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Population models

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Abstract

This thesis will examine mathematical interpretations of biological situations through the study of differential equations. It will first explore the interactions of the lynx and hare populations in Canada based on data retrieved by the Hudson Bay Company. The purpose of this study is to find a suitable mathematical model, namely that of a three-variable Lotka-Volterra system. Also, the paper will explore short-term infectious disease models as they relate to particular epidemics throughout history, including the Iowa Mumps outbreak of 1966 and the Bubonic Plaque. The thesis will then work to make sense of the rise and fall patterns in the data through analysis of the models. Finally, the paper will develop the concept of long-term infectious diseases and cell-to-cell spread as a means for understanding a component of some very complicate diseases such as HIV and herpes; it will not get too deep into examples in this last section, but rather will set up some models to work with and some areas for further research.

Acknowledgements

First and foremost I would like to thank my advisor Dr. Dale Garraway for all his support and help along the way. I would also like to thank my family and friends for all of their support and the EWU Mathematics Department as well as the rest of my thesis committee .

Contents

Chapter 1

Introduction

This thesis will take us on a journey designed to develop understanding of the role differential equations play in the study of mathematical biology. First, we will explore the inter-workings of differential equations, discussing what they are and what their solutions look like. We will also develop how to solve differential equations both in the general setting and with respect to particular criteria. After getting a feel for what differential equations are, we will discuss some ways to work with systems of differential equations. We will establish how to solve systems of differential equations using differentials, which we will define, as well as explore Jacobian matrices as they relate to this study. The topic of equilibria and stability will make up a lot of the material in Chapter 2, as it is the basis for much of what we will be studying in later chapters. We will develop a strong background of how to use eigenvalues and eigenvectors to determine stability as it will be integral to later work. Finally, the last piece to explore before we are ready to move into modeling will be the concept of invariance which we will use in Chapter 3 to show that if a particular species becomes extinct in a mathematical model it will not reappear. Once we have

all these tools in place for working with differential equations, we can begin to develop models using systems of differential equations that we will use in varied biological settings.

The first actual model we will explore is the two-variable Lotka-Volterra predator-prey model. The Lotka-Volterra predator-prey model was proposed independently by the American biophysicist Alfred Lotka in 1925 and the Italian mathematician Vito Volterra in 1926. It was one of the earliest predator-prey models to be based on solid mathematical principles [30]. As we will see, the model is centered around first-order non-linear differential equations. It is used to describe the interactions between two species in an ecosystem, one a predator and the other its prey. This model forms the basis of many of the models used currently in the analysis of population dynamics.

In our study of the Lotka-Volterra model in Chapter 3 we will attempt to describe data from the Hudson Bay Company in Canada, a fur-trading company from western Canada We will be particularly interested in what they discovered regarding the oscillating relationship between the snowshoe hare and the lynx populations. This model will be developed and analyzed as it relates to the data.

After developing the two variable model and analyzing the data from the Hudson Bay Company, we will work to understand a three-variable model as an attempt to find a model better suited to what happens in nature. We will go through much of the same analysis as we did in the two variable case just with an added layer of complexity. After establishing the characteristics of this model we will again evaluate it's reasonableness to the Hudson Bay data. This will conclude our study of predator-prey models.

The next type of models we will examine deal with infectious diseases.

We will develop three different models in Chapter 4, as well as examine how they work in the context of several real life illnesses. We will start with simple compartmental models and add in some different options for what can happen to a person after they have contracted a particular disease. The models for infectious diseases that we will study come from A. G. McKendrick and W.O. Kermack whom together developed a series of models of how infectious disease is spread through a population. Their theory was published in a set of three articles in 1927,1932 and 1933 building off the research of some other important scientists such as Daniel Bernoulli and Ronald Ross. The models discussed by McKendrick and Kermack are vast and encompass several different modifications, thus we will only be able to discuss a few of the proposed models.

All of the models we explore in Chapter 4 deal with a relatively short time scale, thus we are able to neglect non-disease related birth and death rates, but since not all diseases are short in duration relative to the life of their host, discussing diseases in which birth and death play a role in the total population will be an interesting contrast. In Chapter 5, we will develop models that encompass non-disease related birth and death rates within their systems. Specifically, we will discuss models developed to study cell-to-cell spread of diseases, models that could be used to study HIV and herpes for example.

Finally, the thesis will conclude with some limitations and results of the research as well as areas for further study.

