_h^*\left(d_h + 2\mu_h\right)}{\beta_h\left(I_h^* + R_h^*\right)}\left(I_h'\right)\left(\frac{I_h - I_h^*}{I_h}\right) \\
&+ \frac{\left(d_h + 2\mu_h\right)}{2\rho_h}\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\left(\frac{2R_h'\left(R_h - R_h^*\right)}{N_h} - \frac{N_h'\left(R_h - R_h^*\right)^2}{N_h^2}\right) \\
&+ 2AN_h'\left(N_h - N_h^*\right) + 2BR_h'\left(R_h - R_h^*\right) \\
L' = &\Big(\Lambda_h - \mu_h\left(S_h + I_h + R_h\right) - d_h I_h\Big)\left(\frac{N_h - N_h^*}{N_h}\right) \\
&+ \frac{N_h^*\left(d_h + 2\mu_h\right)}{\beta_h\left(I_h^* + R_h^*\right)}\left(\frac{\beta_{a_2} I_a^* S_h}{N_a^*} + \frac{\beta_h I_h S_h}{N_h} - \left(\mu_h + \rho_h + d_h\right) I_h\right)\left(\frac{I_h - I_h^*}{I_h}\right) \\
&+ \frac{\left(d_h + 2\mu_h\right)}{2\rho_h}\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\left(\frac{2\left(\rho_h I_h - \mu_h R_h\right)\left(R_h - R_h^*\right)}{N_h} - \frac{N_h'\left(R_h - R_h^*\right)^2}{N_h^2}\right) \\
&+ 2AN_h'\left(N_h - N_h^*\right) + 2B\left(\rho_h I_h - \mu_h R_h\right)\left(R_h - R_h^*\right).
\end{aligned}
$$

Using the relationships

$$
\Lambda_h = \mu_h\left(S_h^* + I_h^* + R_h^*\right) + d_h I_h^*, \quad \rho_h I_h^* = \mu_h R_h^*, \quad \frac{\beta_{a_2} I_a^* S_h^*}{N_a^*} + \frac{\beta_h I_h^* S_h^*}{N_h^*} = \left(\mu_h + \rho_h + d_h\right) I_h^*,
$$

we obtain

$$
\begin{aligned}
L' = &\Big(\mu_h\left(S_h^* + I_h^* + R_h^*\right) + d_h I_h^* - \mu_h\left(S_h + I_h + R_h\right) - d_h I_h\Big)\left(\frac{N_h - N_h^*}{N_h}\right) \\
&+ \left(\frac{N_h^*\left(d_h + 2\mu_h\right)}{\beta_h\left(I_h^* + R_h^*\right)}\right)\left[\frac{\beta_{a_2} I_a^* S_h}{N_a^*} + \frac{\beta_h I_h S_h}{N_h} - \left(\frac{\beta_{a_2} I_a^* S_h^*}{N_a^* I_h^*} + \frac{\beta_h S_h^*}{N_h^*}\right) I_h\right]\left(\frac{I_h - I_h^*}{I_h}\right) \\
&+ \left[\left(\frac{d_h + 2\mu_h}{2\rho_h}\right)\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\right].
\end{aligned}
$$

$$\left(\frac{2\left(\rho_h I_h-\mu_h R_h-\rho_h I_h^*+\mu_h R_h^*\right)\left(R_h-R_h^*\right)}{N_h}-\frac{N_h'\left(R_h-R_h^*\right)^2}{N_h^2}\right)\Bigg]$$

$$+2AN_h'\left(N_h-N_h^*\right)+2B\left(\rho_h I_h-\mu_h R_h-\rho_h I_h^*+\mu_h R_h^*\right)\left(R_h-R_h^*\right)$$

$$L'=\left(\mu_h\left(S_h^*+I_h^*+R_h^*\right)+d_h I_h^*-\mu_h\left(S_h+I_h+R_h\right)-d_h I_h\right)\left(\frac{N_h-N_h^*}{N_h}\right)$$

$$+\left[\left(\frac{N_h^*\left(d_h+2\mu_h\right)}{\beta_h\left(I_h^*+R_h^*\right)}\right)\left(\frac{\beta_{a_2}I_a^*S_h\left(I_h-I_h^*\right)}{N_a^*I_h}+\frac{\beta_h S_h\left(I_h-I_h^*\right)}{N_h}\right.\right.$$

$$\left.\left.-\left(\frac{\beta_{a_2}I_a^*S_h^*\left(I_h-I_h^*\right)}{N_a^*I_h^*}+\frac{\beta_h S_h^*\left(I_h-I_h^*\right)}{N_h^*}\right)\right)\right]$$

$$+\left[\left(\frac{d_h+2\mu_h}{2\rho_h}\right)\left(1+\frac{S_h^*}{I_h^*+R_h^*}\right)\cdot\right.$$

$$\left.\left(\frac{2\left(\rho_h I_h-\mu_h R_h-\rho_h I_h^*+\mu_h R_h^*\right)\left(R_h-R_h^*\right)}{N_h}-\frac{N_h'\left(R_h-R_h^*\right)^2}{N_h^2}\right)\right]$$

$$+2AN_h'\left(N_h-N_h^*\right)+2B\left(\rho_h I_h-\mu_h R_h-\rho_h I_h^*+\mu_h R_h^*\right)\left(R_h-R_h^*\right)$$

$$L'=\left(\mu_h\left(S_h^*+I_h^*+R_h^*\right)+d_h I_h^*-\mu_h\left(S_h+I_h+R_h\right)-d_h I_h\right)\left(\frac{N_h-N_h^*}{N_h}\right)$$

$$+\left[\left(\frac{N_h^*\left(d_h+2\mu_h\right)}{\beta_h\left(I_h^*+R_h^*\right)}\right)\left(\frac{\beta_{a_2}I_a^*S_hI_h^*\left(I_h-I_h^*\right)}{N_a^*I_hI_h^*}-\frac{\beta_{a_2}I_a^*S_h^*I_h\left(I_h-I_h^*\right)}{N_a^*I_hI_h^*}\right.\right.$$

$$\left.\left.+\frac{\beta_h S_h N_h^*\left(I_h-I_h^*\right)}{N_h^*N_h}-\frac{\beta_h S_h^*N_h\left(I_h-I_h^*\right)}{N_h^*N_h}\right)\right]$$

$$+\left[\left(\frac{d_h+2\mu_h}{2\rho_h}\right)\left(1+\frac{S_h^*}{I_h^*+R_h^*}\right)\cdot\right.$$

$$\left.\left(\frac{2\left(\rho_h I_h-\mu_h R_h-\rho_h I_h^*+\mu_h R_h^*\right)\left(R_h-R_h^*\right)}{N_h}-\frac{N_h'\left(R_h-R_h^*\right)^2}{N_h^2}\right)\right]$$

$$+2AN_h'\left(N_h-N_h^*\right)+2B\left(\rho_h I_h-\mu_h R_h-\rho_h I_h^*+\mu_h R_h^*\right)\left(R_h-R_h^*\right)$$

Since

$$\begin{aligned}
&\beta_h S_h N_h^*\left(I_h-I_h^*\right)-\beta_h S_h^* N_h\left(I_h-I_h^*\right)\\
&\quad=\beta_h\left(I_h-I_h^*\right)\left(S_h N_h^*-S_h^* N_h\right)\\
&\quad=\beta_h\left(I_h-I_h^*\right)\left(S_h\left(S_h^*+I_h^*+R_h^*\right)-S_h^*\left(S_h+I_h+R_h\right)\right)\\
&\quad=\beta_h\left(I_h-I_h^*\right)\left(S_h S_h^*+S_h I_h^*+S_h R_h^*-S_h^* S_h-S_h^* I_h-S_h^* R_h\right)\\
&\quad=\beta_h\left(I_h-I_h^*\right)\left(S_h I_h^*+S_h R_h^*-S_h^* I_h-S_h^* R_h\right)\\
&\quad=\beta_h\left(I_h-I_h^*\right)\left(S_h I_h^*+S_h R_h^*-S_h^* I_h-S_h^* R_h+S_h^* I_h^*-S_h^* I_h^*+S_h^* R_h^*-S_h^* R_h^*\right)\\
&\quad=\beta_h\left(I_h-I_h^*\right)\left(\left(S_h-S_h^*\right)\left(I_h^*+R_h^*\right)-S_h^*\left(I_h-I_h^*\right)-S_h^*\left(R_h-R_h^*\right)\right)
\end{aligned}$$

and

$$\begin{aligned}
&\beta_{a_2} I_a^* S_h I_h^*\left(I_h-I_h^*\right)-\beta_{a_2} I_a^* S_h^* I_h\left(I_h-I_h^*\right)\\
&\quad=\beta_{a_2} I_a^*\left(I_h-I_h^*\right)\left(S_h I_n^*-S_h^* I_h\right)\\
&\quad=\beta_{a_2} I_a^*\left(I_h-I_h^*\right)\left(S_h I_n^*-S_h^* I_h+S_h I_h-S_h I_h\right)\\
&\quad=\beta_{a_2} I_a^*\left(I_h-I_h^*\right)\left(I_h\left(S_h-S_h^*\right)-S_h\left(I_h-I_h^*\right)\right)
\end{aligned}$$

we have

$$L'=\left(\mu_h\left(S_h^*+I_h^*+R_h^*\right)+d_h I_h^*-\mu_h\left(S_h+I_h+R_h\right)-d_h I_h\right)\left(\frac{N_h-N_h^*}{N_h}\right)$$

$$+\left[\left(\frac{N_h^*\left(d_h+2\mu_h\right)}{\beta_h\left(I_h^*+R_h^*\right)}\right)\left(\frac{\beta_{a_2}I_a^*I_h\left(I_h-I_h^*\right)\left(S_h-S_h^*\right)}{N_a^*I_hI_h^*}-\frac{\beta_{a_2}I_a^*S_h\left(I_h-I_h^*\right)^2}{N_a^*I_hI_h^*}\right.\right.$$
$$+\frac{\beta_h\left(I_h-I_h^*\right)\left(S_h-S_h^*\right)\left(I_h^*+R_h^*\right)}{N_h^*N_h}$$
$$\left.\left.-\frac{\beta_hS_h^*\left(I_h-I_h^*\right)^2}{N_h^*N_h}-\frac{\beta_hS_h^*\left(I_h-I_h^*\right)\left(R_h-R_h^*\right)}{N_h^*N_h}\right)\right]$$
$$+\left[\left(\frac{d_h+2\mu_h}{2\rho_h}\right)\left(1+\frac{S_h^*}{I_h^*+R_h^*}\right)\cdot\right.$$
$$\left.\left(\frac{2\left(\rho_hI_h-\mu_hR_h-\rho_hI_h^*+\mu_hR_h^*\right)\left(R_h-R_h^*\right)}{N_h}-\frac{N_h'\left(R_h-R_h^*\right)^2}{N_h^2}\right)\right]$$
$$+2AN_h'\left(N_h-N_h^*\right)+2B\left(\rho_hI_h-\mu_hR_h-\rho_hI_h^*+\mu_hR_h^*\right)\left(R_h-R_h^*\right).$$

Some more algebra yields

$$L'=\left(\mu_h\left(S_h^*+I_h^*+R_h^*\right)+d_hI_h^*-\mu_h\left(S_h+I_h+R_h\right)-d_hI_h\right)\left(\frac{N_h-N_h^*}{N_h}\right)$$
$$+\left[\left(\frac{N_h^*\left(d_h+2\mu_h\right)}{\beta_h\left(I_h^*+R_h^*\right)}\right)\left(\frac{\beta_{a_2}I_a^*\left(I_h-I_h^*\right)\left(S_h-S_h^*\right)}{N_a^*I_h^*}-\frac{\beta_{a_2}I_a^*S_h\left(I_h-I_h^*\right)^2}{N_a^*I_hI_h^*}\right.\right.$$
$$+\frac{\beta_h\left(I_h-I_h^*\right)\left(S_h-S_h^*\right)\left(I_h^*+R_h^*\right)}{N_h^*N_h}-\frac{\beta_hS_h^*\left(I_h-I_h^*\right)^2}{N_h^*N_h}$$
$$\left.\left.-\frac{\beta_hS_h^*\left(I_h-I_h^*\right)\left(R_h-R_h^*\right)}{N_h^*N_h}\right)\right]$$
$$+\left[\left(\frac{d_h+2\mu_h}{2\rho_h}\right)\left(1+\frac{S_h^*}{I_h^*+R_h^*}\right)\cdot\right.$$
$$\left.\left(\frac{2\left(\rho_h\left(I_h-I_h^*\right)-\mu_h\left(R_h-R_h^*\right)\right)\left(R_h-R_h^*\right)}{N_h}-\frac{N_h'\left(R_h-R_h^*\right)^2}{N_h^2}\right)\right]$$

$$+ 2AN_h'\big(N_h - N_h^*\big) + 2B\big(\rho_h\big(I_h - I_h^*\big) - \mu_h\big(R_h - R_h^*\big)\big)\big(R_h - R_h^*\big)$$

$$L' = \Big(\mu_h\big(S_h^* + I_h^* + R_h^*\big) + d_h I_h^* - \mu_h\big(S_h + I_h + R_h\big) - d_h I_h\Big)\left(\frac{N_h - N_h^*}{N_h}\right) \tag{3.12}$$

$$+ \left[\left(\frac{N_h^*\big(d_h + 2\mu_h\big)}{\beta_h\big(I_h^* + R_h^*\big)}\right)\left(\frac{\beta_{a_2} I_a^*\big(I_h - I_h^*\big)\big(S_h - S_h^*\big)}{N_a^* I_h^*} - \frac{\beta_{a_2} I_a^* S_h\big(I_h - I_h^*\big)^2}{N_a^* I_h I_h^*}\right.\right.$$

$$+ \frac{\beta_h\big(I_h - I_h^*\big)\big(S_h - S_h^*\big)\big(I_h^* + R_h^*\big)}{N_h^* N_h} - \frac{\beta_h S_h^*\big(I_h - I_h^*\big)^2}{N_h^* N_h}$$

$$\left.\left. - \frac{\beta_h S_h^*\big(I_h - I_h^*\big)\big(R_h - R_h^*\big)}{N_h^* N_h}\right)\right]$$

$$+ \left[\left(\frac{d_h + 2\mu_h}{2\rho_h}\right)\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\cdot\right.$$

$$\left.\left(\frac{2\rho_h\big(I_h - I_h^*\big)\big(R_h - R_h^*\big)}{N_h} - \frac{2\mu_h\big(R_h - R_h^*\big)^2}{N_h} - \frac{N_h'\big(R_h - R_h^*\big)^2}{N_h^2}\right)\right]$$

$$+ 2AN_h'\big(N_h - N_h^*\big) + 2B\rho_h\big(I_h - I_h^*\big)\big(R_h - R_h^*\big) - 2B\mu_h\big(R_h - R_h^*\big)^2.$$

Notice line (3.12) can be written as

$$\left(\frac{\big(S_h - S_h^*\big) + \big(I_h - I_h^*\big) + \big(R_h - R_h^*\big)}{N_h}\right)\left(-\mu_h\big(S_h - S_h^* + I_h - I_h^* + R_h - R_h^*\big) - d_h\big(I_h - I_h^*\big)\right)$$

$$= \left(\frac{1}{N_h}\right)\Big(-\mu_h\Big[\big(S_h - S_h^*\big)^2 + \big(S_h - S_h^*\big)\big(I_h - I_h^*\big) + \big(S_h - S_h^*\big)\big(R_h - R_h^*\big)$$

$$+ \big(S_h - S_h^*\big)\big(I_h - I_h^*\big) + \big(I_h - I_h^*\big)^2 + \big(I_h - I_h^*\big)\big(R_h - R_h^*\big)$$

$$+ \big(S_h - S_h^*\big)\big(R_h - R_h^*\big) + \big(I_h - I_h^*\big)\big(R_h - R_h^*\big) + \big(R_h - R_h^*\big)^2\Big]$$

$$- d_h\Big[\big(S_h - S_h^*\big)\big(I_h - I_h^*\big) + \big(I_h - I_h^*\big)^2 + \big(I_h - I_h^*\big)\big(R_h - R_h^*\big)\Big]\Big)$$

$$= -\frac{\mu_h\Big(\big(S_h - S_h^*\big) + \big(R_h - R_h^*\big)\Big)^2}{N_h} - \frac{\big(d_h + \mu_h\big)\big(I_h - I_h^*\big)^2}{N_h}$$

$$- \frac{\big(d_h + 2\mu_h\big)\big(S_h - S_h^*\big)\big(I_h - I_h^*\big)}{N_h} - \frac{\big(d_h + 2\mu_h\big)\big(I_h - I_h^*\big)\big(R_h - R_h^*\big)}{N_h} \tag{3.13}$$

so then

$$L' = -\frac{\mu_h\Big(\big(S_h - S_h^*\big) + \big(R_h - R_h^*\big)\Big)^2}{N_h} - \frac{\big(d_h + \mu_h\big)\big(I_h - I_h^*\big)^2}{N_h}$$

$$- \frac{\big(d_h + 2\mu_h\big)\big(S_h - S_h^*\big)\big(I_h - I_h^*\big)}{N_h} - \frac{\big(d_h + 2\mu_h\big)\big(I_h - I_h^*\big)\big(R_h - R_h^*\big)}{N_h}$$

$$+ \left[\left(\frac{N_h^*\big(d_h + 2\mu_h\big)}{\beta_h\big(I_h^* + R_h^*\big)}\right)\cdot\right.$$

$$\left(\frac{\beta_{a_2} I_a^*\big(I_h - I_h^*\big)\big(S_h - S_h^*\big)}{N_a^* I_h^*} - \frac{\beta_{a_2} I_a^* S_h\big(I_h - I_h^*\big)^2}{N_a^* I_h I_h^*}\right.$$

$$+ \frac{\beta_h\big(I_h - I_h^*\big)\big(S_h - S_h^*\big)\big(I_h^* + R_h^*\big)}{N_h^* N_h} - \frac{\beta_h S_h^*\big(I_h - I_h^*\big)^2}{N_h^* N_h}$$

$$\left.\left. - \frac{\beta_h S_h^*\big(I_h - I_h^*\big)\big(R_h - R_h^*\big)}{N_h^* N_h}\right)\right]$$

$$+ \big(d_h + 2\mu_h\big)\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\left(\frac{\big(I_h - I_h^*\big)\big(R_h - R_h^*\big)}{N_h}\right)$$

$$- \frac{\big(d_h + 2\mu_h\big)}{2\rho_h}\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\left(\frac{2\mu_h\big(R_h - R_h^*\big)^2}{N_h} + \frac{N_h'\big(R_h - R_h^*\big)^2}{N_h^2}\right)$$

$$+ 2AN_h'\big(N_h - N_h^*\big) + 2B\rho_h\big(I_h - I_h^*\big)\big(R_h - R_h^*\big) - 2B\mu_h\big(R_h - R_h^*\big)^2.$$

Simplifying and canceling terms yields

$$
\begin{aligned}
L' = &- \frac{\mu_h\Big(\big(S_h - S_h^*\big) + \big(R_h - R_h^*\big)\Big)^2}{N_h} - \frac{\big(d_h + \mu_h\big)\big(I_h - I_h^*\big)^2}{N_h} \\
&+ \left(\frac{N_h^*\big(d_h + 2\mu_h\big)}{\beta_h\big(I_h^* + R_h^*\big)}\right)\left(\frac{\beta_{a_2} I_a^*\big(I_h - I_h^*\big)\big(S_h - S_h^*\big)}{N_a^* I_h^*}\right) \\
&- \left(\frac{N_h^*\big(d_h + 2\mu_h\big)}{\beta_h\big(I_h^* + R_h^*\big)}\right)\left(\frac{\beta_{a_2} I_a^* S_h\big(I_h - I_h^*\big)^2}{N_a^* I_h I_h^*} + \frac{\beta_h S_h^*\big(I_h - I_h^*\big)^2}{N_h^* N_h}\right) \\
&- \left(\frac{d_h + 2\mu_h}{2\rho_h}\right)\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\left(\frac{2\mu_h\big(R_h - R_h^*\big)^2}{N_h} + \frac{N_h'\big(R_h - R_h^*\big)^2}{N_h^2}\right) \\
&+ 2AN_h'\big(N_h - N_h^*\big) + 2B\rho_h\big(I_h - I_h^*\big)\big(R_h - R_h^*\big) - 2B\mu_h\big(R_h - R_h^*\big)^2.
\end{aligned}
$$

Then, using the same method as with the work shown in (3.13), we obtain

$$
\begin{aligned}
L' = &- \frac{\mu_h\Big(\big(S_h - S_h^*\big) + \big(R_h - R_h^*\big)\Big)^2}{N_h} - \frac{\big(d_h + \mu_h\big)\big(I_h - I_h^*\big)^2}{N_h} \\
&+ \left(\frac{N_h^*\big(d_h + 2\mu_h\big)}{\beta_h\big(I_h^* + R_h^*\big)}\right)\left(\frac{\beta_{a_2} I_a^*\big(I_h - I_h^*\big)\big(S_h - S_h^*\big)}{N_a^* I_h^*}\right) \\
&- \left(\frac{N_h^*\big(d_h + 2\mu_h\big)}{\beta_h\big(I_h^* + R_h^*\big)}\right)\left(\frac{\beta_{a_2} I_a^* S_h\big(I_h - I_h^*\big)^2}{N_a^* I_h I_h^*} + \frac{\beta_h S_h^*\big(I_h - I_h^*\big)^2}{N_h^* N_h}\right) \\
&- \left(\frac{d_h + 2\mu_h}{2\rho_h}\right)\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\left(\frac{2\mu_h\big(R_h - R_h^*\big)^2}{N_h} + \frac{N_h'\big(R_h - R_h^*\big)^2}{N_h^2}\right) \\
&- 2A\mu_h\Big(\big(S_h - S_h^*\big) + \big(R_h - R_h^*\big)\Big)^2 - 2A\big(d_h + 2\mu_h\big)\big(I_h - I_h^*\big)^2 \\
&- 2A\big(d_h + 2\mu_h\big)\big(S_h - S_h^*\big)\big(I_h - I_h^*\big) - 2A\big(d_h + 2\mu_h\big)\big(I_h - I_h^*\big)\big(R_h - R_h^*\big) \\
&+ 2B\rho_h\big(I_h - I_h^*\big)\big(R_h - R_h^*\big) - 2B\mu_h\big(R_h - R_h^*\big)^2.
\end{aligned}
$$

Next, we find $A, B > 0$.

