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A Mathematical Model for Malaria with Age-Heterogeneous Biting Rate

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Abstract

We propose a mathematical model for malaria with age-heterogeneous biting rate from mosquitos. The existence of the model, the local behavior of the disease free equilibrium are explored. Furthermore the model is extended to an optimal control problem and the corresponding adjoint equations and optimality conditions are derived. Age dependent parameter values are estimated and numerical simulations are carried out for the model. The new model better accounts for difference in biting rates of mosquitos to different age groups, and improvements in stability to the explicit algorithm. The optimal control is also shown to depend on the age distribution of the biting rate.

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Chapter 1

Introduction

Malaria is a parasitic disease that infects an estimated 228 million individuals and kills an estimated 405,000 [1] people a year. The disease is especially prevalent in Africa and is a major health risk for children, killing 207,000 children a year. The disease is both preventable and curable. Methods and strategies for combatting the spread of malaria continue to be a major issue for the World Health Organization in Africa.

Malaria is caused by 5 different species of Plasmodian Parasites. The parasites vary in the risk they pose to the infected individual. The transmission of malaria occurs as a mosquito feeds on the blood of an infected individual. This infects the mosquito with the parasite. Further transmission back to humans occurs when the mosquito takes another blood meal and injects the parasite into another individual. The parasite is present in red blood cells and can spread through blood transfusions and shared use of needles but do not generally spread from human to human.

There have been large efforts to prevent and treat malaria in recent years. Some efforts have been focused on controling the mosquito population through insecticide treatments, as well as promoting the use of bed nets to lower the contact rate between the vector population and humans. There are also preventative drugs to take preemptively. There are concerns with the development of resistance both by mosquitos to the insecticide and the parasite to the drug.

The focus of this paper is on the recent development of RTS,S, a vaccine for malaria. As of 2019, the vaccine is in a phased introduction stage, starting in the countries of Ghana, Kenya, and Malawi. The goal of this paper is to explore the dynamics of the spread of malaria in the presence of a vaccine. The specific method of transmission, through a mosquito, makes the dynamics of malaria unique and separate from analysis of other diseases.

The use of differential equation in mathematical epidemiology has been going on for at least a century. Ordinary differential equations are use to model the change in susceptible and infected populations with respect to time. The purely time dependent models are heavily explored and are taught usually in an introductory mathematical modeling class. The paper of Kermack and McKendrick [2] in 1927 introduces an extra variable of time since infection. This leads to a set of partial differential equations instead of the traditional ordinary differential equation. The additional variable allows modeling of factors such as recovery rate from infection as a function of the duration of the infection. Some examples of age since infection models and their use can be found in [3]. Although the model in this thesis is not an age since infection model, many of the techniques used in these models also apply to the model in this paper.

Age-demographic structured models look to account for the impact of demographic age on parameters for both modeling population and diseases. For example it is clear that not all countries have the same age profile for their residents. Furthermore, diseases such as malaria have different effect on individuals of different age groups. Children under 5 have been more likely to die as a result of malaria compared to all other age groups. A full introduction to age structured models can be found in [4]. An example of an age-demographic structured model can be found in [5]. In fact in [5], we see an application of techniques in optimal control to evaluate strategies to vaccinate populations, which we follow carefully in this thesis. This thesis will use an age-demographic model to model malaria.

The basic reproduction number is a common measure of the transmission rate of a disease. In epidemiology it describes the number of secondary cases from an infectious individual in a fully susceptible environment. It turns out that there is a mathematical value that can be derived from examining the asymptotic behavior of the model that agrees with the physical definition. For the case of ordinary differential equations, the problem of finding the basic reproduction number has been thoroughly explored in [6]. There are many more examples of the derivation found in [7]. For age-structured models the mathematical derivation of the basic reproduction number is not as simple. In most cases, we can only prove a small potion of the asymptotic stability results given for the case of ordinary differential equations in [6]. An example of the derivation of the basic reproduction number for partial differential equations (both age demographic and age since infection models can be found in [8, 3]

There have been several papers examining mathematical models for malaria. Previous models have been focused on strategies such as bed nets and some models for vaccines [9, 10, 11, 12, 3]. Our model, in contrast with other models explored is an age-structured model that investigates the effects of vaccinations as well as accounts for biting preferences of mosquitos for different age groups.

There are also extensive explorations into the numerical simulations of various aspects of population and disease models. For ODE models, there are extensive texts for simulation of population dynamics in many textbooks, for example [13]. For disease models there are sometimes concerns for preservation of the number of individuals in the total population, leading to invariant preserving algorithms.

For age structured models, there are several approaches for numerical simulations such as Euler-Riemann [4] formulations along the characteristic and estimations of integral equations associated with the partial differential equations for the model [14]. There are also works into higher order numerical methods for the age structured population models [15],[16]. Forward backward sweep methods for optimal control problems are explored in [17, 18]

The thesis is structured as follows. In the second section, we introduce the model of interest and explain the structure of the age heterogeneous force of infection parameter and present the model assumptions. We will place emphasis on the derivation for the force of infection and the important property of preserving the number of total bites.

In the third section we analytically explore the model. We prove the existence of the model using Banach Fixed Point Theorem. We furthermore find the disease free equilibrium and analyze perturbations of the disease free equilibrium. We derive a mathematical formulation of the basic reproduction number and justify why this agrees with the physical definition of the basic reproduction number.

In the fourth section we look at optimal control formulations of the model and derive the formulas for optimal vaccination rates using sensitivities and adjoint function methods. We do not include the proof of existence of the solutions for the adjoint or the optimal control and leave that for a later work.

In the fifth section, we present numerical methods for solving age-structured epidemic models. This includes both explicit and implicit first order Euler-Riemann Methods for both the state equations. We furthermore present an implicit method for solving the adjoint equation and a forward backward sweep method used to solve the optimal control problem.

In the sixth section we present analysis and derivation of age-dependent parameter values. The death and birth rates of Nigeria are modeled. Furthermore, we derive estimates for the age dependent disease induced death rates through data from the World

Health Organization.

The seventh section contains various numerical simulations. First, there are simulations of the initial model and the difference the age dependent force of infection has on our model. Then there are numerical simulations showing the benefits to stability that the added assumption from an age-dependent force of infection allows. Lastly there are some results concerning optimal control.

The appendices include parts of the proofs of theorems in the thesis that were excessively long and similar to previous proofs in other works. They were included for the purpose of completeness.

Chapter 2

Derivation of Model

2.1 Model Formulation

Let $s_h(t,a), i_h(t,a), r_h(t,a), v_h(t,a)$ be the population density of individuals age a at time t for the susceptible, infected, recovered and vaccinated human populations respectively. We use the subscipt h to indicate the density is for human populations. The support of s_h, i_h, r_h and v_h is $[0, A] \times [0, T]$, where A is the maximum age of an individual and maximum time $T > 0$. We have total population density at age a and time t given by

$$n_h(t,a) = s_h(t,a) + i_h(t,a) + r_h(t,a) + v_h(t,a)$$

The total population count at time t is given by integrating over all age groups

$$N_h(t) = \int_0^A n_h(t,a)da$$

Then a logistic death rate is given by

$$\mu_h(a, N_h) = \mu_{h0}(a) + \mu_{h1}N_h \tag{2.1}$$

with the condition that $\lim_{a \to A^-} \mu_0(a) = \infty$. The birth rate is given by a function $b_h(a)$ and the total density of births at time t is given by the integral

$$\int_0^A b_h(a) n_h(t,a) da$$

All individuals are born susceptible, without any immunity and without infection. We closely follow the dynamics of the spread of malaria in formulating the rest of the model. Infected individuals recover at rate $\zeta_h(a)$, recovered individuals lose immunity at rate $\gamma_h(a)$, susceptible individuals are immunized at rate $\xi_h(a)$ and lose vaccine immunity at rate $\eta_h(a)$. There is an additional death rate for infected individuals of $\delta_h(a)$.

Furthermore let $S_v(t)$ and $I_v(t)$ be the number of susceptible and infectious mosquitos at time t. The subscript v is use to indicate the mosquitos, which is usually refered to as a vector. In epidemiology a vector of disease is any agent that carries and transmits infectious pathogens into another living organism. So for the case of malaria, mosquitos are the vectors of disease. They have a death rate of μ_v and a constant recruitment rate of Λ_v. All mosquitos are recruited free of malaria infections. Let $N_v(t) = S_v(t) + I_v(t)$ be total mosquito population.

The force of infection of the disease is from human to mosquito and vice versa. The force of infection from vector to human is given by the formula

$$\lambda_{vh}(a,t) = p_1 \beta \frac{I_v(t)}{N_v(t)} \cdot \frac{N_v(t)\rho(a)}{\int_0^A \rho(a) n_h(t,a)} = \frac{p_1 \beta I_v(t) \rho(a)}{\int_0^A \rho(a) n_h(t,a) da}$$

where $\rho(a)$ is the age distribution which bites are distributed, p_1 is the probability of infection after a bite from an infectious mosquito, β is the contact rate between humans and mosquito. The force of infection from human to mosquito is

$$\lambda_{hv}(t) = p_2\beta\frac{\int_0^A \rho(a)i_h(t,a)da}{\int_0^A \rho(a)n_h(t,a)da}$$

A full explanation of the force of infection is found after the full model.

We have the full model below

$$\frac{\partial s_h(t,a)}{\partial t} + \frac{\partial s_h(t,a)}{\partial a} = -(\lambda_{vh}(a,t) + \mu_h(a,N_h(t)) + \xi_h(a))s_h(t,a) + \gamma_h(a)r_h(t,a) + \eta_h(a)v_h(t,a) \tag{2.2}$$

$$\begin{aligned}
\frac{\partial i_h(t,a)}{\partial t} + \frac{\partial i_h(t,a)}{\partial a} &= \lambda_{vh}(t,a)s_h(t,a) - (\zeta_h(a) + \delta_h(a) + \mu_h(a,N_h(t)))i_h(t,a) \\
\frac{\partial r_h(t,a)}{\partial t} + \frac{\partial r_h(t,a)}{\partial a} &= \zeta_h(a)i_h(t,a) - (\gamma_h(a) + \mu_h(a,N_h(t)))r_h(t,a) \\
\frac{\partial v_h(t,a)}{\partial t} + \frac{\partial v_h(t,a)}{\partial a} &= \xi_h(a)s_h(t,a) - (\mu_h(a,N_h(t)) + \eta_h(a))v_h(t,a) \\
\frac{dS_v(t)}{dt} &= \Lambda_v - (\mu_v + \lambda_{hv}(t))S_v(t) \\
\frac{dI_v(t)}{dt} &= \lambda_{hv}(t)S_v(t) - \mu_v I_v(t)
\end{aligned}$$

We have initial conditions

$$s_{h0}(0,a) = s_{h0}(a), i_{h0}(0,a) = i_{h0}(a), r_{h0}(0,a) = r_{h0}(a), v_{h0}(0,a) = v_{h0}(a)$$

$$S_v(0) = S_{v0}, I_v(0) = I_{v0}$$

and the boundary condition

$$s_h(t,0) = \int_0^A b_h(a)n_h(t,a)da, i_h(t,0) = r_h(t,0) = v_h(t,0) = 0$$

Note: We use $\xi(a)$ as the vaccination rate so that a disease free equilibrium is well

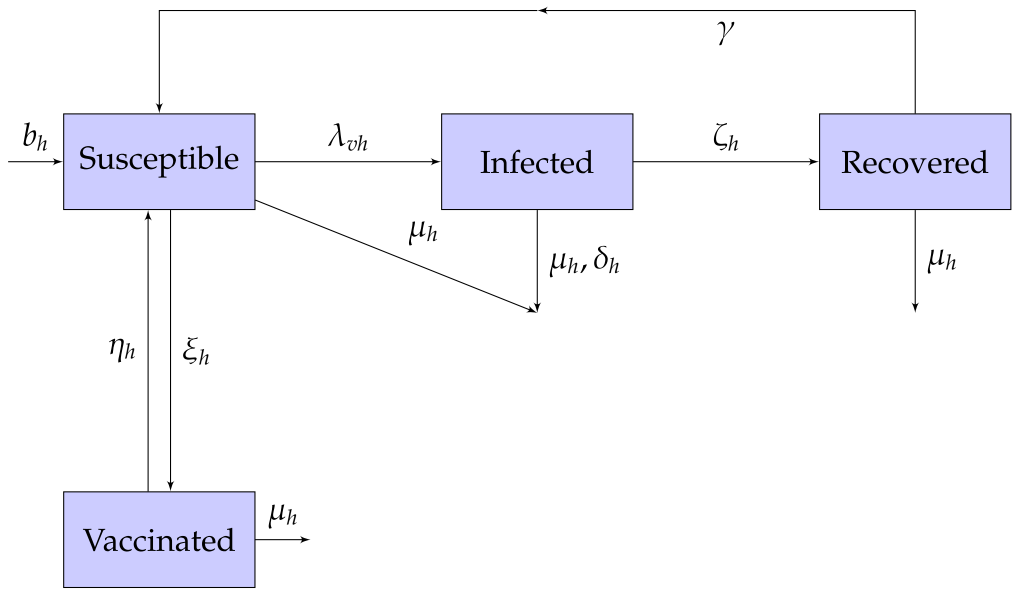

Figure 2.1: Human Population Dynamic

defined. For optimal control formulation in a later section we will use an age and time dependent vaccination rate $\xi_h(a,t)$.

Figure 2.1 has an illustrated flow chart for the dynamics of the human population.

2.2 Derivation of Force of Infection

Many previous models for the spread of malaria contain the assumption, either through omission of an age variable or a force of infection not dependent on age, that the age of an individual does not affect the force of infection of an individual. In previous models, the force of infection from vector to human in previous models took the following form

$$\lambda_{vh}(t) = p_1 \beta \frac{I_v}{N_h}$$

This can be interpreted as the following. There are I_v mosquitos biting at a rate of β. Then since there are a total of N_h humans, the rate that any individual receives a bite from an infectious mosquito is $\beta\frac{I_v}{N_h}$. Then the probability of a bite from an infectious mosquito infecting the human individual is p_1 so the rate at which a susceptible human is infected is $p_1\beta\frac{I_v}{N_h}$. Note that not all of the βI_v bites goes to susceptible humans, some may go to individuals in infected, recovered or vaccinated groups which are not affected by the bites. The total number of bites to susceptible individuals is given by $\beta I_v\frac{S_h}{N_h}$.

The age homogeneous force of infection from human to vector is

$$\lambda_{hv}(t) = p_2\beta\frac{I_h}{N_h}$$

We have that β is the biting rate of a mosquito, and $\frac{I_h}{N_h}$ is the proportion of bites to infected individuals. p_2 is the probability of a mosquito developing infection from biting an infected individual. $p_2\beta\frac{I_h}{N_h}$ is the force of infection from human to vector.

The formulation of the heterogeneous biting rate rests on idea of preserving the total number of bites. This approach differs from other approaches that try to account for the effects of bed nets[11]. The key difference between those examples and our model is treatment like insecticide covered bed nets may change the number of bites that a mosquito gives in its lifetime. In contrast, we are trying to account for difference in the distribution of the bites to different age groups, not variation in the number of bites due to treatments. Given a mosquito bites a person, certain age groups may have a higher chance of receiving that bite. For example, newborns may be isolated in hospitals and indoors and may have less exposure to mosquitos, while individuals of age 5 and older may be more active and spend more time outdoors, increasing their exposure to mosquito bites.

We show the formulation of the heterogeneous force of infection for discrete age groups then extend the idea to the continuous case. Suppose there are a total of B bites between mosquitos and humans. Suppose further that the human group is split into three groups 1, 2 and 3 with M_1, M_2 and M_3 individuals respectively. Let each groups have preference weights ρ_1, ρ_2, ρ_3 respectively. Then let the preference for a person in group M_i being bitten be

$$\frac{\rho_i}{\rho_1 M_1 + \rho_2 M_2 + \rho_3 M_3}$$

We observe that summing the preferences over all people

$$\frac{\rho_i}{\rho_1 M_1 + \rho_2 M_2 + \rho_3 M_3} M_1 + \frac{\rho_i}{\rho_1 M_1 + \rho_2 M_2 + \rho_3 M_3} M_2 + \frac{\rho_i}{\rho_1 M_1 + \rho_2 M_2 + \rho_3 M_3} M_3 = 1$$

Thus we can think of $\frac{\rho_i}{\rho_1 M_1 + \rho_2 M_2 + \rho_3 M_3}$ as the probability of a single individual from group i being bitten given a bite occurs. Then let B be the total number of bites. Then the average number of bites distributed to a person in group M_i is

$$B \cdot \frac{\rho_i}{\rho_1 M_1 + \rho_2 M_2 + \rho_3 M_3}$$

We can also in our case let B be the biting rate instead of the number of bites.

We extend the idea to the continuous case. Let $\rho(a)$ be the preference function over age group for receiving a bite. Given a mosquito bites someone, the probability density of any single individual of age a being infected is

$$\frac{\rho(a)}{\int_0^A \rho(b) n_h(t,b) db}$$

If the biting rate is β, we have by integrating over all humans

$$\int_0^A \beta \frac{\rho(a)}{\int_0^A \rho(b) n_h(t,b) db} n_h(t,a) da = \frac{\int_0^A \beta \rho(a) n_h(t,a) da}{\int_0^A \rho(b) n_h(t,b) db} = \beta$$

preserves the number of bites/biting rate.

Likewise from humans to mosquitos, if β is the number of bites or biting rate, to find the number of bites that infects mosquitos, we want to integrate over the infectious density to see how many mosquito bites were to infected individuals.

$$\int_0^A \frac{\beta\rho(a)}{\int_0^A \rho(b)n_h(t,b)db} i_h(t,a)da = \beta\frac{\int_0^A \rho(a)i_h(t,a)}{\int_0^A \rho(b)n_h(t,b)db}$$

The above is the total number of bites/biting rate of mosquitos to infected individuals.

So the force of infection for an individual of age a is

$$\lambda_{vh}(t,a) = p_1\beta I_v \frac{\rho(a)}{\int_0^A \rho(a)n_h(t,a)da}$$

and the force of infection from vector to human is also modified as

$$\lambda_{hv}(t) = p_2\beta\frac{\int_0^A \rho(a)i_h(t,a)da}{\int_0^A \rho(a)n_h(t,a)da}$$

Chapter 3

Analysis of Model

In this section we work with the model from derived in the previous section. The first part involves proving the existence and uniqueness of a solution to the partial differential equations we provided. This is the necessary starting point to any problem. Then find the disease free equilibrium of the model and we examine the local asymptotic behavior of the disease free equilibrium. Then we explore the threshold value derived for the asymptotic stability of the disease free equilibrium and its interpretation.

3.1 Existence of a solution

We prove theorems concerning the boundedness and existence of the solution to our model.

We have the following assumptions

- $b_h(a)$ is a non-negative function on $L^1(0, A)$ with $|b_h(a)| \leq b$ for some positive bound b.
- $\mu_{h0}(a)$ is an unbounded function on $L^1(0, A)$ and there exists some $\mu_L > 0$ such that $\mu_{h0}(a) \geq \mu_L$
- $\mu_{h1}(a)$ is a non-negative function on $L^1(0, A)$ with $|\mu_{h1}(a)| \leq \mu_{h1}$ for some positive bound μ_{h1}.
- $\eta_h(a)$ is a non-negative function on $L^1(0, A)$ with $|\eta_h(a)| \leq \eta_h$ for some positive bound

η_h.

- $\gamma_h(a)$ is a non-negative function on $L^1(0, A)$ with $|\gamma_h(a)| \leq \gamma_h$ for some positive bound γ_h.

- $\zeta_h(a)$ is a non-negative function on $L^1(0, A)$ with $|\zeta_h(a)| \leq \zeta_h$ for some positive bound ζ_h.

- $\delta_h(a)$ is a non-negative function on $L^1(0, A)$ with $|\delta_h(a)| \leq \delta_h$ for some positive bound δ_h.

- $\xi_h(t, a)$ is a non-negative function on $L^\infty(0, T; L^1(0, A))$ with

$$\sup_{t \geq 0} \xi_h(t, a) da \leq \xi_h$$

  for some positive bound ξ_h. If $\xi_h(t, a)$ is not dependent on t then $|\xi_h(a)| \leq \xi_h$ for all a.

- $p_1, p_2, \beta\Lambda_v, \mu_v$ are positive constants. We let $p_1\beta, p_2\beta \leq C$ for convenience.

- $\rho(a)$ is a non-negative function on $L^1(0, A)$ with $\rho(a) \leq \rho$ for some $\rho > 0$.

The last assumption can be made into $\rho(a) \leq 1$ since if we have some non-negative function $\rho_1(a)$ and K is a positive function then consider $\rho_2(a) = K\rho_1(a)$. Then the force of infection using ρ_1 and ρ_2 are equivalent.

$$\begin{aligned}
\lambda_{vh} : \quad & \frac{\rho_1(a) I_h(t)}{\int_0^A \rho_1(b) n_h(t, b) db} = \frac{K\rho_1(a) I_h(t)}{\int_0^A K\rho_1(b) n_h(t, b) db} = \frac{\rho_2(a) I_h(t)}{\int_0^A \rho_2(b) n_h(t, b) db} \\
\lambda_{hv} : \quad & \frac{\int_0^A \rho_1(a) i_h(t, a) da}{\int_0^A \rho_1(b) n_h(t, b) db} = \frac{\int_0^A K\rho_1(a) i_h(t, a) da}{\int_0^A K\rho_1(b) n_h(t, b) db} = \frac{\int_0^A \rho_2(a) i_h(t, a) da}{\int_0^A \rho_2(b) n_h(t, b) db}
\end{aligned}$$

For proofs it will be more convenient for notation if we assume $\rho(1) \leq 1$. For writing a numerical algorithm it will be more convenient to leave $\rho(a)$ as a reasonable non-negative function

We note that some papers have the assumption $\xi_h(t, a) \leq 1$ based on the idea that we cannot vaccinate more than a proportion of 1 of the population per year. This is not reasonable as $\xi_h(t, a)$ is a rate not a proportion. For example consider the population of Minnesota State University-Mankato. If the University has a campaign to vaccinate all students against the flu in the period of a week then the rate at which the student population is vaccinated is 52 vaccinations per person per year. We see that this formulation is reasonable and so the assumption that $\xi_h(t, a)$ should be bounded by 1 does not necessarily make sense. We do make the assumption that the number of vaccinations at any given time is bounded by some number.

We will further use one more assumption:

$$\int_0^A \rho(a) n_h(t, a) da \geq m$$

for some $m > 0$ for all t. This assumption states that first that n_h does not tend to 0. A proof that $N_h(t) > m'$ for some $m' > 0$ is shown in [19]. The assumption also states that the group of individuals that recieve no bites as a result of the age distribution of the bites i.e. age where $\rho(a) = 0$ is not the support of n_h.If that were the case then the formulation of the age dependent force of infection preserving the number of bites does not make sense since mosquitos may be biting but $\int_0^A \rho(a) n_h(t, a) da = 0$ indicates no person can recieve that bite.

Assume that $p_1\beta, p_2\beta \leq C$. We can make the assumption that the initial conditions integrated ver the age profile is bounded. Let M be some positive number such that the initial conditions satisfy

$$\int_0^A s_{h0}(t,a)da \leq \frac{M}{8}$$
$$\int_0^A i_{h0}(t,a)da \leq \frac{M}{8}$$
$$\int_0^A r_{h0}(t,a)da \leq \frac{M}{8}$$
$$\int_0^A v_{h0}(t,a)da \leq \frac{M}{8}$$
$$S_{v0} \leq \frac{M}{8}$$
$$I_{v0} \leq \frac{M}{8}$$

We then define the state solution space with fixed initial function

$$X = \Big\{(s_h, i_h, r_h, v_h, S_v, I_v) \in L^\infty(Q) \times L^\infty(Q) \times L^\infty(Q) \times L^\infty(Q) \times L^\infty(0,T) \times L^\infty(0,T) \Big|$$
$$\sup_{0\leq t\leq T} \int_0^A |s_h(t,a)|da \leq \frac{M}{4}, \sup_{0\leq t\leq T} \int_0^A |i_h(t,a)|da \leq \frac{M}{4}, \sup_{0\leq t\leq T} \int_0^A |r_h(t,a)|da \leq \frac{M}{4},$$
$$\sup_{0\leq t\leq T} \int_0^A |v_h(t,a)|da \leq \frac{M}{4}, |S_v| \leq \frac{M}{4}, |I_v| \leq \frac{M}{4} a.e.t.$$
$$s_{h0}(0,a) = s_{h0}(a), i_{h0}(0,a) = i_{h0}(a), r_{h0}(0,a) = r_{h0}(a), v_{h0}(0,a) = v_{h0}(a)$$
$$S_v(0) = S_{v0}, I_v(0) = I_{v0}\Big\}$$

where $Q = (0, T; L^1(0, A))$. Then we have the following bounds

$$
\begin{aligned}
|N_h(t)| &= |S_h(t) + I_h(t) + R_h(t) + V_h(t)| \\
&= |S_h(t)| + |I_h(t)| + |R_h(t)| + |V_h(t)| \\
&\leq \int_0^A |s_h(t,a)|da + \int_0^A |i_h(t,a)|da + \int_0^A |r_h(t,a)|da + \int_0^A |v_h(t,a)|da \\
&\leq \frac{M}{4} + \frac{M}{4} + \frac{M}{4} + \frac{M}{4} = M \\
|I_h(t)| &\leq \int_0^A |i_h(t,a)|da \leq \frac{M}{4} \\
|\lambda_{hv}(t)| &= \left| \frac{p_1 \beta I_v \rho(a)}{\int_0^A \rho(a) n_h(t,a)} \right| \leq \frac{CM}{4m} \\
|\lambda_{vh}(t)| &= \left| \frac{p_1 \beta \int_0^A \rho(a) i_h(t,a)da}{\int_0^A \rho(a) n_h(t,a)} \right| \leq \left| \frac{p_1 \beta \int_0^A \rho(a) i_h(t,a)da}{\int_0^A n_h(t,a)} \right| \leq \frac{CM}{4m}
\end{aligned}
$$

Then consider the following functional $L : X \to X$. The functionals are derived by looking at implicit solutions to the partial differential equations for the model. The derivations are included in Appendix A.

$$
\begin{aligned}
L(s_h, i_h, r_h, v_h, S_v, I_v) = \Big(& L_1(s_h, i_h, r_h, v_h, S_v, I_v), L_2(s_h, i_h, r_h, v_h, S_v, I_v), L_3(s_h, i_h, r_h, v_h, S_v, I_v) \\
& , L_4(s_h, i_h, r_h, v_h, S_v, I_v), L_5(s_h, i_h, r_h, v_h, S_v, I_v), L_6(s_h, i_h, r_h, v_h, S_v, I_v) \Big)
\end{aligned}
$$

with

$$L_1(s_h, i_h, r_h, v_h, S_v, I_v) =$$

$$\begin{cases} s_{h0}(a-t)e^{-\int_0^t \lambda_{vh}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\xi(a-t+\tau)d\tau} \\ \quad + \int_0^t (\gamma(a-t+p)r_h(t,a-t+p)+\eta(a-t+p)v_h(t,a-t+p))\times \\ \quad e^{-\int_p^t \lambda_{vh}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\xi(a-t+\tau)d\tau} dp \\ \text{if } t < a \\ \int_0^A b_h(a)n_h(t-a,a)da e^{-\int_0^a \lambda_{vh}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))+\xi(t-a+\tau)d\tau} \\ \quad + \int_0^a (\gamma(t-a+p)r_h(t,t-a+p)+\eta(t-a+p)v_h(t,t-a+p))\times \\ \quad e^{-\int_p^a \lambda_{vh}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))+\xi(t-a+\tau)d\tau} dp \\ \text{if } t \geq a \end{cases}$$

$$L_2(s_h, i_h, r_h, v_h, S_v, I_v) =$$

$$\begin{cases} i_{h0}(a-t)e^{-\int_0^t \zeta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\delta(a-t+\tau)d\tau} \\ \quad + \int_0^t \lambda_{vh}(\tau,a-t+p)s_h(t,a-t+p)e^{-\int_p^t \zeta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\delta(a-t+\tau)d\tau} dp \\ \text{if } t < a \\ \int_0^t \lambda_{vh}(\tau,t-a+p)s_h(t,t-a+p)e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))+\delta(t-a+\tau)d\tau} dp \\ \text{if } t \geq a \end{cases}$$

$$L_3(s_h, i_h, r_h, v_h, S_v, I_v) =$$

$$\begin{cases} r_{h0}(a-t)e^{-\int_0^t \gamma(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))d\tau} \\ \quad + \int_0^t \zeta(a-t+p)i_h(t,a-t+p)e^{-\int_p^t \gamma(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))d\tau}dp \\ \text{if } t < a \\ \int_0^t \zeta(t-a+p)i_h(t,t-a+p)e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))d\tau}dp \\ \text{if } t \geq a \end{cases}$$

$$L_4(s_h, i_h, r_h, v_h, S_v, I_v) =$$

$$\begin{cases} v_{h0}(a-t)e^{-\int_0^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))d\tau} \\ \quad + \int_0^t \xi(a-t+p)s_h(t,a-t+p)e^{-\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))d\tau}dp \\ \text{if } t < a \\ \int_0^t \xi(t-a+p)s_h(t,t-a+p)e^{-\int_p^t \eta(t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))d\tau}dp \\ \text{if } t \geq a \end{cases}$$

$$L_5(s_h, i_h, r_h, v_h, S_v, I_v) = S_{v0}e^{-\int_0^t \lambda_{hv}(\tau)+\mu_v d\tau} + \int_0^t \Lambda_v e^{-\int_p^t \lambda_{hv}(\tau)+\mu_v d\tau}dp$$

and

$$L_6(s_h, i_h, r_h, v_h, S_v, I_v) = I_{v0}e^{-\int_0^t \mu_v d\tau} + \int_0^t \lambda_{hv}(p)e^{-\int_p^t \lambda_{hv}(\tau)+\mu_v d\tau}dp$$

Then we have the following theorem

Theorem 3.1.1. *There exists a unique solutions the system 2.2 with the initial conditions and boundary conditions given with the assumptions given earlier in this section on some finite time domain* $[0, T]$.

Proof. The proof of this theorem is similar to proofs of existence in a previous works for a similar model [19]. For completeness most of the proof is included in the appendix but we explain the general steps here. We used a contraction mapping principal to prove the existence of a unique solution. More specifically we will use Banach Fixed Point Theorem which reads: If (X, d) is a complete metric space with a contraction mapping $T : X \to X$ then there exists a unique fixed point. There are two steps, first we prove that L maps X to X on some finite time interval in Appendix B. Then we prove that it is satisfies a Lipchitz condition on a finite time interval in Appendix C proving that L is a contraction. Then the result of the theorem follows immediately from Banach Fixed Point theorem as a fixed point of L is a set of functions that satisfies the equations 2.2. □

3.2 Basic Reproduction Number

We find and explore the asymptotic stability of the disease free equilibrium of the model 2.2. We first introduce two simpler models, one with just the susceptible compartment and another with the addition of the vaccination compartment. We find the steady states for both models then show the asymptotic stability and derive the basic reproduction number for the full model.