Chapter 2

ODE Basics

The mathematical models that we will explore in the upcoming chapters are centered around ordinary and partial differential equations. Before we can explore these models we must first understand what ODEs and PDEs are in addition to how to work with them.

2.1 Basic Definitions and Terminology

Definition 2.1 *Differential Equation: An equation containing the derivatives or differentials of one or more dependent variables, with respect to one or more independent variables [16].*

The first category of differential equations we will look at are called ordinary differential equations.

Definition 2.2 *Ordinary Differential Equation: A differential equation containing only ordinary derivatives of one or more dependent variables, with respect to a single independent variable [16].*

Example 2.3 *An ODE that we classify as a first order ODE, has highest order differential degree one*

$$\frac{dy}{dt} - 5y = 1.$$

A second order ODE highest order differential of degree two

$$\frac{d^2y}{dx^2} - d\frac{dy}{dx} + 6y = 0.$$

Throughout the majority of this thesis we will be primarily looking at first order ODE's, but it is good to understand ODE's of higher order as well. Another type of differential equation we will see is called a partial differential equation.

Definition 2.4 *Partial Differential Equation: An equation involving the partial derivatives of one or more dependent variables of two or more independent variables [16].*

Example 2.5 *An example of a partial differential equation of first order*

$$\frac{\partial u}{\partial y} = -\frac{\partial v}{\partial x}$$

whereas the following is called a second order partial differential equation

$$\frac{\partial^2 u}{\partial x^2} = \frac{\partial^2 u}{\partial t^2} - 1\frac{\partial u}{\partial t}.$$

In the sections to follow we will be dealing with both linear and non-linear differential equations. Linear differential equations are characterized by two properties:

1. The dependent variable and all its derivatives are of the first degree; that is, the power of each term involving the dependent variable is one.

2. Each coefficient depends on only the independent variable.

All other differential equations are classified as non-linear [16].

Example 2.6

Linear:

$$xdy + ydx = 0$$

$$y'' - 2y' + y = 0$$

Non-linear:

$$yy'' - 2y' = x$$

$$\frac{d^3y}{dx^3} + y^2 = 1$$

Now that we understand what differential equations are, we can begin to explore how to solve differential equations and interpret what their solutions mean.

Definition 2.7 *Solution of a Differential Equation: Any function f defined on some interval I, which when substituted into a differential equation reduces that equation to an identity, is said to be a solution of the equation on the interval [16].*

We can verify that a particular equation is a solution by substituting it into a given differential equation.

Example 2.8 *Verify that*

$$y = e^{3x} + 10e^{2x}$$

is a solution to

$$\frac{dy}{dx} - 2y = e^{3x}.$$

Consider

$$\frac{dy}{dx} = y' = 3e^{3x} + 20e^{2x}$$

then substitute $\frac{dy}{dx}$ *and* y *in to the ODE to get*

$$3e^{3x} + 20e^{2x} - 2(e^{3x} + 10e^{2x}) = e^{3x}.$$

Distributing yields

$$3e^{3x} + 20e^{2x} - 2e^{3x} - 20e^{2x} = e^{3x}.$$

then simplifying leaves

$$e^{3x} = e^{3x}$$

which is always true; therefore y *is a particular solution for the given system.*

When solving differential equations we may get a particular solution, like in the example above, where we have a solution that is independent of arbitrary of parameters or we may end up with a family of solutions. A family of solutions is typically a family of curves or functions containing an arbitrary parameter such that each member of the family is a solution of the differential equation [16]. The following is an example of of a differential equation with a family of solutions.

Example 2.9 *Verify that* $y = cx + c^2$ *is a one-parameter family of solutions to the following equation*