$$-2A\big(d_h + 2\mu_h\big) + 2B\rho_h = 0$$

$$B\rho_h = A\big(d_h + 2\mu_h\big)$$

$$B = \frac{A\big(d_h + 2\mu_h\big)}{\rho_h},$$

$$\frac{N_h^*\big(d_h + 2\mu_h\big)}{\beta_h\big(I_h^* + R_h^*\big)}\left(\frac{\beta_{a_2} I_a^*}{N_a^* I_h^*}\right) - 2A\left(d_h + 2\mu_h\right) = 0$$

$$2A\left(d_h + 2\mu_h\right) = \frac{N_h^*\big(d_h + 2\mu_h\big)}{\beta_h\big(I_h^* + R_h^*\big)}\left(\frac{\beta_{a_2} I_a^*}{N_a^* I_h^*}\right),$$

$$A = \frac{N_h^*\beta_{a_2} I_a^*}{2\beta_h N_a^* I_h^*\big(I_h^* + R_h^*\big)},$$

$$B = \frac{N_h^*\beta_{a_2} I_a^*\big(d_h + 2\mu_h\big)}{2\rho_h\beta_h N_a^* I_h^*\big(I_h^* + R_h^*\big)}.$$

Using these constants, we have

$$\begin{aligned}
L' = &- \frac{\mu_h\Big(\big(S_h - S_h^*\big) + \big(R_h - R_h^*\big)\Big)^2}{N_h} - \frac{\big(d_h + \mu_h\big)\big(I_h - I_h^*\big)^2}{N_h} \\
&- \left(\frac{N_h^*\big(d_h + 2\mu_h\big)}{\beta_h\big(I_h^* + R_h^*\big)}\right)\left(\frac{\beta_{a_2} I_a^* S_h\big(I_h - I_h^*\big)^2}{N_a^* I_h I_h^*} + \frac{\beta_h S_h^*\big(I_h - I_h^*\big)^2}{N_h^* N_h}\right) \\
&- \left(\frac{d_h + 2\mu_h}{2\rho_h}\right)\left(1 + \frac{S_h^*}{I_h^* + R_h^*}\right)\left(\frac{2\mu_h\big(R_h - R_h^*\big)^2}{N_h} + \frac{N_h'\big(R_h - R_h^*\big)^2}{N_h^2}\right) \\
&- \frac{N_h^*\beta_{a_2} I_a^*\mu_h\Big(\big(S_h - S_h^*\big) + \big(R_h - R_h^*\big)\Big)^2}{\beta_h N_a^* I_h^*\big(I_h^* + R_h^*\big)} - \frac{N_h^*\beta_{a_2} I_a^*\big(d_h + 2\mu_h\big)\big(I_h - I_h^*\big)^2}{\beta_h N_a^* I_h^*\big(I_h^* + R_h^*\big)}
\end{aligned}$$

$$- \frac{N_h^* \beta_{a_2} I_a^* \left(d_h + 2\mu_h\right) \mu_h \left(R_h - R_h^*\right)^2}{\rho_h \beta_h N_a^* I_h^* \left(I_h^* + R_h^*\right)}.$$

Finally, since we assume $\mu_h \geq d_h$, it follows that

$$\begin{aligned}
&\frac{2\mu_h \left(R_h - R_h^*\right)^2}{N_h} + \frac{N_h' \left(R_h - R_h^*\right)^2}{N_h^2} \\
&\qquad = \frac{\left(2\mu_h N_h + N_h'\right)\left(R_h - R_h^*\right)^2}{N_h^2} \\
&\qquad = \frac{\left(2\mu_h \left(S_h + I_h + R_h\right) + \Lambda_h - \mu_h \left(S_h + I_h + R_h\right) - d_h I_h\right)\left(R_h - R_h^*\right)^2}{N_h^2} \\
&\qquad = \frac{\left(\mu_h \left(S_h + I_h + R_h\right) + \Lambda_h - d_h I_h\right)\left(R_h - R_h^*\right)^2}{N_h^2} \\
&\qquad = \frac{\left(\mu_h \left(S_h + R_h\right) + \Lambda_h + \left(\mu_h - d_h\right) I_h\right)\left(R_h - R_h^*\right)^2}{N_h^2} \\
&\qquad \geq 0.
\end{aligned}$$

Hence, L' is negative semi-definite in Ω_h, with $L' = 0$ if and only if $S_h = S_h^*$, $I_h = I_h^*$, and $R_h = R_h^*$. Thus the largest compact invariant set in $\left\{\left(S_h, I_h, R_h\right) \in \Omega_h : L' = 0\right\}$ is $\left\{E_h^*\right\}$, therefore, by the LaSalle invariance principle, $\left\{E_h^*\right\}$ is globally asymptotically stable in Ω_h [35, 36]. Now Corollary 3.1.1 implies that $\mathcal{E}_1$ is a globally asymptotically stable equilibrium of (2.1a)-(2.1f).

□

Note that our theorem shows that if the disease is endemic in the animal population, and $\beta_{a_2} > 0$, then irrespective of the reproductive number $\mathcal{R}_{0_h}$ the disease becomes endemic in the human population $\left(\text{if } \mu_h \geq d_h\right)$.

3.4 Stability of the Disease-free Equilibrium

The other equilibrium of the animal subsystem (2.1a)-(2.1c) is the disease-free equilibrium given by $E_a^0 = \left(S_a^0, I_a^0, R_a^0\right) = \left(\Lambda_a/\mu_a, 0, 0\right)$. By Theorem 2.3.2 we know that this equilibrium is globally asymptotically stable if $\mathcal{R}_{0_a} \leq 1$. In this case, $I_a(t) \to 0$ as $t \to \infty$, so in the limit there is no infection in the human population coming from the animal population. Thus, in the limit, dynamics in the human population become exactly the same as the general dynamics in the animal population, and Corollary 3.1.1 applies. Thus we have the following results.

Proposition 3.4.1. *Assume that $\mathcal{R}_{0_a} \leq 1$, so the disease dies out in the animal population. Additionally, let $\mathcal{R}_{0_h} \leq 1$. Then the disease-free equilibrium $\mathcal{E}_0 = \left(\Lambda_a/\mu_a, 0, 0, \Lambda_h/\mu_h, 0, 0\right)$ of (2.1a)-(2.1f) is globally asymptotically stable in Ω.*

Proposition 3.4.2. *Assume that $\mathcal{R}_{0_a} \leq 1$, $\mathcal{R}_{0_h} > 1$ and $\mu_h \geq d_h$. Then the equilibrium $\mathcal{E}_2 = \left(\Lambda_a/\mu_a, 0, 0, S_h^*, I_h^*, R_h^*\right)$ of (2.1a)-(2.1f) is globally asymptotically stable in Ω. $\left($Note that $\left(S_h^*, I_h^*, R_h^*\right)$ are given by the same expressions as (2.3)-(2.6) with the parameters corresponding to the human population.$\right)$*

3.5 Multiple Animal Populations

To finish this chapter, we now consider a scenario where there are multiple animal populations. In this scenario we assume there is no cross-infection between different animal populations. While this results in a fairly straight-forward extension of our results in the previous sections, it is conceivable that such a scenario exists when one group of people hunt multiple species of animals and each species lives in different locations and never cross paths.

Suppose there are n such animal populations, $A_1, A_2, \ldots, A_n$, and one human population denoted H. S_h, I_h, R_h, and N_h are defined as before with S_{a_i}, I_{a_i}, and R_{a_i} representing the susceptible, infected, and recovered individuals in population A_i, for $i = 1, 2, \ldots, n$, with the total number of individuals in population A_i being given as N_{a_i}. Susceptible individuals in A_i are recruited through

migration and birth at the rate Λ_{a_i} and susceptible individuals in H are recruited at a rate of Λ_h. We represent the death rates from disease in population A_i by d_{a_i} and the death rate by disease in population H as d_h. Further, we assume μ_{a_i}, μ_h are the natural death rates for A_i and H, respectively, and ρ_{a_i}, ρ_h are the recovery rates with permanent immunity for A_i and H, respectively. It is assumed that no one in the human population can infect any individual in any A_i population, while individuals in any A_i population can infect those in H on suitable contact. We assume there is no cross-infection between A_i and A_j when $i \neq j$. Disease transmission is modeled using standard incidence, assuming a constant (density-independent) contact rate both within and across the populations resulting in infection rates

$$f_{a_i}\left(S_{a_i}, I_{a_i}, R_{a_i}\right) = \frac{\beta_{a_i^1} I_{a_i}}{N_{a_i}} S_{a_i}, \text{ for } i = 1, 2, \ldots, n, \text{ and}$$

$$f_h\left(S_{a_1}, I_{a_1}, R_{a_1}, \ldots, S_{a_n}, I_{a_n}, R_{a_n}, S_h, I_h, R_h\right) = \left(\left(\sum_{i=1}^{n} \frac{\beta_{a_i^2} I_{a_i}}{N_{a_i}}\right) + \frac{\beta_h I_h}{N_h}\right) S_h,$$

where $\beta_{a_i^1}$ is the effective contact rate within population A_i, $\beta_{a_i^2}$ is the effective contact rate between populations A_i and H, and β_h is the effective contact rate within population H. For $i = 1, 2, \ldots, n$, we assume that $\Lambda_{a_i}, \Lambda_h, \mu_{a_i}, \mu_h, \rho_{a_i}$, and ρ_h are positive parameters and $d_{a_i}, d_h, \beta_{a_i^1}, \beta_{a_i^2}$, and β_h are non-negative parameters. Specifically, this leads to the following model. For $i = 1, 2, \ldots, n$,

$$\frac{dS_{a_i}}{dt} = \Lambda_{a_i} - \mu_{a_i} S_{a_i} - \frac{\beta_{a_i^1} I_{a_i}}{N_{a_i}} S_{a_i}, \tag{3.14a}$$

$$\frac{dI_{a_i}}{dt} = \frac{\beta_{a_i^1} I_{a_i}}{N_{a_i}} S_{a_i} - \left(\mu_{a_i} + \rho_{a_i} + d_{a_i}\right) I_{a_i}, \tag{3.14b}$$

$$\frac{dR_{a_i}}{dt} = \rho_{a_i} I_{a_i} - \mu_{a_i} R_{a_i}, \tag{3.14c}$$

$$\frac{dS_h}{dt} = \Lambda_h - \mu_h S_h - \left(\left(\sum_{i=1}^{n} \frac{\beta_{a_i^2} I_{a_i}}{N_{a_i}}\right) + \frac{\beta_h I_h}{N_h}\right) S_h, \tag{3.14d}$$

$$\frac{dI_h}{dt} = \left(\left(\sum_{i=1}^{n} \frac{\beta_{a_i^2} I_{a_i}}{N_{a_i}}\right) + \frac{\beta_h I_h}{N_h}\right) S_h - \left(\mu_h + \rho_h + d_h\right) I_h, \tag{3.14e}$$

$$\frac{dR_h}{dt} = \rho_h I_h - \mu_h R_h. \tag{3.14f}$$

For $i = 1, 2, \ldots, n$, let

$$\Omega_{a_i} = \left\{ \left(S_{a_i}, I_{a_i}, R_{a_i}\right) \in \mathbb{R}^3_+ : S_{a_i} \geq 0, I_{a_i} \geq 0, R_{a_i} \geq 0, S_{a_i} + I_{a_i} + R_{a_i} \leq \frac{\Lambda_{a_i}}{\mu_{a_i}} \right\}$$

and

$$\Omega_h = \left\{ \left(S_h, I_h, R_h\right) \in \mathbb{R}^3_+ : S_h \geq 0, I_h \geq 0, R_h \geq 0, S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h} \right\}.$$

Then for $i = 1, 2, \ldots, n$, the set $\tilde{\Omega} = \Omega_{a_1} \times \Omega_{a_2} \times \cdots \times \Omega_{a_n} \times \Omega_h$ is positively invariant under the dynamics of (3.14a)-(3.14f) and solutions with initial conditions in $\tilde{\Omega}$ exist globally.

Define $E^{(t)}_{a_i} := \left(S^{(t)}_{a_i}, I^{(t)}_{a_i}, R^{(t)}_{a_i}\right)$ and $E^e_{a_i} := \left(S^e_{a_i}, I^e_{a_i}, R^e_{a_i}\right)$ for $i = 1, 2, \ldots, n$. Depending on the parameters, $E^e_{a_i}$ is either the disease-free equilibrium or the endemic equilibrium. By the structure of the model in (3.14a)-(3.14f) — with animals uninfected by humans and each animal population independent, that is, unable to infect any other animal population — we have that $E^{(t)}_{a_i} \to E^e_{a_i}$ for $i = 1, 2, \ldots, n$, and each $E^e_{a_i}$ is globally asymptotically stable by Theorems 2.3.2 and 2.3.4 under appropriate conditions. Thus, it is straightforward to extend the results of the equilibrium analysis for (2.1a)-(2.1f) and we have the following corollary.

Corollary 3.5.1. *If there exists an $i \in 1, 2, \ldots, n$ such that $\mathcal{R}_{0_{a_i}} > 1, \mu_{a_i} \geq d_{a_i}$, and $\beta_{a_i^2} > 0$, and $\mu_h \geq d_h$, then the unique endemic equilibrium $\tilde{\mathcal{E}} = \left(E^e_{a_1}, \ldots, E^e_{a_n}, E^*_h\right)$ of (3.14a)-(3.14f) is globally asymptotically stable in the interior of $\tilde{\Omega}$.*

4 Numerical Results

We now present numerical results from simulations for the system in (2.1a)-(2.1f) and its extensions. We will present simulation results for the system (2.1a)-(2.1f) as it is, with constant values for all appropriate parameters, and we will present examples where β_{a_2} is no longer a constant, but a function of time. We also present scenarios with more than two populations. We will simulate a scenario with the system in (3.14a)-(3.14f) where we have have two animal populations and one human population. We further introduce a new system where there is one animal population and two interacting human populations. Finding and analyzing an endemic equilibrium for this last model is difficult, but we take the opportunity to show some simulation results for this system and discuss these results. Some of these results appeared in [37], but we present a more extensive study here.

4.1 Scenarios with One Animal Population and One Human Population

In this section we present some numerical results related to the model (2.1a)-(2.1f). Figure 4.1 shows the results of a numerical simulation of (2.1a)-(2.1f) using MATLAB's `ode45` and the parameters $\Lambda_a = 152500/3, \mu_a = 1/8, \rho_a = 1/20, d_a = 1/30, \Lambda_h = 2900/6, \mu_h = 1/6, \rho_h = 17/24, d_h = 1/8$ individuals per month and $\beta_h = 31/24$, $\beta_{a_1} = 3/8$, and $\beta_{a_2} = 41/120$ as the contact rates. The initial values used were $S_h^0 = 2000, I_h^0 = R_h^0 = R_a^0 = 0, S_a^0 = 30000$, and $I_a^0 = 1000$. These are artificial values and are used only for illustration purposes. Under these conditions, the endemic equilibrium of (2.1a)-(2.1f) is globally asymptotically stable.

In the proof of the global asymptotic stability for the co-existence endemic equilibrium, we assumed that $\mu_a \geq d_a$ and $\mu_h \geq d_h$. However, even if we ignore both of those conditions, the numerical results still seem to indicate that the co-existence endemic equilibrium of (2.1a)-(2.1f) is globally asymptotically stable. Figure 4.2 shows the results of a simulation of this kind, with

$\Lambda_a = 152500/3, \mu_a = 1/25, \rho_a = 1/20, d_a = 1/10, \Lambda_h = 2900/6, \mu_h = 1/9, \rho_h = 17/24, d_h = 1/6$ individuals per month and $\beta_h = 31/24$, $\beta_{a_1} = 3/8$, and $\beta_{a_2} = 41/120$ as the contact rates. The initial values used are the same as those in the previous set of results.

4.2 Dependence of Human Infection on the Infection in Each Population

Looking at the system (2.1a)-(2.1f) and revisiting our assumptions, the infection in the human population depends on infection in both populations. In Figure 4.3 we see the change in I_h^*/N_h^* as $\mathcal{R}_{0_a}$ changes. The values used for this figure were $\Lambda_a = 152500/3, \mu_a = 1/25, \rho_a = 1/20, d_a = 1/10, \Lambda_h = 2900/6, \mu_h = 1/9, \rho_h = 17/24, d_h = 1/6$ individuals per month, and $\beta_{a_2} = 0.3$. In order to get the change in $\mathcal{R}_{0_a}$ we use a range of β_{a_1} values; namely $0 \leq \beta_{a_1} \leq 1.9$. The initial values used were $S_h^0 = 2000, I_h^0 = R_h^h = R_a^0 = 0, S_a^0 = 3000$, and $I_a^0 = 1000$. (These values are simply for illustration purposes.) We notice that I_h^*/N_h^* increases after $\mathcal{R}_{0_a} = 1$. When $\beta_h = 1/3$ we have $\mathcal{R}_{0_h} \approx 0.338$ and when $\beta_h = 1/9$ we have $\mathcal{R}_{0_h} \approx 0.113$. Even if $\beta_h = 0$, when $\mathcal{R}_{0_a} \geq 1$, we see there is infection in the human population. Hence, limiting infection from humans to humans is not enough to fully mitigate this disease in humans. In all three curves there is a sharp increase in I_h^*/N_h^* for $1 \leq \mathcal{R}_{0_a} \leq 2$ so that the differences between the different I_h^*/N_h^* curves are nearly indistinguishable the closer $\mathcal{R}_{0_a}$ is to 1. While we do not know what β_{a_1} is in reality, this shows that if it is high enough for there to be endemic infection in the animal population, there will be some level of infection in the human population. This pattern mirrors the belief that it is impossible to eradicate monkeypox due to the endemic infection in animal populations [17, 31, 43, 48, 49].

Figure 4.4 uses the same parameters as in 4.3, but with $\beta_h \geq 1$. Specifically, $\beta_h = 1$ where $\mathcal{R}_{0_h} \approx 1.014$, $\beta_h = 1.5$ when we have $\mathcal{R}_{0_h} \approx 1.521$ and $\beta_h = 2$ when $\mathcal{R}_{0_h} \approx 2.028$. As expected, the increase in β_h results in higher values for I_h^*/N_h^* than in Figure 4.3. While difficult, it is important to continue studying monkeypox in both human and animal populations since infection in the animal population has a substantial impact on infection in the human population.

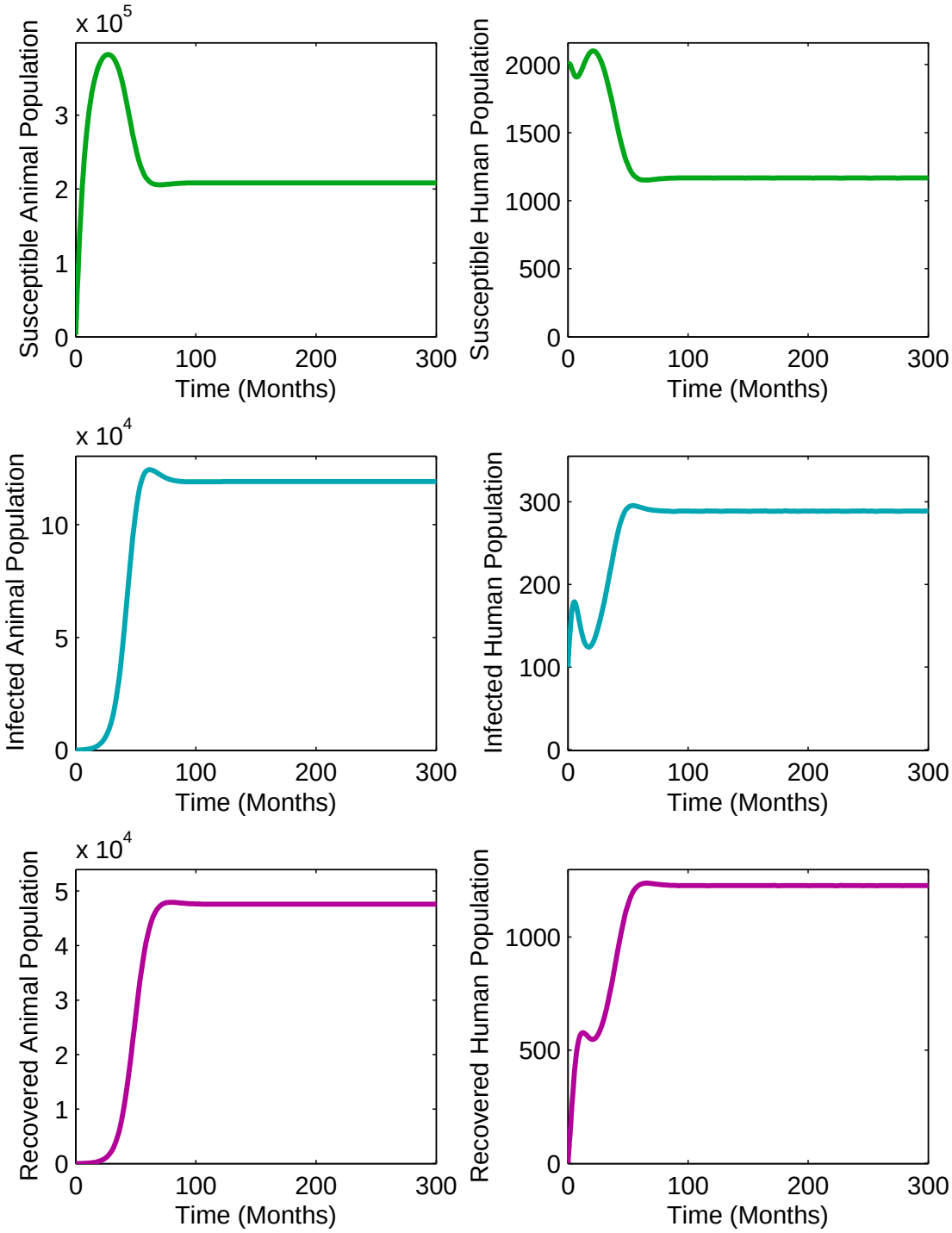

Figure 4.1: The above shows the results for a simulation with all parameters constant and the criteria for Theorem 3.3.1 met.