3.2.1 Logistic Population Model

We first consider a typical age structured population model for logistic growth. First consider the system

$$\begin{aligned} \frac{\partial s_h(t,a)}{\partial t} + \frac{\partial s_h(t,a)}{\partial a} &= -\mu_h(a, N_h(t)) s_h(t,a) \\ s_h(0,a) &= s_{h0}(a) \\ s_h(t,0) &= \int_0^A b_h(a) s_h(t,a) da \end{aligned} \tag{3.1}$$

where we have the logistic death rate $\mu_(a, N_h(t)) = \mu_{h0}(a) + \mu_1 N_h(t)$ of the form described in the original model derivation. The generalization of the following two result for this model can be found in Iannelli and Milner [4] and is adjusted for our specific model

Theorem 3.2.1 (Theorem 5.4 Iannelli and Milner). *If $R_0 = \int_0^A b_h(a) e^{-\int_0^a \mu_{h0}(b)db} da \geq 1$ then the model (3.1) has a unique non-trivial steady state given by*

$$p^*(a) = S^* \frac{e^{-\int_0^a \mu_h(b,S^*)db}}{\int_0^A e^{-\int_0^a \mu_h(b,S^*)db} da}$$

where S^* is the solution to S^* in

$$1 = \int_0^A b_h(a) e^{-\int_0^a \mu_h(b,S^*)db}$$

Theorem 3.2.2 (Proposition 6.6 Iannelli and Milner). *Let the assumptions of Theorem (3.2.1) hold. Then if additionally we have*

$$e^{-\int_0^a \mu_{h0}(b)db}$$

is a non-increasing and convex, we have that for $R_0 > 1$ then the corresponding equilibrium is asymptotically stable.

We will assume all of these conditions are satisfied and we have a non-trivial equilibrium for the total population.

3.2.2 Disease Free Model

We look at the disease free model to find the disease free equilibrium and prove it is asymptotically stable when the disease is not present. The disease free model with just the susceptible and vaccinated compartments is

$$\begin{aligned}\frac{\partial s_h(t,a)}{\partial t} + \frac{\partial s_h(t,a)}{\partial a} &= -(\mu_h(a,N_h(t)) + \xi_h(a))s_h(t,a) + \eta(a)v_h(t,a) \\ \frac{\partial v_h(t,a)}{\partial t} + \frac{\partial v_h(t,a)}{\partial a} &= \xi_h(a)s_h(t,a) - (\mu_h(a,N_h(t)) + \eta_h(a))v_h(t,a)\end{aligned} \tag{3.2}$$

with initial condition

$$s_h(0,a) = s_{h0}(a)$$

$$v_h(0,a) = v_{h0}(a)$$

and boundary conditions

$$s_h(t,0) = \int_0^A b_h(a)n_h(t,a)da$$

$$v_h(t,0) = 0$$

Since the population equilibrium is asymptotically stable, assume the total population

$p(t,a) = s_h(t,a) + v_h(t,a)$ is at equilibrium $p^*(a)$ and consider the variable

$$u_h(t,a) = \frac{v_h(t,a)}{p^*(a)}$$

We have the relation $\frac{s_h(t,a)}{p^*(a)} = 1 - u(t,a)$. Then we have the new reduced system

$$\begin{aligned}\frac{\partial u_h(t,a)}{\partial t} + \frac{\partial u_h(t,a)}{\partial a} &= \frac{\frac{\partial v_h(t,a)}{\partial t}}{p^*(a)} + \frac{\frac{\partial v_h(t,a)}{\partial a}p^*(a) - v_h(t,a)\frac{\partial p^*(a)}{\partial a}}{(p^*(a))^2} \\ &= \frac{\partial v_h(t,a)}{\partial t} + \frac{\partial v_h(t,a)}{\partial a} + \mu_h(a,S^*)v(t,a) \\ &= \xi_h(a)(1-u_h(t,a)) + \eta_h(a)u_h(t,a)\end{aligned} \tag{3.3}$$

with initial condition

$$u_h(0,a) = \frac{v_h(0,a)}{p^*(0)}$$

and boundary condition

$$u_h(t,0) = 0$$

Theorem 3.2.3. *The model (3.2) has the non-trivial equilibrium*

$$\begin{aligned}v^*(a) &= p_\infty(a)\int_0^a \xi_h(\sigma)e^{-\int_\sigma^a(\xi_h(b)+\eta_h(b))db}da \\ s^*(a) &= p_\infty(a) - v^*(a)\end{aligned}$$

and it is globally stable.

Proof. We can in fact solve Equation(3.3) by solving along the characteristic curve in the same way we found the functionals for Model 2.2 and find that the solution is

$$u(t,a) = \begin{cases} \int_{a-t}^{a} \xi_h(\sigma) e^{-\int_\sigma^a \eta(b)+\xi_h(b)db} d\sigma + u_{h0}(a-t) & \text{if } a-t \geq 0 \\ \int_0^a \xi_h(\sigma) e^{-\int_\sigma^a \eta(b)+\xi_h(b)db} d\sigma & \text{if } a-t < 0 \end{cases}$$

Thus for large t, we have that

$$u(t,a) = \int_0^a \xi_h(\sigma) e^{-\int_\sigma^a \eta(b)+\xi_h(b)db} d\sigma$$

which is the steady state. □

3.2.3 The Disease Free Equilibrium and Local Asymptotic Stability

We will linearize the system 2.2 around the disease free equilibrium under the following assumption, when we make perturbations to the equilibrium the total population age profile, $n_h(a)$ will remain the same as the one for the disease free equilibrium, $n_h^*(a)$. The total population N_h^* is also fixed.

After we do so, the solution to the linearized system is assumed to be separable and take a specific form. Then we show that given certain conditions are satisfied, the perturbations converge to 0 and so the disease free equilibrium is asymptotically stable.

The idea of this method is to find the properties of the simpler linearized system and make conclusions about the non-linear system.

Let the disease free equilibrium be the one given in Theorem 3.2.3

$$(s^*(a), i^*(a), r^*(a), v^*(a), S_v^*, I_v^*) = (s^*(a), 0, 0, v^*(a), S_v^*, I_v^*)$$

Let

$$s_h(t,a) = s^*(a) + w(t,a), i_h(t,a) = x(t,a), r_h(t,a) = y(t,a), v_h(t,a) = z(t,a)$$

$$S_v(t) = S_v^* + k(t), I_v(t) = l(t)$$

We now have the following equation for $w(t,a)$

$$\begin{aligned}
\frac{\partial w(t,a)}{\partial t} + \frac{\partial w(t,a)}{\partial a} &= \frac{\partial s_h(t,a)}{\partial t} + \frac{\partial s_h(t,a)}{\partial a} - \frac{ds^*(a)}{da} \\
&= -(\lambda_{vh}(a,t) + \mu_h(a,N_h^*) + \xi_h(a))s_h(t,a) + \gamma_h(a)r_h(t,a) + \eta_h(a)v_h(t,a) \\
&\quad - [-(\mu_h(a,N_h^*) + \xi_h(a))s_h^*(a) + \eta_h(a)v^*(a)] \\
&= -\Big(\frac{p_1\beta\rho(a)l(t)}{\int_0^A \rho(s)n^*(s)ds} + \mu_h(a,N_h^*) + \xi(a)\Big)(s^*(a) + w(t,a)) + \gamma_h(a)y(t,a) \\
&\quad + \eta_h(a)(v^*(a) + z(t,a)) + (\mu_h(a,N_h^*) + \xi(a))s_h^*(a) - \eta(a)v^*(a) \\
&= -\frac{p_1\beta\rho(a)l(t)}{\int_0^A \rho(s)n^*(s)da}(s^*(a) + w(t,a)) - (\mu_h(a,N_h^*) + \xi(a))w(t,a) \\
&\quad + \gamma_h(a)y(t,a) + \eta_h(a)z(t,a)
\end{aligned}$$

We linearize this to get

$$\frac{\partial w(t,a)}{\partial t} + \frac{\partial w(t,a)}{\partial a} = -\frac{p_1\beta\rho(a)s^*(a)}{\int_0^A \rho(s)n^*(s)ds}l(t) - (\mu_h(a,N_h^*) + \xi(a))w(t,a) + \gamma_h(a)y(t,a) + \eta_h(a)z(t,a)$$

We work on $x(t,a)$ next

$$\frac{\partial x(t,a)}{\partial t}+\frac{\partial x(t,a)}{\partial a}=\frac{\partial i_h(t,a)}{\partial t}+\frac{\partial i_h(t,a)}{\partial a}$$
$$=\lambda_{vh}(t,a)s_h(t,a)-(\zeta_h(a)+\delta_h(a)+\mu_h(a,N_h(t)))i_h(t,a)$$
$$=\frac{p_1\beta\rho(a)l(t)}{\int_0^A\rho(s)n_h^*(s)ds}(s^*(a)+w(t,a))-(\zeta_h(a)+\delta_h(a)+\mu_h(a,N_h^*))x(t,a)$$

We linearize this to get

$$\frac{\partial x(t,a)}{\partial t}+\frac{\partial x(t,a)}{\partial a}=\frac{p_1\beta\rho(a)s^*(a)}{\int_0^A\rho(s)n_h^*(s)ds}l(t)-(\zeta_h(a)+\delta_h(a)+\mu_h(a,N_h^*))x(t,a)$$

Next is $y(t,a)$,

$$\frac{\partial y(t,a)}{\partial t}+\frac{\partial y(t,a)}{\partial a}=\frac{\partial r_h(t,a)}{\partial t}+\frac{\partial r_h(t,a)}{\partial a}$$
$$=\zeta_h(a)i_h(t,a)-(\gamma_h(a)+\mu_h(a,N_h^*))r_h(t,a)$$
$$=\zeta_h(a)x(t,a)-(\gamma_h(a)+\mu_h(a,N_h^*))y(t,a)$$

This equation is already linearized. Then for $z(t,a)$,

$$\frac{\partial z(t,a)}{\partial t}+\frac{\partial z(t,a)}{\partial a}$$
$$=\frac{\partial r_h(t,a)}{\partial t}+\frac{\partial r_h(t,a)}{\partial a}-\frac{dv^*(a)}{da}$$
$$=\xi_h(a)s_h(t,a)-(\mu_h(a,N_h^*)+\eta(a))v_h(t,a)-\Big[-(\mu_h(a,N_h^*)+\eta_h(a))v_h^*(a)+\xi(a)v^*(a)\Big]$$
$$=\xi_h(a)(s_h^*(a)+w(t,a))-(\mu_h(a,N_h^*)+\eta_h(a))(v_h^*(a)+z(t,a))$$
$$-\Big[-(\mu_h(a,N_h^*)+\eta_h(a))v_h^*(a)+\xi(a)v^*(a)\Big]$$
$$=\xi(a)w(t,a)-(\mu_h(a,N_h^*)+\gamma(a))z(t,a)$$

We also keep track of the boundary conditions

$$w(t,0) = x(t,0) = \int_0^A b_h(a)n_h^*(a)da$$

$$x(t,0) = i_h(t,0) = 0$$

$$y(t,0) = r_h(t,0) = 0$$

$$z(t,0) = v_h(t,0) = 0$$

Now we move onto the vector equations

$$\begin{aligned}
\frac{dk(t)}{dt} &= \frac{dS_v(t)}{st} \\
&= \Lambda_v - (\mu_v + \lambda_{hv}(t))S_v(t) \\
&= \Lambda_v - \Big(\mu_v + \frac{p_2\beta\int_0^A \rho(a)x(t,a)da}{\int_0^A \rho(s)n^*(s)ds}\Big)(S_v^* + k(t)) \\
&= \Lambda_v - \Big(\mu_v + \frac{p_2\beta\int_0^A \rho(a)x(t,a)da}{\int_0^A \rho(s)n^*(s)ds}\Big)\Big(\frac{\Lambda_v}{\mu_v} + k(t)\Big) \\
&= -\mu_v k(t) - \frac{p_2\beta\int_0^A \rho(a)x(t,a)da}{\int_0^A \rho(s)n^*(s)ds}\Big(\frac{\Lambda_v}{\mu_v} + k(t)\Big)
\end{aligned}$$

We linearize this

$$\frac{dk(t)}{dt} = -\mu_v k(t) - \frac{p_2\beta\Lambda_v}{\mu_v\int_0^A \rho(s)n^*(s)ds}\int_0^A \rho(a)x(t,a)da$$

Lastly we have

$$
\begin{aligned}
\frac{dl(t)}{dt} &= \frac{dI_v(t)}{st} \\
&= \lambda_{hv}(t)S_v(t) - \mu_v I_v(t) \\
&= \frac{p_2\beta \int_0^A \rho(a)x(t,a)da}{\int_0^A \rho(s)n^*(s)ds}\left(\frac{\Lambda_v}{\mu_v} + k(t)\right) - \mu_v l(t)
\end{aligned}
$$

We linearize this to get

$$
\frac{dl(t)}{dt} = -\mu_v l(t) + \frac{p_2\beta\Lambda_v}{\mu_v \int_0^A \rho(s)n^*(s)ds}\int_0^A \rho(a)x(t,a)da
$$

The full linearized system is

$$
\begin{aligned}
\frac{\partial w(t,a)}{\partial t} + \frac{\partial w(t,a)}{\partial a} &= -\frac{p_1 \beta \rho(a) s^*(a)}{\int_0^A \rho(s) n^*(s) ds} l(t) - (\mu_h(a, N_h^*) + \xi(a)) w(t,a) + \gamma(a) y(t,a) + \eta(a) z(t,a) \\
w(t,0) &= \int_0^A b_h(a) n_h^*(a) da \\
\frac{\partial x(t,a)}{\partial t} + \frac{\partial x(t,a)}{\partial a} &= \frac{p_1 \beta \rho(a) s^*(a)}{\int_0^A \rho(s) n_h^*(s) ds} l(t) - (\zeta(a) + \delta(a) + \mu_h(a, N_h^*)) x(t,a) \\
x(t,0) &= 0 \\
\frac{\partial y(t,a)}{\partial t} + \frac{\partial y(t,a)}{\partial a} &= \zeta(a) x(t,a) - (\gamma(a) + \mu_h(a, N_h^*)) y(t,a) \\
y(t,0) &= 0 \\
\frac{\partial z(t,a)}{\partial t} + \frac{\partial z(t,a)}{\partial a} &= \xi(a) w(t,a) - (\mu_h(a, N_h^*) + \gamma(a)) z(t,a) \\
z(t,0) &= 0 \\
\frac{dk(t)}{dt} &= -\mu_v k(t) - \frac{p_2 \beta \Lambda_v}{\mu_v \int_0^A \rho(s) n^*(s) ds} \int_0^A \rho(a) x(t,a) da \\
\frac{dl(t)}{dt} &= -\mu_v l(t) + \frac{p_2 \beta \Lambda_v}{\mu_v \int_0^A \rho(s) n^*(s) ds} \int_0^A \rho(a) x(t,a) da
\end{aligned}
$$

Next we input the eigenfunctions

$$
w(t,a) = \overline{w}(a) e^{\lambda t}, x(t,a) = \overline{x}(t,a) e^{\lambda t}, y(t,a) = \overline{y}(t,a) e^{\lambda t}, z(t,a) = \overline{z}(a) e^{\lambda t}
$$

$$
k(t) = \overline{k} e^{\lambda t}, l(t) = \overline{l} e^{\lambda t}
$$

Then we get the following system

$$
\begin{aligned}
\overline{w}(a)\lambda e^{\lambda t} + e^{\lambda t}\frac{d\overline{w}(a)}{da} &= -\frac{p_1\beta\rho(a)s^*(a)}{\int_0^A \rho(s)n^*(s)ds}\bar{l}e^{\lambda t} - (\mu_h(a,N_h^*) + \xi(a))\overline{w}(a)e^{\lambda t} + \gamma(a)\overline{y}(a)e^{\lambda t} + \eta(a)\overline{z}(a)e^{\lambda t} \\
w(t,0) &= \int_0^A b_h(a)n_h^*(a)da \\
\overline{x}(a)\lambda e^{\lambda t} + e^{\lambda t}\frac{d\overline{x}(a)}{da} &= \frac{p_1\beta\rho(a)s^*(a)}{\int_0^A \rho(s)n_h^*(s)ds}\bar{l}e^{\lambda t} - (\zeta(a) + \delta(a) + \mu_h(a,N_h^*))\overline{x}(a)e^{\lambda t} \\
x(t,0) &= \overline{x}(0)e^{\lambda t} = 0 \\
\overline{y}(a)\lambda e^{\lambda t} + e^{\lambda t}\frac{d\overline{y}(a)}{da} &= \zeta(a)\overline{x}(a)e^{\lambda t} - (\gamma(a) + \mu_h(a,N_h^*))\overline{y}(a)e^{\lambda t} \\
y(t,0) &= \overline{y}(0)e^{\lambda t} = 0 \\
\overline{z}(a)\lambda e^{\lambda t} + e^{\lambda t}\frac{d\overline{z}(a)}{da} &= \xi(a)\overline{w}(a)e^{\lambda t} - (\mu_h(a,N_h^*) + \gamma(a))\overline{z}(a)e^{\lambda t} \\
z(t,0) &= \overline{z}(0)e^{\lambda t} = 0 \\
\bar{k}\lambda e^{\lambda t} &= -\mu_v\bar{k}e^{\lambda t} - \frac{p_2\beta\Lambda_v}{\mu_v\int_0^A \rho(s)n^*(s)ds}\int_0^A \rho(a)\overline{x}(a)e^{\lambda t}da \\
\bar{l}\lambda e^{\lambda t} &= -\mu_v\bar{l}e^{\lambda t} + \frac{p_2\beta\Lambda_v}{\mu_v\int_0^A \rho(s)n^*(s)ds}\int_0^A \rho(a)\overline{x}(a)e^{\lambda t}da
\end{aligned}
$$

We can divide by $e^{\lambda t}$ to get the system

$$\begin{aligned}
\overline{w}(a)\lambda + \frac{d\overline{w}(a)}{da} &= -\frac{p_1\beta\rho(a)s^*(a)}{\int_0^A \rho(s)n^*(s)ds}\bar{l} - (\mu_h(a,N_h^*) + \xi(a))\overline{w}(a) + \gamma(a)\overline{y}(a) + \eta(a)\overline{z}(a) \\
\overline{w}(0) &= \int_0^A b_h(a)n_h^*(a)da \\
\overline{x}(a)\lambda + \frac{d\overline{x}(a)}{da} &= \frac{p_1\beta\rho(a)s^*(a)}{\int_0^A \rho(s)n_h^*(s)ds}\bar{l} - (\zeta(a) + \delta(a) + \mu_h(a,N_h^*))\overline{x}(a) \\
\overline{x}(0) &= 0 \\
\overline{y}(a)\lambda + \frac{d\overline{y}(a)}{da} &= \zeta(a)\overline{x}(a) - (\gamma(a) + \mu_h(a,N_h^*))\overline{y}(a) \\
\overline{y}(0) &= 0 \\
\overline{z}(a)\lambda + \frac{d\overline{z}(a)}{da} &= \xi(a)\overline{w}(a) - (\mu_h(a,N_h^*) + \gamma(a))\overline{z}(a) \\
\overline{z}(0) &= 0 \\
\bar{k}\lambda &= -\mu_v\bar{k} - \frac{p_2\beta\Lambda_v}{\mu_v\int_0^A \rho(s)n^*(s)ds}\int_0^A \rho(a)\overline{x}(a)da \\
\bar{l}\lambda &= -\mu_v\bar{l} + \frac{p_2\beta\Lambda_v}{\mu_v\int_0^A \rho(s)n^*(s)ds}\int_0^A \rho(a)\overline{x}(a)da
\end{aligned}$$

We look at the equations for $\overline{x}(a), \overline{y}(a)$ and $\bar{l}$. We solve for $\overline{x}(a)$ in

$$\overline{x}(a)\lambda + \frac{d\overline{x}(a)}{da} = \frac{p_1\beta\rho(a)s^*(a)}{\int_0^A \rho(s)n_h^*(s)ds}\bar{l} - (\zeta(a) + \delta(a) + \mu_h(a,N_h^*))\overline{x}(a)$$

We have the following

$$\frac{d\overline{x}(a)}{da} + \overline{x}(a)(\lambda + \zeta(a) + \delta(a) + \mu_h(a, N_h^*)) = \frac{p_1\beta\rho(a)s^*(a)}{\int_0^A \rho(s)n_h^*(s)ds}\bar{l}$$

$$\frac{d}{da}\left(\overline{x}(a)e^{\int_0^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}\right) = e^{\int_0^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}\frac{p_1\beta\rho(a)s^*(a)}{\int_0^A \rho(s)n_h^*(s)ds}\bar{l}$$

Then with the initial condition $\overline{x}(0) = 0$ we have

$$\overline{x}(a)e^{\int_0^a \lambda+\zeta(b)+\mu_h(b,N_h^*)db} = \int_0^a e^{\int_0^\sigma \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}\frac{p_1\beta\rho(\sigma)s^*(\sigma)}{\int_0^A \rho(s)n_h^*(s)ds}\bar{l}d\sigma$$

So we have

$$\overline{x}(a) = \int_0^a e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}\frac{p_1\beta\rho(\sigma)s^*(\sigma)}{\int_0^A \rho(s)n_h^*(s)ds}\bar{l}d\sigma$$

For $\overline{y}(a)$ we have

$$\overline{y}(a)\lambda + \frac{d\overline{y}(a)}{da} = \zeta(a)\overline{x}(a) - (\gamma(a) + \mu_h(a, N_h^*))\overline{y}(a)$$

$$\frac{d\overline{y}(a)}{da} + \overline{y}(a)(\lambda + \gamma(a) + \mu_h(a, N_h^*)) = \zeta(a)\overline{x}(a)$$

$$\frac{d}{da}\left(\overline{y}(a)e^{\int_0^a \lambda+\gamma(b)+\mu_h(b,N_h^*)db}\right) = e^{\int_0^a \lambda+\gamma(b)+\mu_h(b,N_h^*)db}\zeta(a)\overline{x}(a)$$

Then with the initial condition $\overline{y}(0) = 0$ we get

$$\overline{y}(a)e^{\int_0^a \lambda+\gamma(b)+\mu_h(b,N_h^*)db} = \int_0^a e^{\int_0^\sigma \lambda+\gamma(b)+\mu_h(b,N_h^*)db}\zeta(\sigma)\overline{x}(\sigma)d\sigma$$

Thus

$$\overline{y}(a) = \int_0^a e^{-\int_\sigma^a \lambda+\gamma(b)+\mu_h(b,N_h^*)db}\zeta(\sigma)\overline{x}(\sigma)d\sigma$$

So we now have the system

$$\begin{aligned}
\overline{x}(a) &= \int_0^a e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}\frac{p_1\beta\rho(\sigma)s^*(\sigma)}{\int_0^A \rho(s)n_h^*(s)ds}\bar{l}d\sigma \\
\overline{y}(a) &= \int_0^a e^{-\int_\sigma^a \lambda+\gamma(b)+\mu_h(b,N_h^*)db}\zeta(\sigma)\overline{x}(\sigma)d\sigma \\
\bar{l}\lambda &= -\mu_v\bar{l} + \frac{p_2\beta\Lambda_v}{\mu_v\int_0^A \rho(s)n^*(s)ds}\int_0^A \rho(a)\overline{x}(a)da
\end{aligned}$$

Now we consider several cases:

- $\overline{x}(a) \neq 0, \bar{l} \neq 0$
- $\overline{x}(a) \neq 0, \bar{l} = 0$
- $\overline{x}(a) = 0, \bar{l} \neq 0$
- $\overline{x}(a) = 0, \bar{l} = 0$

For each of those cases we would like to show that $\mathcal{R}(\lambda) < 0$ under certain conditions.

Since this would imply that for all fixed a,

$$\lim_{t\to\infty} w(t,a) = \lim_{t\to\infty} x(t,a) = \lim_{t\to\infty} y(t,a) = \lim_{t\to\infty} z(t,a) = \lim_{t\to\infty} k(t) = \lim_{t\to\infty} l(t) = 0$$

from which we can conclude the disease free equilibrium is locally asymptotically stable.

- $\bar{x}(a) \neq 0, \bar{l} \neq 0$. This is the most difficult of the cases but also the one that will characterize the behavior of the disease free equilibrium. We plug in $\bar{x}(a)$ into the equation for $\bar{l}$ to get

$$\bar{l}\lambda = -\mu_v \bar{l} + \frac{p_2\beta\Lambda_v}{\mu_v \int_0^A \rho(s)n^*(s)ds} \int_0^A \rho(a) \int_0^a e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db} \frac{p_1\beta\rho(\sigma)s^*(\sigma)}{\int_0^A \rho(s)n_h^*(s)ds} \bar{l} d\sigma da$$

Since $\bar{l} \neq 0$ we have that

$$\lambda = -\mu_v + \frac{p_2\beta\Lambda_v}{\mu_v \int_0^A \rho(s)n^*(s)ds} \int_0^A \rho(a) \int_0^a e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db} \frac{p_1\beta\rho(\sigma)s^*(\sigma)}{\int_0^A \rho(s)n_h^*(s)ds} d\sigma da$$

This is equivalent to

$$1 = \frac{p_2\beta\Lambda_v}{(\mu_v+\lambda)\mu_v \int_0^A \rho(s)n^*(s)ds} \int_0^A \int_0^a \frac{p_1\beta\rho(\sigma)\rho(a)s^*(\sigma)}{\int_0^A \rho(s)n_h^*(s)ds} e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db} d\sigma da$$

We call the right hand side the characteristic equation and let

$$G(\lambda) = \frac{p_2\beta\Lambda_v}{(\mu_v+\lambda)\mu_v \int_0^A \rho(s)n^*(s)ds} \int_0^A \int_0^a \frac{p_1\beta\rho(\sigma)\rho(a)s^*(\sigma)}{\int_0^A \rho(s)n_h^*(s)ds} e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db} d\sigma da$$

This function has the following properties

Lemma 3.2.4. *There exists a real values solution in the interval* $(-\mu_v, \infty)$ *to* $G(\lambda) = 1$. *The solution is only real value solution on the interval* $(-\mu_v, \infty)$ *and is positive if* $G(0) > 1$ *and* *the is negative if* $G(0) < 1$.

Proof. We work on the existence of a solution first. The function $G(\lambda)$ is continuous given the age dependent parameters in it are continuous, which is true by the assumptions of our model. Then since

$$\frac{1}{\mu_v + \lambda} \to \infty, \text{ and } e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db} \text{ approaches a constant as } \lambda \to -\mu_v^+$$

we have that

$$\lim_{\lambda \to -\mu_v^+} G(\lambda) = \infty$$

Furthermore since

$$\frac{1}{\mu_v + \lambda} \to 0, \text{ and } e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db} \to 0 \text{ as } \lambda \to \infty$$

we have that

$$\lim_{\lambda \to \infty} G(\lambda) = 0$$

Thus $G(\lambda) = 1$ has a solution in the interval $(-\mu_v \to \infty)$. For the second claim in the lemma since

$$\frac{1}{\mu_v + \lambda} \text{ and } e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}$$

are both strictly decreasing function of λ on $(-\mu_v, \infty)$ we have that $G(\lambda)$ is strictly decreasing on $(-\mu_v, \infty)$ as well. Then this gives that there is only one real solution to

$G(\lambda) = 1$ in $(-\mu_v, \infty)$ and furthermore if $G(0) > 1$ this solution must be positive and if $G(0) < 1$ then this solution must be negative. □

This lemma tells us that for $G(0) > 1$, the disease free equilibrium is unstable since for fixed a at the perturbations $x(t, a)$ and $l(t)$ have shape $e^{\lambda t}$ which will grow for solutions $\lambda > 0$ From here we can prove the following

Lemma 3.2.5. *If* $G(0) < 1$*, then any solution (including complex) of* $G(\lambda) = 1$ *has negative real part.*

Proof. Let $\lambda = \alpha + \omega i$ be a solution to $G(\lambda) = 1$ and assume for contradiction $\alpha > 0$. In particular we keep in mind from the hypothesis that $G(0) < 1$ we have that $G(\alpha) < 1$. Then we have the relations

$$|\alpha + \omega i + \mu_v| > |\alpha + \mu_v|$$

and

$$|e^{\alpha + \omega i}| = |e^{\alpha}| = e^{\alpha}$$

The first inequality depends on $\alpha > 0$ and the second does not. So

$$
\begin{aligned}
&|G(\alpha+\omega i)| \\
&= \left|\frac{p_1 p_2 \beta^2 \Lambda_v}{(\mu_v+\alpha+\omega i)\mu_v(\int_0^A p(a)s^*(a)da)^2}\int_0^A\int_0^a p(a)p(\sigma)s^*(a)e^{-\int_\sigma^a \alpha+\omega i+\gamma(b)+\delta(b)+\mu_h(b,N_h^*)db}d\sigma da\right| \\
&= \frac{p_1 p_2 \beta^2 \Lambda_v}{|\mu_v+\alpha+\omega i|\mu_v(\int_0^A p(a)s^*(a)da)^2}\int_0^A\int_0^a p(a)p(\sigma)s^*(a)\left|e^{\alpha+\beta i}e^{a-\sigma}\right|e^{-\int_\sigma^a \gamma(b)+\delta(b)+\mu_h(b,N_h^*)db}d\sigma da \\
&\le \frac{p_1 p_2 \beta^2 \Lambda_v}{|\mu_v+\alpha|\mu_v(\int_0^A p(a)s^*(a)da)^2}\int_0^A\int_0^a p(a)p(\sigma)s^*(a)e^{\alpha}e^{a-\sigma}e^{-\int_\sigma^a \gamma(b)+\delta(b)+\mu_h(b,N_h^*)db}d\sigma da \\
&= G(\alpha) < 1
\end{aligned}
$$

We now have a contradiction since $G(\alpha+\omega i) = 1$. Thus $\mathcal{R}(\lambda)$ must be negative for all solutions of $G(\lambda) = 1$ □

Thus we have shown for this case, if $G(0) > 1$ the disease free equilibrium is unstable and if $G(0) < 1$ then the disease free equilibrium is asymptotically stable.

- $\bar{x}(a) \neq 0, \bar{l} = 0$. This case cannot occur as if you plug $\bar{l} = 0$ into the equation for $\bar{x}(a)$ you get $\bar{x}(a) = 0$.

- $\bar{x}(a) = 0, \bar{l} \neq 0$ For this case notice the equation for $\bar{l}$ after plugging in $\bar{x}(a) = 0$ is

$$-\mu_v \bar{l} = \lambda \bar{l}$$

Since $\bar{l} \neq 0$ we get that the only solution is $\lambda = -\mu_v < 0$.

- $\bar{x}(a) = 0, \bar{l} = 0$ We note that by plugging in $\bar{x}(a) = 0$ into $\bar{y}$ that $\bar{y}(a) = 0$. So the only possible non-zero functions are $\bar{x}(a)$ and $\bar{z}(a)$. This is equivalent to studying the asymptotic stability of the system 3.3 which we previously looked at.

We have proven the following

Theorem 3.2.6. *Let*

$$G(\lambda) = \frac{p_2\beta\Lambda_v}{(\mu_v+\lambda)\mu_v\int_0^A \rho(s)n^*(s)ds}\int_0^A\int_0^a \frac{p_1\beta\rho(\sigma)\rho(a)s^*(\sigma)}{\int_0^A \rho(s)n_h^*(s)ds}e^{-\int_\sigma^a \lambda+\zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}d\sigma da$$

then the disease free equilibrium is unstable if $G(0) > 1$ *and locally asymptotically stable if* $G(0) < 1$.