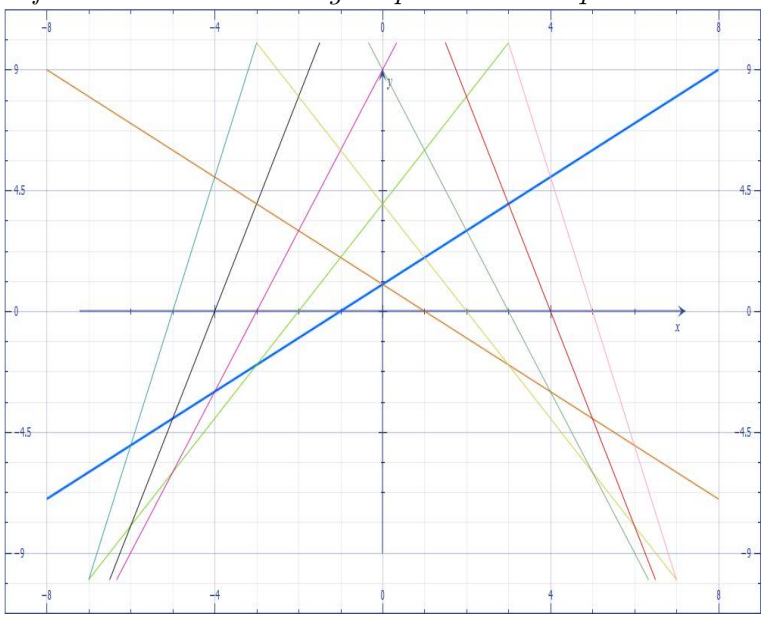
$$y = xy' + (y')^2.$$

Differentiating y *gives* $y' = c$*; therefore*

$$y = xy' + (y')^2 = xc + (c)^2 = cx + c^2$$

which is y *as defined in the family of solutions. The following image shows the family of solutions for this differential equation with each line representative*

of a different pick of for the constant c, including both positive and negative c values. Each of the lines in this image represent a unique solution.



While it is wonderful to be able to verify solutions for differential equations, at some point we do need to be able to solve these equations. Separating variables is a process that allows us to integrate both sides of the equation with respect to a particular variable which equivocally allows us to be able to solve DE's.

2.2 Separable Equations

Definition 2.10 *A differential equation of the form*

$$\frac{dy}{dx} = \frac{g(x)}{h(y)}$$

is said to be separable, or to have separable variables. This means we can write it so that all terms and functions with respect to y can be written on one side and all x on the other side of the equation [16].

Example 2.11 *Solve the following differential equation:*

$$dx - x^2 dy = 0.$$

Adding the second term to both sides yields

$$dx = x^2 dy.$$

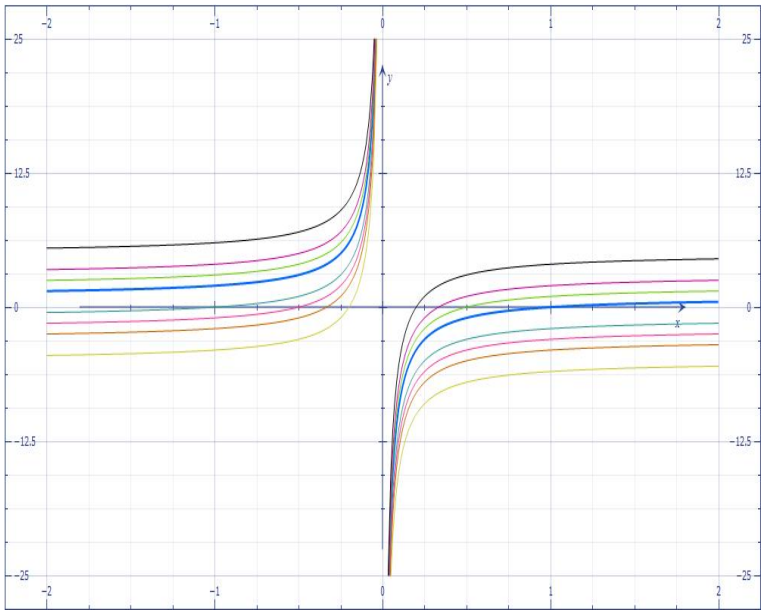
Dividing by x^2 *then gives*

$$\frac{dx}{x^2} = dy$$

then integrating both sides with respect to the respective variables results in

$$-\frac{1}{x} + c = y$$

The following image shows the family of solutions for this differential equation with each line representative of a different pick of for the constant c., each representing a unique solution for the DE.



Separating variables is a technique for solving DE's that will be used in the remaining chapters frequently. The goal is to be able to write the equation

without differentials in order to solve the equation. Now that we are able to write an equation without differentials, we are ready to take the next step of evaluating the DE subject to an initial condition.