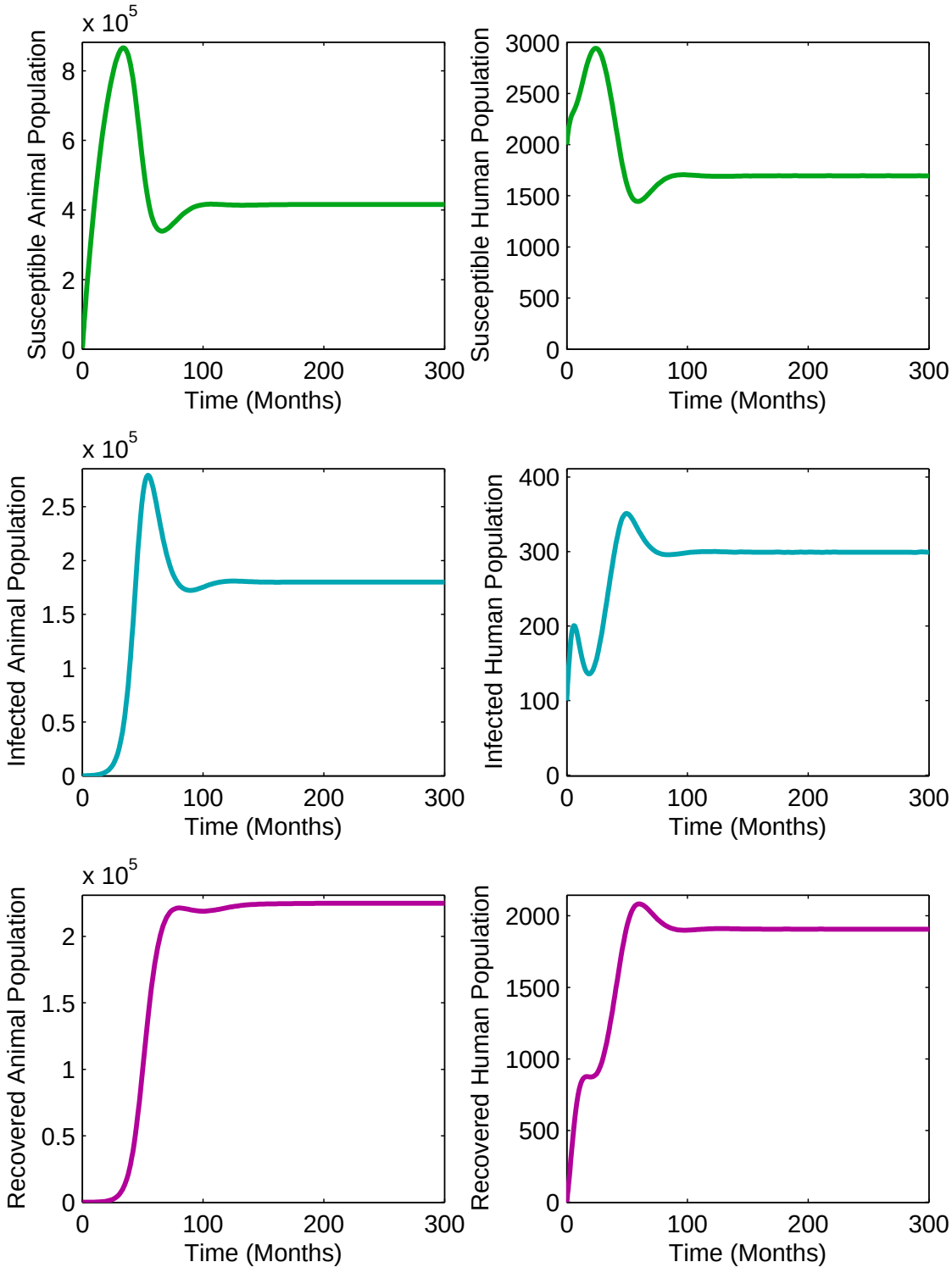

Figure 4.2: The results of a simulation with all parameters constant, but with $\mu_a < d_a$ and $\mu_h < d_h$.

In Figure 4.5, we use the same parameters as in Figure 4.3, but we consider I_a^*/N_a^* as a function of $\mathcal{R}_{0_a}$. Since we changed β_h to obtain three curves in Figure 4.3 but β_h has no role in the value of I_a^*/N_a^*, the curve in Figure 4.5 is the same regardless of β_h. We note that, as expected, changing $\mathcal{R}_{0_a}$ has a greater effect on I_a^*/N_a^* than it did on I_h^*/N_h^* reflected in Figure 4.3.

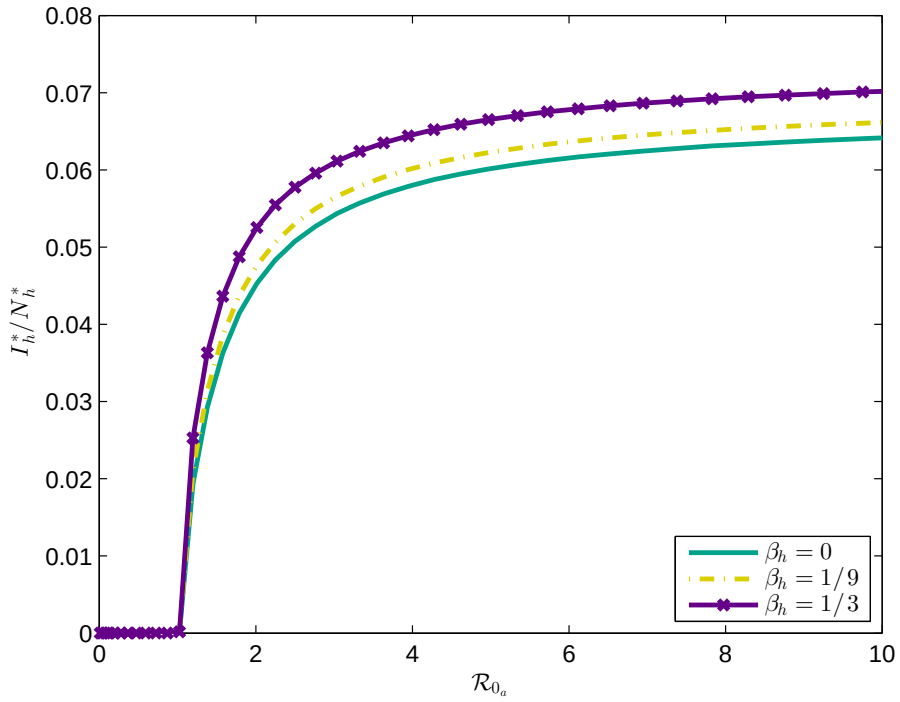

Figure 4.3: The above illustrates the ratio I_h^*/N_h^* as a function of $\mathcal{R}_{0_a}$. The lowest curve represents the case when $\beta_h = 0$ so we see that there is still infection in the human population as long as $\mathcal{R}_{0_a} > 1$.

We also know that changes in β_{a_2} impact the animal-to-human cross-infection. Figure 4.6 shows $\beta_{a_2} I_a^*/N_a^*$ as a function of $\mathcal{R}_{0_a}$ for the same values as in Figure 4.3 with $\beta_h = 0$. These results indicate that, as expected, controlling the disease in the human population also depends on reducing the value of β_{a_2}. Educating individuals in areas affected by monkeypox on how to recognize the symptoms of the disease can be useful in limiting the spread of monkeypox from person-to-person [10, 14, 11, 66]. However, the results presented here indicate that we have to continue to take measures to minimize β_{a_2}. Educating people on how the symptoms of monkeypox present in the animals they interact with and hunt, and on the proper handling of infected animals is crucial in limiting the spread of this disease among humans.

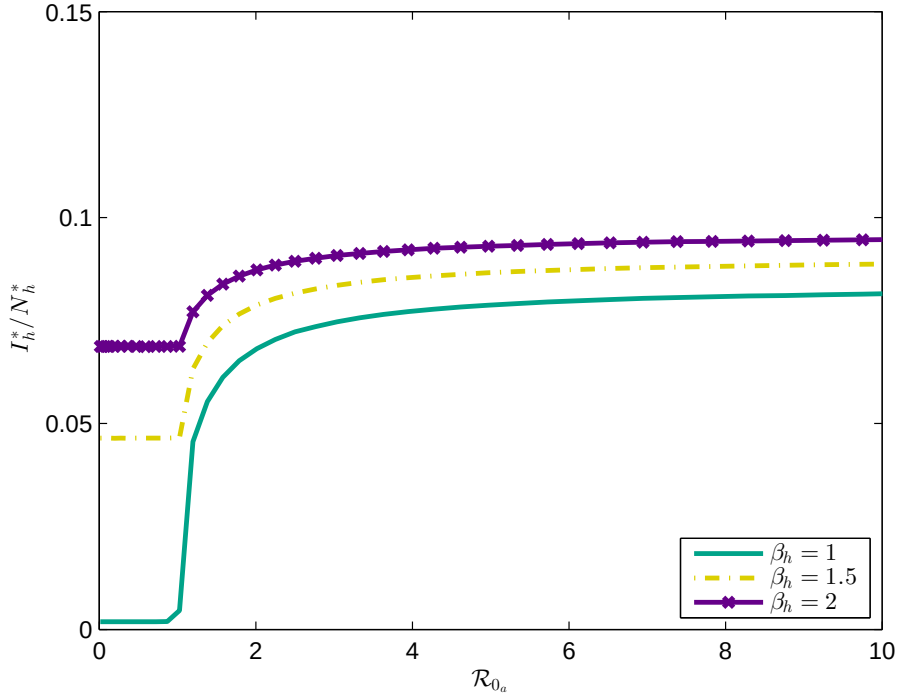

Figure 4.4: The above illustrates the ratio I_h^*/N_h^* as a function of $\mathcal{R}_{0_a}$ for $\mathcal{R}_{0_h} > 1$.

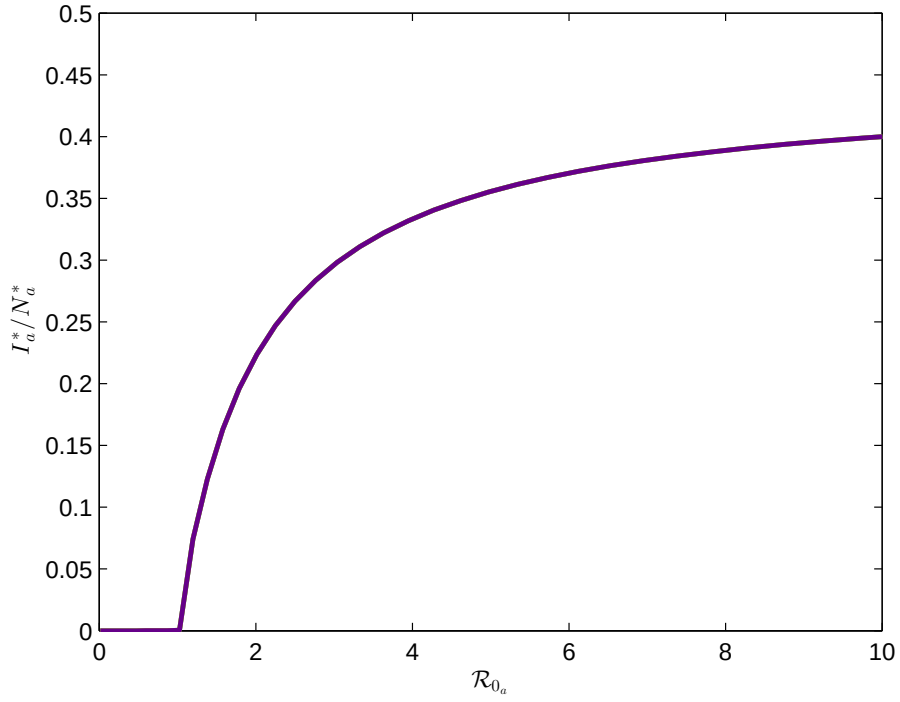

Figure 4.5: The above illustrates I_a^*/N_a^* as a function of $\mathcal{R}_{0_a}$.

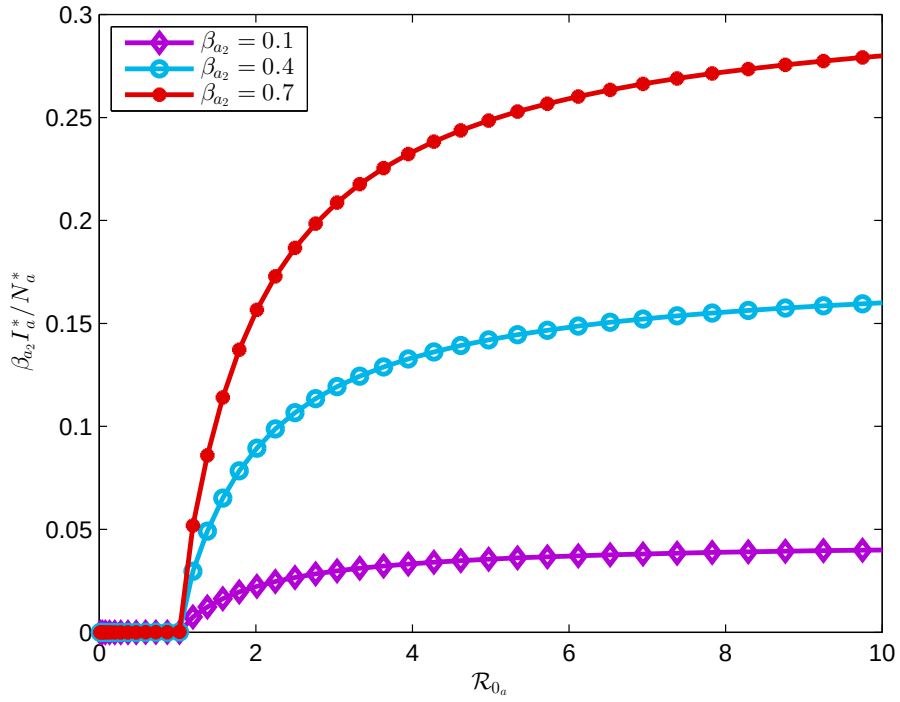

Figure 4.6: The above illustrates $\beta_{a_2} I_a^* / N_a^*$ as a function of $\mathcal{R}_{0_a}$ for three different values of β_{a_2} with $\beta_h = 0$.

4.3 Simulations with β_{a_2} as a Function of Time

Since there is no longer any vaccination against smallpox and this vaccine provided partial immunity against monkeypox, there is waning herd immunity against monkeypox [28, 38, 40, 43, 47, 49, 50, 51]. Thus, in this next example, we assume that as time goes on there is an increasing likelihood that a human will get infected when they come into contact with an infected animal. For this simulation, we use $\beta_{a_2}(t) = \left(1 + 9e^{-t}\right)^{-1}$. Figure 4.7 shows the results of a numerical simulation with this $\beta_{a_2}(t)$ and all other parameters the same as for Figure 4.1. The analysis for our asymptotically autonomous system is still valid because $\beta_{a_2}(t) \to 1$ as $t \to \infty$ and so if we define $g(t) := \beta_{a_2}(t) I_a(t) / N_a(t)$, then $g(t) \to I_a^e / N_a^e$ as $t \to \infty$. Since $\beta_{a_2} \to 1$, it makes sense that Figure 4.7 shows the system approaching a higher I_h^* value than in Figure 4.1.

We are also interested in modeling seasonal oscillations in monkeypox. Figure 4.8 shows the results of a simulation of the system (2.1a)-(2.1f) but with $\beta_{a_2}(t) = \left(\xi_2 - \xi_1\right) \sin(2\pi n t)$ where $\xi_2 = 0.8$,

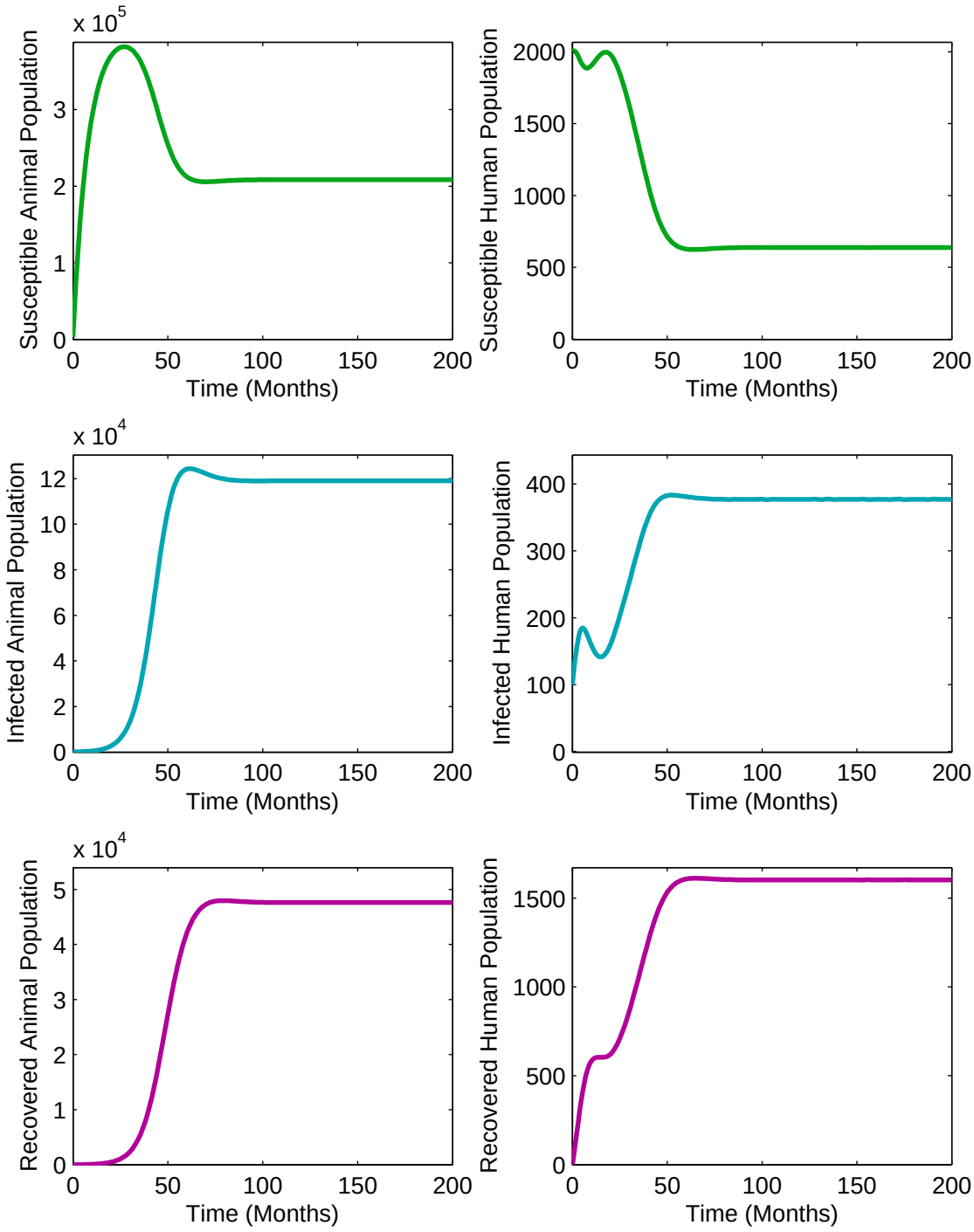

Figure 4.7: The results for a simulation with all parameters constant except $\beta_{a_2}(t)$ which is an increasing function of time.

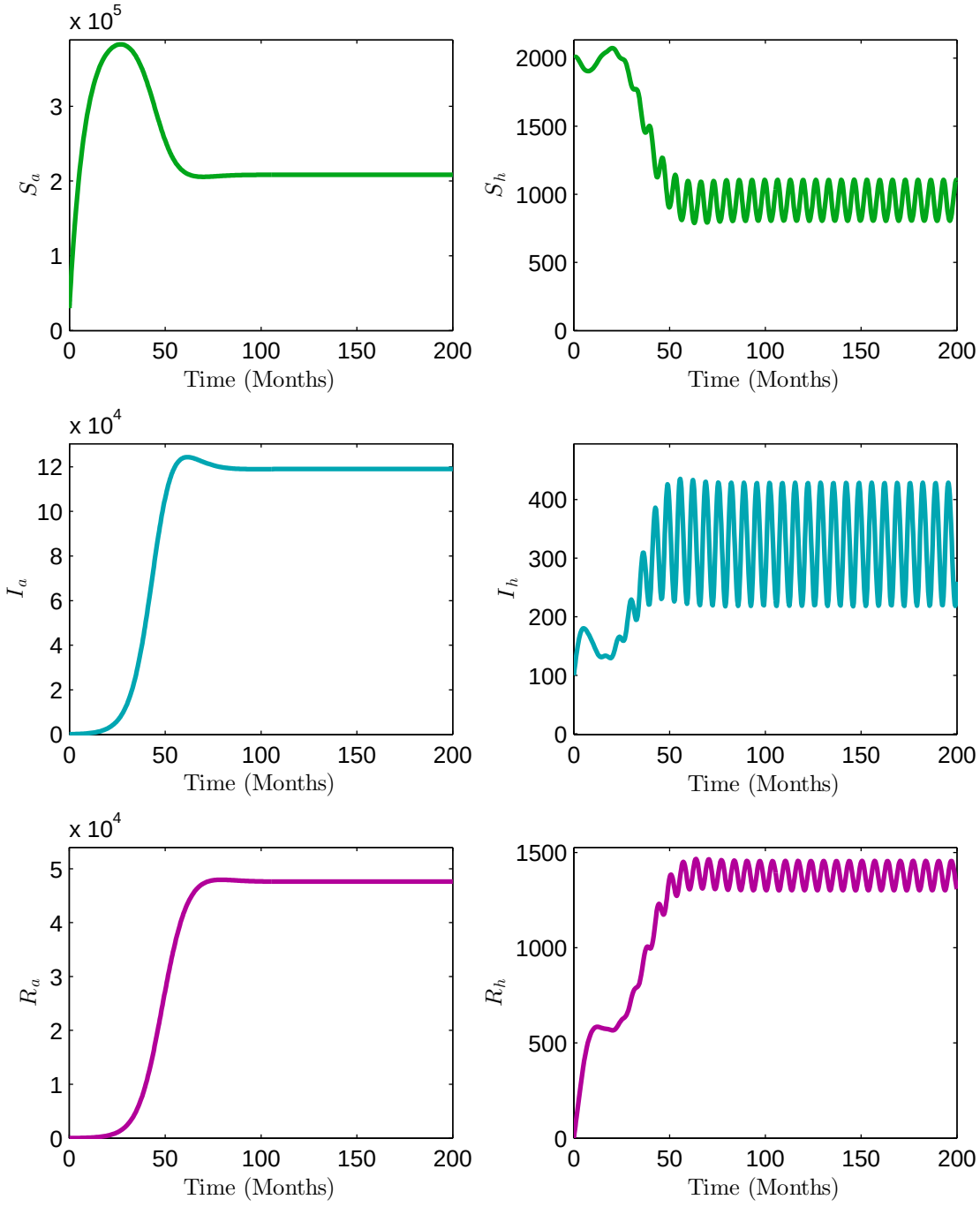

Figure 4.8: The results for a simulation with all parameters constant except $\beta_{a_2}(t)$ is the sinusoidal function of time graphed in Figure 4.9.