The basic reproduction number, which we describe in detail in the next section, is given by

$$R_0 = \sqrt{G(0)} = \sqrt{\frac{p_1p_2\beta^2\Lambda_v}{\mu_v^2(\int_0^A \rho(s)n^*(s)ds)^2}\int_0^A\int_0^a \rho(\sigma)\rho(a)s^*(\sigma)e^{-\int_\sigma^a \zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}d\sigma da}$$

3.3 Interpretation of $R_0 = \sqrt{G(0)}$

We now work on interpreting $R_0 = \sqrt{G(0)}$, which is called the basic reproduction number. We derived the form

$$G(0) = \frac{p_1p_2\beta^2\Lambda_v}{\mu_v^2(\int_0^A \rho(s)n^*(s)ds)^2}\int_0^A\int_0^a \rho(\sigma)\rho(a)s^*(\sigma)e^{-\int_\sigma^a \zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}d\sigma da$$

The previous section showed R_0 is a threshold value for the asymptotic behavior around the disease free equilibrium. Now we compare this to the definition of basic reproduction number in epidemiology, which is the number of secondary cases from a single infectious case in a completely susceptible environment. We can do a change of integration order, keeping in mind $0 < \sigma < a < A$,

$$G(0) = \frac{p_1p_2\beta^2\Lambda_v}{\mu_v^2(\int_0^A \rho(s)n^*(s)ds)^2}\int_0^A\int_\sigma^A \rho(\sigma)\rho(a)s^*(\sigma)e^{-\int_\sigma^a \zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}da d\sigma$$

Then we rearrange to get

$$G(0) = \int_0^A \frac{p_1\beta\rho(\sigma)s^*(\sigma)}{\mu_v \int_0^A \rho(s)n^*(s)ds} \int_\sigma^A \frac{p_2\beta\rho(a)\Lambda_v}{\mu_v \int_0^A \rho(s)n^*(s)ds} e^{-\int_\sigma^a \zeta(b)+\delta(b)+\mu_h(b,N_h^*)db} da d\sigma$$

Suppose we are in a disease free equilibrium and we introduce one infectious mosquito. Then the average lifespan of a mosquito is $\frac{1}{\mu_v}$. Furthermore the rate of people age σ infected by a mosquito is

$$\frac{p_1\beta\rho(\sigma)}{\int_0^A \rho(s)n^*(s)ds}$$

This is $\lambda_{vh}(\sigma)$ with $I_v = 1$. So the total density of susceptible people age σ this mosquito infects is (rate*number of people*lifespan)

$$R_1(\sigma) = \frac{p_1\beta\rho(\sigma)s^*(\sigma)}{\int_0^A \rho(s)n^*(s)ds} \frac{1}{\mu_v}$$

Then consider a person who is infected at age σ. A person may exit the infected category by either dying naturally(μ_h), dying from the disease (σ_h) or recovering (ζ_h). The probability they are still sick at age $a > \sigma$ is

$$e^{-\int_\sigma^a \zeta(b)+\delta(b)+\mu_h(b,N_h^*)db}$$

and the rate at which this person of age a infects mosquitos is

$$\frac{p_2\beta\rho(a)}{\int_0^A \rho(s)n^*(s)ds}$$

Then there are Λ_v/μ_v susceptible mosquitos. So the number of mosquito a person who got sick at age σ infects is given by the integral of the product of the survival probability and the density of mosquitos infected over age a,

$$R_2(\sigma) = \int_\sigma^A \frac{p_2\beta\rho(a)}{\int_0^A \rho(s)n^*(s)ds} \cdot \frac{\Lambda_v}{\mu_v} e^{-\int_\sigma^a \zeta(b)+\delta(b)+\mu_h(b,N_h^*)db} da$$

Thus we see that

$$R_1(\sigma)R_2(\sigma)$$

is the density of mosquitos infected in a disease free environment through an individual infected at age σ by an infectious mosquito. Thus

$$R_0^2 = G(0) = \int_0^A R_1(\sigma)R_2(\sigma)d\sigma$$

is the total number of susceptible mosquitos infected by a single infected mosquito in a disease free environment. Our earlier theorem agrees with the notion that if $R_0 = \sqrt{G(0)} < 1$ then the disease will die out since there are not enough new infections to replace the original, but if $R_0 = \sqrt{G(0)} > 1$ then there will be enough replacements of the original infectious mosquito to keep the disease from dying out. The square root represents the geometric mean, it is sometimes omited from literature since the threshold value remains at 1 for both R_0 and $G(0)$.

Chapter 4

Optimal Control

We now introduce an optimal control formulation of our model. We change $\xi_h(a)$, the vaccination rate to one that is time dependent, $\xi_h(t,a)$. This will allow us to change the value of the vaccination rate as a function of time. Thus we have the system

$$\frac{\partial s_h(t,a)}{\partial t} + \frac{\partial s_h(t,a)}{\partial a} = -(\lambda_{vh}(a,t) + \mu_h(a, N_h(t)) + \xi_h(t,a))s_h(t,a) + \gamma_h(a)r_h(t,a) + \eta_h(a)v_h(t,a) \tag{4.1}$$

$$\begin{aligned}
\frac{\partial i_h(t,a)}{\partial t} + \frac{\partial i_h(t,a)}{\partial a} &= \lambda_{vh}(t,a)s_h(t,a) - (\zeta_h(a) + \delta_h(a) + \mu_h(a, N_h(t)))i_h(t,a) \\
\frac{\partial r_h(t,a)}{\partial t} + \frac{\partial r_h(t,a)}{\partial a} &= \zeta_h(a)i_h(t,a) - (\gamma_h(a) + \mu_h(a, N_h(t)))r_h(t,a) \\
\frac{\partial v_h(t,a)}{\partial t} + \frac{\partial v_h(t,a)}{\partial a} &= \xi_h(t,a)s_h(t,a) - (\mu_h(a, N_h(t)) + \eta_h(a))v_h(t,a) \\
\frac{dS_v(t)}{dt} &= \Lambda_v - (\mu_v + \lambda_{hv}(t))S_v(t) \\
\frac{dI_v(t)}{dt} &= \lambda_{hv}(t)S_v(t) - \mu_v I_v(t)
\end{aligned}$$

We have initial conditions

$$s_{h0}(0,a) = s_{h0}(a), i_{h0}(0,a) = i_{h0}(a), r_{h0}(0,a) = r_{h0}(a), v_{h0}(0,a) = v_{h0}(a)$$

$$S_v(0) = S_{v0}, I_v(0) = I_{v0}$$

and the boundary condition

$$s_h(t,0) = \int_0^A b_h(a)n_h(t,a)da, i_h(t,0) = r_h(t,0) = v_h(t,0) = 0$$

All other parameters and aspects of the system remain unchanged. We then introduce a cost function

$$J(\xi) = \int_0^T \int_0^A [Bi_h(t,a) + C\xi_h(t,a)s_h(t,a) + D\xi_h(t,a)^2]$$

where B is the cost of treating an infected individual per year and C is cost of administering a vaccine to a person. D is some small positive constant. The integral measure the cost of treating sick patients and vaccinating individuals over time span 0 to T. The goal of our analysis will be to find a function $\xi(t,a)$ that will minimize $J(\xi)$ with the restriction of equation 4.1.

Theorem 4.0.1. *The map $L : X \to X$ introduces in an earlier section[ref] is differentiable in the following sense:*

$$\frac{L(u+\epsilon l) - L(u)}{\epsilon} \to (\Psi_s, \Psi_i, \Psi_r . \Psi_v, \Phi_s, \Phi_i)$$

for $u \in X$ and $\epsilon \to 0$ and $l \in L^\infty(Q)$. Furthermore they satisfy equations

$$
\begin{aligned}
\frac{\partial \Psi_s}{\partial t} + \frac{\partial \Psi_s}{\partial t} &= -p_1 \beta \rho(a) \Big(\frac{I_v(t)}{T_h(t)} \Psi_s(t,a) + \frac{\Phi_i(t)}{T_h(t)} s_h(t,a) \\
&\quad - \frac{I_v(t) s_h(t,a) (\int_0^A \rho(a) (\Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a)) da)}{T_h(t)^2} \Big) \\
&\quad - \xi_h(t,a) \Psi_s(t,a) - s_h(t,a) l + \gamma(a) \Psi_r(t,a) + \eta(a) \Psi_v(t,a) \\
&\quad - \mu_h(a, N_h(t)) \Psi_s(t,a) - s_h(t,a) \mu_{h1}(a) \int_0^A \Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a) da \\
\frac{\partial \Psi_i}{\partial t} + \frac{\partial \Psi_i}{\partial t} &= p_1 \beta \rho(a) \Big(\frac{I_v(t)}{T_h(t)} \Psi_s(t,a) + \frac{\Phi_i(t)}{T_h(t)} s_h(t,a) \\
&\quad - \frac{I_v(t) s_h(t,a) (\int_0^A \rho(a) (\Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a)) da)}{T_h(t)^2} \Big) \\
&\quad - (\mu_h(a, N_h(t)) + \delta_h(a) + \zeta_h(a)) \Psi_i(t,a) \\
&\quad - i_h(t,a) \mu_{h1}(a) \int_0^A \Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a) da \\
\frac{\partial \Psi_r}{\partial t} + \frac{\partial \Psi_r}{\partial t} &= \zeta_h(a) \Psi_i - (\mu_h(a, N_h(t)) + \gamma(a)) \Psi_r \\
&\quad - r_h(t,a) \mu_{h1}(a) \int_0^A \Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a) da \\
\frac{\partial \Psi_v}{\partial t} + \frac{\partial \Psi_v}{\partial t} &= \xi_h(t,a) \Psi_s(t,a) - s_h(t,a) l - (\mu_h(a, N_h(t)) + \eta_h(a)) \Psi_v \\
&\quad - v_h(t,a) \mu_{h1}(a) \int_0^A \Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a) da \\
\frac{d\Phi_s}{dt} &= -p_2 \beta \Big(\frac{J_h(t)}{T_h(t)} \Phi_s(t) + \frac{\int_0^A \rho(a) \Psi_i(t,a) da}{T_h(t)} S_v(t) \\
&\quad - \frac{J_h(t) \int_0^A \rho(a) (\Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a)) da}{T_h(t)^2} S_v(t) \Big) - \mu_v \Phi_s(t) \\
\frac{d\Phi_i}{dt} &= p_2 \beta \Big(\frac{J_h(t)}{T_h(t)} \Phi_s(t) + \frac{\int_0^A \rho(a) \Psi_i(t,a) da}{T_h(t)} S_v(t) \\
&\quad - \frac{J_h(t) \int_0^A \rho(a) (\Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a)) da}{T_h(t)^2} S_v(t) \Big) - \mu_v \Phi_i
\end{aligned}
$$

The initial conditions are

$$\Psi_s(0,a) = 0, \Psi_i(0,a) = 0, \Psi_r(0,a) = 0, \Psi_v(0,a) = 0$$

$$\Phi_s(0) = 0, \Phi_i(0) = 0$$

The boundary conditions are

$$\Psi_s(t,0) = \int_0^A b(a)(\Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a))da$$

$$\Psi_i(t,0) = 0, \Psi_r(t,0) = 0, \Psi_v(t,0) = 0$$

Proof. The proof is the first half of Appendix D(Chapter 12) □

Theorem 4.0.2. *The adjoint equations for the system 4.1 are*

$$\begin{aligned}
\frac{\partial p_s}{\partial t} + \frac{\partial p_s}{\partial t} = & \frac{p_1 \beta \rho(a) I_v}{T_h}(p_s - p_i) + \mu_h p_s + \xi_h (p_s - p_v) \\
& - \frac{p_2 \beta J_h S_v}{T_h^2}\rho(a)(q_s - q_i) - \frac{\rho(a) p_1 \beta I_v}{T_h^2}\int_0^A s_h(t,b)\rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
& + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b) + i_h(t,b)p_i(t,b) + r_h(t,b)p_r(t,b) + v_h(t,b)p_v(t,b))db \\
& - C\xi_h
\end{aligned}$$

$$
\begin{aligned}
\frac{\partial p_i}{\partial t} + \frac{\partial p_i}{\partial t} &= (\mu_h + \delta_h)p_i + \zeta_h(p_i - p_r) + \frac{p_2\beta S_v}{T_h}\rho(a)(q_s - q_i) \\
&\quad - \frac{p_2\beta J_h S_v}{T_h^2}\rho(a)(q_s - q_i) - \frac{\rho(a)p_1\beta I_v}{T_h^2}\int_0^A s_h(t,b)\rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b) + i_h(t,b)p_i(t,b) + r_h(t,b)p_r(t,b) + v_h(t,b)p_v(t,b))db \\
&\quad - B \\
\frac{\partial p_r}{\partial t} + \frac{\partial p_r}{\partial t} &= \mu_h p_r + \gamma_h(p_r - p_s) \\
&\quad - \frac{p_2\beta J_h S_v}{T_h^2}\rho(a)(q_s - q_i) - \frac{\rho(a)p_1\beta I_v}{T_h^2}\int_0^A s_h(t,b)\rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b) + i_h(t,b)p_i(t,b) + r_h(t,b)p_r(t,b) + v_h(t,b)p_v(t,b))db \\
\frac{\partial p_v}{\partial t} + \frac{\partial p_v}{\partial t} &= \mu_h p_v + \eta_h(p_v - p_s) \\
&\quad - \frac{p_2\beta J_h S_v}{T_h^2}\rho(a)(q_s - q_i) - \frac{\rho(a)p_1\beta I_v}{T_h^2}\int_0^A s_h(t,b)\rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b) + i_h(t,b)p_i(t,b) + r_h(t,b)p_r(t,b) + v_h(t,b)p_v(t,b))db \\
\frac{dq_s}{dt} &= \mu_v q_s + \frac{p_2\beta J_h}{T_h}(q_s - q_i) \\
\frac{dq_i}{dt} &= \mu_v q_i + \int_0^A \frac{p_1\beta\rho(a)s_h}{T_h}(p_s - p_i)da
\end{aligned}
$$

with initial conditions

$$p_s(T,a) = p_i(T,a) = p_r(T,a) = p_v(T,a) = 0$$

$$q_s(T) = q_i(T) = 0$$

and boundary conditions

$$p_s(t,A) = p_i(t,A) = p_r(t,A) = p_v(t,A) = 0$$

Proof. The proof is in the second half of Appendix D □

We now assume the existence of a solution and uniqueness of the adjoint equations and the optimality conditions. The existence and uniqueness of the adjoint would be proved with the same method as the existence and uniqueness of the state equations, using Banach fixed point theorem. Proof that the optimal control exists uses Ekelands Principal. These are left unfinished due to time restrictions.

Theorem 4.0.3. *Assuming the adjoint equations and the optimal control exists and are unique we have that the optimal control satisfies*

$$\xi_h^* = max(0, \frac{(p_s - p_v - C)s_h}{D})$$

Proof. Again the derivation of these values are included in Appendix D □

The equations above will at the very least allow us to run numerical simulations.

Chapter 5

Numerical Methods for disease model

5.1 State Equations

The Euler-Riemann and Backward Euler-Riemann Methods are used along the characteristic lines of the PDE model to produce simulations. More specifically, we partition the temporal domain $[0, T]$ into M equally sized intervals and the age domain into N equal sized intervals such that $\frac{T}{M} = \frac{A}{N}$, i.e. the step sizes are the same in both variables. Let the step size be denoted by Δt. We now introduce the notation for convenience

$$t_i = i\Delta t, a_j = j\Delta t,$$

and also

$$(\xi_h)_i^j = \xi(t_j, a_i)$$

where ξ_h can be replaced by any of the parameters, the time index is in the superscript and the age index is in the subscript. Furthermore we let $(s_h)_i^j$ be the estimate of s_h at age a_i and time t_j, where we can replace s_h with any of the other state functions. Again the time index is in the superscript and the age index is in the subscript.

Then let

$$A(t,a) = \begin{bmatrix} -(\lambda_{hv} + \mu_h + \xi_h)(t,a) & 0 & \gamma_h(t,a) & \eta_h(t,a) \\ \lambda_{hv}(t,a) & -(\mu_h + \delta_h)(t,a) & 0 & 0 \\ 0 & \zeta_h(t,a) & -(\mu_h + \gamma_h)(t,a) & 0 \\ \xi_h(t,a) & 0 & 0 & -(\mu_h + \eta_h)(t,a) \end{bmatrix}$$

and

$$B(t) = \begin{bmatrix} -(\lambda_{hv}(t) + \mu_v) & 0 \\ \lambda_{hv}(t) & -\mu_v \end{bmatrix}$$

$$b = \begin{bmatrix} \Lambda_v \\ 0 \end{bmatrix}$$

Also let

$$u(t,a) = \begin{bmatrix} s_h(t,a) \\ i_h(t,a) \\ r_h(t,a) \\ v_h(t,a) \end{bmatrix}, v(t) = \begin{bmatrix} S_v(t) \\ I_v(t) \end{bmatrix}$$

Then the state equations of the model 2.2 can be written as

$$\frac{\partial u(t,a)}{\partial t} + \frac{\partial u(t,a)}{\partial a} = A(t,a)u(t,a)$$
$$\frac{dv(t)}{dt} = B(t)v(t) + b$$

Then the Euler method can be used on the characteristic of the PDE to arrive at the first order scheme

$$\frac{u_{i+1}^{j+1} - u_i^j}{\Delta t} = A_i^j u_i^j$$
$$\frac{v^{j+1} - v^j}{\Delta t} = B^j v^j + b$$

Which leads to

$$u_{i+1}^{j+1} = (I + \Delta t A_i^j) u_i^j$$
$$v^{j+1} = (I + \Delta t B^j) v^j + \Delta t b$$

where I is the identity matrix of appropriate size. The boundary values are computed using the trapezoid method. We do not use the value at $a = 0$ since $b_h(0) = 0$.

$$(s_h)_0^j = \frac{\Delta t}{2}\left[b_h(A)(s_h + i_h + r_h + v_h)_N^j + 2\sum_{i=1}^{N-1} b_h(a_i)(s_h + i_h + r_h + v_h)_i^j \right]$$
$$(i_h)_0^j = 0$$
$$(r_h)_0^j = 0$$
$$(v_h)_0^j = 0$$

We have the evaluations used in A_i^j and B^j.

$$(\lambda_{vh})_i^j = p_1 \beta \frac{\rho(a)(I_v)^j}{T_h^j}$$
$$(\lambda_{hv})_i^j = p_2 \beta \frac{J_h^j}{T_h^j}$$
$$(\mu_h)_i^j = \mu_{h0}(a_i) + \mu_{h1}(a_i) N_h^j$$

The values of N_h, T_h, J_h are computed using the trapezoid method as well.

$$N_h^j = \frac{\Delta t}{2}\Big[(n_h)_0^j + 2\sum_{i=1}^{N-1}(p_s)_i^j + (n_h)_N^j\Big]$$
$$T_h^j = \frac{\Delta t}{2}\Big[\rho(0)(n_h)_0^j + 2\sum_{i=1}^{N-1}\rho(a_i)(p_s)_i^j + \rho(A)(n_h)_N^j\Big]$$
$$J_h^j = \frac{\Delta t}{2}\Big[\rho(0)(i_h)_0^j + 2\sum_{i=1}^{N-1}\rho(a_i)(p_s)_i^j + \rho(A)(i_h)_N^j\Big]$$

We define the backward Euler method by the following. Let

$$\widetilde{A}_{i+1}^{j+1} = \begin{bmatrix} -(\xi_h)_{i+1}^{j+1} - (\lambda_{hv} + \mu_h)_{i+1}^j & 0 & (\gamma_h(t,a))_{i+1} & (\eta_h)_{i+1} \\ (\lambda_{hv})_{i+1}^j & -(\mu_h)_{i+1}^j - (\delta_h)_{i+1} & 0 & 0 \\ 0 & (\zeta_h)_{i+1} & -(\mu_h)_{i+1}^j - (\gamma_h)_{i+1} & 0 \\ (\xi_h)_{i+1}^{j+1} & 0 & 0 & -(\mu_h)_{i+1}^j - (\eta_h)_{i+1} \end{bmatrix}$$
$$\widetilde{B}^{j+1} = \begin{bmatrix} -(\lambda_{hv})^j - \mu_v & 0 \\ (\lambda_{hv})^j & -\mu_v \end{bmatrix}$$

Then we have the implicit scheme

$$\frac{u_{i+1}^{j+1} - u_i^j}{\Delta t} = \widetilde{A}_{i+1}^{j+1} u_{i+1}^{j+1}$$
$$\frac{v^{j+1} - v^j}{\Delta t} = \widetilde{B}^{j+1} v^{j+1} + b$$

We note that the population totals such as N_h, T_h and J_h are not implicit. We can rearrange this to get the backward Euler Scheme.

$$u_{i+1}^{j+1} = (I - \Delta t \widetilde{A}_{i+1}^{j+1})^{-1} u_i^j$$
$$v^{j+1} = (I - \Delta t \widetilde{B}^{j+1})^{-1}(v^j + \Delta t b)$$

The inverse matrix is not computed, instead we use LU factorization to solve the system of equations.

5.2 Adjoint Equations

The idea behind evaluating the adjoint equations are the same as the state equations but special care must be given to the fact that the boundary and initial conditions are given on the opposite side of the domain. So in a sense we will be traversing the characteristics used for the state equations backwards. A first order implicit and explicit algorithm will be given below.

Let $p = [p_s, p_i, p_r, p_v]^T$ and $q = [q_s, q_i]^T$ The adjoint equations an be written in the following form.

$$\frac{\partial p}{\partial t} + \frac{\partial p}{\partial a} = D_1(t,a)p + D_2(t,a)q + D_3(t,a)$$
$$\frac{dq}{dt} = E_1(t)q_1 + E_2(t)$$

where

$$D_1(t,a) = \begin{bmatrix} \lambda_{vh}(t,a) + \mu_h(a,t) + \xi_h(t,a) & -\lambda_{vh}(t,a) & 0 & -\xi_h(a) \\ 0 & \mu_h(a,t) + \delta_h(a) + \zeta_h(a) & -\zeta_h(a) & 0 \\ -\gamma_h(a) & 0 & \mu_h(a,t) + \gamma_h(a) & 0 \\ -\eta_h(a) & 0 & 0 & \mu_h(a,t) + \eta_h(a) \end{bmatrix}$$

$$= -A(t,a)^T$$

$$D_2(t,a) = \frac{\lambda_{hv}(t,a)S_v(t)\rho(a)}{T_h(t)} \begin{bmatrix} 1 & -1 \\ 1 & -1 \\ 1 & -1 \\ 1 & -1 \end{bmatrix} + \frac{p_2\beta S_v(t)\rho(a)}{T_h(t)} \begin{bmatrix} 0 & 0 \\ 1 & -1 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$D_3(t,a) = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} \Big(-\frac{\rho(a)p_1\beta I_v}{T_h^2} \int_0^A s_h(t,b)\rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a)$$

$$+ \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b) + i_h(t,b)p_i(t,b) + r_h(t,b)p_r(t,b) + v_h(t,b)p_v(t,b))db \Big)$$

$$- \begin{bmatrix} C\xi_h(a,t) \\ B \\ 0 \\ 0 \end{bmatrix}$$

$$E_1(t) = \begin{bmatrix} \mu_v + \lambda_{hv}(t) & -\lambda_{hv}(t) \\ 0 & \mu_v \end{bmatrix}$$

$$E_2(t) = \left(\int_0^A \frac{p_1\beta\rho(a)s_h(t,a)}{T_h(t)} (p_s(t,a) - p_i(t,a))da \right) \begin{bmatrix} 0 \\ 1 \end{bmatrix}$$

We formulate the explicit first order scheme by the following

$$\frac{p_{i+1}^{j+1} - p_i^j}{\Delta t} = (D_1)_{i+1}^{j+1} p_{i+1}^{j+1} + (D_2)_{i+1}^{j+1} q^{j+1} + (D_3)_{i+1}^{j+1}$$
$$\frac{q^{j+1} - q^j}{\Delta t} = (E_1)^{j+1} q^{j+1} + (E_2)^{j+1}$$

which gives us the schemes

$$p_i^j = (I - \Delta t(D_1)_i^j) p_{i+1}^{j+1} - \Delta t(D_2)_{i+1}^{j+1} q^{j+1} - \Delta t(D_3)_{i+1}^{j+1}$$
$$q_i^j = (I - \Delta t(E_1)^j) q^{j+1} - \Delta t(E_2)^j$$

the implicit scheme is formulated below. All terms except D_3 and E_2 can be made implicit.

$$\frac{p_{i+1}^{j+1} - p_i^j}{\Delta t} = (D_1)_i^j p_i^j + (D_2)_i^j q^j + (D_3)_{i+1}^{j+1}$$
$$\frac{q^{j+1} - q^j}{\Delta t} = (E_1)^j q^j + (E_2)^{j+1}$$

Which leads to

$$q^j = (I + (E_1)^j)^{-1} (q^{j+1} - \Delta t(E_2)^{j+1})$$
$$p_i^j = (I + \Delta t(D_1)_i^j)^{-1} (p_{i+1}^{j+1} - \Delta t(D_2)_i^j q^j - \Delta t(D_3)_{i+1}^{j+1})$$

In practice we do not compute the inverse, we use LU factorization to solve the system. Also note the order of computation, we compute the q first for the time step then compute the p values.

In both the explicit and implicit cases the integrals are evaluated using trapezoid rule :

$$
\begin{aligned}
&\int_0^A s_h(t_j,a)\rho(a)(p_s(t_j,a)-p_i(t_j,a))db \\
&\qquad\approx \frac{\Delta t}{2}\Big[(s_h)_0^j\rho(0)((p_s)_0^j-(p_i)_0^j)+2\sum_{i=1}^{N-1}(s_h)_i^j\rho(a_i)((p_s)_i^j-(p_i)_i^j)+(s_h)_N^j\rho(A)(p_s)_N^j-(p_i)_N^j)\Big] \\
&\int_0^A \mu_{h1}(a)(s_h(t,a)p_s(t,a)+i_h(t,a)p_i(t,a)+r_h(t,a)p_r(t,a)+v_h(t,a)p_v(t,a))da \\
&\qquad\approx \frac{\Delta t}{2}\Big[\mu_{h1}(0)((s_h)_0^j(p_s)_0^j+(i_h)_0^j(p_i)_0^j+(r_h)_0^j(p_r)_0^j+(v_h)_0^j(p_v)_0^j) \\
&\qquad\quad +2\sum_{i=1}^{N-1}\mu_{h1}(a_i)((s_h)_i^j(p_s)_i^j+(i_h)_i^j(p_i)_i^j+(r_h)_i^j(p_r)_i^j+(v_h)_i^j(p_v)_i^j) \\
&\qquad\quad +\mu_{h1}(A)((s_h)_N^j(p_s)_N^j+(i_h)_N^j(p_i)_N^j+(r_h)_N^j(p_r)_N^j+(v_h)_N^j(p_v)_N^j)\Big] \\
&\int_0^A \frac{p_1\beta\rho(a)s_h(t,a)}{T_h(t)}(p_s(t,a)-p_i(t,a))da \approx \frac{\Delta t}{2}\Big[\frac{p_1\beta\rho(0)(s_h)_0^j}{(T_h)^j}((p_s)_0^j-(p_i)_0^j) \\
&\qquad +2\sum_{i=1}^{N-1}\frac{p_1\beta\rho(a_i)(s_h)_i^j}{(T_h)^j}((p_s)_i^j-(p_i)_i^j)+\frac{p_1\beta\rho(A)(s_h)_A^j}{(T_h)^j}((p_s)_A^j-(p_i)_A^j)\Big]
\end{aligned}
$$

the boundary and initial conditions are all set to 0.

5.3 Forward Backward Sweep Method

We present the forward-backward sweep method first introduced in [17] and further application to optimal control problems are explained in [18].

The steps of the algorithm are as follows, set $\epsilon > 0$ small.

1. Initialize $\xi_h = 0$
2. Run the algorithm for the state equation with ξ_h.
3. Run the algorithm for the adjoint equation with the state equation derived from Step 2 and ξ

4. Use the adjoint equations to find the a new ξ_h using the optimality condition

$$\xi_h^* = \min(\max(0, \frac{(p_s - p_v - C)s_h}{D}), \xi)$$

5. If $|\xi_h - \xi_h^*| \leq \epsilon$ then we take ξ_h^* as our approximation of then optimal vaccination rate. If not then take $\xi_h = \xi_h^*$ and repeat from Step 2.

Chapter 6

Parameter Values

The parameters in Table 6.1 and their explanations can be found in Chitnis, Hymen and Cushing [20]. The maximum age was chosen as 90 from the population data available and the recruitment rate for the vector population was chosen so that it is significantly larger than the human population. We make the assumption that the mosquito population should be about 100 times the total human population. We will adjust the μ_{h1} parameter so the total human population is near 300 people and we set the mosquito recruitment to $2 \cdot 10^6$, which will give us a mosquito population of $\Lambda_v \mu_v = 2 \cdot 10^6/(365/21) \approx 115068$ mosquitos.

6.1 Age dependent parameters

We use the age dependent parameters for the country of Nigeria derived in [21].

For birth rate we use

$$b_h(a) = cB_h(a)$$

where

$$B_h(a) = \beta_1 \exp\{-\beta_2(a - \beta_3) - \exp[-\beta_4(a - \beta_3)]\}$$

Parameter	Description	Baseline values and range
age	Max age of adults in years	90 years
Λ_v	Recruitment rate of mosquitoes per year	10^{12}
μ_v	Natural death rate of mosquitoes per year	$\frac{365}{21} \in [365/28, 365/14]$
$p_1\beta$	Contact Rate from vector to human per year	$9 \in [2.6, 32 \cdot 365]$
$p_2\beta$	Contact Rate from human to vector per year	$.8 \in [0.001 \cdot 365, 0.27 \cdot 365]$
γ_h	Rate of loss of immunity per year	$2 \in [1/50, 4]$
η_h	Rate of loss of HV acquired-immunity per year in vaccinated groups of humans	$1/4 \in [1/5, 1]$
ζ_h	Rate of development of temporal immunity per year	$1 \in [1/2, 6]$

Table 6.1: Descriptions of age-independent parameters of the malaria model

with least square estimates

$$\widehat{\beta_1} = 0.0001218$$

$$\widehat{\beta_2} = 0.3022$$

$$\widehat{\beta_3} = 78.38$$

$$\widehat{\beta_4} = 0.04006$$

and constants determined so $s_{h0}(0) = \int_0^A b_h(a) s_h(0, a) da$. This condition gives us that the solution is continuous.

$$c = 0.449569941624713$$

The death rate will take logistic form

$$\mu_h(a, N_h) = \mu_{h0}(a) + \mu_{h1} N_h$$

with

$$\mu_{h0}(a) = \mu_c(a) + \mu_m(a) + \mu_o(a)$$

where

$$\mu_c(a) = \alpha_c \exp\{-\beta_c a\}$$

$$\mu_m(a) = \alpha_m \exp\{-\beta_m(a - \gamma_m) - \exp[\delta_m(a - \gamma_m)]\}$$

$$\mu_o(a) = \frac{\alpha_o}{A - a}$$

$A = 90$ the maximum age and the least square parameter estimates are

$$\widehat{\alpha_c} = 0.09959$$

$$\widehat{\beta_c} = 0.6776$$

$$\widehat{\alpha_m} = 0.1277$$

$$\widehat{\beta_m} = -0.09171$$

$$\widehat{\delta_m} = -0.0006743$$

$$\widehat{\gamma_m} = 66.78$$

$$\widehat{\alpha_o} = 0.05859$$

Figure(6.1) shows the birth and death rate fitted over the data for Nigeria data. For the value of μ_{h1}, we choose it to be constant and set it equal to .0001, which will set the population size to around 300.