2.3 Initial-Value Problems

In the chapters to follow we will often be interested in solving a differential equation

$$\frac{dy}{dx} = f(x, y)$$

subject to a side condition $y(x_0) = y_0$, where x_0 is a number in an interval I and y_0 is an arbitrary real number. Geometrically, we are seeking at least one solution of the differential equation such that the graph of the solution passes through the predetermined point (x_0, y_0). We call problems of this type initial-value problems and the side condition mentioned is known as an initial condition [16]. Initial-value problems usually present themselves as shown below:

$$\text{Solve} \quad \frac{dy}{dx} = f(x, y) \quad \text{subject to} \quad y(x_0) = y_0.$$

The example to follow demonstrates how to solve a particular differential equation subject to a specific the initial condition.

Example 2.12 *Solve*

$$y' + 2y = 1$$

subject to the initial condition

$$y(0) = \frac{5}{2}.$$

Since $y' = \frac{dy}{dt}$ *we can re-write this equation as*

$$\frac{dy}{dx} + 2y = 1.$$

Then separating variables

$$\frac{dy}{dx} = 1 - 2y$$

becomes

$$\frac{dy}{1-2y} = dx.$$

Integrating gives

$$\frac{-\ln(|2y-1|)}{2} = x + c_1$$

and solving for y *yields*

$$\ln(|2y-1|) = -2x - 2c_1.$$

Exponentiating gives

$$2y - 1 = e^{-2x-2c_1}$$

which is equivalent to

$$2y = e^{-2x}e^{-2c_1} + 1.$$

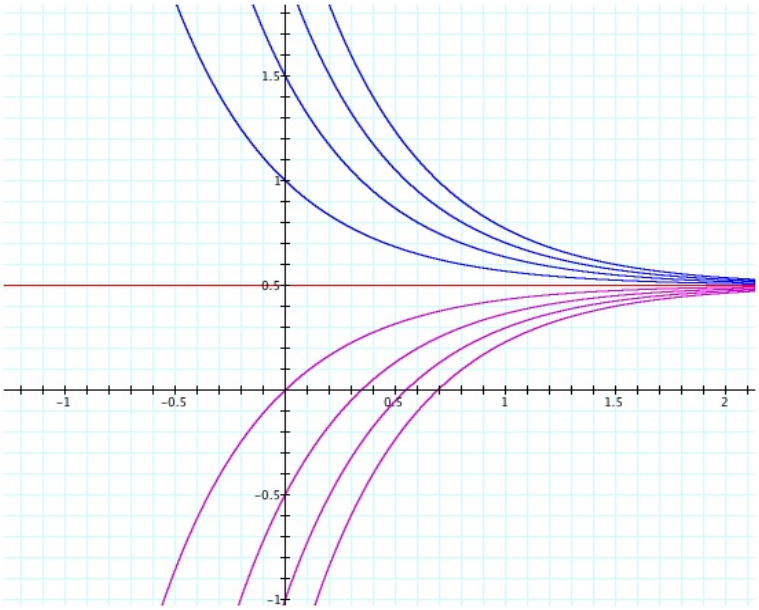
Now since e^{-2c_1} *is just a constant we can replace it with* c *such that* $e^{-2c_1} = c$ *so we can write*

$$2y = ce^{-2x} + 1.$$

Thus,

$$y = \frac{ce^{-2x} + 1}{2}.$$

The following image shows possible solution curves through satisfying this equation. The curves all vary by the constant c *just as in the previous two examples.*



Now that we have solved the differential equation for y we can use the initial condition $y(0) = \frac{5}{2}$ to write

