Migration and Mixing between Populations in Disease Models

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MIGRATION AND MIXING BETWEEN POPULATIONS IN DISEASE MODELS

by

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Abstract

Title of Thesis:
Migration and Mixing between Populations in Disease Models

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The goal of this thesis is to model the spread of disease between populations and find ways to prevent its continued epidemic. This thesis studies disease spread as a function of migration in epidemiological models. The models are constructed using the compartmental approach, and we compare discrete and continuous time approximations. In the discrete model, we will look at ways that induced migration can cause an epidemic case to turn into a dieout case. It will be shown that migration can only effect the size of an outbreak, but cannot create or destroy one. For the continuous cases, we will be looking at periodic solutions and what bifurcations they exhibit. We find that high amplitude outbreaks do not occur for "strong" migration rates. It will be shown from real world data gathered from Cameroon that quarantine does not always reduce the size of the oncoming outbreak.
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Contents

1 Introduction ................................................................. 6

2 Motivations ........................................................................ 7

3 Background ....................................................................... 7
   3.1 Variables and Parameters ............................................. 8
   3.2 Reproductive Ratio ........................................................ 9

4 Measles ........................................................................... 14

5 Discrete Time based Model ............................................. 16
   5.1 Original Model .............................................................. 16
   5.2 Our Model ................................................................. 17
   5.3 Two Population Model .................................................. 18
   5.4 Independent Populations .............................................. 19
   5.5 One Sided Migration ...................................................... 20
   5.6 Multidirectional Migration ............................................ 22
   5.7 Summary of Discrete Model Analysis ............................. 24

6 Continuous SIR Models .................................................. 25
   6.1 Introducing Continuous Systems ................................. 25
   6.2 Our Model ................................................................. 32
      6.2.1 Periodic Solutions ................................................. 34
      6.2.2 Bifurcation Analysis ............................................ 36

7 Continuous SEIR Models ................................................ 38
   7.1 Motivation ................................................................. 38
   7.2 Single Population ....................................................... 39
      7.2.1 Bifurcation Analysis ............................................ 40
7.3 Two Populations ................................................................. 42
  7.3.1 Periodic Behavior changes due to Migration ................. 45

8 Conclusions ........................................................................ 48

List of Figures

1 Logistic model with $r = 2$ ..................................................... 12
2 Susceptibles of two populations during disease dieout ........... 21
3 No net change in population sizes from migration ............... 23
4 Left: Migration $N_1 > N_2$, Right: Migration $N_1 < N_2$ ...... 23
5 Fraction of Susceptibles in two connected populations. ........ 30
6 Change in infectives of populations with serial migration. .... 31
7 Dieout of Epidemic for $R_0 < 1$ ........................................... 33
8 Persistence of Epidemic for $R_0 > 1$ ..................................... 34
9 A period one and period three outbreak ............................... 35
10 Bifurcation diagram for a single population using time series . . . . 36
11 Bifurcation diagram for a single population using automated bifurcation analysis program, AUTO ................................. 37
12 Comparison of amplitude of outbreaks for period one and period three 39
13 Bifurcation for $\mu = 0.0329 \text{ yrs}^{-1}$ using time series ........ 40
14 Bifurcation for $\mu = 0.0428 \text{ yrs}^{-1}$ using time series ........... 41
15 Bifurcation for $\mu = 0.428 \text{ yrs}^{-1}$ using automated bifurcation analysis program, AUTO ................................. 42
16 Increase in migration rate at $time = 20$ ............................. 46
17 Decrease in migration rate at $time = 20$ ............................. 47
1 Introduction

From the bubonic plague to influenza, man has struggled to survive in a dangerous world of diseases. But in our modern time, the struggle against some of the biggest killers has been conquered. We now have vaccines for the most feared childhood diseases, antibiotics that can overcome many more, and better sanitation to help stave off others. There is still a great desire by many to understand and better model diseases and can be attributed to several motivating factors. The first is the prevalence of these “defeated” diseases still being a major killer in developing nations. Without the means and availability of health care like that in industrialized countries, many third world nations are still being ravaged by diseases like malaria. Another cause is the constant mutation of disease strains, which allows treatment resistant strains to replace non-resistant strains. Influenza, for one, is well known for its various strains. Several of the influenza strains have been quite deadly, like the great pandemic of 1918 that claimed an estimated 50 million lives [1]. Perhaps the most important reason to study diseases is to better understand in order to stop or control them. Theoretical biology is continuously improving models to accurately capture the dynamics of real world diseases. These models can than be used to come up with strategies to help control outbreaks that are occurring in countries around the world. With more details, one can better predict a potential outbreak. Also, effective strategies for containment can be developed.

Much of the early work in modeling diseases came from researchers wanting to better understand the spread of bubonic plague in the twelfth century [12]. This modeling motivated many others to use mathematics to model other common diseases. These early models have led others to refine them and develop new models with different goals. Some models evaluate vaccine strategies, others capture spread phenomena, while others look to find quarantine procedures and so on.
2 Motivations

Overall, the goal of this work is to understand, and therefore curb, disease outbreaks. We consider three models that will describe flow dynamics between populations. This flow is of the people of one population into and out of another population. Many times, as will be shown, a single population model cannot exhibit behaviors seen in the real world, like complex periodic orbits or realistic fixed point values. This lack of real world behaviors in isolated population models may be caused by external factors, such as mixing and migration. When populations are connected, we can get a variety of outcomes that were not originally found in the single population. The connections between different populations can change the overall picture. In this thesis, we will consider ways to model migration and study resulting model dynamics.

3 Background

In the field of epidemiology, there are various ways to form a model. These include discretely, continuously, or stochastically. In general, all models depend on how a population can be broken down into groups of people that carry similar traits that are important to the disease [12]. This division is usually done by what stage of the disease a person is in. For this thesis, we will be discussing a compartmental SIR model and a SEIR model. In a SIR model, a population $N$ is divided into three groups: Susceptibles ($S$), those who have the ability to catch the disease; Infected ($I$), those who currently possess the disease; and Recovered ($R$), those who have recovered from the disease. In a SEIR, we add an exposed group ($E$) to the population, people who have the disease but currently do not have any symptoms and are unable to transmit the disease. In both of these types of models, it is assumed that once someone reaches the recovered class, they do not contract the disease again, which is true for measles since one hundred percent immunity is conferred upon recovery.
Many childhood diseases, such as chicken pox and measles, fall into the category of a disease that confers full immunity to the recovered class.

We also further assume that those born to anyone in the population are born into the susceptible class. Except for a short period after birth, a mother passes no natural immunity to the disease, or the disease itself, to her child. In most cases, children are actually more susceptible to disease, as well as environmental problems. This increased susceptibility is caused by their increased breathing, permeability of the skin, and high caloric vs. mass intake [5]. Therefore, the threat of airborne spread is particularly risky for the young.

Numerous papers have shown that breaking a population into these groups based on their current stage of the disease is acceptable and accurate [12, 3, 13]. The compartmentalization approach comes from the fact that we wish only to stratify a population based on the criteria of how they are relative to the disease. We do compartmentalization in the same way as a census poll will stratify people according to age, sex, or race. Since any one individual can only be in one of the groups at a time, we can account for the entire population without worry of double counting anyone or missing someone. With these divisions, we can mark how a disease spreads through a population and monitor the changes.

3.1 Variables and Parameters

Before we can put together a model, we must first establish the intrinsic quantities to the dynamics of disease spread. The first is the contact rate, often denoted $\beta$. The parameter $\beta$ is a measure of how likely a disease will be transmitted when a susceptible person comes in contact with an infected person. The higher the number, the more infectious a disease is. Some diseases, like measles and chicken pox, have very high contact rates. That means it is easier for this type of disease to be passed on when the two classes, susceptible and infective, interact.
The recovery rate, often denoted $\gamma$, is a probabilistic quantity. It is a measure of the average amount of time that passes between a person entering the infected class and leaving to the recovered class [12]. A usefully way to think about it is $\frac{1}{\gamma}$, the mean time that someone stays in the infected class. As more time progresses, it becomes more and more likely that an infected person will recover from the disease. This means that $\frac{1}{\gamma}$ is a decreasing function in relation to time [12].

Finally, we account for people entering and leaving the population. Assuming that the population stays roughly constant and there is no significant death directly caused by the disease, the birth and death rate can be assumed equal, denoted $\mu$. This is an accepted technique used to study disease dynamics [3, 13, 12].