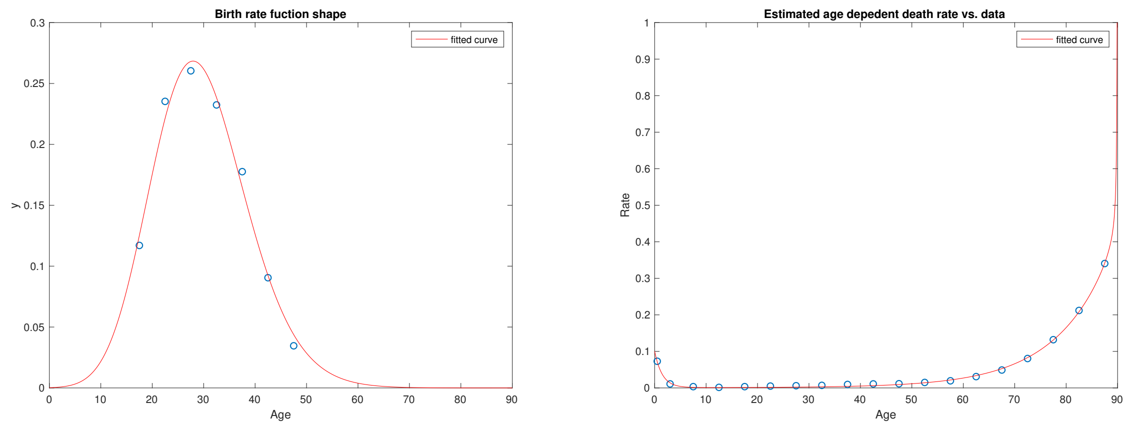

Figure 6.1: Left: Birthrate function shape. Right: Death rate estimates. The open circles are data retrieved from the United Nations website.

We assume the additional death rate due to malaria follows the following distribution

$$\delta_h(a) = \begin{cases} c \cdot \frac{1}{1+e^{2a-14}} & 0 \le a \le 90 \\ 0 & a > 90 \end{cases}$$

The additional death rate will be steady around rate c for age $0-5$. It will then drop quickly to a value close to 0. We will use data obtained from a WHO report in 2009 to determine the value of c. This is the most recent report with estimates for the number of malaria cases and deaths for 0-5 year olds. The shape of the additional death rate allows us to assume for the purpose of finding an appropriate value of c that the additional death rate is constant between ages 0 and 5 at rate c. We use the following relation

$$\begin{aligned} &(\text{\# of infected individuals}) \cdot (\text{averageinfection time}) \cdot (\text{Prob of dying from the disease}) \\ &\qquad = \text{Average number of deaths due to infection} \end{aligned}$$

We restrict to age 0 to 5. The number of infected individuals age 0 to 5 in one year is 34096000 and the number of deaths due to malaria in one year is 219000. The disease induced death rate for 0 to 5 year olds is assumed constant at c, so the probability of dying from the disease over a year is $1 - e^{-c}$.

Then since the death rate $\mu_{h0}(a)$ is smaller than ζ, the recovery rate, and infections last for a relatively short amount of time, we assume that the average time a infected individual stays infected is $\int_0^A e^{-\zeta a} da = \int_0^A e^{-1a} da = 1 - e^{-A} \approx 1$

Then we have the equation

$$34096000 \cdot 1 \cdot (1 - e^{-c}) = 219000$$

We solve for c to arrive at

$$c = -\ln\left(1 - \frac{219000}{34096000}\right) \approx .006444$$

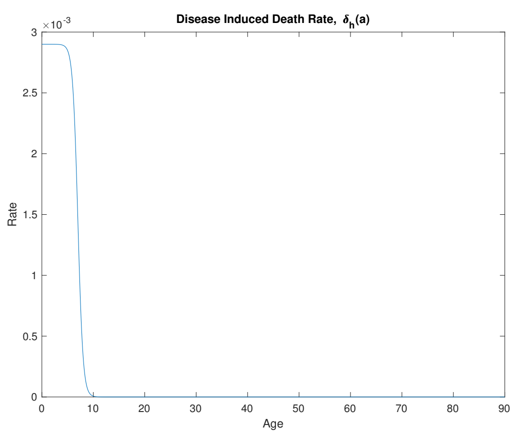

Figure 6.2: Age-dependent disease induced death rate.

The vaccination rate is kept as constant over time at rate .2

6.1.1 Preference Function, $p(a)$

The major advantage of our model is the ability to have heterogeneous biting rates. We use three different functions to model the age exposure likelihood for mosquito bites.

Uniform Distribution: We start with the original preference distribution from the model with homogeneous biting rate.

$$p(a) = \begin{cases} \frac{1}{90} & \text{, if } 0 \leq a \leq 90 \\ 0 & \text{, else} \end{cases} \tag{6.1}$$

Logistic Curve We use an age-dependent function to account for the differences in exposure for different age groups. Newborns are relatively protected from outside factors, having no risk of being bitten at birth, and the opportunity to come in contact with mosquito increases as they gain the ability to walk and become more active. We account for this with the following curve, which has lower values for newborns and drastically increases by the age of 4.

$$p(a) = \begin{cases} 0 & , a < 0 \\ \left(\frac{1}{1+e^{-(x-4)}} - \frac{1}{1+e^{4}} \right) & , 0 \leq a \leq 90 \\ 0 & , a > 60 \end{cases}$$

Figure (6.3) show the curve $p(a)$. The value for newborns is consistent with our previous explanation, $p(0) = 0$. Furthermore for this curve, the preference for humans over 10 is relatively uniform.

Skewed Normal:We have a skewed normal that concentrates bites from the age of

5-30.

$$p(a) = \begin{cases} \frac{2}{\sqrt{1200\pi}} e^{-\frac{(x-10)^2}{1200}} \int_{-\infty}^{4 \cdot \frac{x-10}{\sqrt{600}}} \frac{1}{\sqrt{2\pi}} e^{-\frac{t^2}{2}} dt & \text{, if } 0 \leq a \leq 60 \\ 0 & \text{, else} \end{cases} \tag{6.2}$$

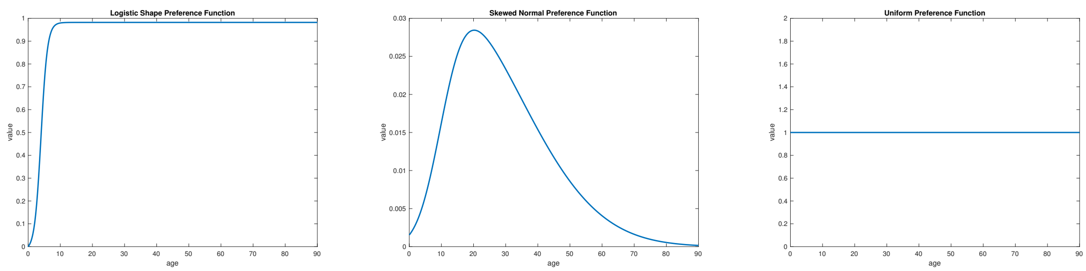

Figure 6.3: Left: Logistic Shape Preference Function. Middle: Skewed Normal Logistic Function. Right: Uniform Preference Function.

6.2 Optimal Control Parameters

We choose $B = 10$ and $C = 1$ as the cost of treating an infected person per year and cost of vaccinating an individual respectively. We choose B larger than C to reflect that treatment of an infected individual costs more than vaccinating an individual. Several tests were done with B larger but they yield similar results.

Chapter 7

Numerical Results

7.1 Numerical Simulations of the State Equation

We first run numerical simulations for the state equations to show the impact of the age-heterogeneous biting rate.

Fugure (7.1) shows the equilibrium population densities under different preference functions. We see that the preference function makes a noticeable difference in the shape of the infected population. The logistic shape preference function has a peak at a larger age. The Skewed Gaussian shows infections concentrated to younger adults reflecting the concentration of the Skewed Gaussian curve in those ages.

The age profile Uniform preference function has sharp changes near age 0. This is due to the fact that $p(0) = 0$ for the logistic shape and Gaussian preference curves while that is not the case for the Uniform preference function. This creates a sharp increase/decrease in the densities near 0 since newborns are moving to the infected compartment immediately at birth. This can cause problems for explicit schemes and may lead to instability on the numerical solution.

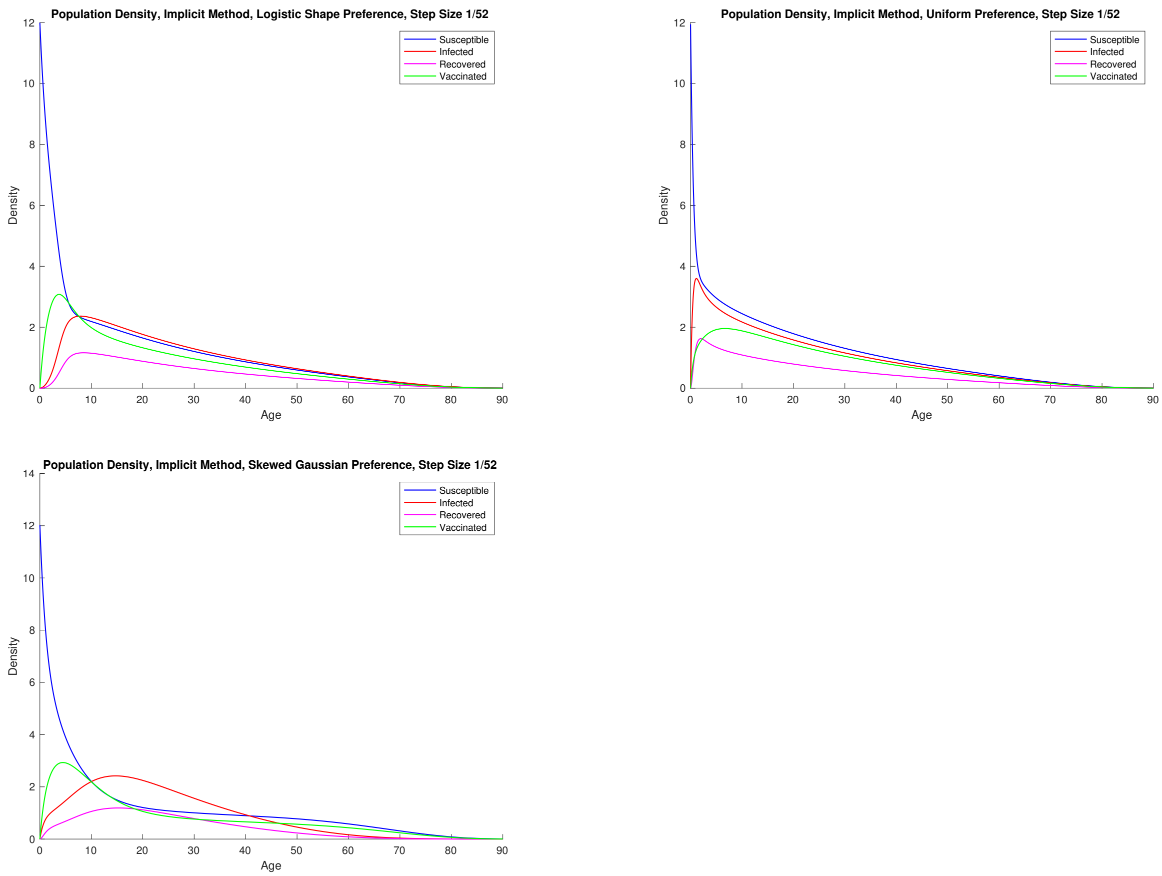

Figure 7.1: Population Densities for model under several preference functions.

7.2 Stability Improvements

The stability of the explicit method for different preference function is shown in Figure (7.2) and Figure(7.3). Figure (7.2) shows the age distributions at several points in time using the Uniform preference function. The smaller time step of $\Delta t = .01$ shows a stable approximation. Comparing the different time steps, we observe with a time step of $\Delta t = .04$, the numerical approximation overshoots the correct value near 0.

Figure(7.3) shows numerical simulations for Skewed Gaussian and Logistic shaped preference functions. We have the same step size of $\Delta t = .04$ but the two numerical approximations do not have stability issues near 0 like the Uniform preference function. The overshoot does not occur since we have that $\rho(0) \approx 0$ for both the Skewed Gaussian

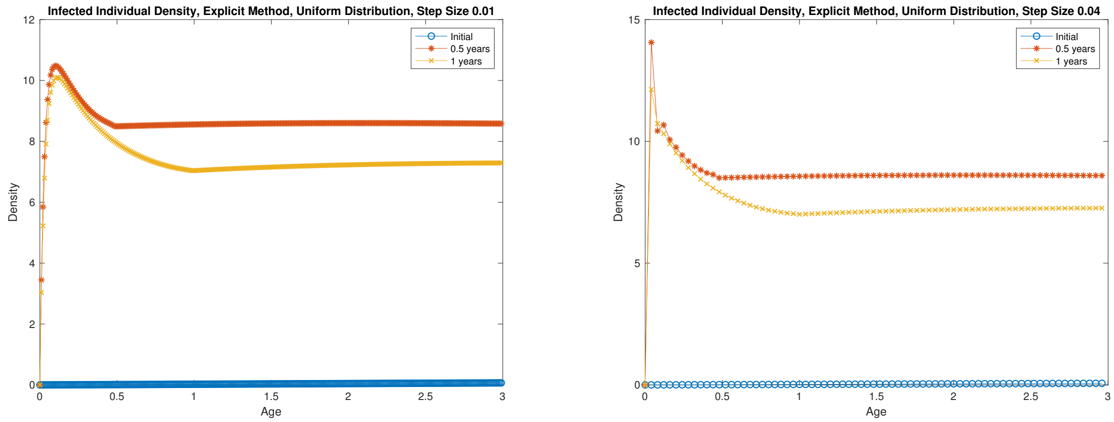

Figure 7.2: Left: Age Profile over time for Uniform Preference Function. Right: Age Profile over time for Skewed Gaussian Shape Preference Function. Both at step size .04

and Logistic Shape preference curves.

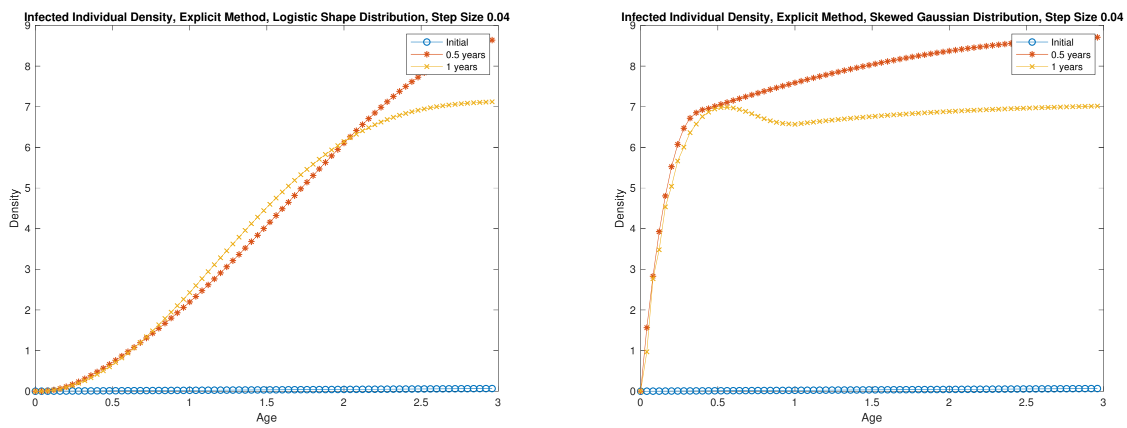

Figure 7.3: Left: Age Profile over time for Logistic Shape Preference Function. Right: Age Profile over time for Skewed Gaussian Preference Function. Both at step size .04

7.3 Optimal Control Simulations

We now examine the results of the optimal control system. For optimal control simulations we used the logistic shape preference function. Figure 7.4 shows the optimal control value for the vaccination rate $\xi_h(t,a)$. We note several features, we have that there is no vaccination for age 0-3. This is due to the shape of the preference function. Children of age 0-3 have significantly smaller force of infection than all other ages. This results in no vaccination at lower ages.

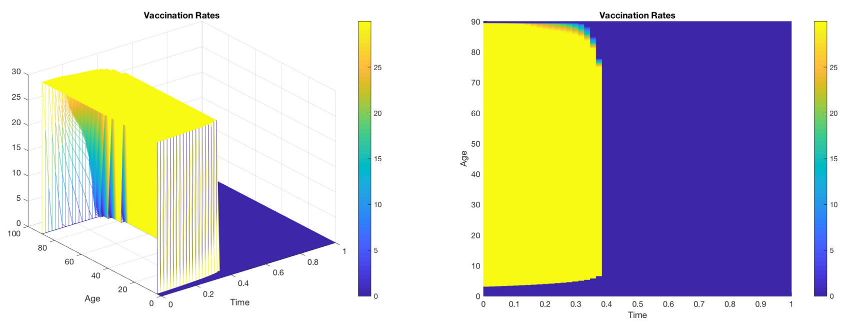

Figure 7.4: Vaccination Rates for $B = 10$ and $C = 1$

Figure 7.5 shows the time profiles under the optimal vaccination rate. We see in general the total infected human and vector population have decreased steadily. In contrast the susceptible and vaccinated population shows changes in behavior at around .4 time. The sharp change in behavior is due to the sudden drop in the vaccination rate at around time .4. The susceptible population decreases and the vaccinated population increase during times the vaccination is active.

Figure 7.6 shows the age profile at time $t = 1$ of the susceptible, infected and vaccinated human populations. The sharp discontinuity observed in the infected age profile and the non-differentiability of the age profile near age 3 in the other profiles are due to the sharp difference in the optimal vaccination rate for individuals between the age of 0-3 and other age groups.

Figure 7.7 shows the Optimal Control under different parameter values. We used treatment cost of infected individual per year $B = 100$ and cost to vaccinate an individual $C = 1$. So the cost of treating an infected individual is even greater than the previous case. We see that the shape is the same but the sharp fall in the vaccination rate occurs later at

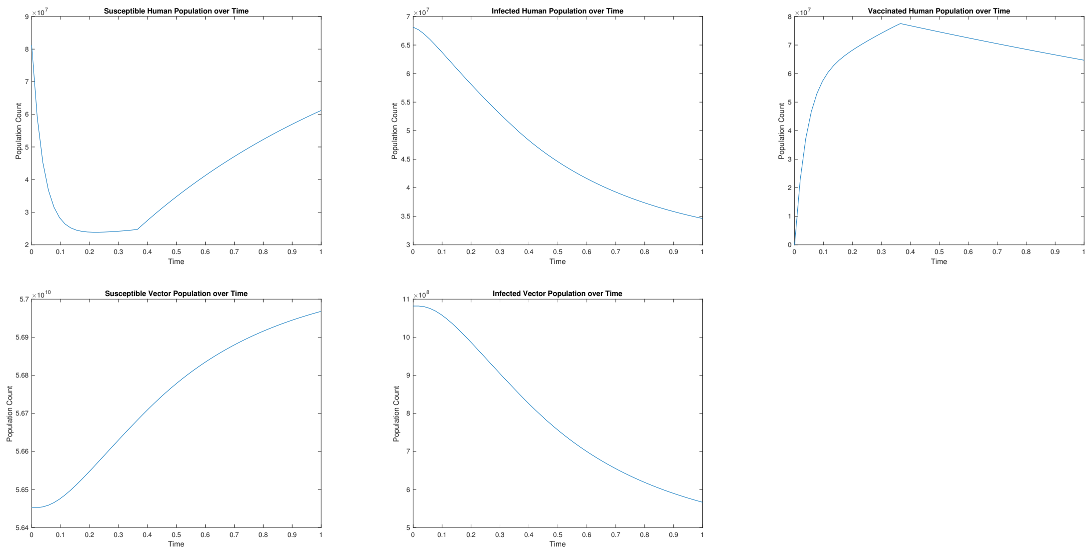

Figure 7.5: Top: Time Profile of Human Populations with Optimal Control Vaccination Rate. Bottom: Time Profile of Vector Population with Optimal Control Vaccination Rate.

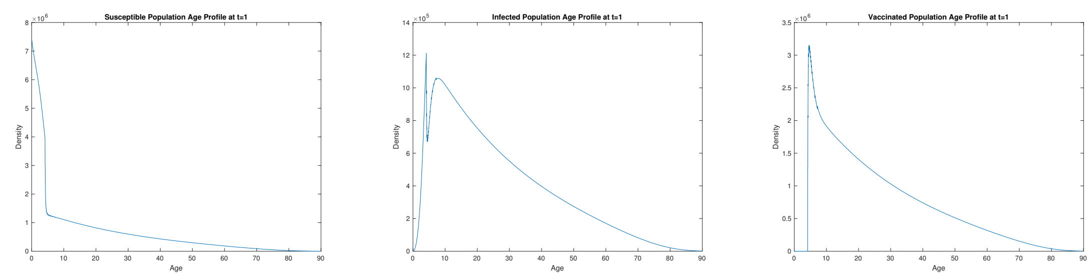

Figure 7.6: Age Profile of Human Populations with Optimal Control Vaccination Rate at $t = 1$. From left to right: Susceptible, Infected, Vaccinated

around time .8. This is due to the increase cost of treatment, it is more cost effective to vaccinate the individual even if they are not vaccinated for a long time. We note we only examine the cost within the 1-year period so if any patients are infected near the end of the time frame then they do not impose a large cost..

We make the observation that the shape of the border between max vaccination and 0 vaccination in the vaccination rate function with respect to age and time has a similar shape to the age preference function shape. In Figure 7.8 we have the optimal vaccination rate when we use the uniform and skewed Gaussian preference functions. The shape of

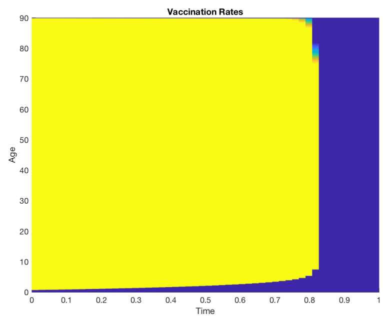

Figure 7.7: Vaccination Rates for $B = 100$ and $C = 1$

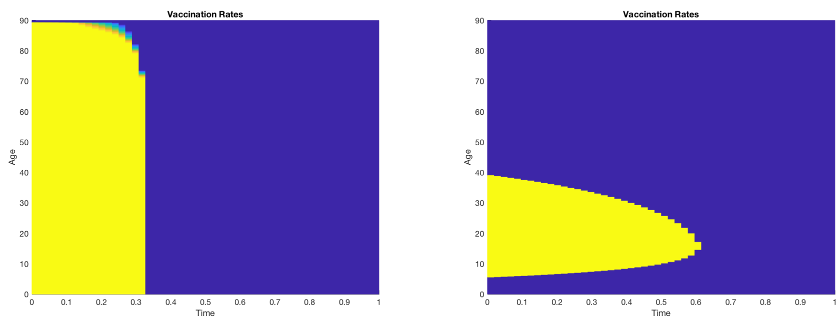

Figure 7.8: Vaccination Rates for $B = 10$ and $C = 1$. Left: Uniform Preference Rate, Right: Skewed Gaussian Preference Rate

the cutoff for the vaccinations reflects the shape of the preference curve. Vaccinations stop after uniform time for the Uniform preference rate except near the maximum age 90. For the skewed Gaussian, the vaccination is only applied to ages 5-40 where the preference function focuses the biting preference. The shape of the cutoff between max vaccination rate and 0 vaccination rate depends on the shape of the preference function.

Chapter 8

Conclusions

In this thesis we introduced an age-demographic model for the spread of malaria. We place emphasis on the age-dependent force of infection, which accounts for difference in biting rates between different age groups from mosquitos while preserving the total number of bites. The existence of a solution to the partial differential equations describing our model was shown. The basic reproduction number was derived by examining the asymptotic stability properties of the disease free equilibrium. Furthermore we interpreted the basic reproduction number derived in this fashion as the number of secondary mosquito infections from a single infectious mosquito through humans. An optimal control problem on minimizing the cost of vaccinations and infections was introduced. The adoint equations and optimality conditions for the optimal control problem was introduced. The paper ends with introduction of numerical schemes and their results with respect to our model. The numerical results show that the age-dependent force of infection changes the shape of the infected individual density, as well as improve stability for explicit schemes. Furthermore the optimal control simulations show the vaccinations should focus longer on age groups that have higher force of infection rate.

Bibliography

[1] World Health Orginization. Fact sheet about malaria, 2020. *https://www.who.int/en/news-room/fact-sheets/detail/malaria*

[2] William Ogilvy Kermack and Anderson G McKendrick. A contribution to the mathematical theory of epidemics. *Proceedings of the royal society of london. Series A, Containing papers of a mathematical and physical character*, 115(772):700–721, 1927.

[3] Liming Cai, Necibe Tuncer, and Maia Martcheva. How does within-host dynamics affect population-level dynamics? insights from an immuno-epidemiological model of malaria. *Mathematical Methods in the Applied Sciences*, 40(18):6424–6450, 2017.

[4] Mimmo Iannelli and Fabio Milner. The basic approach to age-structured population dynamics. *Models Methods and Numerics*, 10:978–94, 2017.

[5] K Renee Fister, Holly Gaff, Suzanne Lenhart, Eric Numfor, Elsa Schaefer, and Jin Wang. Optimal control of vaccination in an age-structured cholera model. In *Mathematical and Statistical Modeling for Emerging and Re-emerging Infectious Diseases*, pages 221–248. Springer, 2016.

[6] Pauline Van den Driessche and James Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical biosciences*, 180(1-2):29–48, 2002.

[7] Pauline van den Driessche. Reproduction numbers of infectious disease models. *Infectious Disease Modelling*, 2(3):288–303, 2017.

[8] Xue-Zhi Li, Ji-Xuan Liu, and Maia Martcheva. An age-structured two-strain epidemic model with super-infection. *Mathematical Biosciences & Engineering*, 7(1):123, 2010.

[9] Jemal Mohammed-Awel, Ruijun Zhao, Eric Numfor, and Suzanne Lenhart. Management strategies in a malaria model combining human and transmission-blocking vaccines. *Discrete & Continuous Dynamical Systems-B*, 22(3):977, 2017.

[10] Ruijun Zhao and Jemal Mohammed-Awel. A mathematical model studying mosquito-stage transmission-blocking vaccines. *Mathematical Biosciences & Engineering*, 11(5):1229, 2014.

[11] Calistus N Ngonghala, Sara Y Del Valle, Ruijun Zhao, and Jemal Mohammed-Awel. Quantifying the impact of decay in bed-net efficacy on malaria transmission. *Journal of theoretical biology*, 363:247–261, 2014.

[12] Folashade B Agusto, Sara Y Del Valle, Kbenesh W Blayneh, Calistus N Ngonghala, Maria J Goncalves, Nianpeng Li, Ruijun Zhao, and Hongfei Gong. The impact of bed-net use on malaria prevalence. *Journal of theoretical biology*, 320:58–65, 2013.

[13] David F Griffiths and Desmond J Higham. *Numerical methods for ordinary differential equations: initial value problems*. Springer Science & Business Media, 2010.

[14] Galena Pelovska and Mimmo Iannelli. Numerical methods for the lotka–mckendrick's equation. *Journal of computational and applied mathematics*, 197(2):534–557, 2006.

[15] Mimmo Iannelli, Tanya Kostova, and Fabio Augusto Milner. A fourth-order method for numerical integration of age-and size-structured population models. *Numerical Methods for Partial Differential Equations*, 25(4):918–930, 2009.

[16] Fabio A Milner and Guglielno Rabbiolo. Rapidly converging numerical algorithms for models of population dynamics. *Journal of mathematical biology*, 30(7):733–753, 1992.

[17] Wolfgang Hackbusch. A numerical method for solving parabolic equations with opposite orientations. *Computing*, 20(3):229–240, 1978.

[18] Michael McAsey, Libin Mou, and Weimin Han. Convergence of the forward-backward sweep method in optimal control. *Computational Optimization and Applications*, 53(1):207–226, 2012.

[19] Dilbar Abdurakhimova. An Age Structured Mathematical Model of Malaria *Unpublished Alternate Plan Paper 2015*

[20] Chitnis, Nakul and Hyman, James M and Cushing, Jim M Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model *Bulletin of mathematical biology*, 70(5):1272, 2008.

[21] Zhao, Ruijun and Kawakami, Sho An Age-structured Mathematical Model of Malaria with Heterogenous Mosquito Biting Pattern *International Journal Of Applied Physics and Mathematics*, submitted and accepted 2020.

Chapter 9

Appendix A

We run through the derivations of the functional and theorems used in the existence theorem in Chapter 3.

First we look at the equation

$$\frac{\partial y}{\partial t} + \frac{\partial y}{\partial a} = c(t,a)y(t,a) + d(t,a)$$

with initial condition $y(0,a) = y_0(a)$ and boundary condition $y_0(t,0) = y^0(t)$. we look for solutions along the characteristic line. Consider the case of $t < a$, and let $\overline{y}(t) = y(t, t+a)$. We have that $\overline{y}(0) = y(0, a_0) = y_0(a_0)$ where $a_0 = a - t$. Then since $\frac{d}{dt}\overline{y}(t) = \frac{\partial y(t,t+a)}{\partial t} + \frac{\partial y(t,t+a)}{\partial a}$. Let $\overline{c}(t) = c(t, t+a_0)$ and $\overline{d}(t) = d(t, t+a_0)$

$$\frac{d}{dt}\overline{y}(t) = \overline{c}(t)\overline{y}(t) + \overline{d}(t)$$

which can be rearranged as

$$\frac{d}{dt}\overline{y}(t) - \overline{c}(t)\overline{y}(t) = \overline{d}(t)$$

which is equivalent to

$$\frac{d}{dt}(e^{-\int_0^t \overline{c}(\tau)d\tau}\overline{y}(t)) = \overline{d}(t)e^{-\int_0^t \overline{c}(\tau)d\tau}$$

So we integrate from $t = 0$ to t.

$$\int_0^t \frac{d}{dp}(e^{-\int_0^p \bar{c}(\tau)d\tau}\overline{y}(p))dp = \int_0^t \bar{d}(p)e^{-\int_0^p \bar{c}(\tau)d\tau}dp$$

which gives along with the initial condition the solution

$$\overline{y}(t) = \overline{y}(0)e^{\int_0^t \bar{c}(\tau)d\tau} + \int_0^t \bar{d}(p)e^{-\int_t^p \bar{c}(\tau)d\tau}dp$$

If we have the case of $t \geq a$, then we integrate from $t - a$ to a instead to get

$$\overline{y}(t) = \overline{y}(t-a)e^{\int_0^t \bar{c}(\tau)dt} + \int_{t-a}^t \bar{d}(p)e^{-\int_t^p \bar{c}(\tau)d\tau}dp$$

where now $\overline{y}(t - a) = y^0(t - a)$.