$$\frac{5}{2} = \frac{ce^{-2(0)} + 1}{2}$$

so

$$\frac{5}{2} = \frac{c+1}{2}.$$

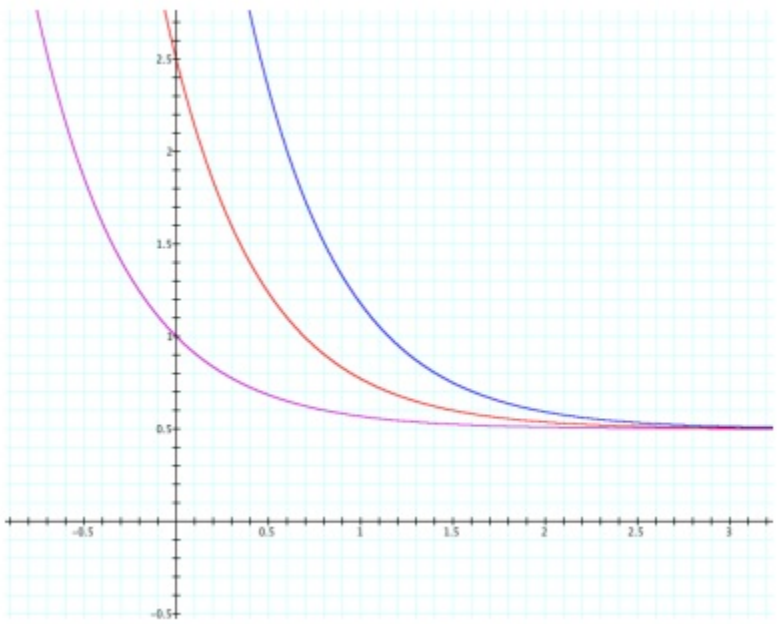
Thus,

$$c = 4.$$

Finally we are able to write the equation for y with respect to this initial value:

$$y = \frac{4e^{-2x} + 1}{2}.$$

Which is represented by the red curve in the image to follow.



The next example we will consider is a rather trivial example of an initial value problem, but it is one that we will see again in our study of infectious diseases thus, it is good to get a feel for it now.

Example 2.13 *Let*

$$\frac{I(\tau)}{d\tau} = -\gamma I,$$

with initial condition

$$I(0) = I_0.$$

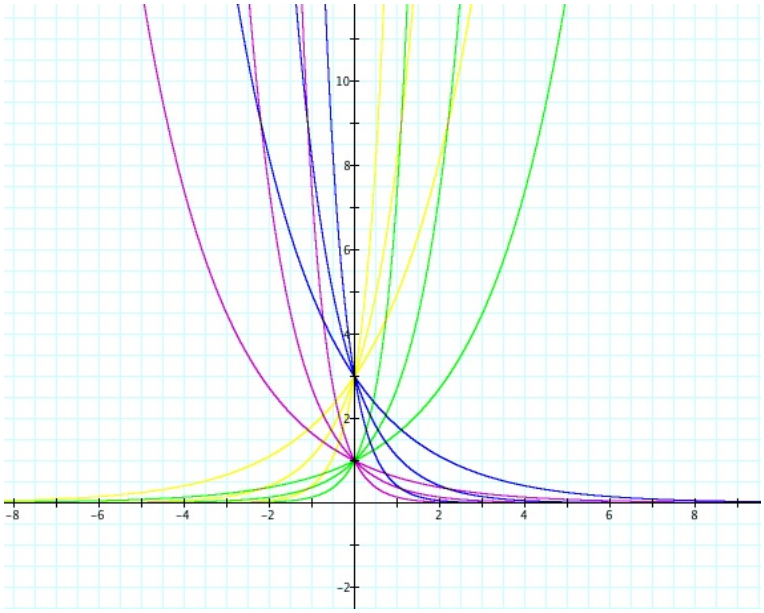
In our study of infectious diseases in Chapter 4, we use I to denote the number of infectious individuals, τ to represent time and γ to denote the rate of recovery from disease. *We can solve this equation to get the number of people in the infectious class at time τ given by*

$$I(\tau) = I_0 e^{-\gamma\tau}$$

since as defined

$$I'(\tau) = -\gamma I_0 e^{-\gamma\tau} = -\gamma I.$$

Notice if $\gamma > 0$ this represents an exponential decay function.



Each family of solution curves corresponds to a particular I_0 with varied γ values.

Also, it is interesting to note that for $\tau \neq 0$,

$$\frac{I(\tau)}{I_0} = e^{-\gamma\tau}$$

gives the proportion of people who are still infectious at time τ. Further from this we can define

$$F(\tau) = 1 - e^{-\gamma\tau}, \quad \tau \neq 0$$

to represent the probability of recovering or leaving the infectious class in the interval of time $[0, \tau)$.

This concludes our study of differential equations in solitary.

2.4 Systems of Differential Equations

Now that we have a feel for differential equations in singular, we will begin our study of how systems of differential equations interact. A system of differential

equations consists of a set of n differential equations with variables $x_1, ..., x_k$. The mathematical models that are introduced in the chapters to follow are based on systems of differential equations, thus it will be useful to obtain a solid understanding of these systems and how they are solved now, so that we have some background exposure as we explore more complicated systems.