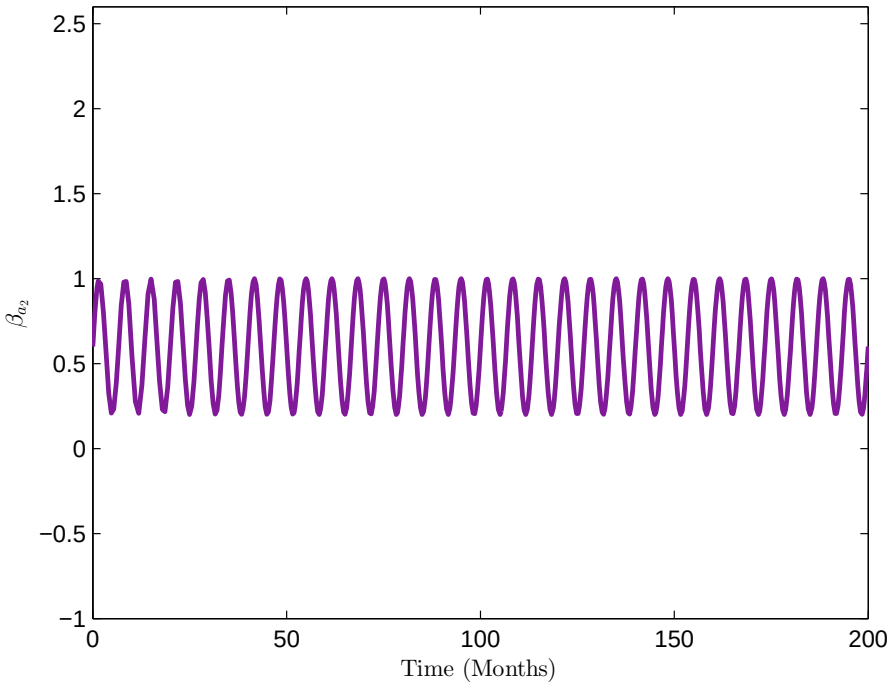

Figure 4.9: A graph of $\beta_{a_2}(t) = \left(\xi_2 - \xi_1\right) \sin(2\pi nt)$ where $n = 0.15$, $\xi_2 = 0.8$ and $\xi_1 = 0.1$. This was used to help create Figure 4.8.

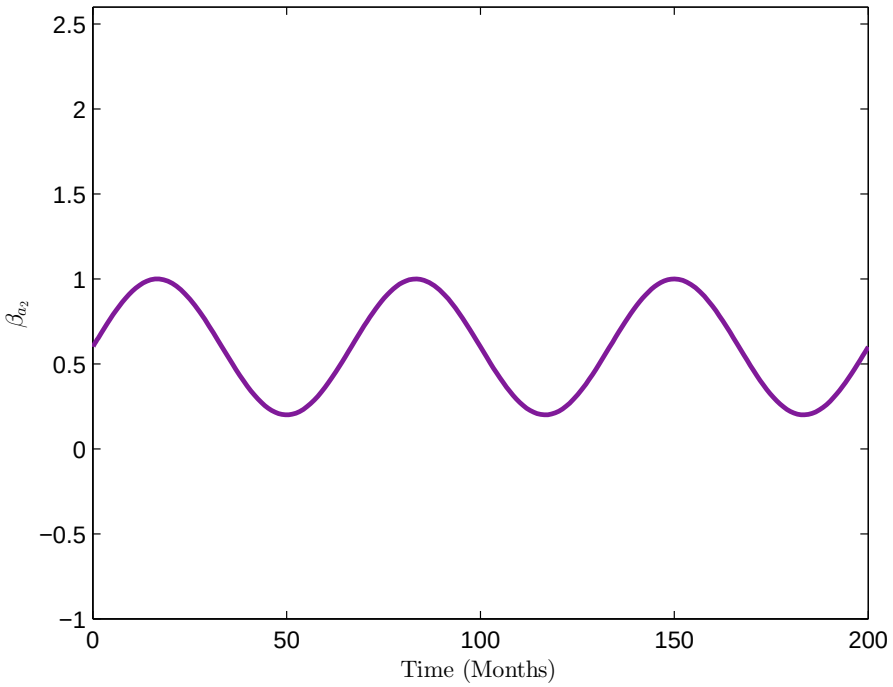

Figure 4.10: A graph of $\beta_{a_2}(t) = \left(\xi_2 - \xi_1\right) \sin(2\pi nt)$ where $n = 0.015$, $\xi_2 = 0.8$ and $\xi_1 = 0.1$. This was used to help create Figure 4.11.

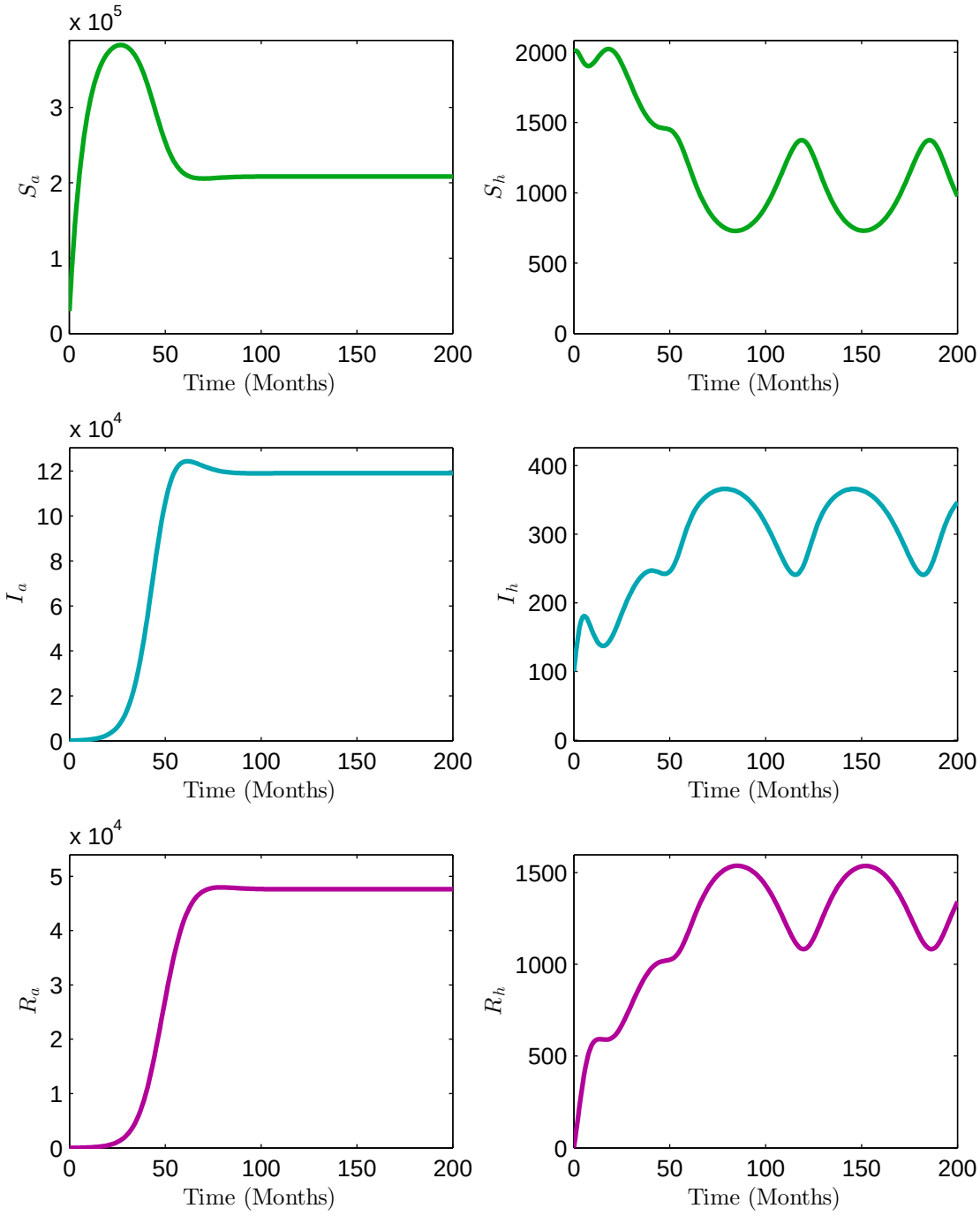

Figure 4.11: The results for a simulation with all parameters constant except $\beta_{a_2}(t)$ is the sinusoidal function of time graphed in Figure 4.10.

$\xi_1 = 0.1$, and $n = 0.15$. Figure 4.9 shows a graph of this $\beta_{a_2}(t)$ function. For the system, we have initial conditions $S_a^0 = 30000, I_a^0 = 100, R_a^0 = 0, S_h^0 = 2000, I_h^0 = 100$, and $R_h^0 = 0$ and parameters $\Lambda_h = 2900/6, \mu_h = 1/6, \rho_h = 17/24, d_h = 1/8, \Lambda_a = 152500/3, \mu_a = 1/8, \rho_a = 1/20$, $d_a = 1/30, \beta_{a_1} = 3/8$, and $\beta_h = 31/24$. In order to see a similar situation but with a longer period, Figure 4.11 shows the results of a simulation using the same conditions as in Figure 4.8 but with $n = 0.015$.

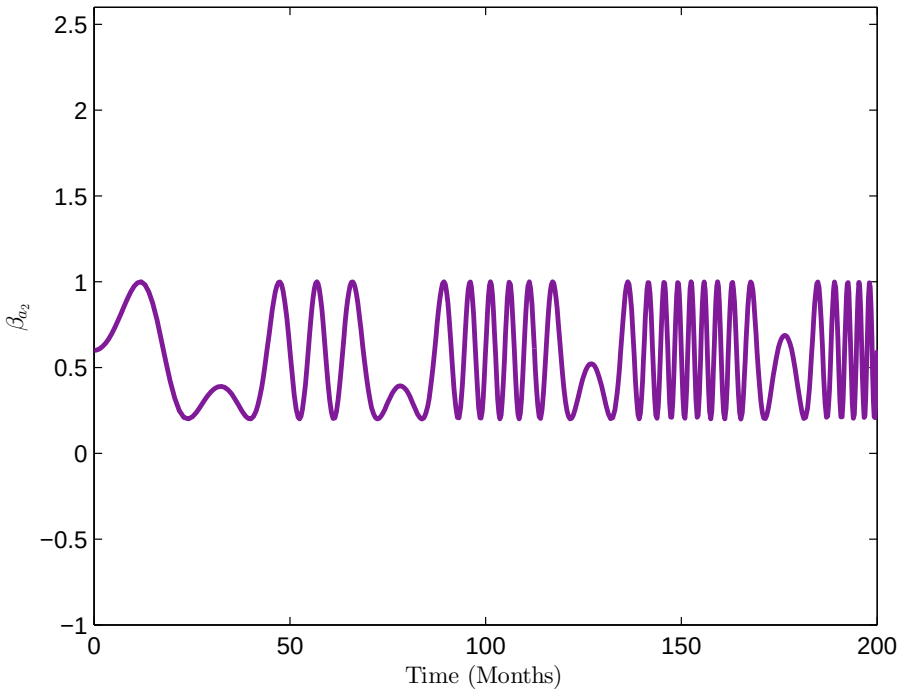

Figure 4.12: A graph of $\beta_{a_2}(t) = \left(\xi_2 - \xi_1\right) \sin(2\pi nt \sin(2\pi mt))$ where $n = 0.315$, $m = 0.01$, $\xi_2 = 0.8$ and $\xi_1 = 0.1$.

As an interesting example, we take this idea further and suppose there is some kind of oscillating behavior, but not it's as direct as in the previous examples. Let $\beta_{a_2}(t) = \left(\xi_2 - \xi_1\right) \sin\left(2\pi nt \sin\left(2\pi mt\right)\right)$ with $\xi_2 = 0.8$, $\xi_1 = 0.1$, $n = 0.315$, and $m = 0.01$. A graph of this $\beta_{a_2}(t)$ is shown in Figure 4.12 and the resulting dynamics of the system are illustrated in Figure 4.13.

Although these examples are only for illustration purposes, with more data we could attempt to find appropriate parameters. It would probably be much easier to find more data from the human population than it is from the animal populations. The fact that we don't even have a complete

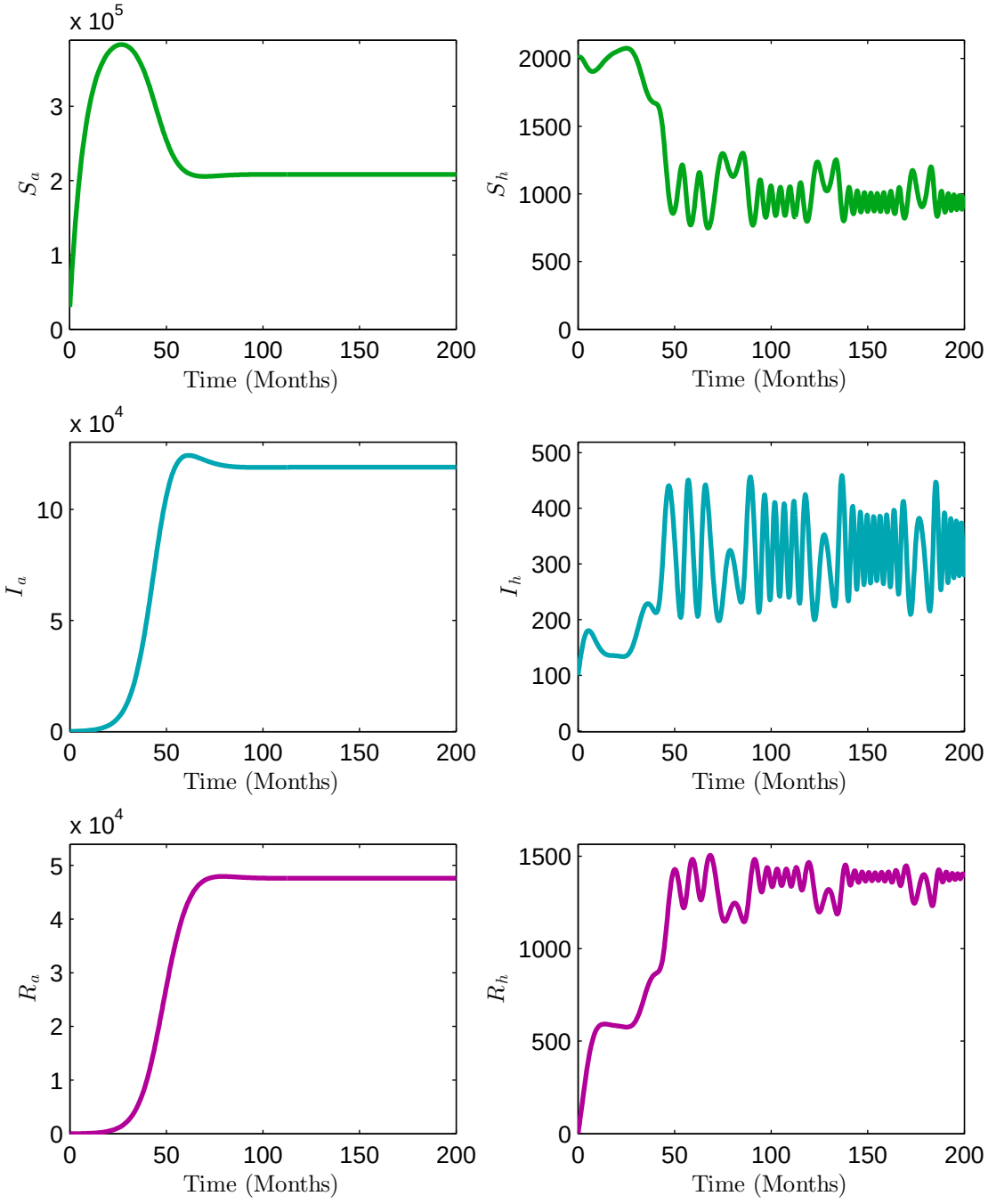

Figure 4.13: The results for a simulation with all parameters constant except that $\beta_{a_2}(t)$ is an oscillating function of time.

list of species affected by monkeypox [48] makes obtaining data among animal populations seem almost impossible, but it would be incredibly helpful to know which species most frequently infect humans and try to find a way to understand how monkeypox impacts those animal populations.

4.4 Multi-host and Meta-population Models

Meta-population models and multi-host models are used for modeling epidemic outbreaks and were also brought into consideration [3, 7, 18, 19, 22, 46, 47, 52, 54, 55, 56]. We simulated an epidemic with multiple animal populations and a single human population. Figure 4.14 shows the results of an epidemic simulation with two animal populations and one human population as given in (3.14a)-(3.14f) for the case of $i = 2$. The initial values used for this simulation are $S^0_{a_1} = 3000$, $I^0_{a_1} = 100$, $S^0_{a_2} = 2500$, $I^0_{a_2} = 40$, $S^0_h = 2000$, $I^0_h = 100$, and $R^0_{a_1} = R^0_{a_2} = R^0_h = 0$. The contact rates are $\beta_{a_1^1} = 1/4$, $\beta_{a_1^2} = 1/9$, $\beta_{a_2^1} = 1/8$, $\beta_{a_2^2} = 1/11$, and $\beta_h = 31/24$. The parameter values, with units of individuals per month, are $\Lambda_h = 2900/6$, $\mu_h = 1/6$, $\rho_h = 17/24$, $d_h = 1/8$, $\Lambda_{a_1} = 152500/2$, $\mu_{a_1} = 1/8$, $\rho_{a_1} = 1/20$, $d_{a_1} = 1/30$, $\Lambda_{a_2} = 500$, $\mu_{a_2} = 1/25$, $\rho_{a_2} = 1/10$, and $d_{a_2} = 1/30$.

Figure 4.15 uses all of the same parameters as for the example shown in 4.14 with the exception that $\beta_h = 0$ and $I^0_h = 0$. Although no humans are infected at the start of the simulation and no humans can be infected by other humans in this scenario, the infection still spreads to humans from the animal population. This may seem like an extreme example since we expect that humans can infect each other, but it again highlights how difficult it would be to eradicate monkeypox entirely, and that is seen numerically in these simulations. As long as animals can infect humans, the disease will persist.

Figure 4.16 takes the results of Figure 4.15 one step further. We add the requirement that $\beta_{a_2^2} = 0$ so that there is no infection spread between humans or from A_2 to humans. We imagine this is a situation where humans take steps to stop human-to-human infection and avoid interacting with some known animal carriers of monkeypox, but still interact with some other animal species that

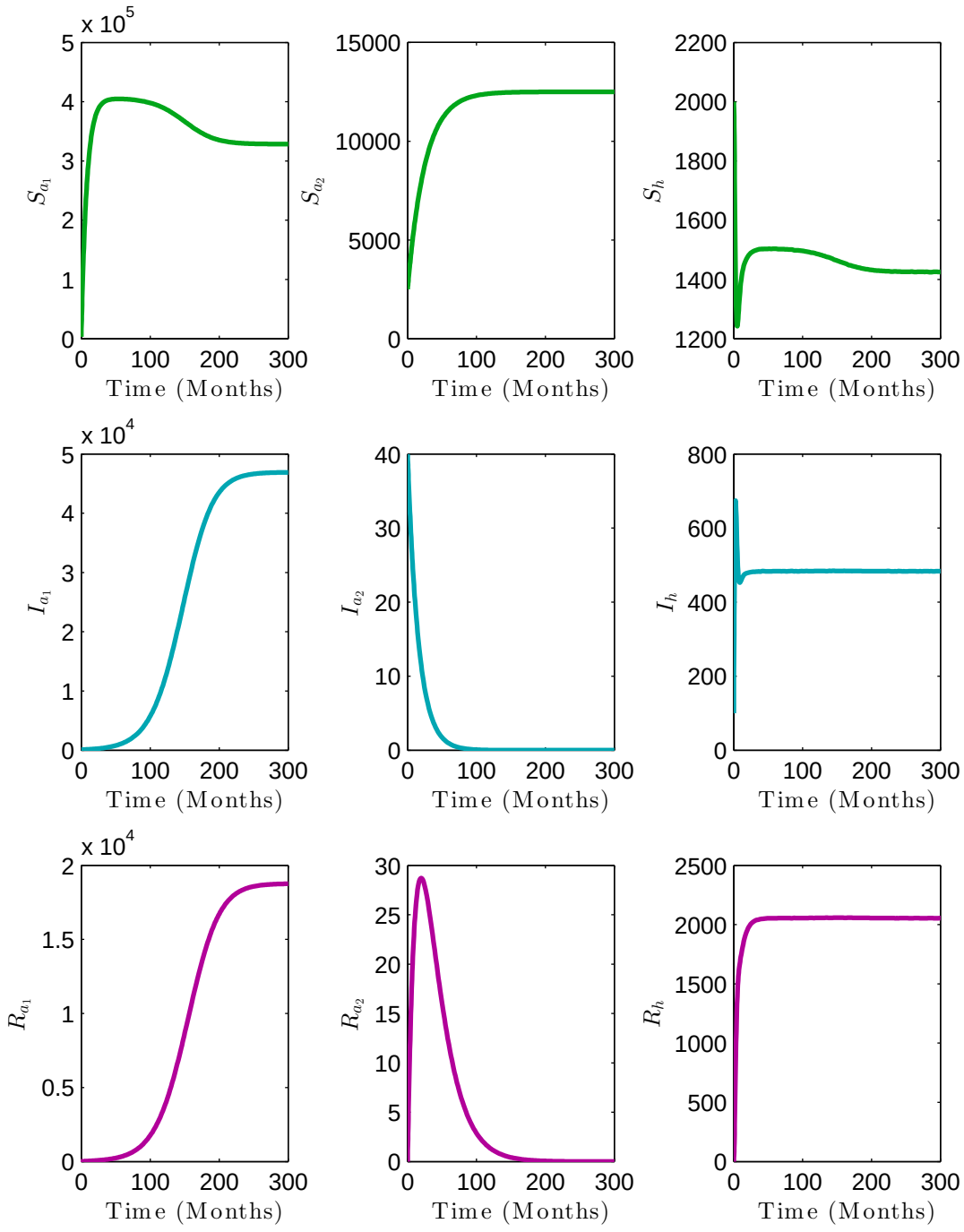

Figure 4.14: The results of a simulation with two animal populations as in (3.14a)-(3.14f) for $i = 2$. The first two columns show the results for populations A_1 and A_2, respectively. The last column shows the results for the human population.