Thus by applying the above to each of the equations in 2.2, we get that the solutions can be written as

$$L_1(s_h, i_h, r_h, v_h, S_v, I_v) = \begin{cases} s_{h0}(a-t)e^{-\int_0^t \lambda_{vh}(\tau, a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))+\xi(a-t+\tau)d\tau} \\ \quad + \int_0^t (\gamma(a-t+p)r_h(t, a-t+p) + \eta(a-t+p)v_h(t, a-t+p))\times \\ \quad e^{-\int_p^t \lambda_{vh}(\tau, a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))+\xi(a-t+\tau)d\tau} dp \\ \text{if } t < a \\ \int_0^A b_h(a)n_h(t-a, a)da e^{-\int_0^a \lambda_{vh}(\tau, t-a+\tau)+\mu_h(t-a+\tau, N_h(\tau))+\xi(t-a+\tau)d\tau} \\ \quad + \int_0^a (\gamma(t-a+p)r_h(t, t-a+p) + \eta(t-a+p)v_h(t, t-a+p))\times \\ \quad e^{-\int_p^a \lambda_{vh}(\tau, t-a+\tau)+\mu_h(t-a+\tau, N_h(\tau))+\xi(t-a+\tau)d\tau} dp \\ \text{if } t \geq a \end{cases}$$

$$L_2(s_h, i_h, r_h, v_h, S_v, I_v) = \begin{cases} i_{h0}(a-t)e^{-\int_0^t \zeta(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))+\sigma(a-t+\tau)d\tau} \\ \quad + \int_0^t \lambda_{vh}(\tau, a-t+p)s_h(t, a-t+p)e^{-\int_p^t \zeta(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))+\sigma(a-t+\tau)d\tau} dp \\ \text{if } t < a \\ \int_0^a \lambda_{vh}(\tau, t-a+p)s_h(t, t-a+p)e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_h(\tau))+\sigma(t-a+\tau)d\tau} dp \\ \text{if } t \geq a \end{cases}$$

$$L_3(s_h, i_h, r_h, v_h, S_v, I_v) =$$

$$\begin{cases} r_{h0}(a-t)e^{-\int_0^t \gamma(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))d\tau} \\ \quad + \int_0^t \zeta(a-t+p)i_h(t, a-t+p)e^{-\int_p^t \gamma(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))d\tau}dp \\ \text{if } t < a \\ \int_0^a \zeta(t-a+p)i_h(t, t-a+p)e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))d\tau}dp \\ \text{if } t \geq a \end{cases}$$

$$L_4(s_h, i_h, r_h, v_h, S_v, I_v) =$$

$$\begin{cases} v_{h0}(a-t)e^{-\int_0^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))d\tau} \\ \quad + \int_0^t \xi(a-t+p)s_h(t, a-t+p)e^{-\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))d\tau}dp \\ \text{if } t < a \\ \\ \text{if } t \geq a \end{cases}$$

We also get that

$$L_5(s_h, i_h, r_h, v_h, S_v, I_v) = S_{v0}e^{-\int_0^t \lambda_{hv}(\tau)+\mu_v d\tau} + \int_0^t \Lambda_v e^{-\int_p^t \lambda_{hv}(\tau)+\mu_v d\tau}dp$$

and

$$L_6(s_h, i_h, r_h, v_h, S_v, I_v) = I_{v0}e^{-\int_0^t \mu_v d\tau} + \int_0^t \lambda_{hv}(p)e^{-\int_p^t \lambda_{hv}(\tau)+\mu_v d\tau}dp$$

Chapter 10

Appendix B

We prove the map L maps X to X as claimed in Chapter 3. We will use the following many times. Consider

$$|e^{-\int_p^a f(\sigma)d\sigma}|$$

If we have the conditions $p < a$, and $f(\sigma) \geq 0$, then the integral $\int_p^a f(\sigma)d\sigma \geq 0$ and so

$$|e^{-\int_p^a f(\sigma)d\sigma}| \leq 1$$

This will case for all of the exponential terms below. Then suppose $(s_h, i_h, r_h, v_h, S_v, I_v) \in X$, then it is clear that all terms including the parameters and inside of integrands are positive almost everywhere,

$$L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t, a) \geq 0$$

$$L_2(s_h, i_h, r_h, v_h, S_v, I_v)(t, a) \geq 0$$

$$L_3(s_h, i_h, r_h, v_h, S_v, I_v)(t, a) \geq 0$$

$$L_4(s_h, i_h, r_h, v_h, S_v, I_v)(t, a) \geq 0$$

$$L_5(s_h, i_h, r_h, v_h, S_v, I_v)(t) \geq 0$$

$$L_6(s_h, i_h, r_h, v_h, S_v, I_v)(t) \geq 0$$

almost everywhere. Then we just need to prove each of these are bounded by $\frac{M}{4}$. For the equation for $t > a$, since t and a are independent, we can switch the order of integration. We need to prove the following

$$\int_0^A |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \leq \frac{M}{4}$$

For $t < A$, we can do this by splitting this into two integrals one 0 to t and t to A on which the function will evaluate differently. The second integral from t to A can be widened to 0 to A since the functions evaluate positively so it works for upper bounds. For the first integral we keep the integration bound 0 to t.

We cover the second segment first

$$\begin{aligned}
&\int_t^A |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&\leq \int_0^A \Big| s_{h0}(a-t)e^{-\int_0^t \lambda_{vh}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\xi(a-t+\tau)d\tau} \\
&\quad + \int_0^t (\gamma(a-t+p)r_h(t,a-t+p) + \eta(a-t+p)v_h(t,a-t+p))\times \\
&\quad e^{-\int_p^t \lambda_{vh}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\xi(a-t+\tau)d\tau}dp\Big|da \\
&\leq \int_0^A \Big|s_{h0}(a-t)\Big| \cdot \Big|e^{-\int_0^t \lambda_{vh}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\xi(a-t+\tau)d\tau}\Big| \\
&\quad + \int_0^t (|\gamma(a-t+p)||r_h(t,a-t+p)| + |\eta(a-t+p)||v_h(t,a-t+p)|)\times \\
&\quad \Big|e^{-\int_p^t \lambda_{vh}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\xi(a-t+\tau)d\tau}dp\Big|da \\
&\leq \int_0^A |s_{h0}|da + \int_0^t \gamma \int_0^A |r_h(t,a-t+p)|dp + \eta \int_0^A |v_h(t,a-t+p)|dpda \\
&\leq \frac{M}{8} + \gamma\frac{M}{4}t + \eta\frac{M}{4}t \\
&= \frac{M}{8} + t\frac{M}{4}(\gamma+\eta)
\end{aligned}$$

and for the equations for $t < a$, we first compute

$$\int_0^A |n_h(t-b,b)|db \le MA$$

from the fact that for fixed t,

$$\int_0^A |n_h(t,b)|db \le M$$

then for t sufficiently small,

$$\int_0^A |n_h(t-b,b)|db \le \int_0^t \int_0^A |n_h(t,b)|dbdt \le Mt \le M$$

Then we can compute

$$\begin{aligned}
&\int_0^t |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&= \int_0^t \bigg| \int_0^A b_h(b)n_h(t-b,b)db e^{-\int_0^a \lambda_{vh}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))+\xi(t-a+\tau)d\tau} \\
&\quad + \int_0^a (\gamma(t-a+p)r_h(t,t-a+p) + \eta(t-a+p)v_h(t,t-a+p))\times \\
&\quad e^{-\int_p^a \lambda_{vh}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))+\xi(t-a+\tau)d\tau} dp\bigg| db \\
&\le \int_0^t \int_0^A |b_h(b)|n_h(t-b,b)db \left| e^{-\int_0^a \lambda_{vh}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))+\xi(t-a+\tau)d\tau} \right| \\
&\quad + \int_0^a (|\gamma(t-a+p)||r_h(t,t-a+p)| + |\eta(t-a+p)v_h(t,t-a+p))|\times \\
&\quad \left| e^{-\int_p^a \lambda_{vh}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))+\xi(t-a+\tau)d\tau} \right| dpdb \\
&= \int_0^t b \int_0^A |n_h(t-b,b)|db + \gamma \int_0^A |r_h(t,t-a+p)|dp + \eta \int_0^A |v_h(t,t-a+p)|dpda \\
&\le \int_0^t bM + \gamma\frac{M}{4} + \eta\frac{M}{4} dt \\
&\le t\left(bM + \gamma\frac{M}{4} + \eta\frac{M}{4}\right)
\end{aligned}$$

So by taking the sum, we see that for t small enough

$$\begin{aligned}\int_0^A |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da &= \int_0^t |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da + \int_t^A |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\ &\leq \frac{M}{8} + t\Big(\frac{M}{4}(\gamma+\eta) + bM + \gamma\frac{M}{4} + \eta\frac{M}{4}\Big) \\ &\leq \frac{M}{4}\end{aligned}$$

If $t > A$ then we can still use the bound derived second above to get for t small enough

$$\int_0^A |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \leq \int_0^t |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \leq \frac{M}{4}$$

We note that t small may force $t < A$.

We have similar results for the other equations, the necessary inequalities are shown below and we have the conclusions at the end.

For L_2,

$$\begin{aligned}&\int_t^A |L_2(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\ &= \int_0^A \Big| i_{h0}(a-t)e^{-\int_0^t \zeta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\sigma(a-t+\tau)d\tau} \\ &\quad + \int_0^t \lambda_{vh}(\tau, a-t+p)s_h(t,a-t+p)e^{-\int_p^t \zeta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\sigma(a-t+\tau)d\tau}dp\Big|da \\ &\leq \int_0^A |i_{h0}(a-t)|\Big|e^{-\int_0^t \zeta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\sigma(a-t+\tau)d\tau}\Big| \\ &\quad + \int_0^t |\lambda_{vh}(\tau, a-t+p)||s_h(t,a-t+p)|\Big|e^{-\int_p^t \zeta(a-t+\tau)+\mu_h(a-t+\tau,N_h(\tau))+\sigma(a-t+\tau)d\tau}\Big|dpda \\ &= \int_0^A |i_{h0}(a-t)|da + \int_0^A \int_0^t |\lambda_{vh}(\tau, a-t+p)||s_h(t,a-t+p)|dpda \\ &\leq \int_0^A |i_{h0}(a-t)|da + \int_0^t \frac{CM}{4m}\int_0^A |s_h(t,a-t+p)|dadp \\ &\leq \frac{M}{8} + t\frac{CM^2}{16m}\end{aligned}$$

and

$$
\begin{aligned}
&\int_0^t |L_2(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&= \int_0^t \left| \int_0^a \lambda_{vh}(\tau, t-a+p) s_h(t, t-a+p) e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_h(\tau))+\sigma(t-a+\tau)d\tau} dp \right| da \\
&\le \int_0^t \int_0^a |\lambda_{vh}(\tau, t-a+p)||s_h(t, t-a+p)| \left| e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_h(\tau))+\sigma(t-a+\tau)d\tau} dp \right| da \\
&\le \int_0^t \int_0^A |\lambda_{vh}(\tau, t-a+p)||s_h(t, t-a+p)| dp da \\
&\le \int_0^t \frac{CM}{4m} \int_0^A |s_h(t, t-a+p)| dp da \\
&\le t \frac{CM}{4m} \frac{M}{4} = t \frac{CM^2}{16m}
\end{aligned}
$$

For L_3

$$
\begin{aligned}
&\int_t^A |L_3(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&\le \int_0^A \Big| r_{h0}(a-t) e^{-\int_0^t \gamma(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))d\tau} \\
&\quad + \int_0^t \zeta(a-t+p) i_h(t, a-t+p) e^{-\int_p^t \gamma(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))d\tau} dp \Big| da \\
&\int_t^A |L_2(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&\le \int_0^A |r_{h0}(a-t)| \left| e^{-\int_0^t \gamma(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))d\tau} \right| \\
&\quad + \int_0^t |\zeta(a-t+p)||i_h(t, a-t+p)| \left| e^{-\int_p^t \gamma(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))d\tau} \right| dp da \\
&\le \int_0^A |r_{h0}(a-t)| + \int_0^t |\zeta(a-t+p)||i_h(t, a-t+p)| dp da \\
&= \int_0^A |r_{h0}(a-t)| da + \int_0^t \zeta \int_0^A |i_h(t, a-t+p)| da dp \\
&\le \frac{M}{8} + \int_0^t \zeta \frac{M}{4} \\
&= \frac{M}{8} + t \frac{\zeta M}{4}
\end{aligned}
$$

and

$$\begin{aligned}
&\int_0^t |L_3(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&\le \int_0^t \left| \int_0^a \zeta(t-a+p) i_h(t, t-a+p) e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau, N_h(\tau))d\tau} dp \right| da \\
&\le \int_0^t \int_0^a |\zeta(t-a+p)||i_h(t, t-a+p)| \left| e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau, N_h(\tau))d\tau} \right| dpda \\
&\le \int_0^t \zeta \int_0^a |i_h(t, t-a+p)| dpda \\
&\le \int_0^t \zeta \int_0^A |i_h(t, t-a+p)| dpda \\
&\le \int_0^t \zeta \frac{M}{4} da \\
&\le t \frac{\zeta M}{4}
\end{aligned}$$

Then for L_4,

$$\begin{aligned}
&\int_t^A |L_4(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&\le \int_0^A \Bigg| v_{h0}(a-t) e^{-\int_0^t \eta(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))d\tau} \\
&\quad + \int_0^t \xi(a-t+p) s_h(t, a-t+p) e^{-\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))d\tau} dp \Bigg| da \\
&\le \int_0^A |v_{h0}(a-t)| \left| e^{-\int_0^t \eta(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))d\tau} \right| \\
&\quad + \int_0^t |\xi(a-t+p)||s_h(t, a-t+p)| \left| e^{-\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau, N_h(\tau))d\tau} \right| dpda \\
&\le \int_0^A |v_{h0}(a-t)| + \int_0^t |\xi(a-t+p)||s_h(t, a-t+p)| dpda \\
&\le \int_0^A |v_{h0}(a-t)| da + \int_0^t \xi \int_0^A ||s_h(t, a-t+p)| dadp \\
&\le \frac{M}{8} + \int_0^t \xi \frac{M}{4} dp \\
&= \frac{M}{8} + t \frac{\xi M}{4}
\end{aligned}$$

and

$$\begin{aligned}
&\int_0^t |L_4(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| da \\
&= \int_0^t \left| \int_0^a \xi(t-a+p) s_h(t, t-a+p) e^{-\int_p^t \eta(t-a+\tau)+\mu_h(t-a+\tau, N_h(\tau)) d\tau} dp \right| dt \\
&\leq \int_0^t \int_0^a |\xi(t-a+p)| |s_h(t, t-a+p)| \left| e^{-\int_p^t \eta(t-a+\tau)+\mu_h(t-a+\tau, N_h(\tau)) d\tau} \right| dp dt \\
&\leq \int_0^t \int_0^a \xi |s_h(t, t-a+p)| dp dt \\
&\leq \int_0^t \xi \int_0^A |s_h(t, t-a+p)| dp dt \\
&\leq \int_0^t \xi \frac{M}{4} da \\
&= t \frac{\xi M}{4}
\end{aligned}$$

Then for L_5 and L_6,

$$\begin{aligned}
&|L_5(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| \\
&= \left| S_{v0} e^{-\int_0^t \lambda_{hv}(\tau)+\mu_v d\tau} + \int_0^t \Lambda_v e^{-\int_p^t \lambda_{hv}(\tau)+\mu_v d\tau} dp \right| \\
&\leq |S_{v0}| \left| e^{-\int_0^t \lambda_{hv}(\tau)+\mu_v d\tau} \right| + \int_0^t |\Lambda_v| \left| e^{-\int_p^t \lambda_{hv}(\tau)+\mu_v d\tau} \right| dp \\
&\leq |S_{v0}| + \int_0^t |\Lambda_v| dp \\
&= \frac{M}{8} + t\Lambda_v
\end{aligned}$$

and

$$
\begin{aligned}
&|L_6(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| \\
&= \left| I_{v0} e^{-\int_0^t \mu_v d\tau} + \int_0^t \lambda_{hv}(p) e^{-\int_p^t \lambda_{hv}(\tau)+\mu_v d\tau} dp \right| \\
&\leq |I_{v0}| \left| e^{-\int_0^t \mu_v d\tau} \right| + \int_0^t |\lambda_{hv}(p)| \left| e^{-\int_p^t \lambda_{hv}(\tau)+\mu_v d\tau} \right| dp \\
&\leq |I_{v0}| + \int_0^t |\lambda_{hv}(p)| dp \\
&\leq \frac{M}{8} + t\frac{CM}{4m}
\end{aligned}
$$

With sufficiently small t, if we have that for $t > A$

$$
\begin{aligned}
\int_0^A |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| da \leq \int_0^t |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| da \leq \frac{M}{4} \\
\int_0^A |L_2(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| da \leq \int_0^t |L_2(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| da \leq \frac{M}{4} \\
\int_0^A |L_3(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| da \leq \int_0^t |L_3(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| da \leq \frac{M}{4} \\
\int_0^A |L_4(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| da \leq \int_0^t |L_4(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| da \leq \frac{M}{4}
\end{aligned}
$$

and if $t < A$

$$\begin{aligned}
\int_0^A |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da &= \int_0^t |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da + \int_t^A |L_1(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&\leq \frac{M}{8} + t\Big(\frac{M}{4}(\gamma + \eta) + bM + \gamma\frac{M}{4} + \eta\frac{M}{4}\Big) \\
&\leq \frac{M}{4} \\
\int_0^A |L_2(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da &= \int_0^t |L_2(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da + \int_t^A |L_2(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&\leq \frac{M}{8} + 2t\frac{CM^2}{16m} \\
&\leq \frac{M}{4} \\
\int_0^A |L_3(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da &= \int_0^t |L_3(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da + \int_t^A |L_3(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&\leq \frac{M}{8} + 2t\frac{\zeta M}{4} \\
&\leq \frac{M}{4} \\
\int_0^A |L_4(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da &= \int_0^t |L_4(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da + \int_t^A |L_4(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)|da \\
&\leq \frac{M}{8} + 2t\frac{\xi M}{4} \\
&\leq \frac{M}{4}
\end{aligned}$$

$$\begin{aligned}
|L_5(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| &\leq \frac{M}{4} \\
|L_6(s_h, i_h, r_h, v_h, S_v, I_v)(t,a)| &\leq \frac{M}{4}
\end{aligned}$$

Thus we have that for finite time interval L maps X to X.

Chapter 11

Appendix C

We prove the Lipchitz continuity. We use the following shorthand, which will simplify the notation. Let $u = (s_h, i_h, r_h, v_h)$ and $v = (S_v, I_v)$ and

$$||u|| = ||s_h||_{L^\infty(Q)} + ||i_h||_{L^\infty(Q)} + ||r_h||_{L^\infty(Q)} + ||v_h||_{L^\infty(Q)}$$

and

$$||v|| = |S_v|_{L^\infty(0,t)} + |I_v|_{L^\infty(0,t)}$$

We first show an inequality we will be taking advantage of. We start with

$$1 + x \leq e^x$$

Then we rearrange this to get

$$-x > 1 - e^x$$

Then for $x < 0$, we have

$$-x \geq 1 - e^x > 0$$

and so

$$|x| \geq |1 - e^x|$$

Then consider the expression

$$\left| e^{-\int g_1(\tau)d\tau} - e^{-\int g_2(\tau)d\tau} \right|$$

where $-\int g_1(\tau)d\tau < 0$ and $-\int g_2(\tau)d\tau < 0$. Then we have two cases, if $-\int g_1(\tau) - g_2(\tau)d\tau < 0$, then

$$\begin{aligned}
\left| e^{-\int g_1(\tau)d\tau} - e^{-\int g_2(\tau)d\tau} \right| &= \left| e^{-\int g_2(\tau)d\tau}\left(e^{-\int g_1(\tau)-g_2(\tau)d\tau} - 1 \right) \right| \\
&\leq \left| e^{-\int g_2(\tau)d\tau} \right| \left| e^{-\int g_1(\tau)-g_2(\tau)d\tau} - 1 \right| \\
&\leq \left| e^{-\int g_1(\tau)-g_2(\tau)d\tau} - 1 \right| \\
&= \left| 1 - e^{-\int g_1(\tau)-g_2(\tau)d\tau} \right| \\
&\leq \left| -\int g_1(\tau) - g_2(\tau)d\tau \right| \\
&= \left| \int g_1(\tau) - g_2(\tau)d\tau \right|
\end{aligned}$$

On the other hand if $-\int g_2(\tau) - g_1(\tau)d\tau < 0$, then

$$\begin{aligned}
\left|e^{-\int g_1(\tau)d\tau} - e^{-\int g_2(\tau)d\tau}\right| &= \left|e^{-\int g_1(\tau)d\tau}\left(1 - e^{-\int g_2(\tau)-g_1(\tau)d\tau}\right)\right| \\
&\leq \left|e^{-\int g_1(\tau)d\tau}\right|\left|1 - e^{-\int g_2(\tau)-g_1(\tau)d\tau}\right| \\
&\leq \left|1 - e^{-\int g_2(\tau)-g_1(\tau)d\tau}\right| \\
&\leq \left|-\int g_2(\tau) - g_1(\tau)d\tau\right| \\
&= \left|\int g_1(\tau) - g_2(\tau)d\tau\right|
\end{aligned}$$

So in either case we have

$$\left|e^{-\int g_1(\tau)d\tau} - e^{-\int g_2(\tau)d\tau}\right| \leq \left|\int g_1(\tau) - g_2(\tau)d\tau\right|$$

We will be able to use the above inequality since $\mu_{h0}(a) > \mu_L > 0$ so int integral in the exponent will be bounded above by a negative number.

We compute the following beforehand:

$$
\begin{aligned}
&|\mu_h(a-t+\tau, N_{h1}(\tau)) - \mu_h(a-t+\tau, N_{h2}(\tau))| \\
&= |\mu_{h0}(a-t+\tau) + \mu_{h1}(a-t+\tau)N_{h1}(\tau) - (\mu_{h0}(a-t+\tau) + \mu_{h1}(a-t+\tau)N_{h2}(\tau))| \\
&= |\mu_{h1}(a-t+\tau)(N_{h1}(\tau) + N_{h2}(\tau))| \\
&= \mu_{h1}\Big|\int_0^A s_{h1}(\tau,b) - s_{h2}(\tau,b) + i_{h1}(\tau,b) - i_{h2}(\tau,b) + r_{h1}(\tau,b) - r_{h2}(\tau,b) + v_{h1}(\tau,b) - v_{h2}(\tau,b)db\Big| \\
&\leq \mu_{h1}\Big(\int_0^A |s_{h1}(\tau,b) - s_{h2}(\tau,b)|db + \int_0^A |i_{h1}(\tau,b) - i_{h2}(\tau,b)|db \\
&\qquad + \int_0^A |r_{h1}(\tau,b) - r_{h2}(\tau,b)|db + \int_0^A |v_{h1}(\tau,b) - v_{h2}(\tau,b)|db\Big) \\
&\leq \mu_{h1}\Big(\sup_{0<\tau<t}\int_0^A |s_{h1}(\tau,b) - s_{h2}(\tau,b)|db + \sup_{0<\tau<t}\int_0^A |i_{h1}(\tau,b) - i_{h2}(\tau,b)|db \\
&\qquad + \sup_{0<\tau<t}\int_0^A |r_{h1}(\tau,b) - r_{h2}(\tau,b)|db + \sup_{0<\tau<t}\int_0^A |v_{h1}(\tau,b) - v_{h2}(\tau,b)|db\Big) \\
&\leq \mu_{h1}\Big(||s_{h1} - s_{h2}||_{L^\infty(Q)} + ||i_{h1} - i_{h2})||_{L^\infty(Q)} + ||r_{h1} - r_{h2}||_{L^\infty(Q)} + ||v_{h1} - v_{h2}||_{L^\infty(Q)}\Big) \\
&\leq \mu_{h1}||u_{h1} - u_{h2}||
\end{aligned}
$$

and

$$
\begin{aligned}
&\left|\int_0^A \rho(b)n_{h1}(\tau,b)db - \int_0^A \rho(b)n_{h2}(\tau,b)db\right| \\
&\leq \left|\int_0^A \rho(b)db\right|\left|\int_0^A n_{h1}(\tau,b) - n_{h2}(\tau,b)db\right| \\
&\leq \rho A\Big(\int_0^A |s_{h1}(\tau,b) - s_{h2}(\tau,b)|db + \int_0^A |i_{h1}(\tau,b) - i_{h2}(\tau,b)|db \\
&\qquad + \int_0^A |r_{h1}(\tau,b) - r_{h2}(\tau,b)|db + \int_0^A |v_{h1}(\tau,b) - v_{h2}(\tau,b)|db\Big) \\
&\leq \rho A\Big(\sup_{0<\tau<t}\int_0^A |s_{h1}(\tau,b) - s_{h2}(\tau,b)|db + \sup_{0<\tau<t}\int_0^A |i_{h1}(\tau,b) - i_{h2}(\tau,b)|db \\
&\qquad + \sup_{0<\tau<t}\int_0^A |r_{h1}(\tau,b) - r_{h2}(\tau,b)|db + \sup_{0<\tau<t}\int_0^A |v_{h1}(\tau,b) - v_{h2}(\tau,b)|db\Big) \\
&= \rho A(||s_{h1} - s_{h2}||_{L^\infty(Q)} + ||i_{h1} - i_{h2}||_{L^\infty(Q)} + ||r_{h1} - r_{h2}||_{L^\infty(Q)} + ||v_{h1} - v_{h2}||_{L^\infty(Q)}) \\
&= \rho A||u_{h1} - u_{h2}||
\end{aligned}
$$

and

$$
\begin{aligned}
&|\lambda_{vh1}(a,\tau)-\lambda_{vh2}(a,\tau)| \\
&=\left|p_1\beta\rho(a)\Big(\frac{I_{v1}(\tau)}{\int_0^A\rho(b)n_{h1}(b,\tau)db}-\frac{I_{v2}(\tau)}{\int_0^A\rho(b)n_{h2}(b,\tau)db}\Big)\right| \\
&\leq C\rho\left|\frac{I_{v1}(\tau)\int_0^A\rho(b)n_{h2}(b,\tau)db+I_{v2}(\tau)\int_0^A\rho(b)n_{h1}(b,\tau)db}{\int_0^A\rho(b)n_{h1}(b,\tau)db\int_0^A\rho(b)n_{h2}(b,\tau)db}\right| \\
&=C\rho\left|\frac{I_{v1}(\tau)\int_0^A\rho(b)n_{h2}(b,\tau)db-I_{v2}(\tau)\int_0^A\rho(b)n_{h2}(b,\tau)db}{\int_0^A\rho(b)n_{h1}(b,\tau)db\int_0^A\rho(b)n_{h2}(b,\tau)db}\right. \\
&\qquad\left.+\frac{I_{v2}(\tau)\int_0^A\rho(b)n_{h2}(b,\tau)db+I_{v2}(\tau)\int_0^A\rho(b)n_{h1}(b,\tau)db}{\int_0^A\rho(b)n_{h1}(b,\tau)db\int_0^A\rho(b)n_{h2}(b,\tau)db}\right| \\
&\leq C\rho\Big(\frac{|I_{v1}(\tau)-I_{v2}(\tau)|}{|\int_0^A\rho(b)n_{h1}(b,\tau)db|}+\frac{I_{v2}(\tau)\int_0^A\rho(b)|(n_{h2}(b,\tau)-n_{h1}(b,\tau)|)db}{|\int_0^A\rho(b)n_{h1}(b,\tau)db||\int_0^A\rho(b)n_{h2}(b,\tau)db|}\Big) \\
&\leq C\rho\Big(\frac{1}{m}|I_{v1}(\tau)-I_{v2}(\tau)| \\
&\qquad+\frac{|I_{v2}(\tau)|\rho}{m^2}(||s_{h1}-s_{h2}||_{L^\infty(Q)}+||i_{h1}-i_{h2}||_{L^\infty(Q)}+||r_{h1}-r_{h2}||_{L^\infty(Q)}+||v_{h1}-v_{h2}||_{L^\infty(Q)})\Big) \\
&\leq C\rho\Big(\frac{1}{m}|I_{v1}-I_{v2}|_{L^\infty(0,t)} \\
&\qquad+\frac{M\rho}{4m^2}(||s_{h1}-s_{h2}||_{L^\infty(Q)}+||i_{h1}-i_{h2}||_{L^\infty(Q)}+||r_{h1}-r_{h2}||_{L^\infty(Q)}+||v_{h1}-v_{h2}||_{L^\infty(Q)})\Big) \\
&\leq\frac{C\rho}{m}||v_1-v_2||+\frac{CM\rho^2}{4m^2}||u_{h1}-u_{h2}||
\end{aligned}
$$

We note that X is the complete metric space with one of the restrictions being they share the same initial conditions. So $s_{h0}(a) = s_{h1}(a)$, then

$$
\begin{aligned}
A_S = &\int_0^A \Big| s_{h1}^0(a-t)e^{-\int_0^t \lambda_{vh1}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))+\xi(a-t+\tau)d\tau} \\
&\quad - s_{h2}^0(a-t)e^{-\int_0^t \lambda_{vh2}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))+\xi(a-t+\tau)d\tau}\Big| da \\
\leq &\int_0^A |s_{h1}^0(a-t) - s_{h2}^0(a-t)| \Big| e^{-\int_0^t \lambda_{vh1}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))+\xi(a-t+\tau)d\tau}\Big| \\
&+ |s_{h2}^0(a-t)| \Big| e^{-\int_0^t \lambda_{vh1}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))+\xi(a-t+\tau)d\tau} - e^{-\int_0^t \lambda_{vh2}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))+\xi(a-t+\tau)d\tau}\Big| da \\
\leq &\frac{M}{8}\int_0^A \int_0^A \Big| -\int_0^t (\lambda_{vh1}(\tau, a-t+\tau) + \mu_h(a-t+\tau, N_{h1}(\tau)) + \xi(a-t+\tau)) \\
&\quad - (\lambda_{vh2}(\tau, a-t+\tau) + \mu_h(a-t+\tau, N_{h2}(\tau)) + \xi(a-t+\tau))d\tau\Big| da \\
\leq &\frac{M}{8}\int_0^A \int_0^t |\lambda_{vh1}(\tau, a-t+\tau) - \lambda_{vh2}(\tau, a-t+\tau)| + |\mu_h(a-t+\tau, N_{h2}(\tau)) - \mu_h(a-t+\tau, N_{h2}(\tau))| d\tau da \\
\leq &\frac{M}{8}\int_0^A \int_0^t \mu_{h1}\|u_{h1} - u_{h2}\| + \frac{C\rho}{m}\|v_1 - v_2\| + \frac{CM\rho^2}{4m^2}\|u_{h1} - u_{h2}\| d\tau da \\
\leq &\frac{tA}{8}(\mu_{h1} + \frac{CM\rho^2}{4m^2})\|u_{h1} - u_{h2}\| + t\frac{ACM\rho}{8m}\|v_1 - v_2\|
\end{aligned}
$$

Similarly we have

$$
\begin{aligned}
A_I = &\int_0^A \Big| i_{h1}^0(a-t)e^{-\int_0^t \zeta(a-t+\tau)+\mu_h(a-t+\tau,N_{h_1}(\tau))+\delta(a-t+\tau)d\tau} - i_{h2}^0(a-t)e^{-\int_0^t \zeta(a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))+\delta(a-t+\tau)d\tau}\Big| da \\
\leq &\int_0^A |i_{h1}^0(a-t)| \Big| -\int_0^t \zeta(a-t+\tau) + \mu_h(a-t+\tau, N_{h_1}(\tau)) + \delta(a-t+\tau) \\
&\quad - (\zeta(a-t+\tau) + \mu_h(a-t+\tau, N_{h2}(\tau)) + \delta(a-t+\tau))d\tau\Big| da \\
\leq &\Big(\int_0^A |i_{h1}^0(a-t)| da\Big) \int_0^A \int_0^t |\mu_h(a-t+\tau, N_{h1}(\tau)) - \mu_h(a-t+\tau, N_{h2}(\tau))| d\tau da \\
\leq &t\frac{M}{8}\mu_{h1}\|u_{h1} - u_{h2}\|
\end{aligned}
$$

$$A_R = \int_0^A \left| r_{h1}^0(a-t)e^{-\int_0^t \gamma(a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))d\tau} - r_{h2}^0(a-t)e^{-\int_0^t \gamma(a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))d\tau} \right| da$$
$$\leq t\frac{M}{8}\mu_{h1}\|u_{h1} - u_{h2}\|$$

$$A_V = \int_0^A \left| v_{h1}^0(a-t)e^{-\int_0^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))d\tau} - v_{h2}^0(a-t)e^{-\int_0^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))d\tau} \right| da$$
$$\leq t\frac{M}{8}\mu_{h1}\|u_{h1} - u_{h2}\|$$