### 3.2 Reproductive Ratio

When studying disease and its epidemic potential, one can use the reproductive ratio, denoted $R_0$, to help determine if an outbreak will persist or dieout. The reproductive ratio tells us how many people a single infected individual can transmit a disease to before they recover. This means how many people on average can one infective infect. If $R_0 < 1$, than the disease will dieout. That follows from a logical argument. If each infective person in a population is averaging less than one new infection, than they are not even replacing themselves. This means it could take two or more infective people at time $t$ to get one infective person at time $t + 1$. Over time, this inability to infect the population will cause a dieout of the disease [11].

If $R_0 > 1$, than the disease will persist. Each infective person in time $t$ is causing more than one infective person to appear at time $t + 1$ and will cause the disease to persist at some relative fraction of the population. The reason the disease will not increase the fraction of infective people is due to the concept of "burn through". If too many people catch a disease at some time $t$, than there will not be enough people at time $t + 1$ to infect to keep the number of infectives as high as they were.
Since no one can catch the disease again, the only pool of people infectives can work with are susceptibles, and they enter the population at the rate $\mu N$, the birth rate for the entire population. If the rate of new infectives is much above this rate, than in time there will not be many susceptibles to infect. This is why most sustained outbreaks see a sharp increase in cases in the beginning of the epidemic, but then a slower leveling off occurs. That is where the disease stays, where infectives have enough susceptibles to keep their group size constant. The stability of the epidemic fixed point for the disease when $R_0 > 1$ will be stable and the disease will persist.

Instead of $R_0$, we can consider a linearization of the system. If we take our system and put it into a vector of $(S, I, R)^T$ or $(S, E, I, R)^T$, we can take the Jacobian of the system. Than we can evaluate the Jacobian matrix at the disease free equilibrium and get its eigenvalues. The dominant eigenvalue, denoted $\lambda$, is the largest eigenvalue of the system. Finding at what values does $\lambda$ have positive real parts gives us a qualitative way at looking at when the disease free equilibrium will become unstable and the disease will move to some other behavior in the phase space. The phase space is designed by considering the infectives. We know that the infectives will be a small percent of the population. We also know that should the number of infectives fall below some threshold, the disease will die out because not even a single person will be infected. We use these two previously stated facts to give us a range to look through when trying to determine stable behaviors. Though $\lambda$ does not hold the biological significance that $R_0$ has, it can alternatively be used to determine disease dynamics in a mathematical model.

To see an application, we look at the $SIS$ model developed in Britton [8]. We start by setting up equations for $S$ and $I$

$$\frac{dS}{dt} = -\beta SI + \gamma I , \quad (1)$$

$$\frac{dI}{dt} = \beta SI - \gamma I , \quad (2)$$
where $\beta SI$ is the interaction between susceptibles and infectives that can lead to disease transmission, and $\gamma I$ is the recovery of the infected.

We now nondimensionalize the variables for susceptible, infective, and time:

$$u = \frac{S}{N}, \quad (3)$$
$$v = \frac{I}{N}, \quad (4)$$
$$t = \gamma r, \quad (5)$$

which gives us our new system as

$$\frac{du}{dr} = -(R_0u - 1)v, \quad (6)$$
$$\frac{dv}{dr} = (R_0u - 1)v, \quad (7)$$

where

$$R_0 = \frac{\beta N}{\gamma}. \quad (8)$$

This fits our definition of $R_0$, since $\beta N$ is the amount of new infections in the population that stay for a time of $\frac{1}{\gamma}$. This means if $\frac{\beta N}{\gamma} > 1$, the disease will persist. Conversely, if $\frac{\beta N}{\gamma} < 1$, the disease will die out.

To illustrate these points, we look at the basic logistic model developed by Pierre Verhulst in 1838 [8]:

$$\frac{dx}{dt} = rx(1 - \frac{x}{k}). \quad (9)$$

In this equation, $r$ is the rate of population change and $k$ is the carrying capacity. Since any isolated populations size is a factor of new births into the population minus the deaths in the population, we have $r = b - d$. The carrying capacity is merely the amount of people, or animals etc., that a population can hold. Since resources
or land can be limited, there is an upper limit on how much of something an area can hold. Any more and those already in the population will not have enough basic materials that are needed for survival.

To find $R_0$, we make a fraction where the numerator is those coming into the population and the denominator is those leaving the population. For the logistic model, we have $R_0 = \frac{b}{d}$. The survival like ratio $R_0$ would be a comparison of people coming into the population $b$ and the time they stay $\frac{1}{d}$. If more people are born than die, $R_0 > 1$, the population will increase to the carrying capacity. If the deaths are greater than the births, $R_0 < 1$, the population will die out. This is analogous to our disease pandemic.

We can also consider the eigenvalue linearized about the zero population size. The linearization tells us $\lambda = r$. So if $r > 0$, the population will grow. If $r < 0$, the population will die out.

As discussed above, both $R_0$ and $\lambda$ will give us the stability of the dieout equilibrium. The difference of $R_0$ and $\lambda$ is what type of information about the disease can it give us. Though $R_0$ tells us biologically significant information, it tells us nothing of the rate of growth or decay for the population. We can use $\lambda$ however, to get a feel for how quickly the population size will change by considering the limit of the linear
solution in the form $e^{\lambda t}$ as $t \to \infty$.

To calculate $R_0$ for more complex continuous models, we use the technique from van den Driessche [14]. In essence, we split the equations into two vectors. The first vector, $F$, is composed of the terms that result in new infections. The second vector, $V$, is composed of all other terms. The entire system of equations then is of the form $G = F - V$. With these, we calculate the Jacobian for both vectors, denoted $F$ and $V$, and multiply them together as $FV^{-1}$ to get a resultant. With these, evaluated at the disease free equilibrium, we can deduce $R_0$ by finding the spectral radius of $FV^{-1}$.

To calculate $R_0$ for all discrete models, we have two methods. If the system is technically simple, than we can find $R_0$ by definition. We do this by creating a fraction in the following fashion. The numerator is the sum of all terms that cause a person to become infected. The denominator is the sum of all terms that cause a person to leave the infected class. Leaving can include recovery, death, or migration. In more complicated models, a good approach is the one outlined in Allen and van den Driessche [4]. In this method, we approach the problem similarly to van den Driessche [14]. We place the disease carrying groups, which would be $E$ and $I$, into a vector $X_0$ and the non disease carrying groups, which are $S$ and $R$, into a vector $X_1$. We then take the Jacobian of $X_1$ with respect to the groups in $X_0$. We further divide this Jacobian matrix into two summed matrices, $F$ and $T$. $F$ contains everyone who still has the disease in the next generation, while $T$ contains all who will leave the disease carrying groups in the next generation. We then calculate the next generation matrix

$$Q = F(I - T)^{-1}, \quad (10)$$

where $I$ is the identity matrix. Finally, we calculate the spectral radius, which is the dominant eigenvalue, of Eqn. (10) to get the reproductive ratio.
To calculate eigenvalues of the system, the approach is the same for both discrete and continuous systems. We set up a vector of the groups and take its Jacobian. We then evaluate this linearization about the disease free equilibrium and get its eigenvalues. Looking at the dominant eigenvalue will give us the our $\lambda$. We then look at the stability. For $\lambda < 0$, the disease free equilibrium is stable. For $\lambda > 0$, the disease free equilibrium will become unstable and the system will move to another behavior in the phase space as discussed earlier.

The final consideration for $R_0$ its validity. As has been discussed in other works [12, 14], $R_0$ is only a good indicator for disease persistence for single populations. Once we move to interactions between populations, $R_0$ turns more into an approximation to determine when the disease will die out. This is due to the off diagonal terms in the matrix that we get the eigenvalues from. To have an accurate $R_0$, we need to be able to diagonalize the matrix. This diagonal matrix can only have terms on the main diagonal, the eigenvalues. A multipatch model will have a less sparse matrix and include off diagonal terms. These terms will not be included in the spectral radius calculation, but are significant to disease dynamics. The loss of $R_0$ as a disease indicator in more complicated models means predicting behaviors is much more complex and needs to be done numerically, which will be done when necessary.

4 Measles

The primary disease we will consider in this thesis is measles. The measles virus belongs to the Morbillivirus group of the Paramyxovirus family for the virus rubella. It is a highly contagious disease that is spread by direct contact with respiratory fluids from an infected person. This occurs mostly from coughing and sneezing, which are symptoms of measles. The virus is found mostly in children due to the diseases high contagious rate. This is further complicated by the high rate of contacts children have in schools. Once someone recovers from measles, they have a lifetime immunity. It
has been found in various biological circles that cross-immunity from different strains is perfect [2].