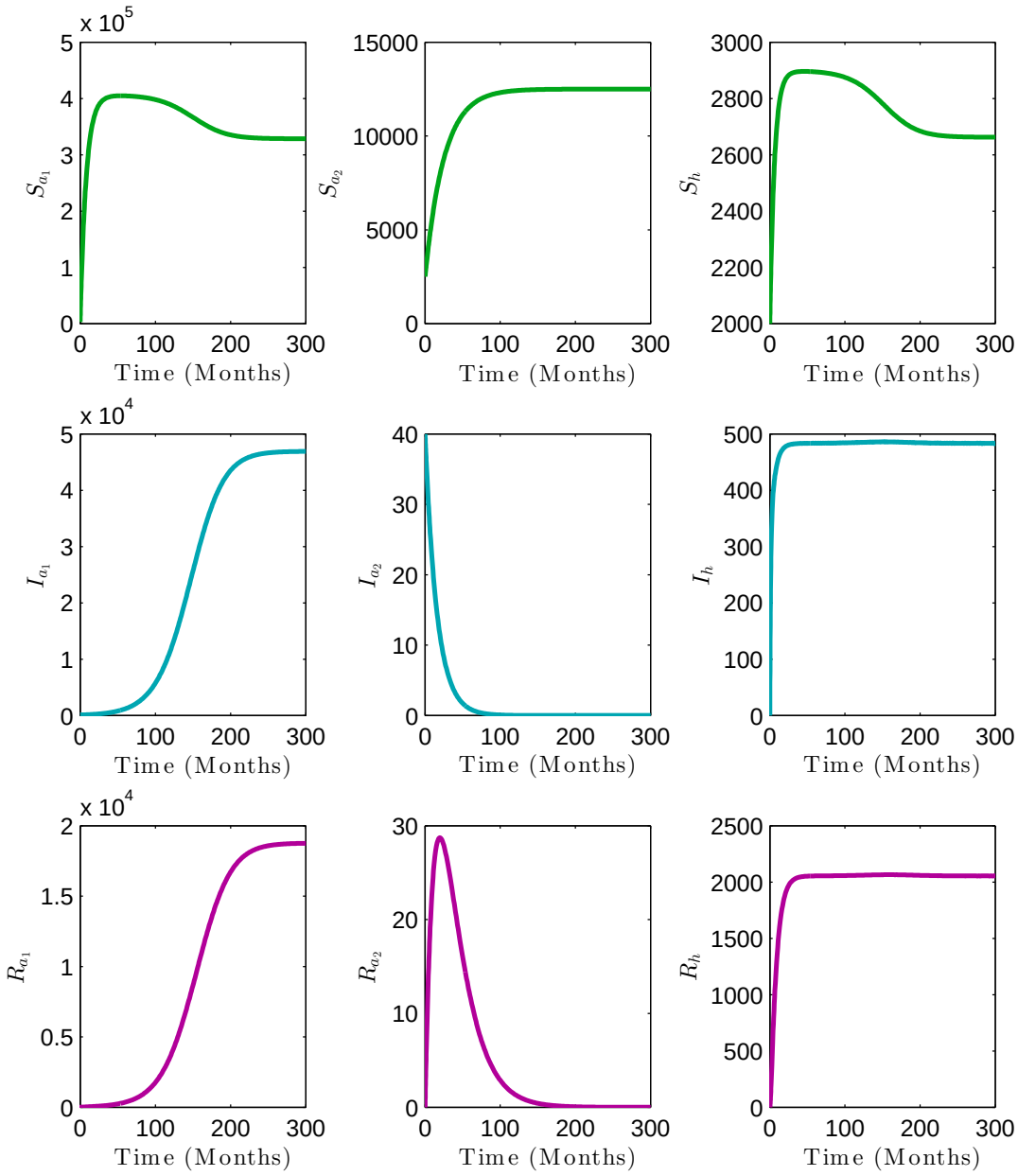

Figure 4.15: The results of a simulation with two animal populations as in (3.14a)-(3.14f) for $i = 2$. These results only differ from Figure 4.14 in that humans can only be infected through contact with animals and $I_h^0 = 0$.

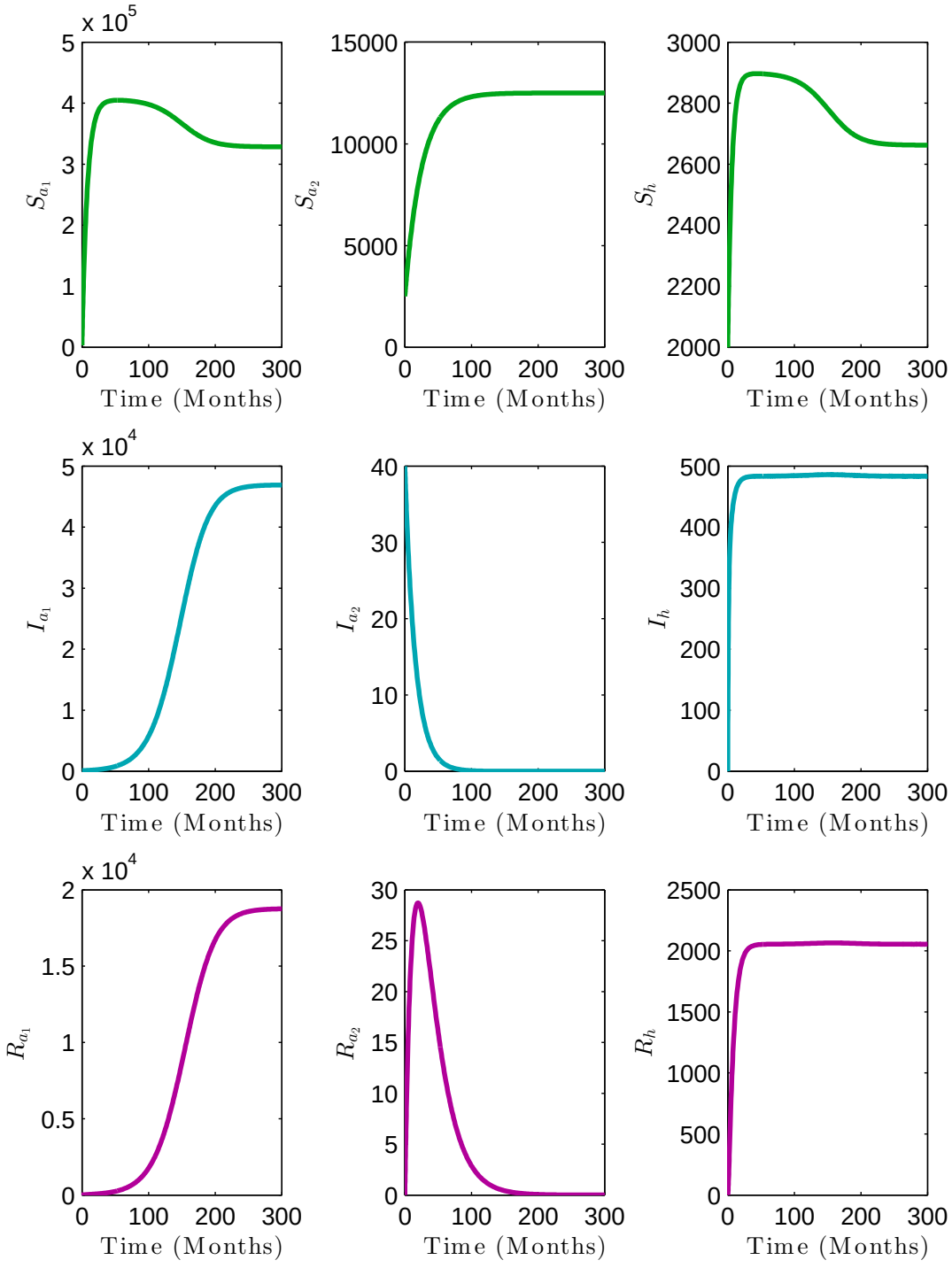

Figure 4.16: The results of a simulation with two animal populations as in (3.14a)-(3.14f) for $i = 2$. These results only differ from Figure 4.14 in that humans can only be infected through contact with animals in A_1 and $I_h^0 = 0$.

carry monkeypox – possibly without knowing it. We see that even though humans can only be infected from animals in A_1 the infection persists. As mentioned earlier, we only know some of the animals that can be infected by monkeypox and these results indicate that even if those different species of animals do not interact, even if infection is eradicated in some animal species, and even if humans cannot spread it among each other, all this is not enough to completely prevent monkeypox in the human population.

For another example of a meta-population model, we divided the human population into subpopulations, assume there is movement of individuals between these human subpopulations and assume that they all have contact with one large animal population with endemic monkeypox infection. We can imagine these human subpopulations represent distinct villages that use the same area to hunt for food. This scenario is particularly difficult to study analytically. Due to the interaction between the human subpopulations, finding a Lyapunov function to prove the global asymptotic stability of the endemic equilibrium is difficult. Regardless, we can still study this situation numerically.

Consider the following system of nine differential equations:

$$\frac{dS_a}{dt} = \Lambda_a - \left(\mu_a + \frac{\beta_a I_a}{N_a}\right) S_a, \tag{4.1a}$$

$$\frac{dI_a}{dt} = \frac{\beta_a I_a}{N_a} S_a - \left(\mu_a + \rho_a + d_a\right) I_a, \tag{4.1b}$$

$$\frac{dR_a}{dt} = \rho_a I_a - \mu_a R_a, \tag{4.1c}$$

$$\frac{dS_{h_1}}{dt} = \Lambda_{h_1} - \left(\mu_{h_1} + \frac{\beta_{a_1} I_a}{N_a} + \frac{\beta_{h_1^1} I_{h_1}}{N_{h_1}} + \frac{\beta_{h_1^2} I_{h_2}}{N_{h_2}}\right) S_{h_1}, \tag{4.1d}$$

$$\frac{dI_{h_1}}{dt} = \left(\frac{\beta_{a_1} I_a}{N_a} + \frac{\beta_{h_1^1} I_{h_1}}{N_{h_1}} + \frac{\beta_{h_1^2} I_{h_2}}{N_{h_2}}\right) S_{h_1} - \left(\mu_{h_1} + \rho_{h_1} + d_{h_1}\right) I_{h_1}, \tag{4.1e}$$

$$\frac{dR_{h_1}}{dt} = \rho_{h_1} I_{h_1} - \mu_{h_1} R_{h_1} \tag{4.1f}$$

$$\frac{dS_{h_2}}{dt} = \Lambda_{h_2} - \left(\mu_{h_2} + \frac{\beta_{a_2} I_a}{N_a} + \frac{\beta_{h_2^1} I_{h_1}}{N_{h_1}} + \frac{\beta_{h_2^2} I_{h_2}}{N_{h_2}}\right) S_{h_2}, \tag{4.1g}$$

$$\frac{dI_{h_2}}{dt} = \left(\frac{\beta_{a_2} I_a}{N_a} + \frac{\beta_{h_2^1} I_{h_1}}{N_{h_1}} + \frac{\beta_{h_2^2} I_{h_2}}{N_{h_2}}\right) S_{h_2} - \left(\mu_{h_2} + \rho_{h_2} + d_{h_2}\right) I_{h_2}, \tag{4.1h}$$

$$\frac{dR_{h_2}}{dt} = \rho_{h_2} I_{h_2} - \mu_{h_2} R_{h_2}. \tag{4.1i}$$

This models a population of animals divided into susceptible, infected, and recovered individuals, denoted S_a, I_a, and R_a, respectively, the first population of humans divided into susceptible, infected and recovered individuals, denoted S_{h_1}, I_{h_1}, and R_{h_1}, respectively, and a second separate population of humans divided into susceptible, infected, and recovered individuals, denoted S_{h_2}, I_{h_2}, and R_{h_2}, respectively. The total number of individuals in the first human population is given as $N_{h_1}(t) = S_{h_1}(t) + I_{h_1}(t) + R_{h_1}(t)$, the total number of individuals in the second human population is given as $N_{h_2}(t) = S_{h_2}(t) + I_{h_2}(t) + R_{h_2}(t)$, and the total animal population is given as $N_a(t) = S_a(t) + I_a(t) + R_a(t)$. For simplicity, from now on we call the first human population H_1 and the second human population H_2. In H_1, susceptible humans are recruited through migration and birth at the rate Λ_{h_1}, susceptible humans in H_2 are recruited through migration and birth at the rate Λ_{h_2}, and susceptible animals are recruited at a rate of Λ_a. Let d_a, d_{h_1}, and d_{h_2} be the death rates by monkeypox for the animals, H_1, and H_2, respectively, μ_a, μ_{h_1}, and μ_{h_2} be the natural death rates for the animals, H_1, and H_2, respectively, and ρ_a, ρ_{h_1}, and ρ_{h_2} be the recovery with permanent immunity for the animals, H_1, and H_2, respectively. It is assumed that hunting of animals by humans is negligible and can be ignored and that animals cannot become infected by humans.

Disease transmission is modeled using standard incidence, assuming a constant (density-independent) contact rate both within and across the populations resulting in infection rates

$$f_a\left(S_a, I_a, R_a\right) = \frac{\beta_a I_a}{N_a} S_a,$$

$$f_{h_1}\left(S_a, I_a, R_a, S_{h_1}, I_{h_1}, R_{h_1}, S_{h_2}, I_{h_2}, R_{h_2}\right) = \left(\frac{\beta_{a_1} I_a}{N_a} + \frac{\beta_{h_1^1} I_{h_1}}{N_{h_1}} + \frac{\beta_{h_1^2} I_{h_2}}{N_{h_2}}\right) S_{h_1}, \text{ and}$$

$$f_{h_2}\left(S_a, I_a, R_a, S_{h_1}, I_{h_1}, R_{h_1}, S_{h_2}, I_{h_2}, R_{h_2}\right) = \left(\frac{\beta_{a_2} I_a}{N_a} + \frac{\beta_{h_2^1} I_{h_1}}{N_{h_1}} + \frac{\beta_{h_2^2} I_{h_2}}{N_{h_2}}\right) S_{h_2},$$

where β_a is the effective contact rate within the animal population, β_{a_1} is the effective contact rate between the animal population and H_1, $\beta_{h_1^1}$ is the effective contact rate within H_1, $\beta_{h_1^2}$ is the effective contact rate between individuals in H_2 affecting those in H_1, β_{a_2} is the effective contact rate between the animal population and H_2, $\beta_{h_2^1}$ is the effective contact rate between individuals in H_1 affecting those in H_2 and $\beta_{h_2^2}$ is the effective contact rate within H_2. We assume all parameters are non-negative.

Figure 4.17 shows the results of a numerical simulation of the model in (4.1a)-(4.1i). The initial values used were $S_a^0 = 30000$, $I_a^0 = 1000$, $S_{h_1}^0 = 2000$, $S_{h_2}^0 = 3000$, and $R_a^0 = I_{h_1}^0 = R_{h_1}^0 = I_{h_2}^0 = R_{h_2}^0 = 0$. The associated contact values are $\beta_a = 3/8$, $\beta_{a_1} = 41/120$, $\beta_{a_2} = 31/24$, $\beta_{h_1^1} = 41/120$, $\beta_{h_2^1} = 5/12$, $\beta h_1^2 = 1/8$, and $\beta_{h_2^2} = 13/40$. The other parameters used, in individuals per month, were $\Lambda_a = 152500/3$, $\Lambda_{h_1} = 1450/3$, $\Lambda_{h_2} = 500/3$, $\mu_a = 1/8$, $\mu_{h_1} = 1/6$, $\mu_{h_2} = 1/3$, $\rho_a = 1/20$, $\rho_{h_1} = 17/24$, $\rho_{h_2} = 13/24$, $d_a = 1/30$, $d_{h_1} = 1/8$, and $d_{h_2} = 1/9$. This shows that even in the meta-population, although no humans in either population are infected at the beginning of the simulation, infection from the animals is enough to cause endemic infection in all three populations.

4.5 Summation

In the systems (2.1a)-(2.1f), (3.14a)-(3.14f), and (4.1a)-(4.1i), there is cross-infection from at least one animal population into a human population. As we have noted, it is believed that it would be impossible to eradicate monkeypox due to the endemic infection in animal populations and the necessary interactions between humans and animals. Our numerical results show that, even when there is no infection between humans, the animal infection does indeed cause endemic infection in both populations in this model. It is clear that more data and information is needed in order to approximate parameter values so that the system (2.1a)-(2.1f) more accurately model monkeypox.

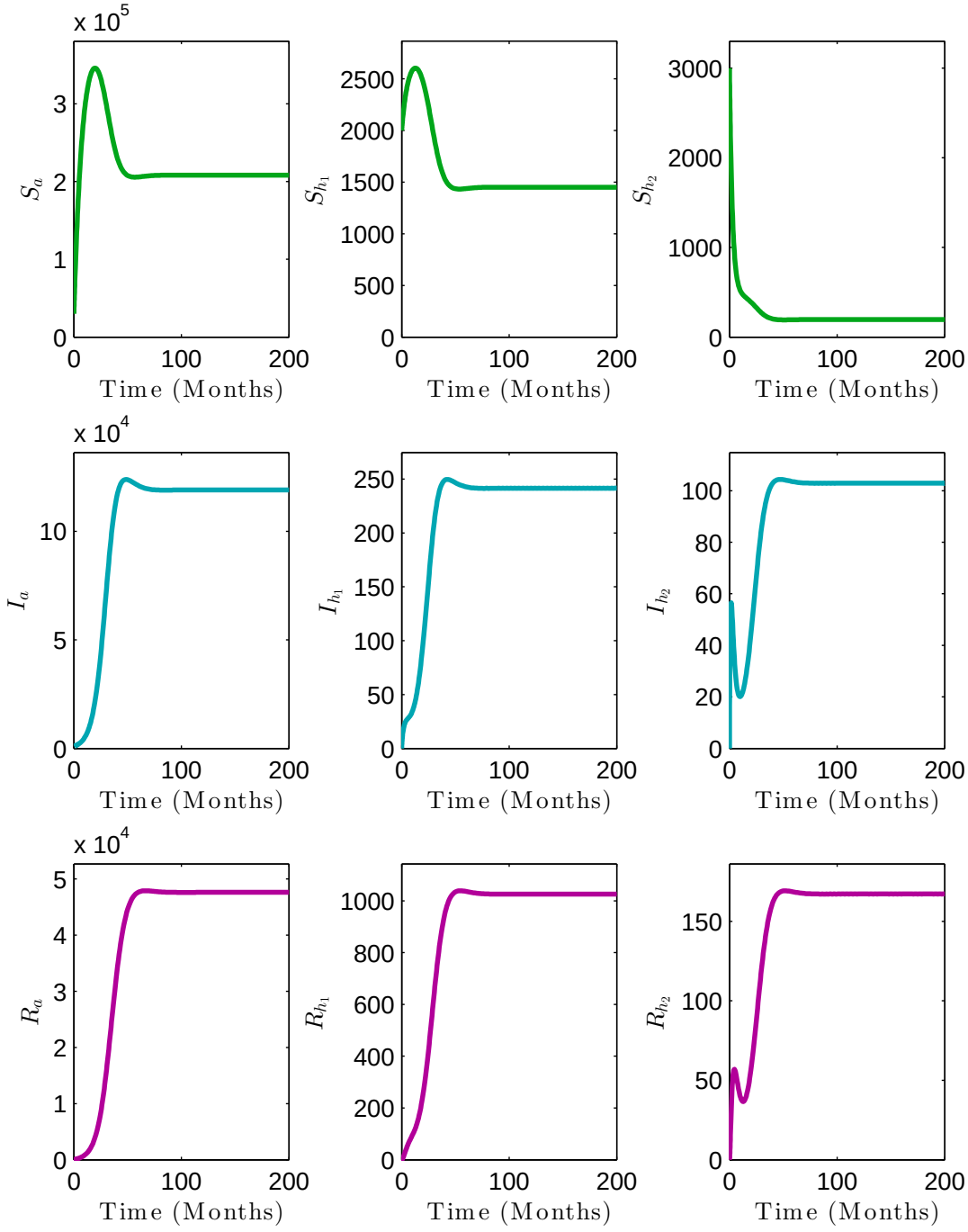

Figure 4.17: Column 1 shows the results for the animal population, the second column shows the results for population H_1 and the last column shows the results for H_2.

5 A Brief Discussion of Cellular Automata Models

Although different from the system of differential equations, network models have become a common way of modeling epidemics [6, 7, 16, 24, 32, 38, 39, 45, 52, 57, 58, 62, 63, 65, 67, 68]. Part of the ongoing investigation into monkeypox modeling can include numerical simulations of the infection spread in a network setting such a small-world network or by using cellular automata.

We present a brief outline of a basic cellular automata model in this chapter. We run some simulations and it becomes clear that more work needs to be done in order to make appropriate assumptions for this model. The intention of this chapter is to explore a different kind of monkeypox model, to present questions and ideas related to monkeypox modeling, and to leave plenty of room for future work.

5.1 Cellular Automata Model Description

Cellular automata can be represented as a grid or lattice of cells changing between states [16, 32, 63, 65, 68]. This idea is applicable when looking for a way to model monkeypox if we want to take each individual human and each individual animal into consideration. We now present a basic cellular automata model for monkeypox.

Consider a grid of cells representing both animal and human populations. We have part of the grid covered in human cells and the rest of the grid covered in animal cells. We have susceptible, infected, and recovered states for both animals and humans. In the systems (2.1a)-(2.1f), (3.14a)-(3.14f), and (4.1a)-(4.1i) we assumed death by monkeypox, natural death by other causes, and a birth rate, but for now let us make the assumption that there is no birth or death, each cell represents one individual animal or individual human, and they can only experience the states of susceptible, infected, and recovered. An example of what a such a cellular automata grid might look like is shown in Figure 5.1. Notice that this grid only has direct connections between some animals and

some humans, but not all animals are connected to humans or vice versa. At this time we believe this assumption is realistic if we consider that those who hunt and cook potentially infected animals are most likely to become infected from an animal versus other humans with less direct contact. The grid may look different from Figure 5.1 depending on the sizes of the populations and other examples will be shown later in the form of simulation results.