Next we have

$$
\begin{aligned}
&B_S \\
&= \int_0^A \int_0^t \Big|(\gamma(a-t+p) r_{h1}(t,a-t+p) + \eta(a-t+p) v_{h1}(t,a-t+p)) \times e^{-\int_p^t \lambda_{vh1}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))+\xi(a-t+\tau)d\tau} \\
&\quad - (\gamma(a-t+p) r_{h2}(t,a-t+p) + \eta(a-t+p) v_{h2}(t,a-t+p)) \times e^{-\int_p^t \lambda_{vh2}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))+\xi(a-t+\tau)d\tau}\Big| dpda \\
&\leq \int_0^A \int_0^t |(\gamma(a-t+p) r_{h1}(t,a-t+p) - \gamma(a-t+p) r_{h2}(t,a-t+p))| \Big| e^{-\int_p^t \lambda_{vh1}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))+\xi(a-t+\tau)d\tau}\Big| dp \\
&\quad + |\gamma(a-t+p) r_{h2}(t,a-t+p)| \Big| e^{-\int_p^t \lambda_{vh1}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))+\xi(a-t+\tau)d\tau} - e^{-\int_p^t \lambda_{vh2}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))+\xi(a-t+\tau)d\tau}\Big| \\
&\quad + |(\eta(a-t+p) v_{h1}(t,a-t+p) - \eta(a-t+p) v_{h2}(t,a-t+p))| \Big| \\
&\quad \times e^{-\int_p^t \lambda_{vh1}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))+\xi(a-t+\tau)d\tau}\Big| dp \\
&\quad + |\eta(a-t+p) v_{h2}(t,a-t+p)| \Big| \\
&\quad \times e^{-\int_p^t \lambda_{vh1}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))+\xi(a-t+\tau)d\tau} - e^{-\int_p^t \lambda_{vh2}(\tau,a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))+\xi(a-t+\tau)d\tau}\Big| da \\
&\leq \gamma \int_0^t \int_0^A |r_{h1}(t,a-t+p) - r_{h2}(t,a-t+p)| dadp + \int_0^t \gamma \frac{M}{4} \int_0^A \int_p^t |\lambda_{vh1}(\tau,a-t+\tau) - \lambda_{vh2}(\tau,a-t+\tau)| \\
&\quad + |\mu_h(a-t+\tau,N_{h1}(\tau)) - \mu_h(a-t+\tau,N_{h2}(\tau))| d\tau dadp \\
&\quad + \eta \int_0^t \int_0^A |v_{h1}(t,a-t+p) - v_{h2}(t,a-t+p)| dadp \\
&\quad + \int_0^t \eta \frac{M}{4} \int_0^A \int_p^t |\lambda_{vh1}(\tau,a-t+\tau) - \lambda_{vh2}(\tau,a-t+\tau)| \\
&\quad + |\mu_h(a-t+\tau,N_{h1}(\tau)) - \mu_h(a-t+\tau,N_{h2}(\tau))| d\tau dadp \\
&\leq \gamma t \|r_{h1} - r_{h2}\|_{L^\infty(Q)} + \eta t \|v_{h1} - v_{h2}\|_{L^\infty(Q)} \\
&\qquad + t \frac{(\gamma+\eta) M A^2}{4} \left(\frac{C\rho}{m} \|v_1 - v_2\| + \frac{CM\rho^2}{4m^2} \|u_{h1} - u_{h2}\| + \mu_{h1} \|u_{h1} - u_{h2}\| \right) \\
&\leq (\gamma+\eta) t \|u_{h1} - u_{h2}\| + t \frac{(\gamma+\eta) M A^2}{4} \left(\frac{C\rho}{m} \|v_1 - v_2\| + \left(\frac{CM\rho^2}{4m^2} + \mu_{h1} \right) \|u_{h1} - u_{h2}\| \right) \\
&= t \frac{(\gamma+\eta) M A^2}{4} \frac{C\rho}{m} \|v_1 - v_2\| + t \left((\gamma+\eta) + \frac{(\gamma+\eta) M A^2}{4} \right) \left(\frac{CM\rho^2}{4m^2} + \mu_{h1} \right) \|u_{h1} - u_{h2}\|
\end{aligned}
$$

Next

$$
\begin{aligned}
&B_I\\
&= \int_0^A \left| \int_0^t \lambda_{vh1}(\tau, a-t+p) s_{h1}(t, a-t+p) e^{-\int_p^t \zeta(a-t+\tau)+\mu_h(a-t+\tau, N_{h1}(\tau))+\delta(a-t+\tau)d\tau} \right.\\
&\quad \left. -\left(\lambda_{vh2}(\tau, a-t+p) s_{h2}(t, a-t+p) e^{-\int_p^t \zeta(a-t+\tau)+\mu_h(a-t+\tau, N_{h2}(\tau))+\delta(a-t+\tau)d\tau}\right) dp \right| da\\
&\leq \int_0^A \int_0^t \left| \lambda_{vh1}(\tau, a-t+p) s_{h1}(t, a-t+p) - \lambda_{vh2}(\tau, a-t+p) s_{h2}(t, a-t+p) \right|\\
&\qquad \times \left| e^{-\int_p^t \zeta(a-t+\tau)+\mu_h(a-t+\tau, N_{h1}(\tau))+\delta(a-t+\tau)d\tau} \right|\\
&\qquad + |\lambda_{vh2}(\tau, a-t+p) s_{h2}(t, a-t+p)|\\
&\qquad \times \left| e^{-\int_p^t \zeta(a-t+\tau)+\mu_h(a-t+\tau, N_{h1}(\tau))+\delta(a-t+\tau)d\tau} - e^{-\int_p^t \zeta(a-t+\tau)+\mu_h(a-t+\tau, N_{h2}(\tau))+\delta(a-t+\tau)d\tau} \right| dpda\\
&\leq \int_0^A \int_0^t |\lambda_{vh1}(\tau, a-t+p) - \lambda_{vh2}(\tau, a-t+p)||s_{h1}(t, a-t+p)|\\
&\qquad + |\lambda_{vh1}(\tau, a-t+p)||s_{h1}(t, a-t+p) - s_{h2}(t, a-t+p)|\\
&\qquad + \frac{CM^2\rho}{16m} \left| -\int_p^t \zeta(a-t+\tau) + \mu_h(a-t+\tau, N_{h1}(\tau)) + \delta(a-t+\tau) \right.\\
&\qquad \left. - (\zeta(a-t+\tau) + \mu_h(a-t+\tau, N_{h2}(\tau)) + \delta(a-t+\tau)) d\tau \right| dpda\\
&\leq \int_0^t \frac{M}{4}\frac{C\rho}{m}\|v_1 - v_2\| + \frac{CM\rho^2}{4m^2}\|u_{h1} - u_{h2}\| + \frac{CM\rho}{4m} \int_0^A |s_{h1}(t, a-t+p) - s_{h2}(t, a-t+p)| dadp\\
&\qquad + \int_0^A \int_0^t \frac{CM^2\rho}{16m} \left| \int_p^t \mu_h(a-t+\tau, N_{h1}(\tau)) - \mu_h(a-t+\tau, N_{h2}(\tau)) d\tau \right| dpda\\
&\leq \int_0^t \frac{C\rho}{m}\|v_1 - v_2\| + \frac{CM\rho^2}{4m^2}\|u_{h1} - u_{h2}\| + \frac{CM\rho}{4m}\|s_{h1} - s_{h2}\|_{L^\infty(Q)} dp + \int_0^A \int_0^t \frac{CM^2\rho\mu_{h1}}{16m}\|u_{h1} - u_{h2}\| dpda\\
&\leq t\frac{C\rho}{m}\|v_1 - v_2\| + t\left(\frac{CM\rho^2}{4m^2} + \frac{CM\rho}{4m} + \frac{ACM^2\rho\mu_{h1}}{16m}\right)\|u_{h1} - u_{h2}\|
\end{aligned}
$$

and

$$
\begin{aligned}
&B_R \\
&= \int_0^A \int_0^t \Bigg| \zeta(a-t+p) i_{h1}(t, a-t+p) e^{-\int_p^t \gamma(a-t+\tau)+\mu_h(a-t+\tau, N_{h1}(\tau))d\tau} \\
&\quad - \left(\zeta(a-t+p) i_{h2}(t, a-t+p) e^{-\int_p^t \gamma(a-t+\tau)+\mu_h(a-t+\tau, N_{h2}(\tau))d\tau} \right) \Bigg| dpda \\
&\leq \int_0^A \int_0^t |\zeta(a-t+p) i_{h1}(t, a-t+p) - \zeta(a-t+p) i_{h2}(t, a-t+p)| \left| e^{-\int_p^t \gamma(a-t+\tau)+\mu_h(a-t+\tau, N_{h1}(\tau))d\tau} \right| \\
&\qquad + |\zeta(a-t+p) i_{h2}(t, a-t+p)| \left| e^{-\int_p^t \gamma(a-t+\tau)+\mu_h(a-t+\tau, N_{h1}(\tau))d\tau} - e^{-\int_p^t \gamma(a-t+\tau)+\mu_h(a-t+\tau, N_{h2}(\tau))d\tau} \right| dpda \\
&\leq \int_0^t \zeta \int_0^A |i_{h1}(t, a-t+p) - i_{h2}(t, a-t+p)| da \\
&\qquad + \gamma \frac{M}{4} \int_0^A \left| -\int_p^t \gamma(a-t+\tau) + \mu_h(a-t+\tau, N_{h1}(\tau)) - (\gamma(a-t+\tau) + \mu_h(a-t+\tau, N_{h2}(\tau))) d\tau \right| dadp \\
&\leq \int_0^t \zeta ||i_{h1} - i_{h2}||_{L^\infty(Q)} + \gamma \frac{M}{4} \int_0^A \left| \int_p^t \mu_h(a-t+\tau, N_{h1}(\tau)) - \mu_h(a-t+\tau, N_{h2}(\tau)) d\tau \right| dadp \\
&\leq \int_0^t \zeta ||u_{h1} - u_{h2}|| + \gamma \frac{M}{4} \int_0^A \int_p^t \mu_{h1} ||u_{h1} - u_{h2}|| d\tau dadp \\
&\leq t \left(\zeta + \frac{\gamma M A^2 \mu_{h1}}{4} \right) ||u_{h1} - u_{h2}||
\end{aligned}
$$

and

$$
\begin{aligned}
&B_V \\
&= \int_0^A \left| \int_0^t \xi(a-t+p)s_{h1}(t,a-t+p)e^{-\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))d\tau} \right. \\
&\quad \left. -\Big(\xi(a-t+p)s_{h2}(t,a-t+p)e^{-\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))d\tau}\Big)dp \right| da \\
&\le \int_0^A \int_0^t |\xi(a-t+p)s_{h1}(t,a-t+p)-\xi(a-t+p)s_{h2}(t,a-t+p)| \left| e^{-\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))d\tau} \right| \\
&\qquad + |\xi(a-t+p)s_{h2}(t,a-t+p)| \left| e^{-\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau))d\tau} - e^{-\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau))d\tau} \right| dpda \\
&\le \int_0^t \xi \int_0^A |s_{h1}(t,a-t+p)-s_{h2}(t,a-t+p)| da \\
&\qquad + \eta \frac{M}{4} \int_0^A \left| -\int_p^t \eta(a-t+\tau)+\mu_h(a-t+\tau,N_{h1}(\tau)) - (\eta(a-t+\tau)+\mu_h(a-t+\tau,N_{h2}(\tau)))d\tau \right| dadp \\
&\le \int_0^t \xi ||s_{h1}-s_{h2}||_{L^\infty(Q)} + \eta \frac{M}{4} \int_0^A \left| \int_p^t \mu_h(a-t+\tau,N_{h1}(\tau)) - \mu_h(a-t+\tau,N_{h2}(\tau))d\tau \right| dadp \\
&\le \int_0^t \xi ||u_{h1}-u_{h2}|| + \eta \frac{M}{4} \int_0^A \int_p^t \mu_{h1} ||u_{h1}-u_{h2}|| d\tau dadp \\
&\le t\Big(\xi + \frac{\eta M A^2 \mu_{h1}}{4}\Big) ||u_{h1}-u_{h2}||
\end{aligned}
$$

Now we also have the following. The calculations are almost identical to the calculations used in B_S

$$
\begin{aligned}
&C_S \\
&= \int_0^t \int_0^a \left|(\gamma(t-a+p)r_h(t,t-a+p) + \eta(t-a+p)v_h(t,t-a+p)) \times e^{-\int_p^a \lambda_{vh}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_h(\tau))+\xi(t-a+\tau)d\tau}\right| dpda \\
&\le \int_0^t \int_0^A |(\gamma(t-a+p)r_{h1}(t,t-a+p) - \gamma(t-a+p)r_{h2}(t,t-a+p))| \left|e^{-\int_p^t \lambda_{vh1}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h1}(\tau))+\xi(t-a+\tau)d\tau}\right| dp \\
&\quad + |\gamma(t-a+p)r_{h2}(t,t-a+p)| \Big| \\
&\quad \times e^{-\int_p^t \lambda_{vh1}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h1}(\tau))+\xi(t-a+\tau)d\tau} - e^{-\int_p^t \lambda_{vh2}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h2}(\tau))+\xi(t-a+\tau)d\tau} \Big| \\
&\quad + |(\eta(t-a+p)v_{h1}(t,t-a+p) - \eta(t-a+p)v_{h2}(t,t-a+p))| \left|e^{-\int_p^t \lambda_{vh1}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h1}(\tau))+\xi(t-a+\tau)d\tau}\right| dp \\
&\quad + |\eta(t-a+p)v_{h2}(t,t-a+p)| \\
&\quad \times \left|e^{-\int_p^t \lambda_{vh1}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h1}(\tau))+\xi(t-a+\tau)d\tau} - e^{-\int_p^t \lambda_{vh2}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h2}(\tau))+\xi(t-a+\tau)d\tau}\right| da \\
&\le \gamma \int_0^t \int_0^A |r_{h1}(t,t-a+p) - r_{h2}(t,t-a+p)| dpda \\
&\quad + \int_0^t \gamma \frac{M}{4} \int_0^A \int_p^t |\lambda_{vh1}(\tau,t-a+\tau) - \lambda_{vh2}(\tau,t-a+\tau)| \\
&\quad + |\mu_h(t-a+\tau,N_{h1}(\tau)) - \mu_h(t-a+\tau,N_{h2}(\tau))| d\tau dpda \\
&\quad + \eta \int_0^t \int_0^A |v_{h1}(t,t-a+p) - v_{h2}(t,t-a+p)| dpda \\
&\quad + \int_0^t \eta \frac{M}{4} \int_0^A \int_p^t |\lambda_{vh1}(\tau,t-a+\tau) - \lambda_{vh2}(\tau,t-a+\tau)| \\
&\quad + |\mu_h(t-a+\tau,N_{h1}(\tau)) - \mu_h(t-a+\tau,N_{h2}(\tau))| d\tau dpda \\
&\le \gamma t \|r_{h1} - r_{h2}\|_{L^\infty(Q)} + \eta t \|v_{h1} - v_{h2}\|_{L^\infty(Q)} \\
&\qquad + t\frac{(\gamma+\eta)MA^2}{4}\left(\frac{C\rho}{m}\|v_1 - v_2\| + \frac{CM\rho^2}{4m^2}\|u_{h1} - u_{h2}\| + \mu_{h1}\|u_{h1} - u_{h2}\|\right) \\
&\le (\gamma+\eta)t\|u_{h1} - u_{h2}\| + t\frac{(\gamma+\eta)MA^2}{4}\left(\frac{C\rho}{m}\|v_1 - v_2\| + \left(\frac{CM\rho^2}{4m^2} + \mu_{h1}\right)\|u_{h1} - u_{h2}\|\right) \\
&= t\frac{(\gamma+\eta)MA^2}{4}\frac{C\rho}{m}\|v_1 - v_2\| + t\left((\gamma+\eta) + \frac{(\gamma+\eta)MA^2}{4}\right)\left(\frac{CM\rho^2}{4m^2} + \mu_{h1}\right)\|u_{h1} - u_{h2}\|
\end{aligned}
$$

$$
\begin{aligned}
C_i &= \Big| \int_0^t \int_0^a \lambda_{vh1}(\tau, t-a+p) s_{h1}(t, t-a+p) e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))+\delta(t-a+\tau)d\tau} \\
&\quad - \Big(\lambda_{vh2}(\tau, t-a+p) s_{h2}(t, t-a+p) e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_{h2}(\tau))+\delta(t-a+\tau)d\tau} \Big) dpda \Big| \\
&\leq \int_0^t \int_0^A \Big| \lambda_{vh1}(\tau, t-a+p) s_{h1}(t, t-a+p) e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))+\delta(t-a+\tau)d\tau} \\
&\quad - \Big(\lambda_{vh2}(\tau, t-a+p) s_{h2}(t, t-a+p) e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_{h2}(\tau))+\delta(t-a+\tau)d\tau} \Big) \Big| dpda \\
&\leq \int_0^t \int_0^A \Big| \lambda_{vh1}(\tau, t-a+p) s_{h1}(t, t-a+p) - \lambda_{vh2}(\tau, t-a+p) s_{h2}(t, t-a+p) \Big| \\
&\qquad \times \Big| e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))+\delta(t-a+\tau)d\tau} \Big| \\
&\qquad + |\lambda_{vh2}(\tau, t-a+p) s_{h2}(t, t-a+p)| \\
&\qquad \times \Big| e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))+\delta(t-a+\tau)d\tau} - e^{-\int_p^t \zeta(t-a+\tau)+\mu_h(t-a+\tau, N_{h2}(\tau))+\delta(t-a+\tau)d\tau} \Big| dpda \\
&\leq \int_0^t \int_0^A |\lambda_{vh1}(\tau, t-a+p) - \lambda_{vh2}(\tau, t-a+p)| |s_{h1}(t, t-a+p)| \\
&\qquad + |\lambda_{vh1}(\tau, t-a+p)| |s_{h1}(t, t-a+p) - s_{h2}(t, t-a+p)| \\
&\qquad + \frac{CM^2\rho}{16m} \Big| - \int_p^t \zeta(t-a+\tau) + \mu_h(t-a+\tau, N_{h1}(\tau)) + \delta(t-a+\tau) \\
&\qquad - (\zeta(t-a+\tau) + \mu_h(t-a+\tau, N_{h2}(\tau)) + \delta(t-a+\tau)) d\tau \Big| dpda \\
&\leq \int_0^t \frac{M}{4} \frac{C\rho}{m} \|v_1 - v_2\| + \frac{CM\rho^2}{4m^2} \|u_{h1} - u_{h2}\| + \frac{CM\rho}{4m} \int_0^A |s_{h1}(t, a-t+p) - s_{h2}(t, a-t+p)| dpda \\
&\qquad + \int_0^t \int_0^A \frac{CM^2\rho}{16m} \Big| \int_p^t \mu_h(a-t+\tau, N_{h1}(\tau)) - \mu_h(a-t+\tau, N_{h2}(\tau)) d\tau \Big| dpda \\
&\leq \int_0^t \frac{C\rho}{m} \|v_1 - v_2\| + \frac{CM\rho^2}{4m^2} \|u_{h1} - u_{h2}\| + \frac{CM\rho}{4m} \|s_{h1} - s_{h2}\|_{L^\infty(Q)} dp + \int_0^t \int_0^A \frac{CM^2\rho\mu_{h1}}{16m} \|u_{h1} - u_{h2}\| dpda \\
&\leq t \frac{C\rho}{m} \|v_1 - v_2\| + t \Big(\frac{CM\rho^2}{4m^2} + \frac{CM\rho}{4m} + \frac{ACM^2\rho\mu_{h1}}{16m} \Big) \|u_{h1} - u_{h2}\|
\end{aligned}
$$

$$
\begin{aligned}
C_R =& \bigg| \int_0^t \int_0^a \zeta(t-a+p) i_{h1}(t, t-a+p) e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))d\tau} \\
&- \left(\zeta(t-a+p) i_{h2}(t, t-a+p) e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau, N_{h2}(\tau))d\tau} \right) dpda \bigg| \\
=& \int_0^t \int_0^A \bigg| \zeta(t-a+p) i_{h1}(t, t-a+p) e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))d\tau} \\
&- \left(\zeta(t-a+p) i_{h2}(t, t-a+p) e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau, N_{h2}(\tau))d\tau} \right) \bigg| dpda \\
\leq& \int_0^t \int_0^A |\zeta(t-a+p) i_{h1}(t, t-a+p) - \zeta(t-a+p) i_{h2}(t, t-a+p)| \left| e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))d\tau} \right| \\
&\quad + |\zeta(t-a+p) i_{h2}(t, t-a+p)| \left| e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))d\tau} - e^{-\int_p^t \gamma(t-a+\tau)+\mu_h(t-a+\tau, N_{h2}(\tau))d\tau} \right| dpda \\
\leq& \int_0^t \zeta \int_0^A |i_{h1}(t, t-a+p) - i_{h2}(t, t-a+p)| da \\
&\quad + \gamma \frac{M}{4} \int_0^A \left| - \int_p^t \gamma(t-a+\tau) + \mu_h(t-a+\tau, N_{h1}(\tau)) - (\gamma(t-a+\tau) + \mu_h(t-a+\tau, N_{h2}(\tau))) d\tau \right| dpda \\
\leq& \int_0^t \zeta \| i_{h1} - i_{h2} \|_{L^\infty(Q)} + \gamma \frac{M}{4} \int_0^A \left| \int_p^t \mu_h(t-a+\tau, N_{h1}(\tau)) - \mu_h(t-a+\tau, N_{h2}(\tau)) d\tau \right| dpda \\
\leq& \int_0^t \zeta \| u_{h1} - u_{h2} \| + \gamma \frac{M}{4} \int_0^A \int_p^t \mu_{h1} \| u_{h1} - u_{h2} \| d\tau dpda \\
\leq& t \left(\zeta + \frac{\gamma M A^2 \mu_{h1}}{4} \right) \| u_{h1} - u_{h2} \|
\end{aligned}
$$

$$\begin{aligned}
C_V &= \Bigg| \int_0^t \int_0^a \xi(t-a+p) s_{h1}(t, t-a+p) e^{-\int_p^t \eta(t-a+\tau)+\mu_h(a-t+\tau, N_{h1}(\tau))d\tau} \\
&\quad - \left(\xi(t-a+p) s_{h2}(t, t-a+p) e^{-\int_p^t \eta(t-a+\tau)+\mu_h(t-a+\tau, N_{h2}(\tau))d\tau} \right) dpda \Bigg| \\
&\leq \int_0^t \int_0^A \Bigg| \xi(t-a+p) s_{h1}(t, t-a+p) e^{-\int_p^t \eta(t-a+\tau)+\mu_h(a-t+\tau, N_{h1}(\tau))d\tau} \\
&\quad - \left(\xi(t-a+p) s_{h2}(t, t-a+p) e^{-\int_p^t \eta(t-a+\tau)+\mu_h(t-a+\tau, N_{h2}(\tau))d\tau} \right) \Bigg| dpda \\
&\leq \int_0^t \int_0^A |\xi(t-a+p) s_{h1}(t, t-a+p) - \xi(t-a+p) s_{h2}(t, t-a+p)| \left| e^{-\int_p^t \eta(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))d\tau} \right| \\
&\qquad + |\xi(t-a+p) s_{h2}(t, t-a+p)| \left| e^{-\int_p^t \eta(t-a+\tau)+\mu_h(t-a+\tau, N_{h1}(\tau))d\tau} - e^{-\int_p^t \eta(t-a+\tau)+\mu_h(t-a+\tau, N_{h2}(\tau))d\tau} \right| dpda \\
&\leq \int_0^t \xi \int_0^A |s_{h1}(t, t-a+p) - s_{h2}(t, t-a+p)| da \\
&\qquad + \eta \frac{M}{4} \int_0^A \left| - \int_p^t \eta(t-a+\tau) + \mu_h(t-a+\tau, N_{h1}(\tau)) - (\eta(t-a+\tau) + \mu_h(t-a+\tau, N_{h2}(\tau))) d\tau \right| dpda \\
&\leq \int_0^t \xi \|s_{h1} - s_{h2}\|_{L^\infty(Q)} + \eta \frac{M}{4} \int_0^A \left| \int_p^t \mu_h(t-a+\tau, N_{h1}(\tau)) - \mu_h(t-a+\tau, N_{h2}(\tau)) d\tau \right| dpda \\
&\leq \int_0^t \xi \|u_{h1} - u_{h2}\| + \eta \frac{M}{4} \int_0^A \int_p^t \mu_{h1} \|u_{h1} - u_{h2}\| d\tau dpda \\
&\leq t \left(\xi + \frac{\eta M A^2 \mu_{h1}}{4} \right) \|u_{h1} - u_{h2}\|
\end{aligned}$$

We also compute the following,

$$
\begin{aligned}
&D_S \\
&= \int_0^t \bigg| \int_0^A b_h(a) n_{h1}(t-a,a) da e^{-\int_0^a \lambda_{vh1}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h1}(\tau))+\xi(t-a+\tau)d\tau} \\
&\qquad - \int_0^A b_h(a) n_{h2}(t-a,a) da e^{-\int_0^a \lambda_{vh2}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h2}(\tau))+\xi(t-a+\tau)d\tau} \bigg| da \\
&\leq b \int_0^t |n_{h1}(t-a,a) - n_{h2}(t-a,a)| \left| e^{-\int_0^a \lambda_{vh1}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h1}(\tau))+\xi(t-a+\tau)d\tau} \right| \\
&\qquad + |n_{h2}(t-a,a)| \bigg| e^{-\int_0^a \lambda_{vh1}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h1}(\tau))+\xi(t-a+\tau)d\tau} \\
&\qquad - e^{-\int_0^a \lambda_{vh2}(\tau,t-a+\tau)+\mu_h(t-a+\tau,N_{h2}(\tau))+\xi(t-a+\tau)d\tau} \bigg| da \\
&\leq b \int_0^t \|u_{h1} - u_{h2}\| da + M \int_0^t \int_0^a \lambda_{vh1}(\tau, t-a+\tau) + \mu_h(t-a+\tau, N_{h1}(\tau)) + \xi(t-a+\tau) \\
&\qquad - (\lambda_{vh2}(\tau, t-a+\tau) + \mu_h(t-a+\tau, N_{h2}(\tau)) + \xi(t-a+\tau)) d\tau da \\
&\leq tb\|u_{h1} - u_{h2}\| + M \int_0^t \int_0^A |\lambda_{vh1}(\tau, t-a+\tau) - \lambda_{vh2}(\tau, t-a+\tau)| \\
&\qquad + |\mu_h(t-a+\tau, N_{h1}(\tau)) - \mu_h(t-a+\tau, N_{h2}(\tau))| da d\tau \\
&\leq tb\|u_{h1} - u_{h2}\| + M \int_0^t \int_0^A \frac{C\rho}{m}\|v_1 - v_2\| + \frac{CM\rho^2}{4m^2}\|u_{h1} - u_{h2}\| + \mu_{h1}\|u_{h1} - u_{h2}\| da d\tau \\
&\leq tb\|u_{h1} - u_{h2}\| + tMA\left(\frac{C\rho}{m}\|v_1 - v_2\| + \frac{CM\rho^2}{4m^2}\|u_{h1} - u_{h2}\| + \mu_{h1}\|u_{h1} - u_{h2}\| \right) \\
&= t\frac{ACM\rho}{m}\|v_1 - v_2\| + t\left(tb + AM\frac{CM\rho^2}{4m^2} + AM\mu_{h1} \right) \|u_{h1} - u_{h2}\|
\end{aligned}
$$

then we assume t is sufficiently small such that $0 < t < A$ then

$$
\begin{aligned}
&\int_0^A |L_1(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_1(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&\leq \int_t^A |L_1(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_1(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&+ \int_0^t |L_1(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_1(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&\leq \int_0^A |L_1(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_1(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&+ \int_0^t |L_1(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_1(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&\leq A_S + B_S + C_S + D_S \\
&\leq tK_S(||u_{h1} - u_{h2}|| + ||v_1 - v_2||)
\end{aligned}
$$

where K_S is a constant. The last equality follows since all A_S, B_S, C_S, D_S all have bound $tK(||u_{h1} - u_{h2}|| + ||v_1 - v_2||)$ for some constant K as calculated above. Then similarly we have

$$
\begin{aligned}
&\int_0^A |L_2(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_2(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&\leq \int_t^A |L_1(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_2(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&+ \int_0^t |L_2(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_1(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&\leq \int_0^A |L_2(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_2(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&+ \int_0^t |L_2(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_2(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})| da \\
&\leq A_I + B_I + C_I + D_I \\
&\leq tK_I(||u_{h1} - u_{h2}|| + ||v_1 - v_2||)
\end{aligned}
$$

where K_I is a constant.

$$\begin{aligned}
&\int_0^A |L_3(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_3(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&\leq \int_t^A |L_3(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_3(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&+ \int_0^t |L_3(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_3(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&\leq \int_0^A |L_3(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_3(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&+ \int_0^t |L_3(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_3(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&\leq A_R + B_R + C_R + D_R \\
&\leq tK_R(\|u_{h1} - u_{h2}\| + \|v_1 - v_2\|)
\end{aligned}$$

where K_R is a constant.

$$\begin{aligned}
&\int_0^A |L_4(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_4(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&\leq \int_t^A |L_4(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_4(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&+ \int_0^t |L_4(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_4(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&\leq \int_0^A |L_4(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_4(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&+ \int_0^t |L_4(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_4(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|da \\
&\leq A_V + B_V + C_V + D_V \\
&\leq tK_V(\|u_{h1} - u_{h2}\| + \|v_1 - v_2\|)
\end{aligned}$$

where K_V is a constant.