Measles has a latency period, an asymptomatic time, of about six days. It also has an infected time of about six days. This means that anyone who contracts measles will have the disease for about two weeks [6]. Furthermore, since it can take about a week for symptoms to show themselves, a person could very well believe they have not contracted the disease and risk spreading it to those they come in contact with. This gives the disease a transmission rate that is dependent not only on those infected, but also those who are exposed. Even though the exposed cannot pass along the disease, they are still able to work themselves into population sections that are full of susceptible people that they can infect once the latency period is over. This causes quarantines to be less effective, since exposed and susceptible groups appear identical. Only medical tests can tell the difference. For measles, the exposed group transmission rate is 46% [9].

Measles has in the past caused a great number of deaths. England had severe cataloged outbreaks from 1940-1967, for example [7, 10]. These outbreaks would occur every three to five years. These outbreaks were later curbed due to the development of a vaccine around 1965 and its mass implication later that decade. In most industrial nations, measles has been on the list of wiped-out disease. A strong requirement of vaccine before school age, coupled with the cross-immunity, means that anyone who is vaccinated cannot get nor carry the disease. Also, since humans are the only carriers of the disease, it cannot be spread or mutated by other animals and passed on to us [7]. For many other diseases, including HIV, that is the current concern.

With these facts, it would seem that by this time in history, the disease should be near non-existent, but that is not the case. The reason for continued prevalence is the lack of immunization efforts in non industrialized countries. Many parts of South America and Africa still have measles outbreaks. Many countries do not have the means for self vaccine supply, and also do not accept help from other countries. This,
combined with the near 50% infection rate generated from asymptomatic people, make the disease both pervasive and hard to control [9]. Another concern is the chance of the disease making a comeback in industrialized countries. This fear of a return of measles comes from many people today do not want to immunize their children. Many fear that the MMR vaccine, which immunizes against measles, mumps and rubella, will actually hurt their children more than catching the disease. Immunity to measles is passed down from mother to child and lasts only about four months, meaning that school age children have no defense against such a pervasive disease. The vaccination has never been shown to be unsafe and as with all safeguards, it is monitored by the CDC and FDA.

5 Discrete Time based Model

5.1 Original Model

The inspiration for this particular model comes from Allen [3]. The variables of the model are: $S_n$, the number of people in the susceptible group of population N; $I_n$, number of people in the infective group of population N; $R_n$, number of people in the recovered group of population N; and $N$, the total size of the population.

\[
S_{n+1} = S_n\left(1 - \frac{\beta \Delta t I_n}{N}\right) + \mu \Delta t (N - S_n), \quad (11)
\]
\[
I_{n+1} = I_n\left(1 - \gamma \Delta t - \mu \Delta t + \frac{\beta \Delta t S_n}{N}\right), \quad (12)
\]
\[
R_{n+1} = R_n(1 - \mu \Delta t) + \gamma \Delta t I_n. \quad (13)
\]

The parameters are $\beta$, $\mu$, $\gamma$, and $\Delta t$; the infection rate, birth and death rate, recovery rate, and time step respectively. In Allen’s model, interactions between groups represent the infectives of one group coming in contact with the susceptible of
the other group. This is termed mass action. In the multipopulation model we have:

\[
S_{n+1}^i = S_n^i \left(1 - \sum_{k=1}^{K} \frac{\beta_{ik} \Delta t I_k^j}{N_i} \right) + \mu_i \Delta t (N_i - S_n^i), \quad (14)
\]

\[
I_{n+1}^i = I_n^i \left(1 - \gamma \Delta t - \mu_i \Delta t + S_n^i \sum_{k=1}^{K} \frac{\beta_{ik} \Delta t I_k^j}{N_i} \right), \quad (15)
\]

\[
R_{n+1}^i = R_n^i (1 - \mu_i \Delta t) + \gamma \Delta t I_n^i. \quad (16)
\]

### 5.2 Our Model

For our model, we removed the intrapopulational mass action and replaced it by the migration term from Liebovitch and Schwartz [13]. This term corresponds to the susceptibles or infectives of one population moving to the susceptible or infective class of another population. This move is of temporary permanence, for the only way to move back to the population one originated from is to migrate back in the same manner they originally left by. This means that the migration rates can affect the total size of a population and therefore its endemic behaviors. This change causes our model to become:

\[
S_{n+1}^i = S_n^i \left(1 - \beta \Delta t I_n^i \right) + \mu_i \Delta t (N_i - S_n^i) - \frac{\chi_i \Delta t S_n^i}{N_i} + \sum_{k=2}^{K} \frac{\chi_k \Delta t S_n^k}{N_k}, \quad (17)
\]

\[
I_{n+1}^i = I_n^i \left(1 - \gamma \Delta t - \mu_i \Delta t + \frac{\beta \Delta t S_n^i}{N_i} \right) - \frac{\rho_i \Delta t I_n^i}{N_i} + \sum_{k=2}^{K} \frac{\rho_k \Delta t I_n^k}{N_k}, \quad (18)
\]

\[
R_{n+1}^i = R_n^i (1 - \mu_i \Delta t) + \gamma \Delta t I_n^i. \quad (19)
\]

The only difference in parameters is the additions of \( \rho \), the rate of migration of the infectives, and \( \chi \), the rate of migration of the susceptibles.

Overall, the disease is not fatal and is only spread by human interactions. The migration, as compared to mass action, causes a populations size change. In mass action, someone from another population only acts on a different population. Under migration, someone from another population joins the different population, thus
increasing their numbers while decreasing the size of the group from which he came.

5.3 Two Population Model

The complete model for two populations is:

\[ S_{n+1}^1 = S_n^1(1 - \frac{\beta \Delta t I_{n}^1}{N_1}) + \mu_1 \Delta t (N_1 - S_n^1) - \frac{\chi_1 \Delta t S_n^1}{N_1} + \frac{\chi_2 \Delta t S_n^2}{N_2}, \]  
\[ I_{n+1}^1 = I_n^1(1 - \gamma \Delta t - \mu_1 \Delta t + \frac{\beta \Delta t S_n^1}{N_1}) - \frac{\rho_1 \Delta t I_n^1}{N_1} + \frac{\rho_2 \Delta t I_n^2}{N_2}, \]  
\[ R_{n+1}^1 = R_n^1(1 - \mu_1 \Delta t) + \gamma \Delta t I_{n}^1, \]  
\[ S_{n+1}^2 = S_n^2(1 - \frac{\beta \Delta t I_{n}^2}{N_2}) + \mu_2 \Delta t (N_2 - S_n^2) - \frac{\chi_2 \Delta t S_n^2}{N_2} + \frac{\chi_1 \Delta t S_n^1}{N_2}, \]  
\[ I_{n+1}^2 = I_n^2(1 - \gamma \Delta t - \mu_2 \Delta t + \frac{\beta \Delta t S_n^2}{N_2}) - \frac{\rho_2 \Delta t I_n^2}{N_2} + \frac{\rho_1 \Delta t I_n^1}{N_2}, \]  
\[ R_{n+1}^2 = R_n^2(1 - \mu_2 \Delta t) + \gamma \Delta t I_{n}^2. \]

We then normalize the equation by letting \( S_n^i = s_n^i N_i, I_n^i = i_n^i N_i, R_n^i = r_n^i N_i \) for \( i = 1, 2 \):

\[ s_{n+1}^1 = s_n^1(1 - \beta \Delta t i_{n}^1 N_1) + \mu_1 \Delta t (1 - s_n^1) - \frac{\chi_1 \Delta t s_n^1}{N_1} + \frac{\chi_2 \Delta t s_n^2}{N_2}, \]  
\[ i_{n+1}^1 = i_n^1(1 - \gamma \Delta t - \mu_1 \Delta t + \beta \Delta t s_n^1) - \frac{\rho_1 \Delta t i_n^1}{N_1} + \frac{\rho_2 \Delta t i_n^2}{N_2}, \]  
\[ r_{n+1}^1 = r_n^1(1 - \mu_1 \Delta t) + \gamma \Delta t i_{n}^1, \]  
\[ s_{n+1}^2 = s_n^2(1 - \beta \Delta t i_{n}^2 N_2) + \mu_2 \Delta t (1 - s_n^2) - \frac{\chi_2 \Delta t s_n^2}{N_2} + \frac{\chi_1 \Delta t s_n^1}{N_2}, \]  
\[ i_{n+1}^2 = i_n^2(1 - \gamma \Delta t - \mu_2 \Delta t + \beta \Delta t s_n^2) - \frac{\rho_2 \Delta t i_n^2}{N_2} + \frac{\rho_1 \Delta t i_n^1}{N_2}, \]  
\[ r_{n+1}^2 = r_n^2(1 - \mu_2 \Delta t) + \gamma \Delta t i_{n}^2. \]

For this model, there are several cases that can be examined: both populations independent of the other, one way migration, and multidirectional migration. We examine each part separately.
5.4 Independent Populations