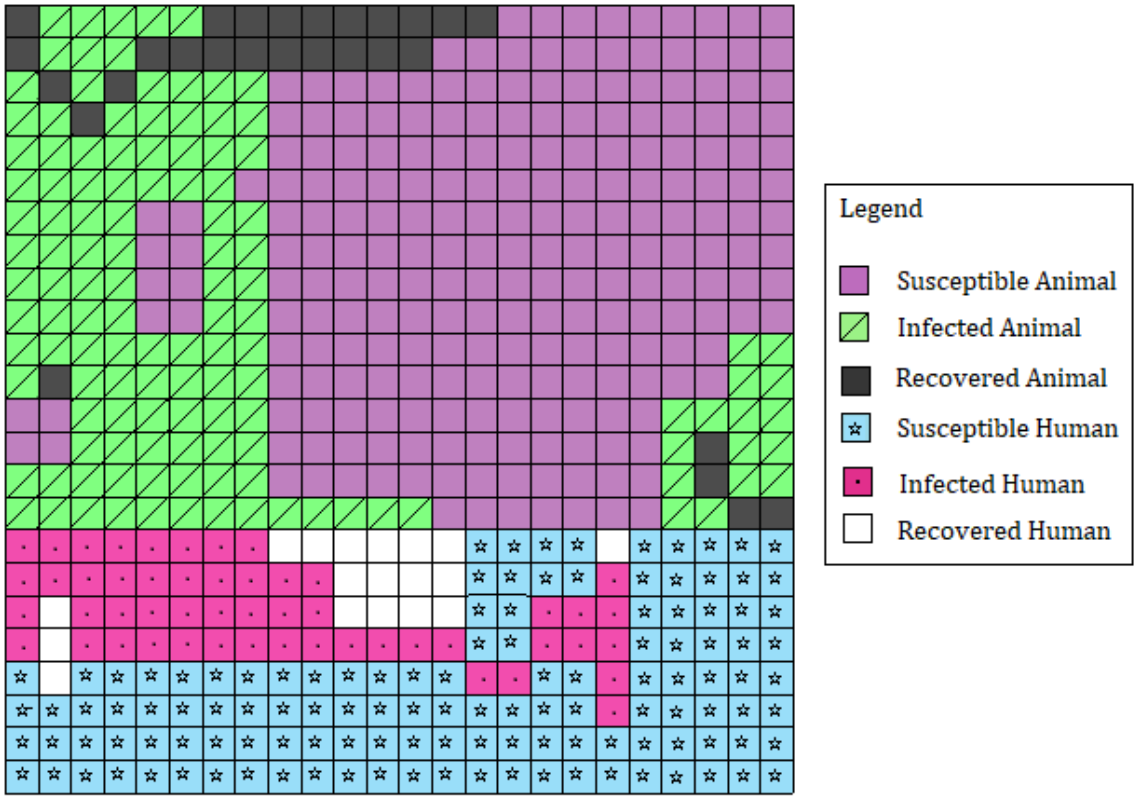

Figure 5.1: This figure shows a cellular automata grid where violet cells are in A_S, green cells are in A_I, black cells are in A_R, blue cells are in H_S, magenta cells are in H_I and white cells are in H_R.

For all the examples presented here, let the grid be toroidally connected so that the top row connects to the bottom row and the left side connects to the right. This way each cell has the same number of neighbors. For the simplest case, a cell has four neighbors – the cell above, the cell below, the cell to the left and the cell to the right.

Define the cell states as follows: a susceptible animal is in the state denoted A_S, an infected animal is in the state denoted A_I, an animal who has recovered from monkeypox is in the state denoted A_R,

a susceptible human is in the state denoted H_S, an infected human is in the state denoted H_I, and a human who has recovered from monkeypox is in the state H_R. Let ϕ_a be the number of a susceptible cell's infected animal neighbors and ϕ_h be a susceptible cell's infected human neighbors [58]. Let η_a^a be the probability that a susceptible animal with one infected animal neighbor becomes infected, η_h^a be the probability that a susceptible human with one infected animal neighbor becomes infected, and η_h^h be the probability that a human with one infected human neighbor becomes infected. Initialize the grid so that there is at least one infected animal. Let δ_a be the probability that an infected animal recovers and δ_h be the probability that a human recovers in one time step. We define $\Phi_a^a := 1 - \left(1 - \eta_a^a\right)^{\phi_a}$ to be the probability that an animal with ϕ_a infected neighbors will become infected, $\Phi_h^a := 1 - \left(1 - \eta_h^a\right)^{\phi_a}$ to be the probability that a human with ϕ_a animal neighbors will become infected, and $\Phi_h^h := 1 - \left(1 - \eta_h^h\right)^{\phi_h}$ to be the probability that a human with ϕ_h infected human neighbors will become infected [58]. We will calculate Φ_a^a, Φ_h^a, and Φ_h^h at each time step and update the grid according to the following rules:

- Each cell in state A_S with $\phi_a > 0$ changes state to A_I with probability Φ_a^a.
- Each cell in state H_S with $\phi_a > 0$ changes state to H_I with probability Φ_h^a.
- Each cell in state H_S with $\phi_h > 0$ changes state to H_I with probability Φ_h^h.
- Each cell in state A_I changes state to A_R with probability δ_a.
- Each cell in state H_I changes to state H_R with probability δ_h.

These rules are not definitive and may be changed to best reflect reality. For instance, changing the order these rules are followed may change the outcome.

5.2 Preliminary Simulation Results

Figure 5.2 shows the results of a simulation on a 100×100 grid where the left half of the grid contains cells representing animals and the right side contains cells representing humans. For this

simulation, $\eta_a^a = 0.25$, $\eta_h^a = 0.3$, $\eta_h^h = 0.2$, $\delta_a = 0.1$, and $\delta_h = 0.1$. This grid was set up with a cluster of infected animals and humans in the middle of the grid shown, and two independent clusters – one in the human section of the grid and one in the animal section. In Figure 5.2 we can roughly see where these infected clusters are located. At the start of the simulation $A_S = 116$ and $H_S = 124$. It should be noted that these values are simply for illustration purposes.

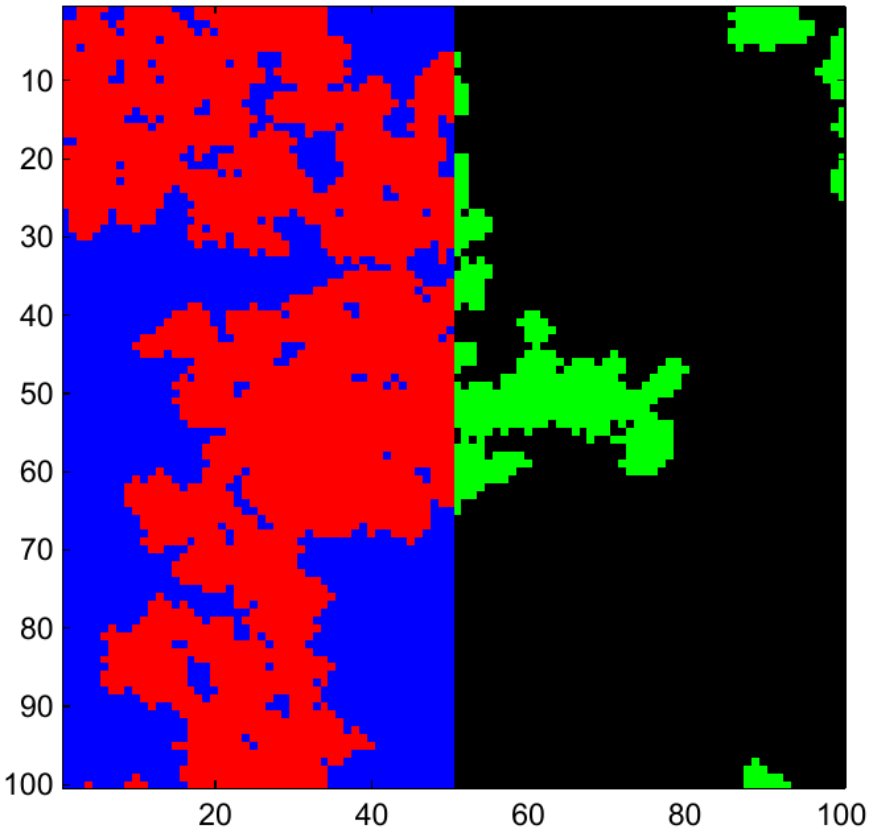

Figure 5.2: An example of a cellular automata model is shown. The cells in blue are in the state A_S, the red cells are in the state of A_R, the black cells are in the state of H_S, and the cells in the state of H_R are in green.

Table 5.1 shows the averaged results from this same cellular automata set up as was used in Figure 5.2 run 1000 times.

Mean A_S	Mean A_I	Mean A_R	Mean H_S	Mean H_I	Mean H_R
2604.992	0	2395.008	4601.289	0	398.711

Table 5.1: The averages for relevant population values after 1000 simulations.

When we change some of the probabilities in this set up, we immediately see a difference. Suppose

the grid is initialized the same way as was done for the results in Table 5.1 and Figure 5.2, but $\eta_a^a = 0.3$, $\eta_h^a = 0.3$, $\eta_h^h = 0.25$, $\delta_a = 0.07$, and $\delta_h = 0.1$. An example grid from a simulation run under these conditions is shown in Figure 5.3 and Table 5.2 shows the mean averaged results after running 1000 of these simulations. Since $\eta_h^h < \eta_a^a$, $\eta_h^h < \eta_h^a$, and $\delta_a < \delta_h$, it is expected that more animals will spread infection than humans, but the result of a relatively small difference in probabilities was more striking than one may expect.

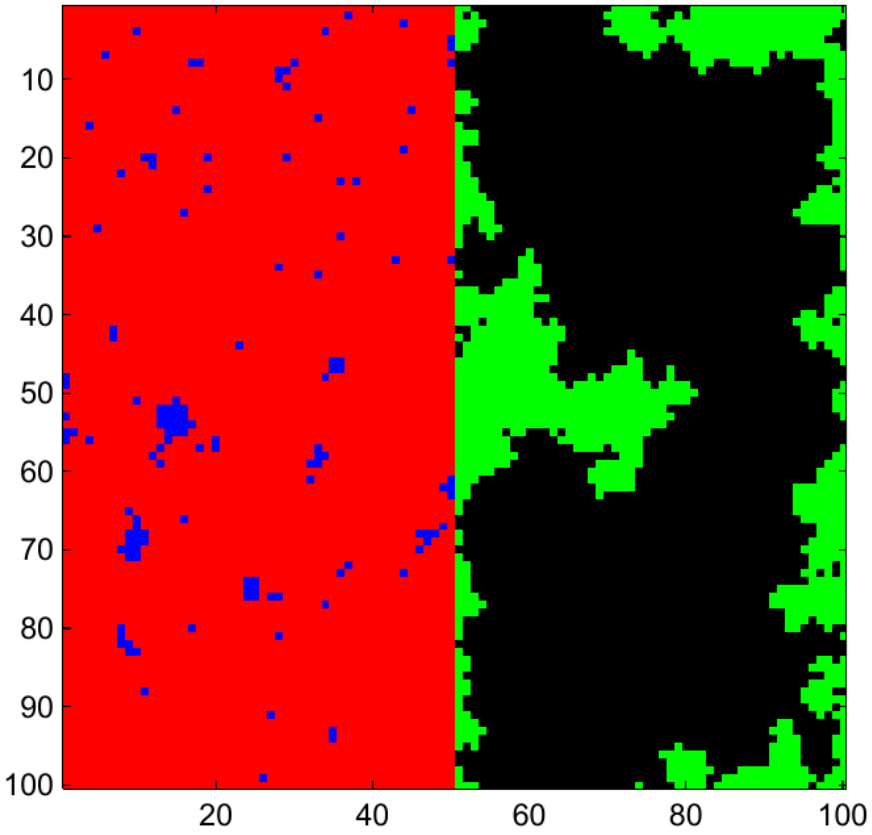

Figure 5.3: Another example of a cellular automata model is shown above. The cells in blue are in the state A_S, the red cells are in the state of A_R, the black cells are in the state of H_S, and the cells in the state of H_R are in green.

Mean A_S	Mean A_I	Mean A_R	Mean H_S	Mean H_I	Mean H_R
152.855	0	4847.145	3567.632	0	1432.368

Table 5.2: The averages for relevant population values after 1000 simulations.

The results of a cellular automata model depend on more than just the probabilities. The initial states and structure of the model are of the utmost importance. In Figure 5.4 and Table 5.3, we see

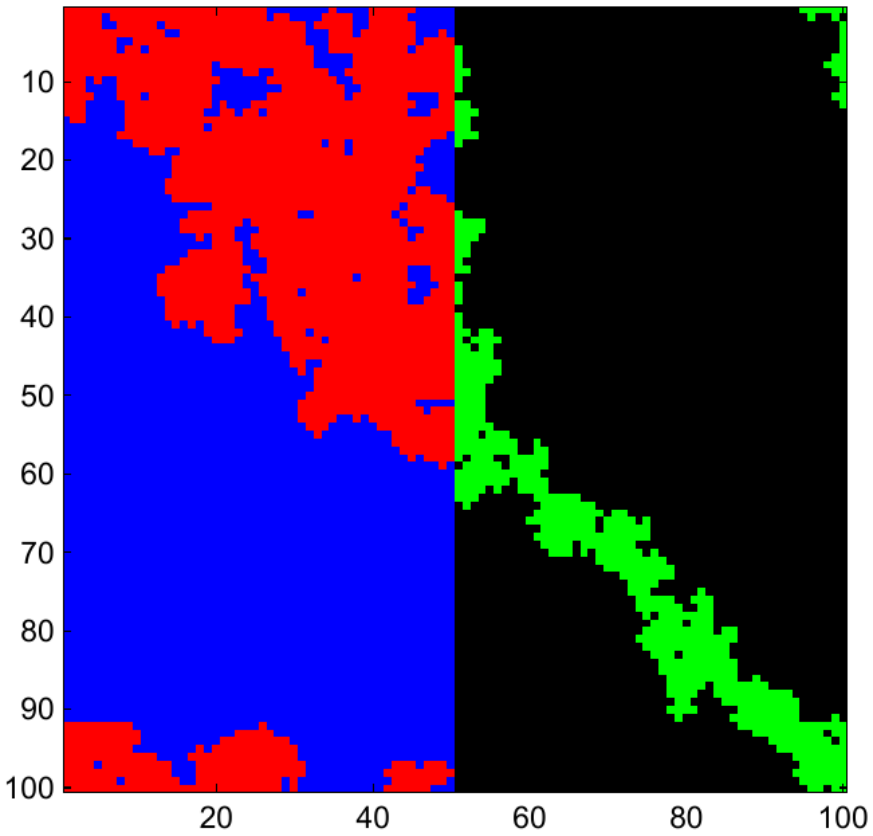

Figure 5.4: Another example of a cellular automata model is shown above. The initial infected cells were along the diagonal. The cells in blue are in the state A_S, the red cells are in the state of A_R, the black cells are in the state of H_S, and the cells in the state of H_R are in green.

Mean A_S	Mean A_I	Mean A_R	Mean H_S	Mean H_I	Mean H_R
2493.252	0	2506.748	4493.359	0	506.641

Table 5.3: The averages for relevant population values after 1000 simulations.

the results of a simulation with the same probabilities as was used in Figure 5.2 and Table 5.1, but in the initial grid, those who are infected do not exist in three clusters, but along the diagonal of the grid. Also for comparison, Figure 5.5 and Table 5.4 show the results of a simulation with the same probabilities as was used in Figure 5.3 and Table 5.2, but with the infected individuals only along the diagonal initially. Since the initial infected individuals are down the diagonal, for these grid dimensions, each simulation starts with 50 infected animals and 50 infected humans.

This is only a simple outline for a cellular automata model and it can certainly be made more

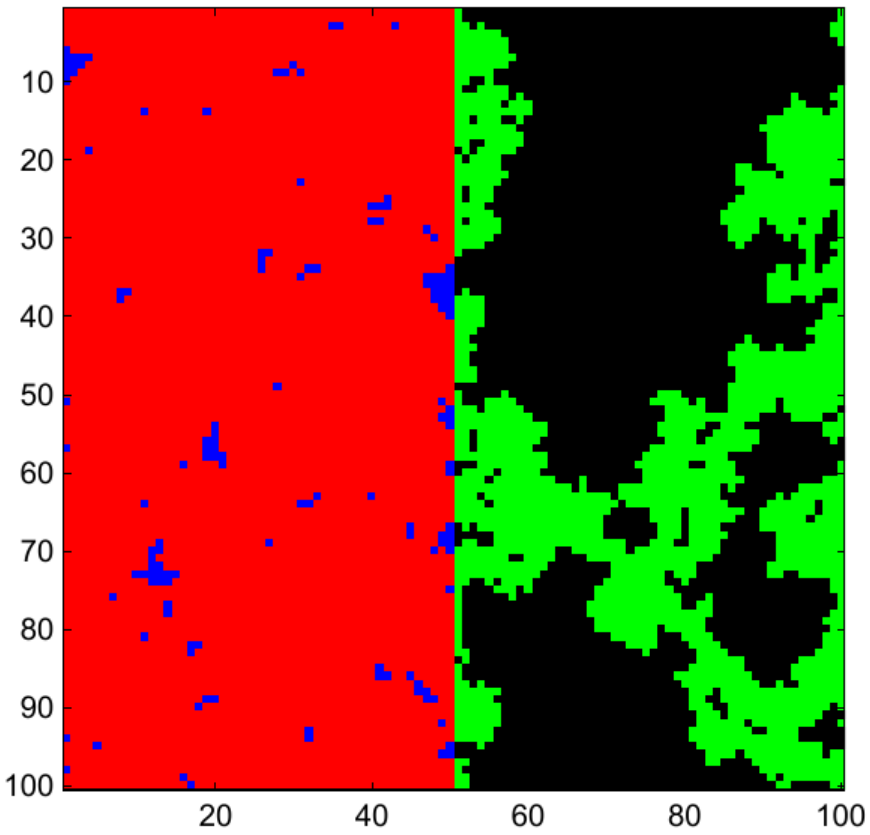

Figure 5.5: Another example of a cellular automata model is shown above. The initial infected cells were along the diagonal. The cells in blue are in the state A_S, the red cells are in the state of A_R, the black cells are in the state of H_S, and the cells in the state of H_R are in green.

Mean A_S	Mean A_I	Mean A_R	Mean H_S	Mean H_I	Mean H_R
145.54	0	4854.46	3443.601	0	1556.399

Table 5.4: The averages for relevant population values after 1000 simulations.

realistic and complicated. Since these are closed systems with no birth, migration, or death, the epidemic is always mitigated and $A_I = H_I = 0$ at the end of each simulation. Unlike the model in (2.1a)-(2.1f), the disease in this cellular automata is not endemic as long as there is disease in the animal population. Since monkeypox is endemic in parts of the world, particularly in the animal population, we believe that the problem is with the accuracy of this cellular automata model in this form.

5.3 A Slight Modification

In this section, in an attempt to make the model more accurate, we allow the state of death and then revive cells with a certain probability. This means that each cell can then go through the states of susceptible, infected, recovered, and dead. If the cell is revived then it represents another individual and can then go through the states again as a new individual. Although this may seem like an easy fix, we will see that whether or not the epidemic remains endemic depends on the probabilities.

To adapt our cellular automata model to include a state of death, let τ_a, τ_h be the probabilities of natural death for an animal cell and a human cell, respectively, let ω_a, ω_h be the probabilities of death due to monkeypox for an animal cell and a human cell, respectively, and let σ_a, σ_h be the probabilities of revival of a dead animal cell and a dead human cell, respectively. In addition to the states A_S, A_I, A_R, H_S, H_I, and H_R, add the state of A_D for dead animal cells and the state of H_D for dead human cells. Initialize the grid with at least one infected animal cell and then at each time step, update the grid accordingly with the following rules:

- Each cell in state A_D changes to state A_S with probability σ_a.
- Each cell in state H_D changes to state H_S with probability σ_h.
- Each cell in state A_S, A_I, A_R changes to state A_D with probability τ_a.
- Each cell in state H_S, H_I, H_R changes to state H_D with probability τ_h.
- Each cell in state A_I changes to state A_D with probability ω_a.
- Each cell in state H_I changes to state H_D with probability ω_h.
- Each cell in state A_S with $\phi_a > 0$ changes state to A_I with probability Φ_a^a.
- Each cell in state H_S with $\phi_a > 0$ changes state to H_I with probability Φ_h^a.
- Each cell in state H_S with $\phi_h > 0$ changes state to H_I with probability Φ_h^h.
- Each cell in state A_I changes state to A_R with probability δ_a.

- Each cell in state H_I changes to state H_R with probability δ_h.

For clarity in our figures, we will only show the animal population or the human population and the other population will be blacked out. This allows us to focus on all of the states in each population, but also reminds us that we are looking at two distinct populations.

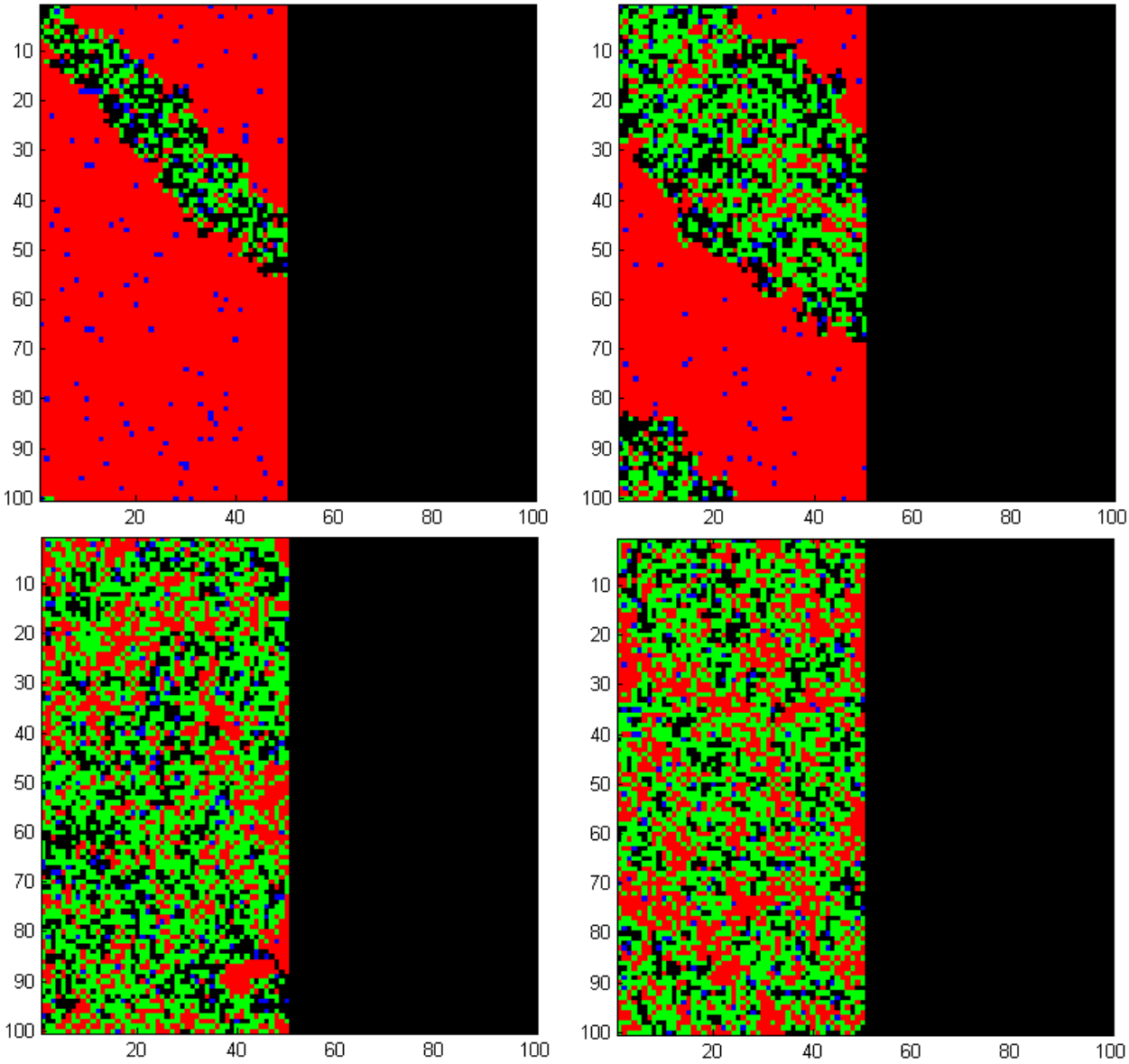

Figure 5.6: This figure shows a picture of an ongoing simulation and highlights the animal population.