Then we finish the other two components of L.

$$
\begin{aligned}
&||L_5(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_5(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|| \\
&= \left| S_{v0} e^{-\int_0^t \lambda_{hv1}(\tau)+\mu_v d\tau} + \int_0^t \Lambda_v e^{-\int_p^t \lambda_{hv1}(\tau)+\mu_v d\tau} dp - \left(S_{v0} e^{-\int_0^t \lambda_{hv2}(\tau)+\mu_v d\tau} + \int_0^t \Lambda_v e^{-\int_p^t \lambda_{hv2}(\tau)+\mu_v d\tau} dp \right) \right| \\
&\leq ||S_{v0}|| ||e^{-\int_0^t \lambda_{hv1}(\tau)+\mu_v d\tau} - e^{-\int_0^t \lambda_{hv2}(\tau)+\mu_v d\tau}|| + \Lambda_v \int_0^t ||e^{-\int_p^t \lambda_{hv1}(\tau)+\mu_v d\tau} - e^{-\int_p^t \lambda_{hv2}(\tau)+\mu_v d\tau}|| dp \\
&\leq \frac{M}{8} || \int_0^t \lambda_{hv1}(\tau) + \mu_v d - (\lambda_{hv2}(\tau) + \mu_v)\tau || + \Lambda_v \int_0^t \left| \int_p^t \lambda_{hv1}(\tau) + \mu_v - (\lambda_{hv1}(\tau) + \mu_v) d\tau \right| dp \\
&= \frac{M}{8} \int_0^t |\lambda_{hv1}(\tau) - \lambda_{hv1}(\tau)| d\tau + \Lambda_v \int_0^t \int_0^A |\lambda_{hv1}(\tau) - \lambda_{hv1}(\tau)| d\tau dp \\
&\leq t \frac{M}{8} \frac{C\rho}{m} ||v_1 - v_2|| + t \frac{CM\rho^2}{4m^2} ||u_{h1} - u_{h2}|| + t \Lambda_v A \frac{C\rho}{m} ||v_1 - v_2|| + t \frac{CM\rho^2}{4m^2} ||u_{h1} - u_{h2}|| \\
&\leq t K_{SV} (||u_{h1} - u_{h2}|| + ||v_1 - v_2||)
\end{aligned}
$$

where K_{SV} is a constant. and

$$
\begin{aligned}
&||L_6(s_{h1}, i_{h1}, r_{h1}, v_{h1}, S_{v1}, I_{v1}) - L_6(s_{h2}, i_{h2}, r_{h2}, v_{h2}, S_{v2}, I_{v2})|| \\
&= |I_{v0} e^{-\int_0^t \mu_v d\tau} + \int_0^t \lambda_{hv1}(p) e^{-\int_p^t \lambda_{hv1}(\tau)+\mu_v d\tau} dp - \left(I_{v0} e^{-\int_0^t \mu_v d\tau} + \int_0^t \lambda_{hv2}(p) e^{-\int_p^t \lambda_{hv2}(\tau)+\mu_v d\tau} dp \right)| \\
&\leq \int_0^t |\lambda_{hv1}(p) - \lambda_{hv2}(p)| \left| e^{-\int_p^t \lambda_{hv1}(\tau)+\mu_v d\tau} \right| dp + \int_0^t |\lambda_{hv2}(p)| \left| e^{-\int_p^t \lambda_{hv1}(\tau)+\mu_v d\tau} - e^{-\int_p^t \lambda_{hv2}(\tau)+\mu_v d\tau} \right| dp \\
&\leq \int_0^t \frac{M}{8} \frac{C\rho}{m} ||v_1 - v_2|| + \frac{CM\rho^2}{4m^2} ||u_{h1} - u_{h2}|| dp + \frac{C\rho M}{4m} \int_0^t \int_p^t |\lambda_{hv1}(\tau) + \mu_v - (\lambda_{hv2}(\tau) + \mu_v)| d\tau dp \\
&\leq \int_0^t \frac{M}{8} \frac{C\rho}{m} ||v_1 - v_2|| + \frac{CM\rho^2}{4m^2} ||u_{h1} - u_{h2}|| dp + \frac{C\rho M}{4m} \int_0^t \int_0^A |\lambda_{hv1}(\tau) - \lambda_{hv2}(\tau)| d\tau dp \\
&\leq t \frac{M}{8} \frac{C\rho}{m} ||v_1 - v_2|| + t \frac{CM\rho^2}{4m^2} ||u_{h1} - u_{h2} + t \frac{C\rho MA}{4m} \left(\frac{C\rho}{m} ||v_1 - v_2|| + \frac{CM\rho^2}{4m^2} ||u_{h1} - u_{h2}|| \right) \\
&\leq t K_{IV} (||u_{h1} - u_{h2}|| + ||v_1 - v_2||)
\end{aligned}
$$

where K_{IV} is a constant.

Thus L has Lipshitz properties.

Chapter 12

Appendix D

We derive the results of several theorems for the optimal control results of our model. The cost function is

$$J(\xi) = \int_0^T \int_0^A [Bi_h(t,a) + C\xi_h(t,a)s_h(t,a) + D\xi_h(t,a)^2]$$

Given control ξ_h, let $\xi_h^\epsilon = \xi_h + \epsilon l$ for some variation l and $\epsilon > 0$. Then the partial differential equation corresponding to ξ_h is

$$\begin{aligned}
\frac{\partial s_h}{\partial t} + \frac{\partial s_h}{\partial a} &= -(\lambda_{vh}(t,a) + \mu_h(a,N_h) + \xi_h(t,a))s_h(t,a) + \gamma_h(a)r_h(t,a) \\
\frac{\partial i_h}{\partial t} + \frac{\partial i_h}{\partial a} &= \lambda_{vh}(t,a)s_h(t,a) - (\mu_h(a,N_h) + \delta_h(a) + \zeta_h(a))i_h(t,a) \\
\frac{\partial r_h}{\partial t} + \frac{\partial r_h}{\partial a} &= \zeta_h(a)i_h(t,a) - (\mu_h(a,N_h) + \gamma_h(a))r_h(t,a) \\
\frac{\partial v_h}{\partial t} + \frac{\partial v_h}{\partial a} &= \xi_h(t,a)s_h(t,a) - \zeta_h(a)v_h(t,a) \\
\frac{dS_v}{dt} &= \Lambda_v - \lambda_{hv}S_v - \mu_v S_v \\
\frac{dI_v}{dt} &= \lambda_{hv}S_v - \mu_v I_v
\end{aligned}$$

The partial differential equations associated with ξ_h^ϵ are

$$
\begin{aligned}
\frac{\partial s_h^\epsilon}{\partial t} + \frac{\partial s_h^\epsilon}{\partial a} &= -(\lambda_{vh}^\epsilon(t,a) + \mu_h^\epsilon(a, N_h^\epsilon) + \xi_h^\epsilon(t,a))s_h^\epsilon(t,a) + \gamma_h(a) r_h^\epsilon(t,a) \\
\frac{\partial i_h^\epsilon}{\partial t} + \frac{\partial i_h^\epsilon}{\partial a} &= \lambda_{vh}^\epsilon(t,a) s_h^\epsilon(t,a) - (\mu_h^\epsilon(a, N_h^\epsilon) + \delta_h(a) + \zeta_h(a)) i_h^\epsilon(t,a) \\
\frac{\partial r_h^\epsilon}{\partial t} + \frac{\partial r_h^\epsilon}{\partial a} &= \zeta_h(a) i_h^\epsilon(t,a) - (\mu_h^\epsilon(a, N_h^\epsilon) + \gamma_h(a)) r_h^\epsilon(t,a) \\
\frac{\partial v_h^\epsilon}{\partial t} + \frac{\partial v_h^\epsilon}{\partial a} &= \xi_h^\epsilon(t,a) s_h^\epsilon(t,a) - \zeta_h(a) v_h^\epsilon(t,a) \\
\frac{dS_v^\epsilon}{dt} &= \Lambda_v - \lambda_{hv}^\epsilon S_v^\epsilon - \mu_v S_v^\epsilon \\
\frac{dI_v^\epsilon}{dt} &= \lambda_{hv}^\epsilon S_v^\epsilon - \mu_v I_v^\epsilon
\end{aligned}
$$

Let

$$
J_h(t) = \int_0^A \rho(a) i_h(t,a) da, T_h(t) = \int_0^A \rho(a) n_h(t,a) da
$$

and

$$
J_h^\epsilon(t) = \int_0^A \rho(a) i_h^\epsilon(t,a) da, T_h^\epsilon(t) = \int_0^A \rho(a) n_h^\epsilon(t,a) da
$$

and so

$$
\lambda_{vh}(t,a) = p_1 \beta \frac{\rho(a) I_v(t)}{T_h(t)}, \lambda_{hv}(t) = p_2 \beta \frac{J_h(t)}{N_h(t)}
$$

and

$$
\lambda_{vh}^\epsilon(t,a) = p_1 \beta \frac{\rho(a) I_v^\epsilon(t)}{T_h^\epsilon(t)}, \lambda_{hv}^\epsilon(t) = p_2 \beta \frac{J_h^\epsilon(t)}{N_h^\epsilon(t)}
$$

We introduce the following

$$
\Psi_s = \lim_{\epsilon \to 0} \frac{s_h^* - s_h}{\epsilon}, \Psi_i = \lim_{\epsilon \to 0} \frac{i_h^* - i_h}{\epsilon}, \Psi_r = \lim_{\epsilon \to 0} \frac{r_h^* - r_h}{\epsilon}, \Psi_v = \lim_{\epsilon \to 0} \frac{v_h^* - v_h}{\epsilon}
$$

and

$$\Phi_s = \lim_{\epsilon \to 0} \frac{S_v^* - S_v}{\epsilon}, \Phi_i = \lim_{\epsilon \to 0} \frac{I_v^* - I_v}{\epsilon}$$

Then we calculate the following preemptively

$$\begin{aligned}
-\lambda_{vh}^{\epsilon}(t,a)s_h^{\epsilon}(t,a) + \lambda_{vh}(t,a)s_h(t,a) &= -p_1\beta\rho(a)\Big(\frac{I_v^{\epsilon}(t)}{T_h^{\epsilon}(t)}s_h^{\epsilon}(t,a) - \frac{I_v(t)}{T_h(t)}s_h(t,a)\Big) \\
&= -p_1\beta\rho(a)\Big(\frac{I_v^{\epsilon}(t)}{T_h^{\epsilon}(t)}s_h^{\epsilon}(t,a) - \frac{I_v^{\epsilon}(t)}{T_h^{\epsilon}(t)}s_h(t,a) + \frac{I_v^{\epsilon}(t)}{T_h^{\epsilon}(t)}s_h(t,a) \\
&\quad - \frac{I_v(t)}{T_h^{\epsilon}(t)}s_h(t,a) + \frac{I_v(t)}{T_h^{\epsilon}(t)}s_h(t,a) - \frac{I_v(t)}{T_h(t)}s_h(t,a)\Big) \\
&= -p_1\beta\rho(a)\Big(\frac{I_v^{\epsilon}(t)}{T_h^{\epsilon}(t)}(s_h^{\epsilon}(t,a) - s_h(t,a)) + \frac{I_v^{\epsilon}(t) - I_v(t)}{T_h^{\epsilon}(t)}s_h(t,a) \\
&\quad - \frac{I_v(t)(T_h^{\epsilon}(t) - T_h(t))}{T_h^{\epsilon}(t)T_h(t)}s_h(t,a)\Big)
\end{aligned}$$

If we divide by ϵ and take the limit as $\epsilon \to 0$ then

$$\begin{aligned}
\lim_{\epsilon \to 0} \frac{-\lambda_{vh}^{\epsilon}(t,a)s_h^{\epsilon}(t,a) + \lambda_{vh}(t,a)s_h(t,a)}{\epsilon} &= -p_1\beta\rho(a)\Big(\frac{I_v(t)}{T_h(t)}\Psi_s(t,a) + \frac{\Phi_i(t)}{T_h(t)}s_h(t,a) \\
&\quad - \frac{I_v(t)s_h(t,a)(\int_0^A \rho(a)(\Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a))da)}{T_h(t)^2}\Big)
\end{aligned}$$

Similarly

$$
\begin{aligned}
-\lambda_{hv}^{\epsilon}(t)S_v^{\epsilon}(t) + \lambda_{hv}(t)S_v(t) &= -p_2\beta\Big(\frac{J_h^{\epsilon}(t)}{T_h^{\epsilon}(t)}S_v^{\epsilon}(t) - \frac{J_h(t)}{T_h(t)}S_v(t)\Big) \\
&= -p_2\beta\Big(\frac{J_h^{\epsilon}(t)}{T_h^{\epsilon}(t)}S_v^{\epsilon}(t) - \frac{J_h^{\epsilon}(t)}{T_h^{\epsilon}(t)}S_v(t) + \frac{J_h^{\epsilon}(t)}{T_h^{\epsilon}(t)}S_v(t) \\
&\quad - \frac{J_h(t)}{T_h^{\epsilon}(t)}S_v(t) + \frac{J_h(t)}{T_h^{\epsilon}(t)}S_v(t) - \frac{J_h(t)}{T_h(t)}S_v(t)\Big) \\
&= -p_2\beta\Big(\frac{J_h^{\epsilon}(t)}{T_h^{\epsilon}(t)}(S_v^{\epsilon}(t) - S_v(t)) + \frac{J_h^{\epsilon}(t) - J_h(t)}{T_h^{\epsilon}(t)}S_v(t) \\
&\quad - \frac{J_h(t)(T_h^{\epsilon}(t) - T_h(t))}{T_h^{\epsilon}(t)T_h(t)}S_v(t)\Big)
\end{aligned}
$$

dividing by ϵ and taking he limit as $\epsilon \to 0$

$$
\begin{aligned}
\lim_{\epsilon\to 0}\frac{-\lambda_{hv}^{\epsilon}(t)S_v^{\epsilon}(t) + \lambda_{hv}(t)S_v(t)}{\epsilon} &= -p_2\beta\Big(\frac{J_h(t)}{T_h(t)}\Phi_s(t) + \frac{\int_0^A \rho(a)\Psi_i(t,a)da}{T_h(t)}S_v(t) \\
&\quad - \frac{J_h(t)\int_0^A \rho(a)(\Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a))da}{T_h(t)^2}S_v(t)\Big)
\end{aligned}
$$

We also have

$$
-\xi_h^{\epsilon}(t,a)s_h^{\epsilon}(t,a) + \xi_h(t,a)s_h(t,a) = -\xi_h^{\epsilon}(t,a)(s_h^{\epsilon}(t,a) - s_h(t,a)) - s_h(t,a)(\xi_h^{\epsilon}(t,a) - \xi_h(t,a))
$$

We again divide by ϵ and take the limit as $\epsilon \to 0$.

$$
\lim_{\epsilon\to 0}\frac{-\xi_h^{\epsilon}(t,a)s_h^{\epsilon}(t,a) + \xi_h(t,a)s_h(t,a)}{\epsilon} = -\xi_h^{\epsilon}(t,a)\Psi_s(t,a) - s_h(t,a)l
$$

Also

$$\mu_h^\epsilon(a, N_h^\epsilon(t)) - \mu_h(a,_h(t)) = (\mu_{h0}(a) + \mu_{h1}(a)N_h^\epsilon(t)) - (\mu_{h0}(a) + \mu_{h1}(a)N_h(t))$$
$$= \mu_{h1}(a)(N_h^\epsilon(t) - N_h(t)))$$

We divide by ϵ and take the limit as $epsilon \to 0$.

$$\lim_{\epsilon\to 0} \frac{\mu_h^\epsilon(a, N_h^\epsilon(t)) - \mu_h(a,_h(t))}{\epsilon} = \mu_{h1}(a)\int_0^A \Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a)da$$

Thus we have

$$\begin{aligned}
\frac{\partial(s_h^\epsilon - s_h)}{\partial t} + \frac{\partial(s_h^\epsilon - s_h)}{\partial t} &= -\lambda_{vh}^\epsilon(t,a)s_h^\epsilon(t,a) - \lambda_{vh}(t,a)s_h(t,a) - \xi_h^\epsilon(t,a)s_h^\epsilon(t,a) + \xi_h(t,a)s_h(t,a) \\
&\quad + \gamma(a)(r_h^\epsilon(t,a) - r_h(t,a)) + \eta(a)(v_h^\epsilon(t,a) - v_h(t,a)) \\
&\quad - \mu_h(a, N_h(t))(s_h^\epsilon(t,a) - s_h(t,a)) - s_h^\epsilon(t,a)(\mu_h^\epsilon(a, N_h^\epsilon(t)) - \mu_h(a,_h(t))) \\
\frac{\partial(i_h^\epsilon - i_h)}{\partial t} + \frac{\partial(i_h^\epsilon - i_h)}{\partial t} &= \lambda_{vh}^\epsilon(t,a)s_h^\epsilon(t,a) + \lambda_{vh}(t,a)s_h(t,a) \\
&\quad - (\mu_h(a, N_h(t)) + \delta_h(a) + \zeta_h(a))(i_h^\epsilon(t,a) - i_h(t,a)) \\
&\quad - i_h^\epsilon(t,a)(\mu_h^\epsilon(a, N_h(t)) - \mu_h(a, N_h)) \\
\frac{\partial(r_h^\epsilon - r_h)}{\partial t} + \frac{\partial(r_h^\epsilon - r_h)}{\partial t} &= \zeta_h(a)(i_h^\epsilon(t,a) - i_h(t,a)) - (\mu_h(a, N_h(t)) + \gamma(a))(r_h^\epsilon(t,a) - r_h(t,a)) \\
&\quad - r_h^\epsilon(t,a)(\mu_h^\epsilon(a, N_h(t)) - \mu_h(a, N_h)) \\
\frac{\partial(v_h^\epsilon - v_h)}{\partial t} + \frac{\partial(v_h^\epsilon - v_h)}{\partial t} &= \xi_h^\epsilon(t,a)s_h(t,a) - \xi_h(t,a)s_h(t,a) - (\mu_h(a, N_h(t)) + \eta_h(a))(v_h^\epsilon(t,a) - v_h(t,a)) \\
&\quad - v_h^\epsilon(t,a)(\mu_h^\epsilon(a, N_h(t)) - \mu(a, N_h(t))) \\
\frac{d(S_v^\epsilon(t) - S_v(t))}{dt} &= -p_2\beta\Big(\frac{J_h^\epsilon(t)}{T_h^\epsilon(t)}S_v^\epsilon(t) - \frac{J_h(t)}{T_h(t)}S_v(t)\Big) - \mu_v(S_v^\epsilon(t) - S_v(t)) \\
\frac{d(I_v^\epsilon(t) - I_v(t))}{dt} &= p_2\beta\Big(\frac{J_h^\epsilon(t)}{T_h^\epsilon(t)}S_v^\epsilon(t) - \frac{J_h(t)}{T_h(t)}S_v(t)\Big) - \mu_v(I_v^\epsilon(t) - I_v(t))
\end{aligned}$$

Then we divide each one by ϵ and take the limit as $\epsilon \to 0$.

$$
\begin{aligned}
\frac{\partial \Psi_s}{\partial t} + \frac{\partial \Psi_s}{\partial t} &= -p_1 \beta \rho(a)\Big(\frac{I_v(t)}{T_h(t)}\Psi_s(t,a) + \frac{\Phi_i(t)}{T_h(t)}s_h(t,a) \\
&\quad - \frac{I_v(t)s_h(t,a)(\int_0^A \rho(a)(\Psi_s(t,a)+\Psi_i(t,a)+\Psi_r(t,a)+\Psi_v(t,a))da)}{T_h(t)^2}\Big) \\
&\quad - \xi_h(t,a)\Psi_s(t,a) - s_h(t,a)l + \gamma(a)\Psi_r(t,a) + \eta(a)\Psi_v(t,a) \\
&\quad - \mu_h(a,N_h(t))\Psi_s(t,a) - s_h(t,a)\mu_{h1}(a)\int_0^A \Psi_s(t,a)+\Psi_i(t,a)+\Psi_r(t,a)+\Psi_v(t,a)da \\
\frac{\partial \Psi_i}{\partial t} + \frac{\partial \Psi_i}{\partial t} &= p_1 \beta \rho(a)\Big(\frac{I_v(t)}{T_h(t)}\Psi_s(t,a) + \frac{\Phi_i(t)}{T_h(t)}s_h(t,a) \\
&\quad - \frac{I_v(t)s_h(t,a)(\int_0^A \rho(a)(\Psi_s(t,a)+\Psi_i(t,a)+\Psi_r(t,a)+\Psi_v(t,a))da)}{T_h(t)^2}\Big) \\
&\quad - (\mu_h(a,N_h(t)) + \delta_h(a) + \zeta_h(a))\Psi_i(t,a) \\
&\quad - i_h(t,a)\mu_{h1}(a)\int_0^A \Psi_s(t,a)+\Psi_i(t,a)+\Psi_r(t,a)+\Psi_v(t,a)da \\
\frac{\partial \Psi_r}{\partial t} + \frac{\partial \Psi_r}{\partial t} &= \zeta_h(a)\Psi_i - (\mu_h(a,N_h(t)) + \gamma(a))\Psi_r \\
&\quad - r_h(t,a)\mu_{h1}(a)\int_0^A \Psi_s(t,a)+\Psi_i(t,a)+\Psi_r(t,a)+\Psi_v(t,a)da \\
\frac{\partial \Psi_v}{\partial t} + \frac{\partial \Psi_v}{\partial t} &= \xi_h(t,a)\Psi_s(t,a) - s_h(t,a)l - (\mu_h(a,N_h(t)) + \eta_h(a))\Psi_v \\
&\quad - v_h(t,a)\mu_{h1}(a)\int_0^A \Psi_s(t,a)+\Psi_i(t,a)+\Psi_r(t,a)+\Psi_v(t,a)da \\
\frac{d\Phi_s}{dt} &= -p_2\beta\Big(\frac{J_h(t)}{T_h(t)}\Phi_s(t) + \frac{\int_0^A \rho(a)\Psi_i(t,a)da}{T_h(t)}S_v(t) \\
&\quad - \frac{J_h(t)\int_0^A \rho(a)(\Psi_s(t,a)+\Psi_i(t,a)+\Psi_r(t,a)+\Psi_v(t,a))da}{T_h(t)^2}S_v(t)\Big) - \mu_v\Phi_s(t) \\
\frac{d\Phi_i}{dt} &= p_2\beta\Big(\frac{J_h(t)}{T_h(t)}\Phi_s(t) + \frac{\int_0^A \rho(a)\Psi_i(t,a)da}{T_h(t)}S_v(t) \\
&\quad - \frac{J_h(t)\int_0^A \rho(a)(\Psi_s(t,a)+\Psi_i(t,a)+\Psi_r(t,a)+\Psi_v(t,a))da}{T_h(t)^2}S_v(t)\Big) - \mu_v\Phi_i
\end{aligned}
$$

The initial conditions are

$$\Psi_s(0,a) = 0, \Psi_i(0,a) = 0, \Psi_r(0,a) = 0, \Psi_v(0,a) = 0$$

$$\Phi_s(0) = 0, \Phi_i(0) = 0$$

The boundary conditions are

$$\Psi_s(t,0) = \int_0^A b(a)(\Psi_s(t,a) + \Psi_i(t,a) + \Psi_r(t,a) + \Psi_v(t,a))da$$

$$\Psi_i(t,0) = 0, \Psi_r(t,0) = 0, \Psi_v(t,0) = 0$$

Let

$$u = \begin{bmatrix} \Psi_2 \\ \Psi_i \\ \Psi_r \\ \Psi_v \\ \Phi_S \\ \Phi_I \end{bmatrix}, f = \begin{bmatrix} -s_h(t,a)l \\ 0 \\ 0 \\ s_h(t,a)l \\ 0 \\ 0 \end{bmatrix}$$

Then we have that $L(u) = \begin{bmatrix} L_1(u) & L_2(u) & L_3(u) & L_4(u) & L_5(u) & L_6(u) \end{bmatrix} = f$ where

$$\begin{aligned} L_1(u) = {} & \frac{\partial \Psi_s}{\partial t} + \frac{\partial \Psi_s}{\partial t} + \frac{p_1 \beta \rho s_h}{T_h} \Phi_i + (\frac{p_1 \beta \rho I_v}{T_h} + \xi_h + \mu_h)\Psi_s - \gamma \Psi_r - \eta \Psi_v \\ & - \frac{p_1 \beta \rho I_v s_h}{T_h^2} \int_0^A \rho(a)(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da + s_h \mu_{h1} \int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da \end{aligned}$$

$$L_2(u) = \frac{\partial \Psi_i}{\partial t} + \frac{\partial \Psi_i}{\partial t} - \frac{p_1 \beta \rho I_v}{T_h}\Psi_s - \frac{p_1 \beta \rho s_h}{T_h}\Phi_i + (\mu_h + \delta_h + \zeta_h)\Psi_i$$
$$+ \frac{p_1 \beta \rho I_v s_h}{T_h^2}\int_0^A \rho(a)(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da + i_h \mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da$$

$$L_3(u) = \frac{\partial \Psi_r}{\partial t} + \frac{\partial \Psi_r}{\partial t} - \zeta_h \Psi_i + (\mu_h + \gamma_h)\Psi_r + r_h \mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da$$

$$L_4(u) = \frac{\partial \Psi_v}{\partial t} + \frac{\partial \Psi_v}{\partial t} - \xi_h \Psi_s + (\mu_h + \eta_h)\Psi_v + v_h \mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da$$

$$L_5(u) = \frac{d\Phi_s}{dt} + \left(\frac{p_2 \beta J_h}{T_h} + \mu_v\right)\Phi_s + \frac{p_2 \beta S_v}{T_h}\int_0^A \rho \Psi_i da - \frac{p_2 \beta J_h S_v}{T_h^2}\int_0^A \rho(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da$$

$$L_6(u) = \frac{d\Phi_i}{dt} - \frac{p_2 \beta J_h}{T_h}\Phi_s + \mu_v \Phi_i - \frac{p_2 \beta S_v}{T_h}\int_0^A \rho \Psi_i da + \frac{p_2 \beta J_h S_v}{T_h^2}\int_0^A \rho(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da$$

Next we work on the adjoint, let

$$v = \begin{bmatrix} p_2 \\ p_i \\ p_r \\ p_v \\ q_s \\ q_i \end{bmatrix}$$

Then we find adjoint L^* such that

$$\langle v, L(u)\rangle = \langle l^* v, u\rangle$$

Using integration by parts, if we set $p_s(T,a) = 0$

$$\begin{aligned}
\int_0^T \int_0^A \frac{\partial \Psi_s}{\partial t} p_s dadt &= \int_0^A [\Psi_s p_s]_0^T da - \int_0^T \int_0^A \frac{\partial p_S}{\partial t} \Psi_s dadt \\
&= \int_0^A [\Psi_s(T,a)p_s(T,a) - \Psi_s(0,a)p_s(0,a)]da - \int_0^T \int_0^A \frac{\partial p_S}{\partial t} \Psi_s dadt \\
&= -\int_0^T \int_0^A \frac{\partial p_S}{\partial t} \Psi_s dadt
\end{aligned}$$

Likewise if we set $p_s(t,A) = 0$,

$$\begin{aligned}
\int_0^T \int_0^A \frac{\partial \Psi_s}{\partial a} p_s dadt &= \int_0^T [\Psi_s p_s]_0^A dt - \int_0^T \int_0^A \frac{\partial p_S}{\partial a} \Psi_s dadt \\
&= \int_0^T [\Psi_s(t,A)p_s(t,A) - \Psi_s(t,0)p_s(t,0)]dt - \int_0^T \int_0^A \frac{\partial p_S}{\partial a} \Psi_s dadt \\
&= -\int_0^T \int_0^A \frac{\partial p_S}{\partial a} \Psi_s dadt - \int_0^T \int_0^T p_s(t,0)b(a)(\Psi_s + \Psi_i + \Psi_r + \Psi_v)dadt
\end{aligned}$$

Likewise by if we set $p_i(T,a) = 0, p_i(t,A) = 0, p_r(T,a) = 0, p_r(t,A) = 0, p_v(T,a) = 0, p_v(t,A) =$

$0, q_s(T) = 0, q_i(T) = 0,$

$$\int_0^T \int_0^A \frac{\partial \Psi_i}{\partial t} p_i dadt = -\int_0^T \int_0^A \frac{\partial p_i}{\partial t} \Psi_i dadt$$
$$\int_0^T \int_0^A \frac{\partial \Psi_i}{\partial a} p_i dadt = -\int_0^T \int_0^A \frac{\partial p_i}{\partial a} \Psi_i dadt$$
$$\int_0^T \int_0^A \frac{\partial \Psi_r}{\partial t} p_r dadt = -\int_0^T \int_0^A \frac{\partial p_r}{\partial t} \Psi_r dadt$$
$$\int_0^T \int_0^A \frac{\partial \Psi_r}{\partial a} p_r dadt = -\int_0^T \int_0^A \frac{\partial p_r}{\partial a} \Psi_r dadt$$
$$\int_0^T \int_0^A \frac{\partial \Psi_v}{\partial t} p_v dadt = -\int_0^T \int_0^A \frac{\partial p_v}{\partial t} \Psi_v dadt$$
$$\int_0^T \int_0^A \frac{\partial \Psi_v}{\partial a} p_v dadt = -\int_0^T \int_0^A \frac{\partial p_v}{\partial v} \Psi_v dadt$$

Thus we have that

$$
\begin{aligned}
\langle v, L(u)\rangle = \int_0^T \int_0^A \Big\{ & \frac{\partial \Psi_s}{\partial t} + \frac{\partial \Psi_s}{\partial t} + \frac{p_1\beta\rho s_h}{T_h}\Phi_i + (\frac{p_1\beta\rho I_v}{T_h} + \xi_h + \mu_h)\Psi_s - \gamma\Psi_r - \eta\Psi_v \\
& - \frac{p_1\beta\rho I_v s_h}{T_h^2}\int_0^A \rho(a)(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da + s_h\mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da\Big\} p_s da dt \\
+ \int_0^T \int_0^A \Big\{ & \frac{\partial \Psi_i}{\partial t} + \frac{\partial \Psi_i}{\partial t} - \frac{p_1\beta\rho I_v}{T_h}\Psi_s - \frac{p_1\beta\rho s_h}{T_h}\Phi_i + (\mu_h + \delta_h + \zeta_h)\Psi_i \\
& + \frac{p_1\beta\rho I_v s_h}{T_h^2}\int_0^A \rho(a)(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da + i_h\mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da\Big\} p_i da dt \\
+ \int_0^T \int_0^A \Big\{ & \frac{\partial \Psi_r}{\partial t} + \frac{\partial \Psi_r}{\partial t} - \zeta_h\Psi_i + (\mu_h + \gamma_h)\Psi_r + r_h\mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da\Big\} p_r da dt \\
+ \int_0^T \int_0^A \Big\{ & \frac{\partial \Psi_v}{\partial t} + \frac{\partial \Psi_v}{\partial t} - \xi_h\Psi_s + (\mu_h + \eta_h)\Psi_v + v_h\mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da\Big\} p_v da dt \\
+ \int_0^T \Big\{ & \frac{d\Phi_s}{dt} + \Big(\frac{p_2\beta J_h}{T_h} + \mu_v\Big)\Phi_s + \frac{p_2\beta S_v}{T_h}\int_0^A \rho\Psi_i da \\
& - \frac{p_2\beta J_h S_v}{T_h^2}\int_0^A \rho(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da\Big\} q_s dt \\
+ \int_0^T \Big\{ & \frac{d\Phi_i}{dt} - \frac{p_2\beta J_h}{T_h}\Phi_s + \mu_v\Phi_i - \frac{p_2\beta S_v}{T_h}\int_0^A \rho\Psi_i da \\
& + \frac{p_2\beta J_h S_v}{T_h^2}\int_0^A \rho(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da\Big\} q_i dt
\end{aligned}
$$

$$
\begin{aligned}
\langle v, L(u)\rangle = \int_0^T \int_0^A & -\Big(\frac{\partial p_s}{\partial t} + \frac{\partial p_s}{\partial t}\Big)\Psi_s - p_s(t,0)b(a)(\Psi_s + \Psi_i + \Psi_r + \Psi_v) \\
& + \Big\{\frac{p_1\beta\rho s_h}{T_h}\Phi_i + (\frac{p_1\beta\rho I_v}{T_h} + \xi_h + \mu_h)\Psi_s - \gamma\Psi_r - \eta\Psi_v \\
& - \frac{p_1\beta\rho I_v s_h}{T_h^2}\int_0^A \rho(a)(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da + s_h\mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da\Big\} p_s dadt \\
+ \int_0^T \int_0^A & -\Big(\frac{\partial p_i}{\partial t} + \frac{\partial p_i}{\partial t}\Big)\Psi_i + \Big\{ - \frac{p_1\beta\rho I_v}{T_h}\Psi_s - \frac{p_1\beta\rho s_h}{T_h}\Phi_i + (\mu_h + \delta_h + \zeta_h)\Psi_i \\
& + \frac{p_1\beta\rho I_v s_h}{T_h^2}\int_0^A \rho(a)(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da + i_h\mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da\Big\} p_i dadt \\
+ \int_0^T \int_0^A & -\Big(\frac{\partial p_r}{\partial t} + \frac{\partial p_r}{\partial t}\Big)\Psi_r + \Big\{ - \zeta_h\Psi_i + (\mu_h + \gamma_h)\Psi_r + r_h\mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da\Big\} p_r dadt \\
+ \int_0^T \int_0^A & -\Big(\frac{\partial p_v}{\partial t} + \frac{\partial p_v}{\partial t}\Big)\Psi_v + \Big\{ - \xi_h\Psi_s + (\mu_h + \eta_h)\Psi_v + v_h\mu_{h1}\int_0^A \Psi_s + \Psi_i + \Psi_r + \Psi_v da\Big\} p_v dadt \\
+ \int_0^T & -\frac{dq_s}{dt}\Phi_s + \Big\{\Big(\frac{p_2\beta J_h}{T_h} + \mu_v\Big)\Phi_s + \frac{p_2\beta S_v}{T_h}\int_0^A \rho\Psi_i da \\
& - \frac{p_2\beta J_h S_v}{T_h^2}\int_0^A \rho(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da\Big\} q_s dt \\
+ \int_0^T & -\frac{dq_i}{dt}\Phi_i + \Big\{ - \frac{p_2\beta J_h}{T_h}\Phi_s + \mu_v\Phi_i - \frac{p_2\beta S_v}{T_h}\int_0^A \rho\Psi_i da \\
& + \frac{p_2\beta J_h S_v}{T_h^2}\int_0^A \rho(\Psi_s + \Psi_i + \Psi_r + \Psi_v)da\Big\} q_i dt
\end{aligned}
$$