In the independent populations model, the migration rates $\rho_1$ and $\rho_2$ are set to zero causing the model to become:

\begin{align*}
S_{n+1} &= S_n \left( 1 - \frac{\beta \Delta t I_n}{N} \right) + \mu_1 \Delta t (N - S_n), \quad (32) \\
I_{n+1} &= I_n \left( 1 - \gamma \Delta t - \mu_1 \Delta t + \frac{\beta \Delta t S_n}{N} \right), \quad (33) \\
R_{n+1} &= R_n (1 - \mu_1 \Delta t) + \gamma \Delta t I_n. \quad (34)
\end{align*}

For this system, we continue with an analysis of a single population. There are two possible behaviors, dieout of the disease or persistence of the disease. Since we are considering the amount of people in each group at some future time after the asymptotic approach to the steady state, we let $(S_n, I_n, R_n) \to (S^*, I^*, R^*)$ denote our equilibrium values. Dieout occurs when the contact rate $\beta \leq \gamma + \mu$. For this case the equilibrium becomes the standard dieout equilibrium: $(S^*, I^*, R^*) = (N, 0, 0)$

The population reaches endemic behavior at $\beta > \gamma + \mu$. For this case, the equilibria are given by:

\begin{align*}
S_n &= \frac{N(\gamma + \mu)}{\beta}, \quad (35) \\
I_n &= \frac{\mu N(\beta - \gamma - \mu)}{\beta(\gamma + \mu)}, \quad (36) \\
R_n &= N - S_n - I_n. \quad (37)
\end{align*}

What we find is that the endemic state does not exist for $R_0 < 1$ since $I^* = 0$. Once $R_0 > 1$, then both the disease free and endemic equilibrium exist, though the stability of these equilibrium tells us where the groups will go.
5.5 One Sided Migration

In the one sided migration, we set $\chi_2$ and $\rho_2$ to zero and get the system as:

\begin{align*}
S_{n+1}^1 &= S_n^1 \left(1 - \frac{\beta \Delta t I_n^2}{N_1}\right) + \mu_1 \Delta t(N_1 - S_n^1) - \frac{\chi_1 \Delta t S_n^1}{N_1}, \quad (38) \\
I_{n+1}^1 &= I_n^1 \left(1 - \gamma \Delta t - \mu_1 \Delta t + \frac{\beta \Delta t S_n^1}{N_1}\right) - \frac{\rho_1 \Delta t I_n^1}{N_1}, \quad (39) \\
R_{n+1}^1 &= R_n^1 \left(1 - \mu_1 \Delta t\right) + \gamma \Delta t I_n^1, \quad (40) \\
S_{n+1}^2 &= S_n^2 \left(1 - \frac{\beta \Delta t I_n^2}{N_2}\right) + \mu_2 \Delta t(N_2 - S_n^2) + \frac{\chi_1 \Delta t S_n^1}{N_2}, \quad (41) \\
I_{n+1}^2 &= I_n^2 \left(1 - \gamma \Delta t - \mu_2 \Delta t + \frac{\beta \Delta t S_n^2}{N_2}\right) + \frac{\rho_1 \Delta t I_n^1}{N_2}, \quad (42) \\
R_{n+1}^2 &= R_n^2 \left(1 - \mu_2 \Delta t\right) + \gamma \Delta t I_n^2. \quad (43)
\end{align*}

For this type of system, where population one has a migration into population two, one find three behaviors: Dieout in both populations, dieout in population one with persistence in population two, or persistence in both populations. This migration causes population one to become lower than it normally would, while population two is larger than it normally would be.

Dieout again sets $(I_1, I_2, R_1, R_2) = (0, 0, 0, 0)$, while the other terms become:

\begin{align*}
S_1 &= \frac{\mu N_1^2}{\lambda}, \quad (44) \\
S_2 &= \frac{\mu N_1 N_2 + \chi_1 (N_2 + N_1)}{\lambda}, \quad (45)
\end{align*}

where $\lambda = \mu N_1 + \chi_1$.

The reason why $S_1 \neq N_1$ or $S_2 \neq N_2$ is due to the migration term. Since the susceptibles of population one are allowed to move to population two, we see the terms have a factor of $\chi$. If one sets $\chi = 0$ than the populations again assume standard non-interaction dynamics.

To illustrate this point, consider two populations, where $N_1 = 1000$ people and
$N_2 = 2000$ people. For parameter values: $\mu = 2 \text{ yrs}^{-1}$, $\gamma = 0.1 \text{ yrs}^{-1}$, $\rho_1 = 0$, $\beta = 1 \text{ yrs}^{-1}$, and $\chi_1 = 50$, These values will cause the dieout equilibrium to be stable, and therefore the disease will dieout. The migration of susceptibles, however, will cause a small fraction of their numbers to move and change the population sizes of each population. As can be seen in Figure 2, once the disease is completely out of the populations, the end results give different $N_1$ and $N_2$ values than they started with.

![Figure 2: Susceptibles of two populations during disease dieout](image)

Persistence in population two occurs when

$$\beta > \frac{N_2(\gamma\mu N_1 + \gamma \chi_1 + \mu^2 N_1 + \mu \chi_1)}{\mu N_2 N_1 + \chi_1(N_2 + N_1)},$$

but persistence in population one does not occur until

$$\beta > \frac{N_1 \mu (N_1 \gamma + N_1 \mu + \chi_1 + \rho_1) + \chi_1 (N_1 \gamma + \rho_1)}{\mu N_1^2}.$$  \hspace{1cm} (47)

Since population two will reach epidemic bifurcation first, Eqn. (47) must be a more strict requirement than Eqn. (46). This also means that fulfillment of Eqn. (47) means that Eqn. (46) has been met.
5.6 Multidirectional Migration

For multidirectional migration, the model becomes:

\[ S_{n+1}^1 = S_n^1 \left(1 - \frac{\beta \Delta t I_n^1}{N_1}\right) + \mu_1 \Delta t (N_1 - S_n^1) - \frac{x_1 \Delta t S_n^1}{N_1} + \frac{x_2 \Delta t S_n^2}{N_2}, \]  
\[ I_{n+1}^1 = I_n^1 \left(1 - \gamma \Delta t - \mu_1 \Delta t + \frac{\beta \Delta t S_n^1}{N_1}\right) - \frac{\rho_1 \Delta t I_n^1}{N_1} + \frac{\rho_2 \Delta t I_n^2}{N_2}, \]  
\[ R_{n+1}^1 = R_n^1 \left(1 - \mu_1 \Delta t\right) + \gamma \Delta t I_n^1, \]  
\[ S_{n+1}^2 = S_n^2 \left(1 - \frac{\beta \Delta t I_n^2}{N_2}\right) + \mu_2 \Delta t (N_2 - S_n^2) - \frac{x_2 \Delta t S_n^2}{N_2} + \frac{x_1 \Delta t S_n^1}{N_2}, \]  
\[ I_{n+1}^2 = I_n^2 \left(1 - \gamma \Delta t - \mu_2 \Delta t + \frac{\beta \Delta t S_n^2}{N_2}\right) - \frac{\rho_2 \Delta t I_n^2}{N_2} + \frac{\rho_1 \Delta t I_n^1}{N_2}, \]  
\[ R_{n+1}^2 = R_n^2 \left(1 - \mu_2 \Delta t\right) + \gamma \Delta t I_n^2. \]

One cannot get a closed form solution to this model. One set \( \chi_1 = \chi_2 = \rho_1 = \rho_2 \) or \( \chi_1 = \chi_2 \) and \( \rho_1 = \rho_2 \). This will lead to three possible solutions, dieout in both populations and two forms of persistence in both populations. Only the one form of persistence is ever stable, so the other can be disregarded. Both of these cases however will lead to determined dynamics that mimic a single population, due to symmetry.

This is not the interesting case. Instead, we use numerical techniques to explore the dynamics. In the case where we do not equate \( \rho \)'s, there are two possible solutions, dieout in both populations or persistence in both populations. This means that no amount of migration can cause the disease to dieout in a population. Transferring the infected out of one population and into the other, short of total migration, will not cause the disease free equilibrium to become stable in the migrating population. What the migration does account for is the overall outbreak size for each population. A positive net change in migration into a population will cause the outbreak size to increase greater than it naturally could sustain. Similarly, the other population, which would be experiencing a negative net migration, will have an endemic state that is lower than it would naturally sustain.
We again use the same parameter values and population sizes that were used for Figure 2 except for changing $\beta = 3$. This increase will mean that the disease will persist in both populations. We then compare what happens as we change the net migrations for each population.