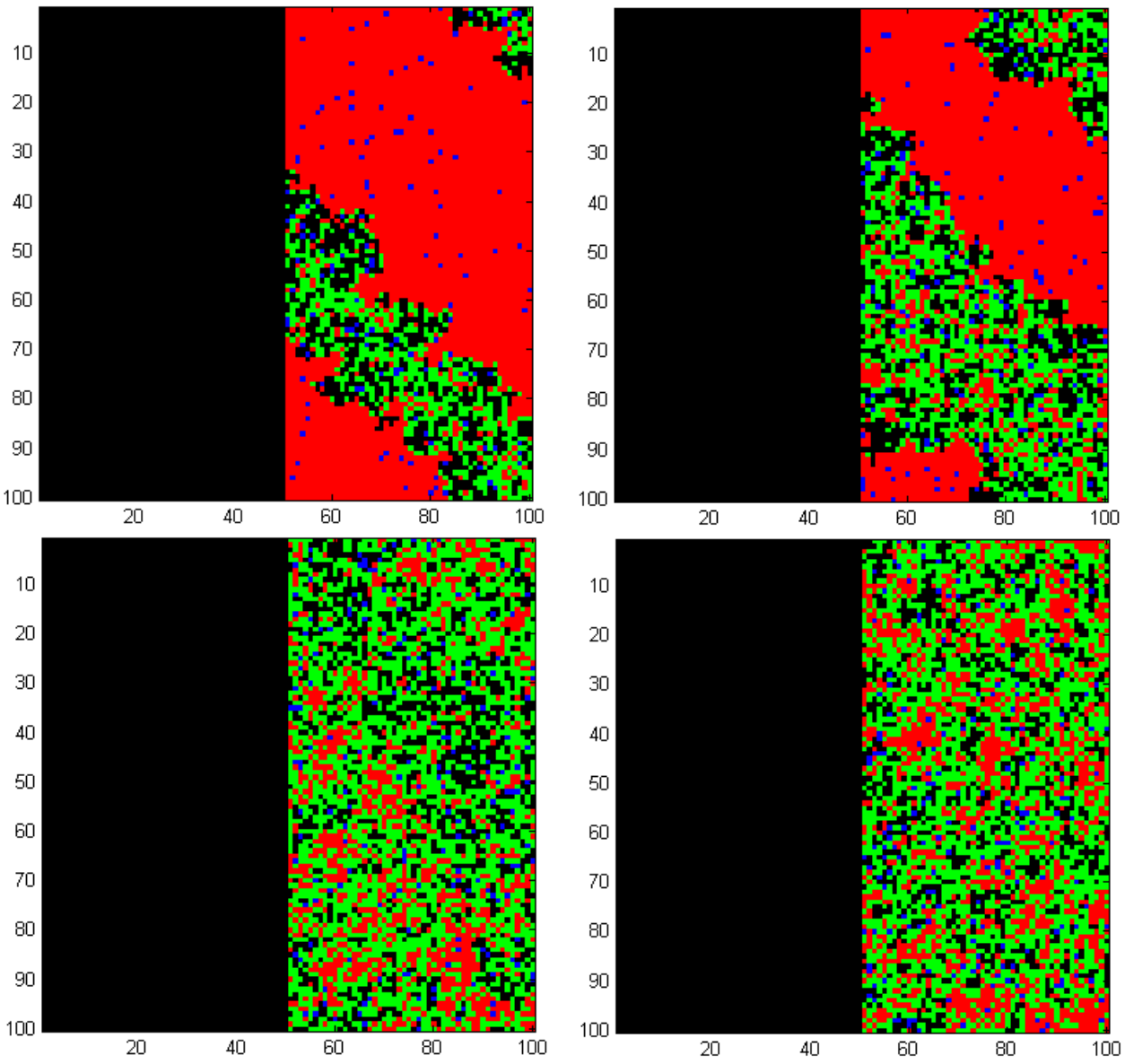

Figure 5.7: This figure shows a picture of an ongoing simulation and highlights the human population.

Figure 5.6 shows an example of modeling monkeypox with cellular automata with the probability values of $\eta_a^a = 0.3, \eta_h^a = 0.25, \eta_h^h = 0.3, \rho_a = 0.1, \rho_h = 0.1, \tau_a = 0.02, \tau_h = 0.02, \sigma_a = 0.9, \sigma_h = 0.9, \omega_a = 0.08$, and $\omega_h = 0.08$. The grid is initialized with infected individuals down the diagonal and with all remaining cells in the state of susceptible. (All of our remaining simulations will be initialized this way.) Figure 5.6 shows the model in four stages, but only shows what is happening among the animals. On the left hand side in this figure, the red cells are in the state A_S, the black cells are in the state A_I, the green cells are in the state A_R, and the cells in the state A_D are in

blue. On the right hand side, all human cells are black. Figure 5.7 shows an example of modeling monkeypox with cellular automata with the same probabilities as were used in 5.6, but highlights the human population. On the left hand side, the animal cells are shown in black. On the right hand side, the cells in red are in the state H_S, the black cells are in the state H_I, the green cells are in the state H_R, and the blue cells in the state H_D. The bottom right portions of Figures 5.6 and 5.7 are good representations of what the simulation looks like when it is continued even further. We see that the epidemic is endemic in both populations in this scenario. The high probabilities of σ_a and σ_h result in a cell being revived almost immediately after it has died and this fuels the epidemic.

Table 5.5 shows the averaged results of 1000 simulations for a different scenario. The values averaged were taken at time step 500. The probability values used for these simulations were $\eta_a^a = 0.3, \eta_h^a = 0.25, \eta_h^h = 0.3, \rho_a = 0.1, \rho_h = 0.1, \tau_a = 0.02, \tau_h = 0.02, \sigma_a = 0.15, \sigma_h = 0.15, \omega_a = 0.08$, and $\omega_h = 0.08$. At these values of σ_a and σ_h and for higher values of σ_a and σ_h like in the examples illustrated in Figures 5.6 and 5.7, when the other values are left as they are, our results indicated there is enough revival to maintain the infection. In other words, the results presented here indicate that for these values there are enough new susceptible individuals entering the population for the epidemic to be endemic. An example of how the epidemic spreads in this situation is shown in Figure 5.8.

Mean A_S	Mean A_I	Mean A_R	Mean A_D	Mean H_S	Mean H_I	Mean H_R	Mean H_D
3838.13	79.842	383.822	698.206	3619.454	115.125	553.268	712.153

Table 5.5: The averages for relevant population values after 1000 simulations of 500 time steps each. These values indicate that the epidemic continues since $A_I, H_I > 0$.

When we change the rate of revival so that the parameters are $\eta_a^a = 0.3, \eta_h^a = 0.25, \eta_h^h = 0.3, \rho_a = 0.1, \rho_h = 0.1, \tau_a = 0.02, \tau_h = 0.02, \sigma_a = 0.14, \sigma_h = 0.14, \omega_a = 0.08$, and $\omega_h = 0.08$, we see that the infection is mitigated. This is true when we ran 1000 simulations. Those averaged results

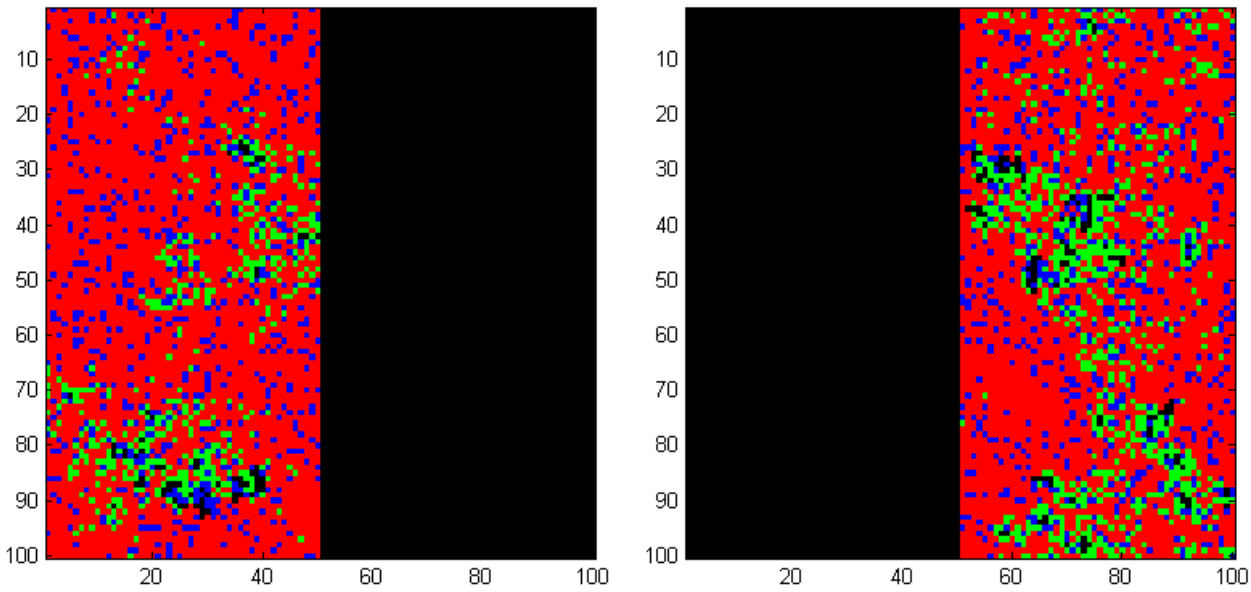

Figure 5.8: This figure shows a picture of an ongoing simulation with the same parameters as those used for the results in Table 5.5. The animal population is shown on the right and the human population is shown on the left. For the corresponding population, the susceptible individuals are in red, the infected individuals are in black, the recovered individuals are in green, and the dead individuals are in blue.

are shown in Table 5.6. Figure 5.9 shows an example of what this looks like in the GUI. In this figure, the top row shows how the epidemic progresses in the animal population and the bottom row shows how the epidemic spreads in the human population. The left column of Figure 5.9 shows the progression after 50 time steps and the right hand side shows what happens after 300 time steps. In each population, we see that the disease will die out eventually in this example.

Mean A_S	Mean A_I	Mean A_R	Mean A_D	Mean H_S	Mean H_I	Mean H_R	Mean H_D
4247.78	0	19.756	715.466	4216.174	0	66.713	717.113

Table 5.6: The averages for relevant population values after 1000 completed simulations.

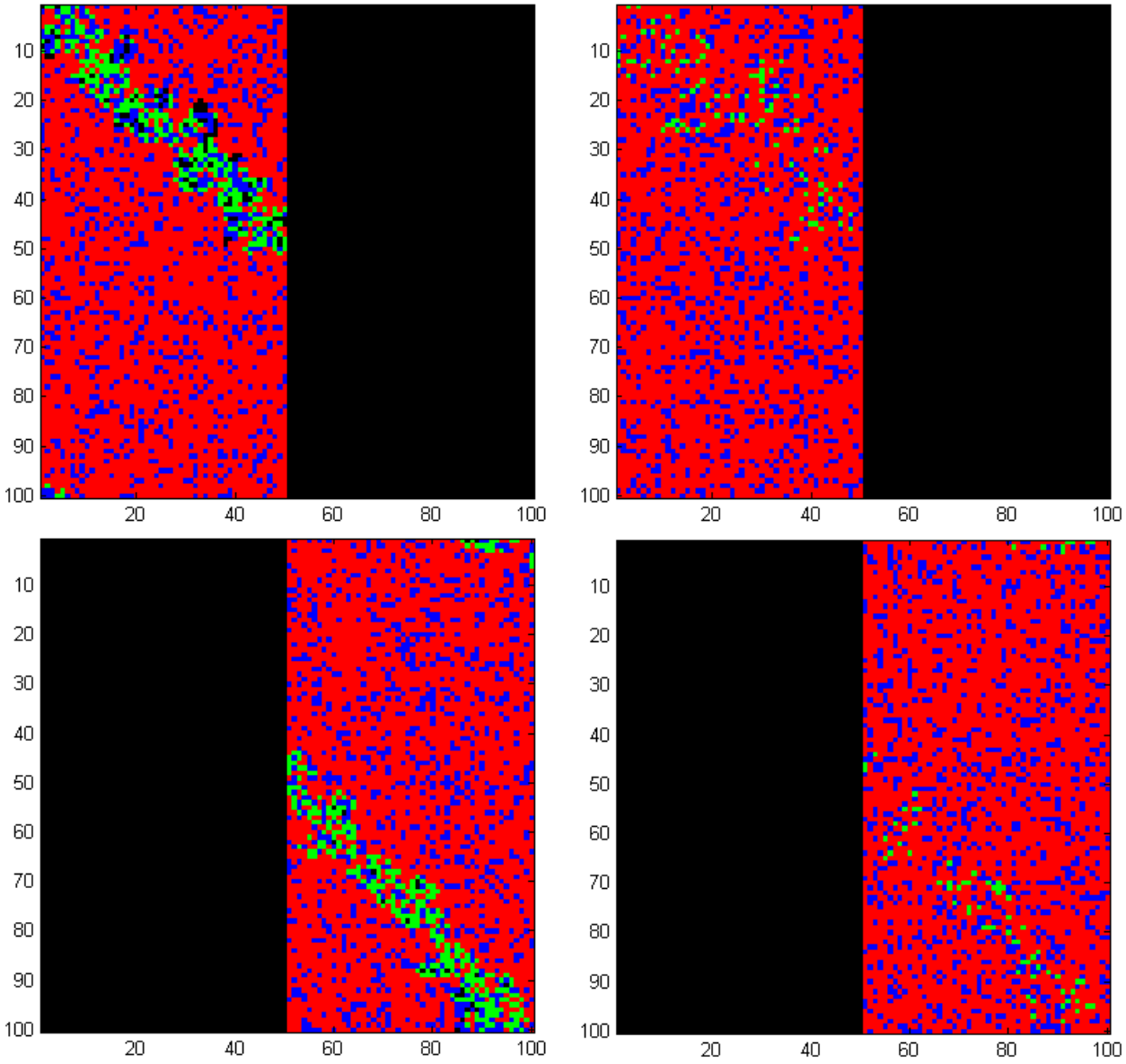

Figure 5.9: This figure shows a picture of an ongoing simulation with the same parameters as those used for the results in Table 5.6. The animal population is shown in the top row and the human population is shown in the bottom row. For the corresponding population, the susceptible individuals are in red, the infected individuals are in black, the recovered individuals are in green, and the dead individuals are in blue.

6 Future Work

In addition to obtaining more data and finding actual parameter values, we can consider other modeling approaches to further understand monkeypox and similar epidemic models.

A natural mathematical extension of the work in the previous chapters related to system (2.1a)-(2.1f) is an optimal control problem to determine if there is a threshold where monkeypox can remain endemic at some low level in the animal population while mitigating it in the human population using a range of controls. Since there is currently no vaccine for monkeypox available for wide use, the most realistic control would be a parameter changing the incidence of infection in the human population as a result of education. Many people in areas affected with monkeypox are not always aware of the difference between monkeypox and other diseases or ways of preventing the spread of infection, hence education efforts in these areas may decrease the incidence of monkeypox [48, 51, 53]. Additionally, people in these areas can have increased contact with infected animals because they have a difficult time finding food and safety from local socioeconomic turbulence and so there could also be other methods to keep people from becoming infected that are related to these issues [1, 17, 21, 23, 27, 40, 44, 10, 14, 11, 48, 49, 51, 53, 54, 66, 67].

While it is interesting to consider network models, a lot of work needs to be done in order for those models to reflect what we know from ongoing monkeypox research. A cellular automata model was presented in this work, but only as a catalyst for future work.

Another way of modeling the states of individuals during an epidemic is with a small-world network. An example of a small-world network is shown in Figure 6.1. This network was created in MATLAB by starting with a series of nodes connected to their neighbor on each side, then disconnecting each node from a neighboring node with a certain probability, and then connecting each node by a shortcut to another node across the network with another probability. In general, a small-world network can most simply be created by taking a lattice network and adding some random

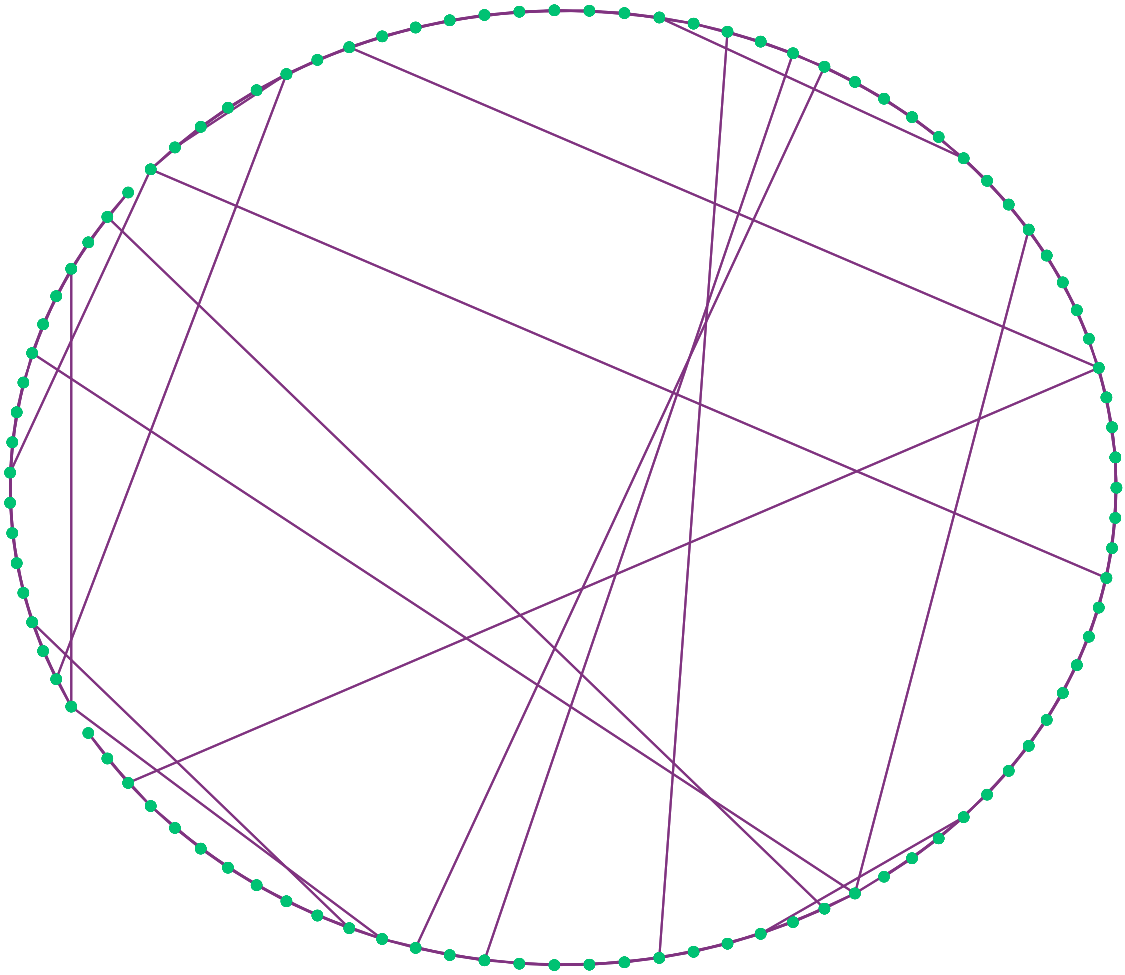

Figure 6.1: An example of a small-world network without specified states.

connections. Even just two or three of these shortcuts can have a major impact on the spread of the epidemic versus a lattice without shortcuts. Since each individual in a cellular automata network is only connected to its four nearest neighbors, this is like a person who can only get infected from the people they live with or who live right next to them. We know this is not entirely accurate since people interact with others from different locations at community areas such as schools, churches, and markets. A small-world network accounts for these kind of interactions [32, 57, 63].

Although we could use a model like the one shown in Figure 6.1 and use rules similar to those proposed in the previous section for the cellular automata model, it would possibly be more realistic

to have one such network for the animal population and another for the human population with some connections between the two networks representing the influence of the animal population on the human population. As with the cellular automata model, we start with at least one infected animal node and update each node based on its state and the states of their connections given certain probabilities.

In order to use network models to better understand the spread of monkeypox, a better understanding of the interactions between humans and animals in areas with endemic monkeypox is needed.

Although we have been solely focused on monkeypox, the ideas presented here are applicable to a range of diseases that affect humans and animals. Ebola viruses are thought to have a natural reservoir in apes, bats, and other animals, avian flu viruses are carried by birds but can adapt to infect humans as well, and bats are a reservoir for rabies since they can spread it to humans and other animals [12, 13, 15, 25, 37].

The differential equation models considered in this work corroborate the epidemiological evidence that once the disease becomes endemic in the reservoir (animal) population, there will be endemic disease in the human population. While we might wish to suggest a guaranteed way of mitigating monkeypox in the human population, this is incredibly difficult. The mass culling of birds is one strategy used to prevent the spread of avian flu, but this is not practical or even possible for the cases of monkeypox, rabies, or ebola within wild populations. In the case of monkeypox, there are too many different species of wild animals that can harbor the disease so it is difficult to know what ways of controlling this disease in the animal populations will work best.

The study and understanding of monkeypox is crucial given its resurgence. The system presented in (2.1a) - (2.1f) is important in our understanding of monkeypox – as are its extensions. As more data is collected and as epidemiologists learn more about this disease, the model can be made more accurate and new insights can be gained.