Then we rearrange to get

$$
\begin{aligned}
\langle v, L(u)\rangle = \int_0^T \int_0^A \Big\{ &-\Big(\frac{\partial p_s}{\partial t} + \frac{\partial p_s}{\partial t}\Big) - p_s(t,0)b(a) + (\frac{p_1\beta\rho I_v s_h}{T_h} + \xi_h + \mu_h)p_s - \rho(a)\int_0^A \frac{p_1\beta\rho I_v p_s}{T_h^2}da \\
&+ \int_0^A s_h\mu_{h1}p_s da - \frac{p_1\beta\rho I_v s_h}{T_h}p_i + \rho(a)\int_0^A \frac{p_1\beta\rho I_v p_i}{T_h^2}da + \int_0^A i_h\mu_{h1}p_i da + \int_0^A r_h\mu_{h1}p_r da \\
&+ \int_0^A v_h\mu_{h1}p_v da - \xi_h p_v - \frac{p_2\beta J_h S_v}{T_h^2}\rho q_s + \frac{p_2\beta J_h S_v}{T_h^2}\rho q_i \Big\}\Psi_s dadt \\
+ \int_0^T \int_0^A \Big\{ &-\Big(\frac{\partial p_i}{\partial t} + \frac{\partial p_i}{\partial t}\Big) - p_s(t,0)b(a) - \rho(a)\int_0^A \frac{p_1\beta\rho I_v s_h p_s}{T_h^2}da + \int_0^A s_h\mu_{h1}p_s da \\
&+ (\mu_h + \delta_h + \zeta_h)p_i + \rho(a)\int_0^A \frac{p_1\beta\rho I_v s_h p_i}{T_h^2}da + \int_0^A i_h\mu_{h1}p_i da + \int_0^A r_h\mu_{h1}p_r da \\
&+ \int_0^A v_h\mu_{h1}p_v da - \zeta_h p_r + \frac{p_2\beta S_v}{T_h}\rho q_s - \frac{p_2\beta S_v}{T_h}\rho q_i - \frac{p_2\beta J_h S_v}{T_h^2}\rho q_s + \frac{p_2\beta J_h S_v}{T_h^2}\rho q_i \Big\}\Psi_i dadt \\
+ \int_0^T \int_0^A \Big\{ &-\Big(\frac{\partial p_r}{\partial t} + \frac{\partial p_r}{\partial t}\Big) - p_s(t,0)b(a) - \gamma p_s - \rho(a)\int_0^A \frac{p_1\beta\rho I_v s_h p_s}{T_h^2}da + \int_0^A s_h\mu_{h1}p_s da \\
&+ \rho(a)\int_0^A \frac{p_1\beta\rho I_v s_h p_i}{T_h^2}da + \int_0^A i_h\mu_{h1}p_i da + \int_0^A r_h\mu_{h1}p_r da + \int_0^A v_h\mu_{h1}p_v da \\
&+ (\mu_h + \gamma_h)p_r - \frac{p_2\beta J_h S_v}{T_h^2}\rho q_s + -\frac{p_2\beta J_h S_v}{T_h^2}\rho q_i \Big\}\Psi_r dadt \\
+ \int_0^T \int_0^A \Big\{ &-\Big(\frac{\partial p_v}{\partial t} + \frac{\partial p_v}{\partial t}\Big) - p_s(t,0)b(a) - \eta p_s - \rho(a)\int_0^A \frac{p_1\beta\rho I_v s_h p_s}{T_h^2}da + \int_0^A s_h\mu_{h1}p_s da \\
&+ \rho(a)\int_0^A \frac{p_1\beta\rho I_v s_h p_i}{T_h^2}da + \int_0^A i_h\mu_{h1}p_i da + \int_0^A r_h\mu_{h1}p_r da + \int_0^A v_h\mu_{h1}p_v da \\
&+ (\mu_h + \eta_h)p_v - \frac{p_2\beta J_h S_v}{T_h^2}\rho q_s + -\frac{p_2\beta J_h S_v}{T_h^2}\rho q_i \Big\}\Psi_v dadt \\
+ \int_0^T \Big\{ &-\frac{dq_s}{dt} + \Big(\frac{p_2\beta J_h}{T_h} + \mu_v\Big)q_s - \frac{p_2\beta J_h}{T_h}q_i \Big\}\Phi_s dt \\
+ \int_0^T \Big\{ &-\frac{dq_i}{dt} + \int_0^A \frac{p_1\beta\rho s_h}{T_h}p_s - \int_0^A \frac{p_1\beta\rho s_h}{T_h}p_i + \mu_v q_i da \Big\}\Phi_i dt
\end{aligned}
$$

We rearrange this

$$
\begin{aligned}
&\langle v, L(u)\rangle \\
&= \int_0^T \int_0^A \Big\{ -\Big(\frac{\partial p_s}{\partial t} + \frac{\partial p_s}{\partial t}\Big) + \frac{p_1\beta\rho I_v}{T_h}(p_s - p_i) + \mu_h p_s + \xi_h(p_s - p_v) \\
&\quad - \frac{p_2\beta J_h S_v}{T_h^2}\rho(q_s - q_i) - \frac{\rho(a)p_1\beta I_v}{T_h^2}\int_0^A s_h(t,b)\rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b)da + i_h(t,b)p_i(t,b)da + r_h(t,b)p_r(t,b)da + v_h(t,b)p_v(t,b))db\Big\}\Psi_s da dt \\
&+ \int_0^T \int_0^A \Big\{ -\Big(\frac{\partial p_i}{\partial t} + \frac{\partial p_i}{\partial t}\Big) + (\mu_h + \delta_h)p_i + \zeta_h(p_i - p_r) + \frac{p_2\beta S_v}{T_h}\rho(q_s - q_i) \\
&\quad - \frac{p_2\beta J_h S_v}{T_h^2}\rho(q_s - q_i) - \frac{\rho(a)p_1\beta I_v}{T_h^2}\int_0^A s_h(t,b)\rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b)da + i_h(t,b)p_i(t,b)da + r_h(t,b)p_r(t,b)da + v_h(t,b)p_v(t,b))db\Big\}\Psi_i da dt \\
&+ \int_0^T \int_0^A \Big\{ -\Big(\frac{\partial p_r}{\partial t} + \frac{\partial p_r}{\partial t}\Big) + \mu_h p_r + \gamma_h(p_r - p_s) \\
&\quad - \frac{p_2\beta J_h S_v}{T_h^2}\rho(q_s - q_i) - \frac{\rho(a)p_1\beta I_v}{T_h^2}\int_0^A s_h(t,b)\rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b)da + i_h(t,b)p_i(t,b)da + r_h(t,b)p_r(t,b)da + v_h(t,b)p_v(t,b))db\Big\}\Psi_r da dt \\
&+ \int_0^T \int_0^A \Big\{ -\Big(\frac{\partial p_v}{\partial t} + \frac{\partial p_v}{\partial t}\Big) + \mu_h p_v + \eta_h(p_v - p_s) \\
&\quad - \frac{p_2\beta J_h S_v}{T_h^2}\rho(q_s - q_i) - \frac{\rho(a)p_1\beta I_v}{T_h^2}\int_0^A s_h(t,b)\rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b)da + i_h(t,b)p_i(t,b)da + r_h(t,b)p_r(t,b)da + v_h(t,b)p_v(t,b))db\Big\}\Psi_v da dt \\
&+ \int_0^T \Big\{ -\frac{dq_s}{dt} + \mu_v q_s + \frac{p_2\beta J_h}{T_h}(q_s - q_i)\Big\}\Phi_s dt \\
&+ \int_0^T \Big\{ -\frac{dq_i}{dt} + \mu_v q_i + \int_0^A \frac{p_1\beta\rho s_h}{T_h}(p_s - p_i)da\Big\}\Phi_i dt
\end{aligned}
$$

Then the adjoint PDE is

$$L^{*}(v) = \frac{\text{Integrand of } J(\xi)}{\partial x} = \begin{bmatrix} C\xi \\ B \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

We have the adjoint equations

$$
\begin{aligned}
\frac{\partial p_s}{\partial t} + \frac{\partial p_s}{\partial t} &= \frac{p_1 \beta \rho I_v}{T_h}(p_s - p_i) + \mu_h p_s + \xi_h (p_s - p_v) \\
&\quad - \frac{p_2 \beta J_h S_v}{T_h^2} \rho (q_s - q_i) - \frac{\rho(a) p_1 \beta I_v}{T_h^2} \int_0^A s_h(t,b) \rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b)da + i_h(t,b)p_i(t,b)da + r_h(t,b)p_r(t,b)da + v_h(t,b)p_v(t,b))db \\
&\quad - C\xi_h \\
\frac{\partial p_i}{\partial t} + \frac{\partial p_i}{\partial t} &= (\mu_h + \delta_h)p_i + \zeta_h(p_i - p_r) + \frac{p_2 \beta S_v}{T_h} \rho (q_s - q_i) \\
&\quad - \frac{p_2 \beta J_h S_v}{T_h^2} \rho (q_s - q_i) - \frac{\rho(a) p_1 \beta I_v}{T_h^2} \int_0^A s_h(t,b) \rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b)da + i_h(t,b)p_i(t,b)da + r_h(t,b)p_r(t,b)da + v_h(t,b)p_v(t,b))db \\
&\quad - B \\
\frac{\partial p_r}{\partial t} + \frac{\partial p_r}{\partial t} &= \mu_h p_r + \gamma_h (p_r - p_s) \\
&\quad - \frac{p_2 \beta J_h S_v}{T_h^2} \rho (q_s - q_i) - \frac{\rho(a) p_1 \beta I_v}{T_h^2} \int_0^A s_h(t,b) \rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b)da + i_h(t,b)p_i(t,b)da + r_h(t,b)p_r(t,b)da + v_h(t,b)p_v(t,b))db \\
\frac{\partial p_v}{\partial t} + \frac{\partial p_v}{\partial t} &= \mu_h p_v + \eta_h (p_v - p_s) \\
&\quad - \frac{p_2 \beta J_h S_v}{T_h^2} \rho (q_s - q_i) - \frac{\rho(a) p_1 \beta I_v}{T_h^2} \int_0^A s_h(t,b) \rho(b)(p_s(t,b) - p_i(t.b))db - p_s(t,0)b(a) \\
&\quad + \int_0^A \mu_{h1}(b)(s_h(t,b)p_s(t,b)da + i_h(t,b)p_i(t,b)da + r_h(t,b)p_r(t,b)da + v_h(t,b)p_v(t,b))db \\
\frac{dq_s}{dt} &= \mu_v q_s + \frac{p_2 \beta J_h}{T_h}(q_s - q_i) \\
\frac{dq_i}{dt} &= \mu_v q_i + \int_0^A \frac{p_1 \beta \rho s_h}{T_h}(p_s - p_i) da dt
\end{aligned}
$$

with initial conditions

$$p_s(T,a) = p_i(T,a) = p_r(T,a) = p_v(T,a) = 0$$

$$q_s(T) = q_i(T) = 0$$

and boundary conditions

$$p_s(t,A) = p_i(t,A) = p_r(t,A) = p_v(t,A) = 0$$

Then for the optimality condition

$$\begin{aligned}
0 &\leq \lim_{\epsilon \to 0} \frac{J(\xi_h^* + \epsilon l) - J(\xi_h^*)}{\epsilon} \\
&= \frac{\int_0^T \int_0^A [Bi_h^\epsilon + C(\xi_h^* + \epsilon l)s_h^\epsilon + D(\xi_h^* + \epsilon l)^2] - [Bi_h + C\xi_h^* s_h + D(\xi_h^*)^2] dadt}{\epsilon} \\
&= \int_0^T \int_0^A [B\Psi_i + C\xi_h^* \Psi_s + Cs_h l + D\xi_h^* l] dadt \\
&= \langle u, L^*(v) \rangle + \int_0^T \int_0^A [Cs_h l + D\xi_h^* l] dadt \\
&= \langle L(u), v \rangle + \int_0^T \int_0^A [Cs_h l + D\xi_h^* l] dadt \\
&= \int_0^T \int_0^A \begin{bmatrix} -s_h l \\ 0 \\ 0 \\ s_h l \end{bmatrix} \cdot \begin{bmatrix} p_s \\ p_i \\ p_r \\ p_v \end{bmatrix} dadt + \int_0^T \begin{bmatrix} 0 \\ 0 \end{bmatrix} \cdot \begin{bmatrix} q_s \\ q_i \end{bmatrix} dt + \int_0^T \int_0^A [Cs_h l + D\xi_h^* l] dadt \\
&= \int_0^T \int_0^A l(-s_h p_s + p_v s_h + Cs_h + D\xi_h^*) dadt
\end{aligned}$$

Thus the optimality condition is

$$\xi_h^* = \max(0, \frac{(p_s - p_v - C)s_h}{D})$$

Chapter 13

Appendix E: Code

```
function OptimalControl()

clc;

clear;

close all;


%%Find Equillibrium of state

%Range

af=90;

tf=1;

deltat = 1/52;


%Boundary Conditions

function y=sh0(a)

y=1500000-(1500000/90)*a;

end


function y=ih0(a)

%y=.2-(.2/90)*a;

y=0;

end
```

```
function y=rh0(a)

y=0;

end


function y=vh0(a)

y=0;

end


%Initial vacination rate matrix

N=floor(tf/deltat);

M=floor(af/deltat);

apartition = 0:deltat:af;

tpartition = 0:deltat:tf;


%% Get equillibrium

%{

xih=0*ones(M+1,N+1);


sh0mat = arrayfun(@sh0,apartition);

ih0mat = arrayfun(@ih0,apartition);

rh0mat = arrayfun(@rh0,apartition);

Sv0=10000;

Iv0=1000;%1000

vh0mat = arrayfun(@vh0,apartition);
```

```
tic

[sh,ih,rh,vh,State,tpartition,apartition,Th,Iph]=ImplicitState(...

sh0mat,ih0mat,rh0mat,vh0mat,Sv0,Iv0,xih,tf,deltat,af);

toc

figure(1)

plot(apartition,sh(:,end))

figure(2)

plot(apartition,ih(:,end))



sheq=sh(:,end);

iheq=ih(:,end);

rheq=rh(:,end);

vheq=vh(:,end);

Sveq=State(6,end);

Iveq=State(7,end);


%save('StateEquillibrium','sheq','iheq','rheq','vheq','Sveq','Iveq');

%}


%% Run optimization loop%{

S=load('StateEquillibrium.mat');


B=100;%try these

C=1;

D=1;
```

```
sh0mat = S.sheq;

ih0mat = S.iheq;

rh0mat = S.rheq;

vh0mat = S.vheq;

Sv0=S.Sveq;

Iv0=S.Iveq;


%initialize xih

xihold=0*ones(M+1,N+1);

xihnew=0*ones(M+1,N+1);


z=0;


while z<100


tic

[sh,ih,rh,vh,State,tpartition,apartition,Th,Iph]=ImplicitState(...

sh0mat,ih0mat,rh0mat,vh0mat,Sv0,Iv0,xihnew,tf,deltat,af);

toc


tic

[pas,pai,par,pav,q,tpartition,apartition]=ImplicitAdjoint(...

sh,ih,rh,vh,State,tf,deltat,af,xihnew,B,C,Th,Iph);

toc

z=z+1
```

```
xihold=xihnew;


xihnew = max(zeros(M+1,N+1),((pas-pav-C).*sh)/D);

xihnew = min(30*ones(M+1,N+1),xihnew);

xihnew = (.5)*xihnew+(.5)*xihold;


norm(xihnew-xihold,2)

if norm(xihnew-xihold,2)<10^(-4)

break;

end

end




figure(1)

mesh(tpartition,apartition,xihnew)

ylabel('Age')

xlabel('Time')

title('Vaccination Rates')

%}


%% Generate plots

%{

S=load('StateEquillibrium.mat');

T=load('OptimizedResult');
```

```
figure(1)
mesh(T.tpartition,T.apartition,T.xihnew)
ylabel('Age')
xlabel('Time')
title('Vaccination Rates')
colorbar
figure(2)
plot(apartition,T.sh(:,end))
xlabel('Age')
ylabel('Density')
title('Susceptible Population Age Profile at t=1')
figure(3)
plot(apartition,T.ih(:,end))
xlabel('Age')
ylabel('Density')
title('Infected Population Age Profile at t=1')
figure(4)
plot(apartition,T.vh(:,end))
xlabel('Age')
ylabel('Density')
title('Vaccinated Population Age Profile at t=1')
figure(5)
plot(tpartition,T.State(1,:))
xlabel('Time')
ylabel('Population Count')
title('Susceptible Human Population over Time')
```

```
figure(6)
plot(tpartition,T.State(2,:))
xlabel('Time')
ylabel('Population Count')
title('Infected Human Population over Time')
figure(7)
plot(tpartition,T.State(4,:))
xlabel('Time')
ylabel('Population Count')
title('Vaccinated Human Population over Time')
figure(8)
plot(tpartition,T.State(6,:))
xlabel('Time')
ylabel('Population Count')
title('Susceptible Vector Population over Time')
figure(9)
plot(tpartition,T.State(7,:))
xlabel('Time')
ylabel('Population Count')
title('Infected Vector Population over Time')
%}
end


function y=muh0(x)
a = 0.09959;
b = 0.6776;
```

```
c = 0.1277;

d = -0.09171;

e = 66.78;

f = -0.0006743;

g = 0.05859;


if a==90

y=0;

else

y=a*exp(-b*x)+c*exp(-d*(x-e)-exp(f*(x-e)))+(g/(90-x));

end


end


function y=muh1(a)

%y=.0000000001;

y=0.00000000016;

end


function y=muh(a,Nh)

y=muh0(a)+muh1(a)*Nh;

end


%% Birth Rates

function y=bh(x)

a = 0.0001218;
```

```
b = 0.3022;

c = 78.38;

d = 0.04006;

out= a*exp(-b*(x-c)-exp(-d*(x-c)));

y=out;

y=out*0.449569941624713;

end


%% liklihood of bite by age

%Probability function for contact

%Logistic Shape

function y=p(a)

y = ((1/(1+exp(-(a-4)))))-((1/(1+exp(4))));

end


%Skewed gaussian

% function y = p(x)

% y=2*(1/sqrt((400*pi))*exp(-(x-10).^2/400))*normcdf(4*(x-10)/sqrt(200));

% end


% %Uniform

%    function y=p(a)

%       y=1/60;

%    end


function y= deltah(a)
```

```
y=.006444/(1+exp(2*a-14));
end

%% Implicit Methods
function [sh,ih,rh,vh,State,tpartition,apartition,Th,Iph]=ImplicitState(...
sh0mat,ih0mat,rh0mat,vh0mat,Sv0,Iv0,xih,tf,deltat,af)
%Evaluates the system of pdes using implicit forward difference
%Inputs: boundary conditions as functions, vaccination rate xih, maximum age and
    time
%af,tf anf step size deltat
%Output: Soultion to pde system from initial values

%%%%%Things to check, are boundary conditions row or column vectors. Does
%%%%%deltat match row length

%Constants
Lambdav=10^(12);
% p1beta=9;
% p2beta=.8;
p1=.0246575;
p2=.00219178;
beta=365;
p1beta=p1*beta;
p2beta=p2*beta;
gammah=2;
etah=1/4;%younger recover faster
```

```
zetah=1;
muv=365/21;

%Number intervals for each variable, should be an integer
N=floor(tf/deltat);
M=floor(af/deltat);
tpartition = 0:deltat:tf;
apartition = 0:deltat:af;

%Initialize age in first index, time in second index
sh = zeros(M+1,N+1);
ih = zeros(M+1,N+1);
rh = zeros(M+1,N+1);
vh = zeros(M+1,N+1);
State=zeros(7,N+1);%Sh,Ih,Rh,Vh,Nh,Sv,Iv in that order
Th=zeros(1,N+1);
Iph=zeros(1,N+1);

%Set boundary points into initialized matrices
sh(:,1) = sh0mat;
ih(:,1) = ih0mat;
rh(:,1) = rh0mat;
vh(:,1) = vh0mat;
State(6,1) = Sv0;
State(7,1) = Iv0;
```

```
%Matrix used later for Vector equations

bv=[Lambdav;0];


%Run thru time variable

for j=1:N

%Current time

t=deltat*(j-1);


%compute Sh,Ih,Rh,Vh etc with trapezoid method

%also compute the denominator and numerator of force of infection

%endpoints

State(1,j)=(deltat/2)*(sh(1,j)+sh(M+1,j));

State(2,j)=(deltat/2)*(ih(1,j)+ih(M+1,j));

State(3,j)=(deltat/2)*(rh(1,j)+rh(M+1,j));

State(4,j)=(deltat/2)*(vh(1,j)+vh(M+1,j));

J=(deltat/2)*(p(0)*ih(1,j)+p(af)*ih(M+1,j));

K=(deltat/2)*(p(0)*(sh(1,j)+ih(1,j)+rh(1,j)+vh(1,j))...

+p(af)*(sh(M+1,j)+ih(M+1,j)+rh(M+1,j)+vh(M+1,j)));

%middle points

for i=2:M

State(1,j)=State(1,j)+deltat*sh(i,j);

State(2,j)=State(2,j)+deltat*ih(i,j);

State(3,j)=State(3,j)+deltat*rh(i,j);

State(4,j)=State(4,j)+deltat*vh(i,j);

J=J+p(deltat*(i-1))*ih(i,j);

K=K+p(deltat*(i-1))*(sh(i,j)+ih(i,j)+rh(i,j)+vh(i,j));
```

```
end
State(5,j) = State(1,j)+State(2,j)+State(3,j)+State(4,j);
Th(j)=K;
Iph(j) = J;

%compute explicit lambda for steps
lambdahv=p2beta*J/K;

%matrix for vector
Av = [-(lambdahv+muv) 0;lambdahv -muv];

%Solve Vector for time j+1 Euler
State(6:7,j+1) = (eye(2)-deltat*Av)\(State(6:7,j)+deltat*bv);

%run thorough age variable
for i=1:M-1
%current age
a=deltat*(i);
mu=muh(a,State(5,j));
lambdavh=p1beta*State(7,j)*p(a)/K;

%Construct matrix
A = [-(lambdavh+mu+xih(i+1,j+1)) 0 gammah etah;
lambdavh -(mu+deltah(a)+zetah) 0 0;
0 zetah -(mu+gammah) 0;
xih(i+1,j+1) 0 0 -(mu+etah)];
```

```
%Compute time j+1 step for human densities%need to make all var age
%time dep
i;
newsol=(eye(4)-deltat*A)\[sh(i,j);ih(i,j);rh(i,j);vh(i,j)];
sh(i+1,j+1) = newsol(1);
ih(i+1,j+1) = newsol(2);
rh(i+1,j+1) = newsol(3);
vh(i+1,j+1) = newsol(4);
end
sh(M+1,j+1) = 0;
ih(M+1,j+1) = 0;
rh(M+1,j+1) = 0;
vh(M+1,j+1) = 0;

%Compute susceptible at age 0(newborn density) using trapezoid
sh(1,j+1)=(deltat/2)*bh(M*deltat)*(sh(M+1,j+1)+ih(M+1,j+1)+rh(M+1,j+1)+vh(M+1,j+1));
for i=2:M
%age at step i
a=deltat*(i-1);
%trapezoid
sh(1,j+1)=sh(1,j+1)+(deltat)*bh(a)*(sh(i,j+1)+ih(i,j+1)+rh(i,j+1)+vh(i,j+1));
end
end

%compute Ih,Nh at last step for time(N+1) using trapezoid
```

```
State(1,N+1)=(deltat/2)*(sh(1,N+1)+sh(M+1,N+1));
State(2,N+1)=(deltat/2)*(ih(1,N+1)+ih(M+1,N+1));
State(3,N+1)=(deltat/2)*(rh(1,N+1)+rh(M+1,N+1));
State(4,N+1)=(deltat/2)*(vh(1,N+1)+vh(M+1,N+1));

J=(deltat/2)*(p(0)*ih(1,j)+p(af)*ih(M+1,j));
K=(deltat/2)*(p(0)*(sh(1,N+1)+ih(1,N+1)+rh(1,N+1)+vh(1,N+1))...
+p(af)*(sh(M+1,N+1)+ih(M+1,N+1)+rh(M+1,N+1)+vh(M+1,N+1)));

%middle points
for i=2:M
State(1,N+1)=State(1,N+1)+deltat*sh(i,N+1);
State(2,N+1)=State(2,N+1)+deltat*ih(i,N+1);
State(3,N+1)=State(3,N+1)+deltat*rh(i,N+1);
State(4,N+1)=State(4,N+1)+deltat*vh(i,N+1);
J=J+p(deltat*(i-1))*ih(i,N+1);
K=K+p(deltat*(i-1))*(sh(i,N+1)+ih(i,N+1)+rh(i,N+1)+vh(i,N+1));
end
State(5,N+1) = State(1,N+1)+State(2,N+1)+State(3,N+1)+State(4,N+1);
Th(N+1)=K;
Iph(N+1) = J;
end

function [pas,pai,par,pav,q,tpartition,apartition]=ImplicitAdjoint(...
sh,ih,rh,vh,State,tf,deltat,af,xih,B,C,Th,Iph)
%The Adjoint part, solves backwards
```

```
%Constants

Lambdav=10^(12);

% p1beta=9;

% p2beta=.8;

p1=.0246575;

p2=.00219178;

beta=365;

p1beta=p1*beta;

p2beta=p2*beta;

gammah=2;

etah=1/4;%younger recover faster

zetah=1;

muv=365/21;


%Number intervals for each variable, should be an integer

N=floor(tf/deltat);

M=floor(af/deltat);

tpartition = 0:deltat:tf;

apartition = 0:deltat:af;


%Initialize, initial values for most of these are 0

pas = zeros(M+1,N+1);

pai = zeros(M+1,N+1);

par = zeros(M+1,N+1);

pav = zeros(M+1,N+1);
```

```
q=zeros(2,N+1);%qs and qi


Intg1 = zeros(1,N+1);

Intg2 = zeros(1,N+1);

Intg3 = zeros(1,N+1);


%Boundary values

%All boundary values are 0

%run through time backwards

for j=N:-1:1


%Trapezoid Rule on integral found in qi, as well as P_is

Intg1(j+1) = (deltat/2)*(sh(1,j+1)*p(0)*(pas(1,j+1)-pai(1,j+1))

   +sh(M+1,j+1)*p(af)*(pas(M+1,j+1)-pai(M+1,j+1)));

Intg2(j+1) = (deltat/2)*(muh1(0)*(sh(1,j+1)*pas(1,j+1)+ih(1,j+1)*pai(1,j+1)

   +rh(1,j+1)*par(1,j+1)+vh(1,j+1)*pav(1,j+1))...

+muh1(af)*(sh(M+1,j+1)*pas(M+1,j+1)+ih(M+1,j+1)*pai(M+1,j+1)

   +rh(M+1,j+1)*par(M+1,j+1)+vh(M+1,j+1)*pav(M+1,j+1)));

Intg3(j+1) = (deltat/2)*(p(0)*sh(1,j+1)*(pas(1,j+1)-pai(1,j+1))/Th(j));


for i=2:M

Intg1(j+1) = Intg1(j+1)+deltat*sh(1,j+1)*p(deltat*(i-1))...

*(pas(i,j+1)-pai(i,j+1));

Intg2(j+1) = Intg2(j+1)+deltat*(muh1(deltat*(i-1))*...

(sh(i,j+1)*pas(i,j+1)+ih(i,j+1)*pai(i,j+1)...

+rh(i,j+1)*par(i,j+1)+vh(i,j+1)*pav(i,j+1)));
```

```
Intg3(j+1) =
    Intg3(j+1)+deltat*(p(deltat*(i-1))*sh(i,j+1)*(pas(i,j+1)-pai(i,j+1))/Th(j));
end

%matrix for q
Avimp=[p2beta*Iph(j)/Th(j)+muv -p2beta*Iph(j)/Th(j);0 muv];
bvimp=[0;p1beta*Intg3(j+1)];

%Euler
q(:,j)=(eye(2)+deltat*Avimp)\(q(:,j+1)-deltat*bvimp);

%loop for age
for i=1:M
%age value for loop
aimp=(i-1)*deltat;

%Compute the H
lambdavhimp = p1beta*p(aimp)*State(7,j)/Th(j);

Aimp=[lambdavhimp+muh(aimp,State(5,j))+xih(i,j) -lambdavhimp 0 -xih(i,j);
0 muh(aimp,State(5,j))+deltah(aimp)+zetah -zetah 0;
-gammah 0 muh(aimp,State(5,j))+gammah 0;
-etah 0 0 muh(aimp,State(5,j))+etah];
bimp=(p2beta*State(6,j)*Iph(j)*p(aimp)/(Th(j)^2))*[-1 1;-1 1;-1 1;-1 1]...
+(p2beta*State(6,j)*p(aimp)/Th(j))*[0 0;1 -1;0 0;0 0];
```

```
cimp =
    (Intg2(j+1)-(p(aimp)*lambdavhimp*Intg1(j+1)/Th(j)))*[1;1;1;1]-[C*xih(i,j);B;0;0];

%Compute
sol=(eye(4)+deltat*Aimp)\([pas(i+1,j+1);pai(i+1,j+1);
    par(i+1,j+1);pav(i+1,j+1)]-deltat*(bimp*q(:,j)+cimp));
pas(i,j)=sol(1);
pai(i,j)=sol(2);
par(i,j)=sol(3);
pav(i,j)=sol(4);
end
end
end
```