As Figures 3 and 4 show, when experiencing migration, a net gain for a population causes an increase in the infected group for that population, while the other population has a smaller infected group than it would normally have. The overall maximum for both populations can be found to be
What Eqn. (54) tell us is that the migration that gives the largest outbreak size depends on the population sizes. If the migration rate $\rho$ is chosen without considering how the sizes of the two populations compare, there is a risk of burn through if the migration is too high. If too many people catch the disease at time $t$ and the birth rate does not replace all the susceptibles infected, than at time $t + 1$ less people are available to be infected than at time $t$. These less potential infections mean the disease will decrease in endemic size. This burning though of the susceptibles will keep the disease at a lower rate than it would have sustained with smaller migration. Similarly, if the migrations are very low, no appreciable difference is detected in the infected classes.

\[ \rho_1 = \frac{N_1}{N_2} \rho_2. \] (54)

5.7 Summary of Discrete Model Analysis

This model analyzed the endemic behavior within a population and also how other populations can affect this behavior through migration. When the populations are separated, they can either have no disease outbreak or an epidemic. When we allow migration only in one direction, we have three possible outcomes: a dieout in both populations, an outbreak in the population receiving the migration while the migrating population experiences a dieout, or an outbreak in both populations. When multidirectional migration is allowed, there are again only two cases: a dieout in both populations or an outbreak in both populations.

The migration rate cannot induce an outbreak where one will not naturally occur. Migration simply influences the size of an epidemic, pandemic, or the population itself. If one population is gaining more infectives than it loses, it will have a larger outbreak than it naturally would, while the other population which is giving away
more infectives than it is receiving will experience a smaller outbreak than it naturally would have. Susceptible movement also works in this same manner. It seems the ultimate key to keeping outbreaks and epidemics from occurring is to control the contact rate. This is the only logical parameter that can be changed. Altering the birth rate would require governmental sanctions into personal rights, which in most countries is not an acceptable practice. Along the same lines, altering the recover rate would require some form of cure or antibiotic to be created, which is not a short term appropriate. This leaves contact rate, which is plausible by means like quarantines. Overall, if an outbreak is going to occur, there is not much that can be done to stop it besides sectioning off those with the disease in hopes that enough separation will cause non persistence.

6 Continuous SIR Models

6.1 Introducing Continuous Systems

We begin our discussion of continuous models by first introducing how the models are derived. This is done in much the same way as we did in the discrete case. The population has several internal parameters included in an SIR model. The first is $\mu$, the birth rate. This parameter simply refers to the people born into the population as a constant fraction of the population. For many developed countries, this parameter is about 2% per year. Next is $\gamma$, the recovery rate. This is the average amount of time a person spends in the infected class. The parameter will vary depending on what disease is being modeled, from 3 days for influenza to 6 days for measles. The final parameter is $\beta$, the contact rate. It is how many susceptibles will one infected person infect on average in the given time period. This determines how infectious the disease is.

People move from the susceptible class to the infected class by the contact term
\( \beta SI \). This is referred to as mass action. The number of interactions between the two classes, along with the probability of spreading the disease, models the movement \[3\]. People move from the infected class to the recovered class by the recovery term \( \gamma I \).

Since the diseases we are working with have a very low probability of mortality from the disease, we do not include a term for death from the disease. There is also the birth term \( \mu N \). This means that everyone born into the population is born into the same class, in this case, the susceptible class. People leave the population through the death rate \(-\mu S, -\mu I, \) or \(-\mu R\) depending on if the person is in the susceptible, infected, or recovered class. We use \( \mu \) for both births and deaths to show that the rates for both are the same. Since \( S + I + R = N \), the entire death rate is \(-\mu N\).

Also the entire birth rate is \( \mu N \), meaning that we have a constant population size with exact replacement.

With these terms, we can now build one of the simplest \( SIR \) models:

\[
\frac{dS}{dt} = \mu N - \beta IS - \mu S, \quad (55)
\]

\[
\frac{dI}{dt} = \beta IS - \gamma I - \mu I, \quad (56)
\]

\[
\frac{dR}{dt} = \gamma I - \mu R. \quad (57)
\]

First, we test if this is a well posed problem by adding up the equations. If a constant population size is assumed, there should be no overall change and the sum should be zero. Since the model assumes births and deaths to be equal, this is the case we have.

The system has two steady steady state, or equilibrium, solutions. The first corresponds to the disease free equilibrium, \( (S, I, R) = (N, 0, 0) \). In this steady state, the disease is not present and every person stays in the susceptible class. The second steady state is \( (S, I, R) = \left( \frac{\gamma + \mu}{\beta}, \frac{\mu (N \beta - \gamma + \mu)}{\beta (\gamma + \mu)}, \frac{(N \beta - \gamma + \mu) \gamma}{\beta (\gamma + \mu)} \right) \). This corresponds to the endemic state. As we can see, the particular values for each group depend on the parameters that the model is given. Solutions will tend towards one of the two equilibria depending on the value of the reproductive ratio, \( R_0 = \frac{\beta}{\mu + \gamma} \). The reproductive
ratio is the average number of new infectives in the next time period that are caused by an infective in the current time period. This gives us the average replacement rate for the infected class. If the reproductive ratio is less than one, it means that every infective is not replaced by another infective in the next time period. This means that as time goes on, we are decreasing in infectives until all die out. If the reproductive ratio is greater than one, then each infective in a time period is being replaced by more than one infective in the next time period. This means the infective class will approach the equilibrium value.

Next, we nondimensionalize our variables to represent the fraction of the population that the class represents. In this case, divide each variable by $N$ to find the new groups: $s = S/N$, $i = I/N$, $r = R/N$. Note that $s + i + r = 1$ and by solving the system for $s$ and $i$, we can determine $r$ with this relationship.

We now divide the population into $n$ homogeneous patches, with separate SIR models in each. Consider $s_n$ as the susceptibles in patch $n$ and $i_n$ as the infectives in patch $n$. We divide the population in this fashion in order to more easily model the dynamics. Since we know how the groups, susceptibles, infectives, and recovereds, interact with one another, we can split any population into these groups. Once split, we can use the terms of interaction to mimic the mixing of these groups. In any population, all three groups of people will come in constant contact with one another. However, only some form of these interactions give any change to the disease dynamics, which is our focus. An interaction between susceptible and recovered, or infective and recovered, does not change how the disease is propagating through the population. This is why, in modeling an epidemic, we can ignore these interactions in favor of ones that matter, such as the one between susceptible and infective. Breaking a population into these patches lets us account for all important interactions that will occur in a population, while still allowing for a model we can work with.

Taking the ideas from the discrete model in Allen [3] and adding the migration term from Liebovitch and Schwartz [13], define $\chi_n$ as the ratio of the rate of decline
of infectives in patch \( n \) from migration compared to recovery. We developed a model that uses migration to cause movement between the two populations:

\[
\begin{align*}
\frac{ds_1}{dt} &= \mu - \beta s_1 i_1 - \mu s_1, \\
\frac{di_1}{dt} &= \beta s_1 i_1 - \gamma i_1 - \mu i_1 + \left(\frac{\chi_2 \gamma N_2}{N_1}\right) i_2 - (\chi_1 \gamma) i_1, \\
\frac{ds_2}{dt} &= \mu - \beta s_2 i_2 - \mu s_2, \\
\frac{di_2}{dt} &= \beta s_2 i_2 - \gamma i_2 - \mu i_2 + \left(\frac{\chi_1 \gamma N_1}{N_2}\right) i_1 - (\chi_2 \gamma) i_2. 
\end{align*}
\]

The goal is to find out how to stop an infection that has occurred in one of the two populations when considering one sided migration versus multidirectional. To study how migration can induce an epidemic in a susceptible patch, we connect it to a second patch under various \( R_0 \) and \( r_i \) conditions. Our initial analysis is for two populations, but can be extended to more. We describe our results for several cases.

We start by setting the parameters, which are \( \mu = 2 \text{ yrs}^{-1}, \gamma = 0.1 \text{ yrs}^{-1}, \Delta t = 0.001, r_1 = r_2 = 0.01, N_1 = 100 \text{ people}, \) and \( N_2 = 200 \text{ people}. \) We also set the initial conditions \( S_1 = 90, I_1 = 10, R_1 = 0, S_2 = 180, I_2 = 20, R_2 = 0. \) We have left \( \beta \) as a variable, since that is the parameter we wish to control. We consider two scenarios that this model gives us when migration occurs from population two to population one. If the second population is larger than the first, there can be either dieout in both, persistence in the first population, or persistence in both. If we reverse the sizes and make the first population larger than the second, we see the same three behaviors, though the outbreak numbers for the endemic case in both are more drastic. For this case, the first population will have a much higher endemic state, while the second population will have a much lower endemic state.