References

[1] Abdullahi, M., Hasan, Y. & Abdullah, F. (2014) *Modeling and optimal control of* Plasmodium knowlesi *malaria spread from infected humans to mosquitoes*. Annu. Res. Rev. Biol. **4**(**24**), 4482-4501. (DOI: 10.9734/ARRB/2014/12044)

[2] Afassinou, K., Chirove, F. & Govinder, K. S. (2017). *Pre-exposure prophylaxis and antiretroviral treatment interventions with drug resistance*. Math Biosci. **285**, 92-101.

[3] Begon, M., Bowers, R.G., Kadianakis, N. & Hodgkinson, D.E. (1992) *Disease and community structure: the importance of host self-regulation in a host-host-pathogen model*. Am. Nat. **139**, 1131-1150.

[4] Bhunu C.P. & Mushayabasa, C. (2011) *Modelling the transmission dynamics of pox-like infections*. IAENG Int. J. Appl. Math. **41**(**2**), 141-149.

[5] Bhunu C.P., Mushayabasa, C. & Hyman, J.M. (2012) *Modelling HIV/AIDS and monkeypox co-infection*. Appl. Math. Comput. **218**, 9504-9518.

[6] Blumberg, S., Funk, S. & Pulliam, J.R.C. (2014) *Detecting differential transmissiblilities that affect the size of self-limited outbreaks*. PLOS Pathogens. **10**, `https://doi.org/10.1371/journal.ppat.1004452`.

[7] Brauer, F., van den Driessche, P., & Wu, J., Eds. (2008) *Mathematical Epidemiology*. Springer, Berlin.

[8] Castillo-Chavez, C., Feng, Z. & Huang, W. (2001) *On the computation of $\mathcal{R}_0$ and its role on global stbility*. Institute for Mathematics and Its Applications. **125**, 229.

[9] Castillo-Chavez, C. & Thieme, H. (1994) *Asymptotically Autonomous Epidemic Models*. Biometrics Unit Technical Reports. **BU-1248-M**, `http://hdl.handle.net/1813/31834`.

[10] The Center for Food Security & Public Health. *Monkeypox*. (2013) Retrieved on April 22, 2016 from `http://www.cfsph.iastate.edu/Factsheets/pdfs/monkeypox.pdf`.

[11] The Center for Food Security & Public Health. *Monkeypox Fast Facts*. (2013) Retrieved on April 22, 2016 from `http://www.cfsph.iastate.edu/FastFacts/pdfs/monkeypox_F.pdf`.

[12] Centers for Disease Control and Prevention. *About Ebola Virus Disease*. (2017) Retrieved on June 19, 2017 from `https://www.cdc.gov/vhf/ebola/about.html`.

[13] Centers for Disease Control and Prevention. *Information on Avian Influenza*. (2017) Retrieved on June 19, 2017 from`https://www.cdc.gov/flu/avianflu/index.htm`.

[14] Centers for Disease Control and Prevention. (2015) *Monkeypox*. Retrieved on April 22, 2016 from `https://www.cdc.gov/poxvirus/monkeypox/`.

[15] Centers for Disease Control and Prevention. *Rabies: How is rabies transmitted?* (2011) Retrieved on June 19, 2017 from `https://www.cdc.gov/rabies/transmission/index.html`.

[16] Cisse, B., El Yacoubi, S., & Tridane, A. (2013) *Impact of neighborhood structure on epidemic spreading by means of cellular automata approach*. Procedia Computer Science. **18**, 2603-2606.

[17] Damon, I.K (2011) *Status of human monkeypox: clinical disease, epidemiology and research*. Vaccine. **29**(**Suppl4**), D54-D59. (DOI: 10.1016/j.vaccine.2011.04.014)

[18] Dobson, A. (2004) *Population dynamics of pathogens with multiple host species*. Am. Nat. **164**, S64-S78.

[19] Dobson, A. & Foufopoulos, J. (2001) *Emerging infectious pathogens of wildlife*. Phil. Trans. R. Soc. Lond. **356**, 1001-1012.

[20] Emeka, P.C., Ounorah, M.O., Eguda, F.Y. & Babangida, B.G. (2018) *Mathematical model for monkeypox virus transmission dynamics*. Epidemiology (Sunnyvale). **8(3):348**. (DOI: 10.4172/2161-1165.1000348)

[21] Epanchin-Niell, R.S. & Wilen, J.E. (2011) *Optimal control of spatial-dynamic processes: the case of biological invasions*. Resources for the Future. RFF DP 11-07. Retrieved on March 27, 2014 from: `http://www.rff.org/rff/Documents/RFF-DP-11-07.pdf`.

[22] Gaff, H. & Gross, L.L. (2007) *Modeling tick-bourne disease: a metapopulation model*. Bull. of Math. Biol. **69**, 265-288. (DOI: 10.1007/s11538-006-9125-5)

[23] Gaff, H. & Schaefer, E. (2009) *Optimal control applied to vaccination and treatment strategies for various epidemiological models*. Math. Biosci. Eng. **6**, 469-492. (DOI: 10.3934/mbe.2009.6.469)

[24] Graziano Ceddia, M. (2010) *Managing infectious diseases over connected populations: a non-convex optimal control*. MPRA Paper No. 22344. Retrieved on March 27, 2014 from `http://mpra.ub.uni-muenchen.de/22344/`.

[25] Gilbert, A.T., McCracken, G.F., Sheeler, L.L., et al. (2015) *Rabies surveillance among bats in Tennessee, USA, 1996-2010*. J. Wildl. Dis. **15(4)**, 821-832.

[26] Hammarlund, E., Lewis, M.W., Carter, S.V., et al. (2005) *Multiple diagnostic techniques identify previously vaccinated individuals with protective immunity against monkeypox*. Nat. Med. **11(9)** 1005-1011.

[27] Hansen, K. & Day, T. (2011) *Optimal control of epidemics with limited resources*. J. Math. Biol. **62**, 423-451. (DOI: 10.1007/s00285-010-0341-0)

[28] Hutin, Y.J.F, Williams, R.J., Malfait, P., et al. (2001) *Outbreak of human monkeypox, Democratic Republic of Congo, 1996-1997*. Emerg. Infect. Dis. **7**, 434-438.

[29] Jeẑek, Z., Arita, I., Mutombo, M. Dunn, C., Nakano, J.H. & Szczeniowski, M. (1986) *Four generations of probable person-to-person transmission of human monkeypox*. Am. J Epidemiol. **123(6)**. 1004-1012.

[30] Jeẑek, Z., Grab, B., Szczeniowski, M.V., Paluku, K.M. & Mutombo, M. (1988) *Human monkeypox: secondary attack rates*. Bull. World Health Organ. **66(4)**. 465-470.

[31] Kantele, A., Chickering, K., Vapalahti, Q. & Rimoin, A.W. (2016) *Emerging diseases - the monkeypox epidemic in the Democratic Republic of the Congo*. Clin. Microbiol. Infec. **22**, 658-659. (DOI: http://dx.doi.org/10.1016/j.cmi.2016.07.004)

[32] Keeling, M.J. & Eames, T.D. (2005) *Networks and epidemic models*. J. R. Sos. Interface **2**, 295-307. (DOI: 10.1098/rsif.2005.0051)

[33] Korobeinikov, A. (2006) *Lyapunov functions and global stability for SIR and SIRS epidemiological models with non-linear transmission*. Bull. Math. Biol. **68**, 615-626. (DOI: 10.1007/s11538-005-9037-9)

[34] Korobeinikov, A. & Maini, P.K. (2004) *A Lyapunov function and global properties for SIR and SEIR epidemiological models with nonlinear transmission*. Math. Biosci. Eng. **68**, 57-60.

[35] LaSalle, J.P. (1976) *The stability of dynamical systems*. SIAM, Philadelphia, PA.

[36] LaSalle, J.P. & Lefschetz, S. (1961) *Stability by Liapunovs direct method with applications*. New York: Academic Press.

[37] Lauko, I., Pinter, G. & TeWinkel, R.E. (2018) *Equilibrium analysis for an epidemic model with a reservoir for infection*. Letters in Biomathematics. **5**(**1**), 255-274.

[38] Levine, R.S., Townsend Peterson, A., Yorita, K.L., Carroll, D., Damon, I.K. & Reynolds, M.G. (2007) *Ecological niche and geographic distribution of human monkeypox in Africa*. PLoS ONE **2**(**1**) : **e176**, `https://doi.org/10.1371/journal.pone.0000176`.

[39] Li, M.Y. & Shuai, Z. (2010) *Global-stability problem for coupled systems of differential equations on networks*. J. Diff. Equations. **248**, 1-20.

[40] Lloyd-Smith, J.O., George, D., Pepin, K.M., et. al. (2009) *Epidemic dynamics at the human-animal interface*. Science. **326**, 1362-1367.

[41] Markus, L. (1956). *Asymptotically autonomous differential systems.* Contributions to the Theory of Nonlinear Oscillations III. S. Lefschetz (Ed.) Ann. of Math. Stud. **36**, London: Princeton Univ. Pres.

[42] McCluskey, C.C. (2006) *Lyapunov functions for tuberculosis models with fast and slow progression*. Math. Biosci. Eng. **3**, 603-614.

[43] McCollum, A.M. & Damon, I.K. (2014) *Human monkeypox*. Clin. Infect. Dis. **58**, 260-267. (DOI: https://doi.org/10.1093/cid/cit703)

[44] Meseda, C.A. & Weir, J.P. (2010) *Third-generation smallpox vaccines: challenges in the absence of clinical smallpox*. Future Microbiol. **5**(**9**), 1367-1382.

[45] Neilan, R.M. & Lenhart, S. (2011) *Optimal vaccine distribution in a spatiotemporal epidemic model with an application to rabies and raccoons*. J. Math, Anal. Appl. **378**, 603-619.

[46] Njagarah, J.B.H. & Nyabadza, R. (2014) *A metapopulation model for cholera transmission dynamics between communities linked by migration*. Appl. Math. Comp. **241**, 317-331.

[47] Nolen, L.D., Osadebe, L., Katomba, J., et. al. (2016) *Extended human-to-human transmission during a monkeypox outbreak in the Democratic Republic of the Congo*. Emerg. Infect. Dis. **22**, 1014-1021.

[48] Reynolds, M.G., Emerson, G.L., Pukuta, E., et. al. (2013) *Detection of human monkeypox in the Republic of the Congo following intensive community education*. Am. J. Trop. Med. Hyg. **88(5)**, 982-985.

[49] Rimoin, A.W. & Graham, B.S. (2011) *Whither monkeypox vaccination*. Vaccine. **29**(**Suppl4**), D60-D64. (DOI: 10.1016/j.vaccine.2011.09.004)

[50] Rimoin, A.W., Kisalu, N., Kebela-Ilunga, B., et. al. (2007) *Endemic human monkeypox, Democratic Republic of Congo, 2001-2004*. Emerg. Infect. Dis. **13**, 934. (DOI: https://dx.doi.org/10.3201/eid1306.061540)

[51] Rimoin, A.W., Mulembakani, P.M., Johnston, S.C., et. al. (2010) *Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo*. PNAS. **107**, 16262-16267. (DOI: 10.1073/pnas.1005769107)

[52] Roche, B., Benbow, M.E. & Merritt, R. (2013) *Identifying the Achilles heel of multi-host pathogens: the concept of keystone 'host' species illustrated by* Mycobacterium ulcerans *transmission*. Environ. Res. Lett. **8**, 045009. (DOI: 10.1088/1748-9326/8/4/045009)

[53] Roess, A.A., Monroe, B.P., Kinzoni, E.A., et. al. (2011) *Assessing the effectiveness of a community intervention for monkeypox prevention in the Congo Basin*. PLOS Neglected Tropical Diseases. **5**, `https://doi.org/10.1371/journal.pntd.0001356`.

[54] Rowthorn, R., Laxminarayan, R., & Gilligan, C. (2009) *Optimal control of epidemics in metapopulations*. J. R. Soc. Interface 1-10. (DOI: 10.1098/rsif.2008.0402)

[55] Shchelkunov, S.N. (2013) *An increasing danger of zoonotic orthopoxvirus infections*. PLOS Pathogens. **9**, `https://doi.org/10.1371/journal.ppat.1003756`.

[56] Song, X. & Z. Xiang, (2006) *The prey-dependent consumption two-prey one-predator models with stage structure for the predator and impulsive effects*. J. Theor. Biol. **242**, 683-698.

[57] TeWinkel, R.E. (2015, October) *Control of Network Epidemic Models*. Poster session presented at the International Symposium on Biomathematics and Ecology Education and Research, Normal, IL.

[58] TeWinkel, R.E. (2015, January) *Epidemic Modeling with Optimal Controls in a Setting with Limited Resources and Spatial Dynamics*. Preliminary report presented at the Joint Mathematics Meetings, San Antonio, TX.

[59] Thieme, H. (1992) *Convergence results and a Poincaré-Bendixson trichotomy for asymptotically autonomous differential equations*. J Math. Biol. **30**, 755-763.

[60] van den Driessche, P. & Watmough, J. (2002) *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*. Math. Biosci. **180**, 29-48.

[61] Vargas De-León, C. (2011) *On the global stability of SIS, SIR and SIRS epidemic models with standard incidence*. Chaos Solitons & Fractals. **44**, 1106-1110.

[62] Vynnycky, E. & White, R.G. (2010) *An Introduction to Infectious Disease Modelling*. Oxford University Press.

[63] Watts, D.J. & Strogatz, S.H. (1998) *Collective dynamics of'small-world' networks*. Nature. **393**, 440–442.

[64] Weaver, J.R. & Isaacs, S.N. (2009) *Monkeypox virus and insights into its immunomodulatory proteins*. Immunol. Rev. **225** 96-113.

[65] White, S.H., del Rey, A.M. & Sanchez, G.R. (2007) *Modeling epidemics using cellular automata*. Appl. Math. Comput. **186**, 193-202.

[66] World Health Organization. *Monkeypox Fact Sheet*. (2016) Retrieved on April 22, 2016 from `http://www.who.int/mediacentre/factsheets/fs161/en/`.

[67] Youssef, M. & Scoglio, C. (2013) *Mitigation of epidemics in contact networks through optimal contact adaptation*. Math. Biosci. Eng. **10**, 1227-1251.

[68] Zhi-Zhen, Z. & Ai-Ling, W. (2009) *Phase transitions in cellular automata models of spatial susceptible-infected- resistant-susceptible epidemics*. Chinese Phys. B. **18**, 489-500.

Curriculum Vitae

Rachel Elizabeth TEWINKEL

Education

SEPT 2014 - MAY 2019	PhD Candidate in Mathematics, University of Wisconsin-Milwaukee, Dissertation: "Stability Analysis for the Equilibria of a Monkeypox Model" | Advisor: Istvan Lauko
SEPT 2012 - MAY 2014	MS in Mathematics, University of Wisconsin-Milwaukee, Thesis: "A Mathematical Model of Moisture Movement and Bacterial Growth in Two-Dimensional Porous Medium" Advisor: Istvan Lauko
AUG 2004 - DEC 2007	BS in Mathematics, Salisbury University, Salisbury, MD Thesis: "Using Viruses to Defeat Cancer : A Mathematical Model of Virotherapy" | Advisor: Steven Hetzler Graduated Magna Cum Laude and Honors with Distinction

Work Experience

APR 2019 - PRESENT	Content Author (Remote), Macmillan Authored online content for Calculus II and III in Raptor
SEPT 2012 - MAY 2019	Graduate Teaching Assistant Department of Mathematical Sciences, University of Wisconsin-Milwaukee
APR 2008 - JUN 2011, NOV 2016 - MAY 2018	Private Tutor Tutored elementary school students in math, science, reading, writing Tutored high school and middle school students in algebra and geometry
SEPT 2009 - JAN 2011	Independent Contractor with Tutor.com
JAN 2005 - DEC 2007	Student Assistant for the Honors Department, Salisbury University Assisted director of the program by processing paperwork, managing incoming students, and processing applications to the program

Skills and Experience

- Designed network models and differential equation models pertaining to biology, physics and business
- Extensive experience modeling epidemics, impacts of vaccination, disease in the body, networks, population dynamics, water and heat flow and symbiotic relationships
- Illustrated population dynamics and biological processes
- Research includes applications of differential equations, optimal controls, statistical models, finite element and finite volume methods, cellular automata and small-world networks
- Gathered and organized data on monkeypox, avian flu, rabies and plague
- Developed code to run simulations and better understand math models
- Adapted models to include an optimization component
- Tested algorithms and code
- Interpreted patterns found in data
- Created posters and slide presentations to communicate model results at seminars and conferences
- Authored research papers and project proposals
- Collaborated with faculty in the Department of Mathematical Sciences and the Zilber School of Public Health
- Critiqued colleagues' work and adapted own work in response to their critiques
- Authored Calculus II and III content in Raptor and wrote students with error-specific feedback on online exercises
- Advanced knowledge in LaTeX, including producing visualizations using LaTeXpackages
- Coding experience: proficient in scripting with Matlab, basic knowledge of C++, Maple, Mathematica, SQL and Python
- Experienced with Google Drive, Microsoft Office Suite and Zoom video conferencing

Teaching Experience

Graduate Teaching Assistant, University of Wisconsin-Milwaukee
Course Co-coordinator:

Precalculus (*MATH 115*) FALL 2016, SPRING 2017

Taught as Sole Instructor:

Matrices and Applications (*MATH 240*) SPRING 2018
Calculus and Analytic Geometry I (*MATH 231*) SPRING 2015
Calculus and Analytic Geometry II (*MATH 232*) FALL 2017

Calculus and Analytic Geometry III (MATH 233)	SUMMER 2017, SUMMER 2018
Calculus with Life Sciences Applications(MATH 213)	FALL 2018, SPRING 2019
Survey in Calculus and Analytic Geometry (MATH 211)	SUMMER 2016
College Algebra (MATH 116)	SPRING 2014, SPRING 2016
Precalculus (MATH 115)	FALL 2016, SPRING 2017
Intermediate Algebra (MATH 105)	FALL 2013
Preparation for College Mathematics (MATH 094)	FALL 2014

Discussion Instructor:

Survey in Calculus and Analytic Geometry (MATH 211)	FALL 2012, SPRING 2013, FALL 2016
Preparation for College Mathematics (MATH 094)	SPRING 2015

Publication

Lauko, I., Pinter, G. & TeWinkel, R.E. (2018) *Equilibria Analysis for a Two-Population Epidemic Model with One Population Being a Reservoir for Infection*. Letters in Biomathematics, 5:1, 255-274. (Math publications list authors in alphabetical order.)

Conference Presentations

JAN 2019	"Exploration of a Monkeypox Model," The Joint Mathematics Meetings, Baltimore, MD
JAN 2018	"Equilibria Analysis for a Two-Population Epidemic Model with One Population Being a Reservoir for Infection," The Joint Mathematics Meetings, San Diego, CA
APR 2017	"A Small-World Network Epidemic Model with a Ring Vaccination Strategy," The 2017 Annual Mathematical Association of America - Wisconsin Section Meeting, Milwaukee, WI
OCT 2016	"Math vs. Disease," Wisconsin Science Festival: Big Ideas for Busy People - PhD Edition, Milwaukee, WI
OCT 2015	"Control of Network Epidemic Models," International Symposium on Biomathematics and Ecology Education and Research, Normal, IL
JAN 2015	"Epidemic Modeling with Optimal Controls in a Setting with Limited Resources and Spatial Dynamics," The Joint Mathematics Meeting, San Antonio, TX
JUL 2014	"A Mathematical Model of Moisture Movement and Bacterial Growth in Two-Dimensional Porous Medium," Society for Industrial and Applied Mathematics Annual Meeting, Chicago, IL
APR 2007	"The Airplane Boarding Problem," Salisbury University Annual Student Research Conference, Salisbury, MD

Memberships and Service

FEB 2019 Organized a morning of math workshops for students at Oostburg

	Christian School through the Association for Women in Mathematics
JAN 2018 - MAY 2019	Secretary of new Association for Women in Mathematics Chapter
APR 2017	Session Moderator, The 2017 Annual Mathematical Association of America - Wisconsin Section Meeting Milwaukee, WI
AUG 2016	Panelist at New Teaching Assistant Orientation: Session for graduate student teaching assistants in math and science, University of Wisconsin - Milwaukee
APR 2016	"An Honest Take on Graduate School," Invited Guest Speaker, Math Club, University of Wisconsin - Milwaukee
OCT 2015	Invited Guest Speaker, Teaching Math to Undergraduates Seminar, University of Wisconsin - Milwaukee
MAR 2014	Scientific Process Judge, Badger State Science and Engineering Fair, Milwaukee, WI
JAN 2014 - PRESENT	Association for Women in Mathematics
JAN 2014 - PRESENT	Society for Industrial and Applied Mathematics
OCT 2012 - PRESENT	American Mathematical Society
2007	Student Vice President, Salisbury University Chapter 168, The Honor Society of Phi Kappa Phi
MAY 2006 - PRESENT	The Honor Society of Phi Kappa Phi
MAY 2005 - PRESENT	Pi Mu Epsilon

Scholarships, Awards and Distinctions

MAY 2019	Morris and Miriam Marden Award in Mathematics, University of Wisconsin - Milwaukee: Given for a mathematical paper of high quality with respect to both exposition and mathematical content
SEPT 2017, SEPT 2018	Math Research Excellence Award, University of Wisconsin - Milwaukee
MAY 2015	Summer Research Excellence Award, University of Wisconsin - Milwaukee
SEPT 2012 - 2016	Chancellor's Award, University of Wisconsin - Milwaukee: Given for up to five years to graduate students in excellent standing
MAY 2013, MAY 2018	Ernst Schwandt Graduate Teaching Award, University of Wisconsin - Milwaukee: Recognizes demonstrated outstanding teaching performance by Mathematical Sciences Graduate Student Teaching Assistants and may be won at most once in any three year period
FEB 2007	Mathematical Contest in Modeling, Honorable Mention
DEC 2004	Ensemble Scholarship (Symphony Orchestra)
SEPT 2004 - DEC 2007	Henson Scholarship, Salisbury University: Given to three to four incoming students per year with support continued until degree

	completed for up to four years
SEPT 2004 - DEC 2007	Presidential Scholarship, Salisbury University

Professional Development

OCT 2018, NOV 2017	"Checkpoint: Data Security & Privacy" online training, University of Wisconsin - Milwaukee
SEPT 2017	"Think About It" Title IX Training, University of Wisconsin System-wide online training
FEB, MAR 2017	Safe Space Training, LGBT+ Center, University of Wisconsin - Milwaukee
FEB 2015	Title IX Training, Office of Equity/Diversity Services, University of Wisconsin - Milwaukee
NOV 2014	Workshop with Dr. Paul Nolting: "Improving Math Study Skills and Reducing Test Anxiety"
SEPT - DEC 2012	Responsible Conduct in Research Seminar, University of Wisconsin - Milwaukee
AUG 2012	Teaching Assistant Orientation, University of Wisconsin - Milwaukee