When considering multidirectional migration, we find two scenarios. We again assume all the same parameters and initial conditions as the first set. The first is with equal migration rates. There are only two possible outcome, dieout in both or
persistence in both, occurring when \( R_0 > 1 \). This corresponds to \( \beta = 2.1 \text{ yrs}^{-1} \) for our particular initial conditions and parameter values. The other possibility is different migration rates, which still only have those two outcomes, dieout in both or persistence in both, but the size of the endemic states change. Overall, the endemic states of both populations are lower than that of the symmetric case, and it can be shown that the maximum outbreak occurs along the line \( \chi_1 = \frac{x_2}{2} \).

These results also answer our second question, of whether migration alone can induce an epidemic in our model. It was found that for our model, this cannot happen. Migration merely causes a change in the size of the endemic state for infective people, but nothing more. The key to curbing an outbreak is to control the contact rate \( \beta \).

The motivation of this thesis comes from questions raised by the model derived by Liebovitch and Schwartz [13] for \( i = 1, 2 \):

\[
\frac{ds_i}{dt} = \mu - \beta_i i_i s_i, \tag{62}
\]

\[
\frac{d\gamma_i}{dt} = \beta_i i_i s_i - \gamma_i - \chi_i \gamma_i + \sum_{k=1, k \neq i}^{n} \frac{\chi_k \gamma_i n_k}{n_i}. \tag{63}
\]

In this model, several populations are connected through a migration term of the infectives, \( r_i \gamma_i \). The rate \( r \) is defined as the ratio of the rate of decline of infectives in a patch from migration compared to recovery. This causes the interactions between populations to consist of infective people of one patch moving into the infective group of another patch. By studying the endemic steady state, they hoped to see the effects of the migration on the infectives in both size and outbreak time.

In example one, two populations are connected and given the following parameters using Eqn. (62): \( \beta_1 = 1200 \text{ yrs}^{-1}, \beta_2 = 1000 \text{ yrs}^{-1}, \mu = .02 \text{ yrs}^{-1}, r_1 = .1, r_2 = 0, n_1 = 1,000,000 \text{ people}, \) and \( n_2 = 500,000 \text{ people} \). Observe the long term behavior in Figure 5. The infected classes of the two populations move towards separate steady states. Each infected class approaches a value that it will stay fixed near or at specifically depending on the periodicity of disease, an innate characteristic of it.
and the model.

Once this is established, the next consideration is connecting several populations together. In doing this, one can observe how the migrational movement affects the outbreaks. It is assumed that the populations are serially connected. Serial connection means each population is connected to all populations next to them, so 1 connects to 2, 2 connects to one and three, and so on. We give the values of the first population $n_1$ the same as before. For all other populations, we define their parameters in terms of the previous population. The migration rates between all populations in the serial migration are constant and migration only occurs between populations that are next to one another. Each successive population has half the size of the previous one. Finally, ever population is given the same birth and death rate as population one. These conventions of parameters can be shown as: $\chi_{k,k+1} = .002$, $n_k/n_{k+1} = 2$, and $\mu_k/\mu_{k+1} = 1$. Observe the long term behavior in Figure 6. The outbreaks occur one after another, not succinctly. This means the the endemic state propagates outward from the epicenter of the disease, much like the ripples produced by a drop of water in a pond. This is caused by the connectivity of the populations with the migration rate $r$.

Two major changes now occur for the model being analyzed for the thesis. The
first is to include the movement of the susceptible class. This is more logical since noticeably infected people do not usually travel. This can be due to either not feeling well enough for it, or not being allowed to as is indicative with the airlines industry. In this case, since we are considering migration, we will also consider the change in size of the populations. In the model for Liebovitch and Schwartz [13], the populations are considered constant since the size of migrating population compared to total population is negligible. Though small, there is general curiosity if it will matter or not. Since we will also be considering movement of the susceptibles, this increase in the total migrational population, which could cause a significant change to the overall population of any one population class to warrant its tracking. We still assume that the sum of all populations is constant.

We hope to answer several questions and observe several situations. The first question is can migrational effects induce an endemic state in a population where one does not currently exist. The second is can curbing the rates of migration, or any other term, cause an endemic state to turn to a dieout state. We will look at both continuous and discrete models for our situation considerations. We will also compare how the different coupling terms, linear migration and mass action mixing, affect the results and long term behaviors of our systems. Lastly, we will look at

![Figure 6: Change in infectives of populations with serial migration.](image-url)
emergent behavior in continuous models with seasonality, using bifurcation software such as AUTO. Included in the analysis will also be typical questions of epidemiology: bifurcations, stability, and long term behavior.

6.2 Our Model

We continue our discussion by considering a continuous $SIR$ system. The main difference between continuous models and discrete models is what aspects of the population we need to keep track of. In discrete systems, we are using more of a mapping idea. We take the dynamics at time $t$ and use it to find the dynamics at time $t+1$. For discrete systems, we need to keep track of all terms that give us the current conditions of the population as well as terms that cause a change to the overall state. In a continuous system, we need only use the terms that cause a change in the particular group we are considering. This can mean that the equations are shorter with less terms, though can still give us all the relevant information that we need. For a single population, we have the normalized continuous model

\[
\begin{align*}
\frac{ds}{dt} &= \mu - \beta si - \mu s, \\
\frac{di}{dt} &= \beta si - \gamma i - \mu i, \\
\frac{dr}{dt} &= \gamma i - \mu r.
\end{align*}
\]

In this model, we have $\mu$ as the birth and death rate, $\beta$ as the contact rate, and $\gamma$ as the recovery rate. From this basic model, we can look into several important characteristics. The first is the reproductive ratio, $R_0$. Using the method discussed earlier, we find the reproductive ratio is $\frac{\beta}{\mu+\gamma}$. When this value is less than zero, the disease will die out

\[(s, i, r) = (1, 0, 0)\]
Figure 7: Dieout of Epidemic for $R_0 < 1$

This can also be seen graphically in from Figure 7. As is clear, the disease is fully removed from the population in under three months. When this value is greater than one, the disease will have a stable endemic state. We find this endemic state by setting each equation equal to zero and solving for the variables. Doing so we find

$$s = \frac{\gamma + \mu}{\beta},$$  \hspace{1cm} (68)

$$i = \frac{-\mu (-\beta + \gamma + \mu)}{\beta (\gamma + \mu)},$$  \hspace{1cm} (69)

$$r = \frac{-\gamma (-\beta + \gamma + \mu)}{\beta (\gamma + \mu)}.$$  \hspace{1cm} (70)

This will give us the endemic stable state is, and what fraction of the population each group contains. Once we fill in our parameters, we will have the percentages. For this model, we let $\beta = 1200 \text{ yrs}^{-1}$, $\mu = 0.02 \text{ yrs}^{-1}$, and $\gamma = 100 \text{ yrs}^{-1}$ These values tell us that in the population, roughly eight percent of people will be susceptible, nearly ninety-two percent of people will be recovered, and a very small amount, far less than one percent, will be infected. This can also be seen from Figure 8.

Though this may sound small, it can still present a very large problem when
one considers the size of the population. For example, let us say the disease, whose parameters fit measles, is in the USA. This would mean the endemic stable state is

\[(s, i, r) = (2.1671 \times 10^7, 47656, 2.3828 \times 10^8).\]  

This would be a larger outbreak than reported cases of influenza strains A and B for all of 2008 [2]. The infected class may not make up a significant portion of the population, but having at a steady state of tens of thousand of people sick is alarming.

### 6.2.1 Periodic Solutions

Though the current model can predict disease behavior, it is not indicative of an important disease dynamic, periodicity. Most diseases have a time of year, or several, in which it is much more likely to catch them then others. The flu, for instance, is much more prevalent in the spring than it is in the winter. To give us this periodicity,
we change the contact rate term

$$\beta(t) = \beta (1 + \rho \cos(2\pi t)) .$$  \hspace{1cm} (72)

This method has been used in numerous works [12, 10, 13, 7] and has been verified by real world data. The introduction of \( \cos(2\pi t) \) gives a variable fluctuation to the term that is determined by the coefficient \( \rho \). This causes the disease to become periodic. What period is induced depends on what values of the parameters the model is given.

This changes our model to

\[
\begin{align*}
\frac{ds}{dt} &= \mu - \beta (1 + \rho \cos(2\pi t)) s i - \mu s , \\
\frac{di}{dt} &= \beta (1 + \rho \cos(2\pi t)) s i - \gamma i - \mu i , \\
\frac{dr}{dt} &= \gamma i - \mu r ,
\end{align*}
\hspace{1cm} (73, 74, 75)
\]

Where the only difference from Eqn. (64) is the forcing term on the contact rate. This new population system can lead to different outbreak behaviors.

From Figure 9, it can be seen that if the model is given parameter values for a typical measles outbreak, the value of \( \rho \) changes the periodic nature of the disease.
With this periodic nature, we cannot find a steady state solution, since none exists. What we do have is a stable limit cycle. The periodic repetition we see comes about as a multiple of the forcing period. In a period two outbreak, for example, the disease is seen to follow a fixed pattern that repeats every two years. We can determine what will happen in the future based on the periodic nature.

6.2.2 Bifurcation Analysis

We continue with a bifurcation analysis of the system as we vary the forcing rate $\rho$. Our first method is by iteration using Matlab. In this program we will trace the stable orbits for different $\rho$ values. Once we have covered all initial condition combinations and allowed our time series to continue long enough to fully remove transients, we can see the periodic solutions.

Figure 10 shows the the period one bifurcation in blue and the period three bifurcation in red. Looking at the blue curve, we see that around $\rho = .05$ the period one becomes a period two. This is one of the bifurcations we were looking for. We can also see that the period three has a saddle node around $\rho = .05$, since to the left of
the point the periodic orbit does not exist, and to the right it has two branches.

In order to fully understand how the population will move from one periodic solution to another, we do a full bifurcation analysis in AUTO. AUTO is a standard bifurcation analysis software program that will trace out the bifurcations of the periodic orbits, whether they are stable or not. It then determines what kinds of bifurcations the system undergoes. We see from Figure 11 that the full bifurcation picture is much more detailed than the one we found by iteration using Matlab in Figure 10. We can now see just how the population dynamics changes as we alter the forcing amplitude parameter $\rho$. For small enough values, $\rho < .04$ the only stable behavior is a period one. As $\rho$ increases, other behaviors begin to appear. Which behavior the system will undergo depends on where the population is at that time. If $\rho = .06$, the population could experience either a period two or period three outbreak. The actual behavior of the infective class will be determined by the initial conditions for the system. We also see that after about $\rho = .1$, the period doubling cascade leads to chaos. After that point, it is not possible to predict with any certainty what behavior the population will experience over a long period of time. Chaos is marked by the inability to accurately predict long-term behavior in a deterministic system.
7 Continuous SEIR Models

We now further our study of measles from a theoretical model to a real world simulation. Further, we add another class to the populations, exposed. Exposed are people who have come in contact with the disease but are not yet infectious, often called a latency period. The disease is in an incubation stage for several days until it becomes a full blown infection. As before, we will look at the case of one population, than examine two populations. With these two populations connected through migration, we wish to see what sorts of dynamics are present and how best to control them through the migration.

7.1 Motivation

The country of Cameroon, located on the western side of Africa, has experienced outbreaks of measles in the recent past. Not until a few years ago their was no vaccination strategy, so therefore the disease was endemic in the country. The size of these outbreaks and timing are split across an unofficial north south division. The northern half of the country experiences an outbreak every year. The southern half of the country experiences a severe outbreak every three years. As can be seen in Figure 12, a period three outbreak might occur less often, but the amount of people who catch a disease from it is far greater than other who catch it in a period one. In general, it can be seen that the higher the period, the higher the amplitude of the outbreak. These outbreaks have lead to some persistent problems for the country as a whole. The goal is to find out how the migration of people between the north and south affects the outbreak potentials. It is considered if there is a movement strategy that would decrease the overall outbreaks the two halves experience. Could an increase or decrease in migration destabilize the high amplitude outbreaks and lead to lower amplitude outbreaks?
7.2 Single Population

The normalized model we are working with is

\[
\frac{ds}{dt} = \mu - \beta(1 + \rho \cos(2\pi t))si - \mu s , \tag{76}
\]

\[
\frac{de}{dt} = \beta(1 + \rho \cos(2\pi t))si - \delta e - \mu e , \tag{77}
\]

\[
\frac{di}{dt} = \delta e - \gamma i - \mu i , \tag{78}
\]

\[
\frac{dr}{dt} = \gamma i - \mu r . \tag{79}
\]

Since the values for these compartmental groups can often be very small for all but \( s \), we instead use an exponential substitutions

\[
X_1 = e^s , \tag{80}
\]

\[
X_2 = e^e , \tag{81}
\]

\[
X_3 = e^i , \tag{82}
\]

\[
X_4 = e^r . \tag{83}
\]

The second part of the substitution follows directly from the chain rule. Using these
conversions, we find the reformed equations to be

\[
\begin{align*}
\frac{dX_1}{dt} &= \mu \exp(-s) - \beta(1 + \rho \cos(2\pi t)) \exp(i) - \mu, \\
\frac{dX_2}{dt} &= \beta(1 + \rho \cos(2\pi t)) \exp(-e + s + i) - \delta - \mu, \\
\frac{dX_3}{dt} &= \delta \exp(e - i) - \gamma - \mu, \\
\frac{dX_4}{dt} &= \gamma \exp(i - r) - \mu.
\end{align*}
\]

(84) (85) (86) (87)

7.2.1 Bifurcation Analysis

With this model complete, we can now begin to study its bifurcations. We have two different tools to study bifurcations. The first is Matlab, which can find us stable periodic orbits. Using Matlab, we can judge what happens to the observed behavior of the system while varying the forcing rate \( \rho \). We are going to set the parameters as follows: \( \delta = 35.84 \text{ yrs}^{-1}, \ \gamma = 100 \text{ yrs}^{-1}, \ \text{and} \ \beta = 900 \text{ yrs}^{-1}. \) We will also consider this varied forcing for both populations, so \( \mu \) is defined for the particular picture we wish to find.

![Figure 13: Bifurcation for \( \mu = 0.0329 \text{ yrs}^{-1} \) using time series](image)

As can be seen, a birth rate of \( \mu = 0.0329 \text{ yrs}^{-1} \) we see a predominately stable period one. As \( \rho \) is increased, this predominate behavior gives way to a period two
around \( \rho = 0.18 \). We also see there is a small window of a stable period three giving way to a period six and so on down the doubling cascade. This behavior, however, appears to fully destabilize and join back up with the period one at around \( \rho = 0.14 \).

Now that we know the stable behaviors of one population, we can look and see what happens in the other.

Figure 14 has many similar characteristics of the first that just occur and different values. The period doubling from one to two now occurs around \( \rho = 0.55 \), where the period three behavior occurs later and lasts for longer. Also, the period 3 doubling cascade has a larger amplitude in this population than it did in the first.

These two pictures show us what the general behaviors of the two populations do as we increase the forcing rate \( \rho \). Since these are the stable behaviors, we know what visible behaviors to expect in the population and which groupings have a bi-stability.

For \( \mu = 0.0329 \text{ yr}^{-1} \), the coexisting behaviors are a period one with the period three doubling cascade. As for \( \mu = 0.0428 \text{ yr}^{-1} \), we have the period two being stable with the period three doubling cascade. These differences in possible stable outbreaks are what will lead us to interesting connection outbreaks.

We again look to the bifurcation diagram compiled by AUTO in order to get a
complete understanding of the system.

From Figure 15, we can see the same stable behaviors that were shown in Matlab. The difference here is that we notice how and where the stability changes occur. We see that the period three behavior and its associated period doubling cascade comes into existence around $\rho = .1$. This agrees with the simulation in Matlab and gives us a better accuracy. We know then that when we traced $\rho$ in the Matlab plot, it seemed that the period three just came into existence. From Auto, we can tell that the period three cascade only occurs in a certain region and can see its stable and unstable branches.

### 7.3 Two Populations

We now consider the case of two connected populations. Since we are using parameters from Cameroon, we need to set one population as the northern region and one as the
southern region.

\[
\begin{align*}
\frac{ds_1}{dt} & = \mu_1 - \beta_1 (1 + \rho_1 \cos(2\pi t) s_1 i_1) - \mu_1 s - c\chi_1 s_1 + \frac{\chi_2 s_2 n_2}{n_1}, \\
\frac{de_1}{dt} & = \beta_1 (1 + \rho_1 \cos(2\pi t) s_1 i_1) - \delta e_1 - \mu_1 e_1 - c\chi_1 e_1 + \frac{\chi_2 e_2 n_2}{n_1}, \\
\frac{di_1}{dt} & = \delta e_1 - \gamma i_1 - \mu_1 i_1 - c\chi_1 i_1 + \frac{\chi_2 i_2 n_2}{n_1}, \\
\frac{dr_1}{dt} & = \gamma i_1 - \mu_1 r_1 - c\chi_1 r_1 + \frac{\chi_2 r_2 n_2}{n_1}, \\
\frac{ds_2}{dt} & = \mu_2 - \beta_2 (1 + \rho_2 \cos(2\pi t) s_2 i_2) - \mu_2 s_2 - c\chi_2 s_2 + \frac{c\chi_1 s_1 n_1}{n_2}, \\
\frac{de_2}{dt} & = \beta_2 (1 + \rho_2 \cos(2\pi t) s_2 i_2) - \delta e_2 - \mu_2 e_2 - c\chi_2 e_2 + \frac{c\chi_1 e_1 n_1}{n_2}, \\
\frac{di_2}{dt} & = \delta e_2 - \gamma i_2 - \mu_2 i_2 - c\chi_2 i_2 + \frac{c\chi_1 i_1 n_1}{n_2}, \\
\frac{dr_2}{dt} & = \gamma i_2 - \mu_2 r_2 - c\chi_2 r_2 + \frac{c\chi_1 r_1 n_1}{n_2}.
\end{align*}
\] (88-95)

where population one is the northern half and population two is the southern half. The parameter \( \chi \) is the migration rate for the populations and \( c \) is a scaling parameter. We wish to keep the size of both populations constant to ensure survival of the population. Since population one is larger than population two, we use the factor \( c \) to scale the migration to keep the population sizes constant.

We arrive at the value of \( c \) through a simple calculation. First, we consider only the migrating parts of each population.
At this point we sum up the compartments of population one and set it equal to the sum of the compartments of population 2

\[
\frac{ds_1}{dt} + \frac{de_1}{dt} + \frac{di_1}{dt} + \frac{dr_1}{dt} = \frac{ds_2}{dt} + \frac{de_2}{dt} + \frac{di_2}{dt} + \frac{dr_2}{dt}.
\]

(104)

At this point we solve Eqn. (104) for \(c\) and find

\[
c = \left(\frac{n_2}{n_1}\right)^2
\]

(105)

For this model of measles in Cameroon, we find \(c = 5.26\). So, in order to keep the population sizes constant, we must move about five times the amount of people from population one as that of population two.

A consideration needed before analysis of this multipopulation model is the reasoning we use. The first piece we consider is that even though the populations are of constant size and migration rate for given \(\chi\), the population is changing. The change occurs in the makeup of the population. Since each population is migrating a
proportional size of each compartment that makes up the population, a net change in a compartment can happen between populations even when a net change of population size does not occur. This is because each population could be having a different dynamic in relation to the disease. Population two could be experiencing a high amplitude outbreak while population one experiences a low amplitude outbreak. More people would be in the exposed and infected compartments for the high amplitude outbreak as compared to the low amplitude outbreak. This causes the high amplitude population to send more exposed and infected into the low amplitude population than they receive. The migration is a snapshot of the dynamics of the population it comes from, and can therefore have an impact on the other population.

One last consideration needed before analyzing the system is the assumptions we will be making. The first assumption is that a population is homogeneously mixed, and that this even mixing allows us to pull the correct amount of each compartment for migration. We also assume that the the recovereds migration will not affect the disease dynamics. This is probably not the case, but for this model we will not consider that group to be moving. Since we know that $S + E + I + R = N$ and that each population is held at a constant size, if we keep track of the number of people in three of the compartments, we can know how many people are in the last. We track the recovereds by knowing the sizes of the other groups in order to decrease the number of equations needed in our solution methods and as a result means that the recovered group is not taken into consideration since they can no longer contribute to the disease in any way.

7.3.1 Periodic Behavior changes due to Migration

We now consider what happens to an outbreak in each population as we change the migration rate. To begin with, we will consider a theoretical outbreak. In this outbreak, both the northern and southern portions experience a period six epidemic. The period six is really just a period three where two outbreak peaks differ by a slight
amount. This scenario agrees with the high amplitude period three outbreaks we see in Cameroon.

We start by connecting the populations with a migration rate of $r_2 = .007$. This small migration rate is then changed to see what new behaviors, if any, the two populations will experience as a result of either an increase in movement or a decrease in movement.

![Figure 16: Increase in migration rate at time = 20](image)

We first increase the migration rate of the populations to observe what happens. As we see from Figure 16, the outbreak sizes in both populations decrease. The outbreak maximum in population two, corresponding to $\mu = .0329 \text{ yrs}^{-1}$, is decreased more than that of population one, which corresponds to $\mu = .0428 \text{ yrs}^{-1}$. This, however, is a bit misleading. Since population one is over twice as large as population two, a small decrease in its outbreak size causes a much more drastic reduction in the number of infectives in that population. Figure 16 shows that each population has its period six behavior destabilize into a period two behavior. This period modification causes a substantial reduction in the infective class of each population, where population one feels the reduction most.

We now decrease the migration rate of the populations. In this case, a strict quarantine is placed upon the populations in which no movement between them is allowed.
Figure 17: Decrease in migration rate at \textit{time} = 20

This leads to some unexpected behaviors. As shown in Figure 17, each population sees a decrease in their respective period behaviors, but an increase in epidemic size. Though the increase for population two is slight, there is a significant increase in epidemic size for population one. This increase means thousands more people in that population will catch measles, each with a chance of spreading the disease to others. This shows that once a disease is injected into a population, a quarantine is not effective at stopping an outbreak. A quarantine is only truly effective if it can be placed between the populations before the disease is introduced into both populations. Once the disease is endemic in both groups, it is too late for a quarantine to be effective. Also, placing a quarantine before an outbreak occurs is difficult. In the beginning of a disease being introduced into a population, it undergoes exponential growth. So in a very short amount of time, the disease has already approached the endemic state. Also, since measles has a latency period, people in the exposed group could migrate into another population and will not show the fact they have the disease for up to nine days. Once a population starts to see people with the disease among its people, it is too late. If a disease will naturally persist in a population, than nothing can be done to keep that from happening in terms of migration.
8 Conclusions

In this thesis, we have studied different models for measles and the results we can obtain from them. Though the outcomes we were looking for are similar, the methods and practices to reach them were different.

In the discrete SIR model, we primarily studied how migration affects outbreaks in steady state cases. For these cases, exact solutions can be found, though they might be too complicated as to allow for meaningful understanding. The stability of these exact solutions can be analyzed and a method of destabilization of the endemic equilibria was studied. It was found that once two populations are connected, either unilaterally or bilaterally, an endemic cannot be stopped. If one population is going to experience an outbreak of measles, nothing short of eliminating the infected from the population can cause the disease to die out. The migration only changed the size of the outbreaks, but could not stop them. We also found that the maximum outbreak in two connected populations can be found by a ratio of their migration rates. For the case of population two being larger than population one, the maximum outbreak occurred at $r_1 = .5r_2$.

In the continuous models, we changed our steady state equations into periodic equations. By adding a forcing term, we are able to more accurately describe disease transmission in a year. We add seasonality since most diseases are more prevalent in certain seasons than in others. The purely biological reasons for seasonality behavior aside, we found that now only periodic solutions would present themselves, and no fixed point solutions exist. We turned to the bifurcation analysis in order to study the stable periodic orbits. The bifurcation analysis allows us to monitor the changes in periodic behaviors as different parameters changed.

In the SIR system, we studied a theoretical model that exhibited a deep bifurcation picture as the forcing rate $\rho$ was changed. We saw a multitude of possible behaviors with their own attractors and stable manifolds. In further work, the man-
ifolds and basins of attraction could be analyzed at to see what periodic solutions are most likely. The migration induced between the populations led to many more unique periodic couplings than a single population could see. If one population was undergoing a period two behavior, and the other was undergoing a period three behavior, we were able to find a stable period six that did not exist in the region or population. These findings help to show just how much the solutions of a system can change when it goes from isolation to migrational mixing.

For SEIR models, we applied the techniques to a real world example, the country of Cameroon. With their different periodic measles outbreaks between the northern and southern regions, we were able to look at the situation from a bifurcation perspective. In the analysis, it was found that the behavior seem in the country could not be explained solely with migration, leading to the conclusion that it must be more of a mixing, or mixing and migration, problem. We did find, however, that quarantines are not always the best option. Though there might be an overall drop in the percent of infectives when considering both populations, the actual numbers can increase. This increase is due to the fact that the two populations are very different in size. A small increase in the percent of infectives of one population could mean a very substantial increase in the other population when considering actual amounts. We learned that in order to do what is best for a population, one must be able to accurately demonstrate the behavior seen and analyze the bifurcations in order to come to a usable solution.

In the end, the only way to curb an outbreak, or to stop it outright, is to understand the dynamics behind it. If we wish to make the world safer, we must first know how exactly the disease is behaving or will behave in a population. We must also know how interactions with other population groups will play a role in the overall dynamics of the population we are considering. Only when we are armed with this knowledge will policy be at its most effective.
References