Definition 2.14 *Solution of a System: A solution of a system of differential equations is a set of differentiable functions $f_i(t)$ that satisfies each equation of the system on some interval I for any t.*

Example 2.15 *Solve the following system of linear equations*

$$\begin{cases} \frac{dx}{dt} &= 4x + 7y \\ \frac{dy}{dt} &= x - 2y \end{cases}$$

In order to make these easier to deal with we will re-write them with differential operators. The symbol D, called a differential operator possesses a linearity property which means that if D is operating on a linear combination of two differentiable functions, this is equivalent to the linear combination of D operating on the individual functions. Thus, this will allow us to solve the system using simple algebraic techniques.

Re-writing the system with differential operators yields

$$\begin{cases} Dx - 4x &= 7y \\ x &= Dy + 2y \end{cases}$$

Factoring out the x in the first equation and a y in the second equation, then multiplying the second equation by $D - 4$ yields

$$\begin{cases} (D-4)x &= 7y \\ (D-4)x &= (D^2 - 2D - 8)y \end{cases}$$

Subtracting the equations using a process of algebraic elimination gives

$$0 = (D^2 - 2D - 15)y.$$

This is a second-order equation in terms of the differential D.

Note that if this was a first-order equation $\frac{dy}{dx} + ay = 0$, where a is a constant, we would have a general solution of the form $y = c_1 e^{-ax}$. For a second order equation $ay'' + by' + cy = 0$. A solution of the form $y = e^{mx}$ implies that $y' = me^{mx}$ and $y'' = m^2 e^{mx}$, thus we have $am^2 e^{mx} + bme^{mx} + ce^{mx} = 0$ or equivalently $e^{mx}(am^2 + bm + c) = 0$. Then since $e^{mx} \neq 0$ for any real value of x, it is clear that the only way we can satisfy the differential equation is to choose m so that it is a root of the quadratic equation $am^2 + bm + c = 0$. This equation is called the characteristic or auxiliary equation. If the roots of the characteristic equation are real and different from each other we end up with a solution of the from $y = c_1 e^{m_1 x} + c_2 e^{m_2 x}$ [16].

Going back to our example with $0 = (D^2 - 2D - 15)y$ we now consider the characteristic equation,

$$m^2 - 2m - 15 = 0.$$

Factoring gives

$$(m - 5)(m + 3) = 0$$

so that

$$m_1 = 5 \quad \textit{and } m_2 = -3.$$

Thus, since our characteristic equation has distinct real roots, according to [16] the general solution is of the form

$$y(t) = c_1 e^{m_1 t} + c_2 e^{m_2 t}.$$

Therefore, for the particular m-values found we have

$$y(t) = c_1 e^{5t} + c_2 e^{-3t}.$$

Now to find an equation for $x(t)$ we can proceed using the same process or take our solution above and substitute this value into one of the equations in our system. Since we have

$$\begin{cases} Dx - 4x &= 7y \\ x &= Dy + 2y \end{cases}$$

with

$$y(t) = c_1 e^{5t} + c_2 e^{-3t}$$

choosing either equation from the system (the second chosen here) and substituting y yields

$$\begin{aligned} x &= D\left(c_1 e^{5t} + c_2 e^{-3t}\right) + 2\left(c_1 e^{5t} + c_2 e^{-3t}\right) \\ &= 5c_1 e^{5t} - 3c_2 e^{-3t} + 2c_1 e^{5t} + 2c_2 e^{-3t} \\ &= 7c_1 e^{5t} - c_2 e^{-3t} \end{aligned}$$

Thus we conclude

$$x(t) = 7c_1 e^{5t} - c_2 e^{-3t}$$

and

$$y(t) = c_1 e^{5t} + c_2 e^{-3t}.$$

This example shows a particular method for solving systems of differential equations which we will see later on in this thesis. In addition to solving systems however, we will also be highly interested in finding equilibria points and determining their stability, thus in the section and subsequent subsections to follow, we will extensively develop these ideas. In order to make sense of solutions to systems such as these we will be using phase portraits or phase

diagrams. The next subsection will discuss what these are and how they are developed.

2.4.1 Phase Portraits

For a system of linear differential equations $X' = AX$, we can create a phase portrait, or graph showing a representative set of its solutions plotted as parametric curves with parameter t. Similar to a vector field (direction field), a phase portrait is a tool used to visualize how the solutions of a given system behave in the long run. It can also be used to predict the behaviors of a systems solutions, and is especially useful for systems that are difficult to solve.

We will explore the phase portrait attributed to the system from the previous example

$$\begin{cases} \frac{dx}{dt} &= 4x + 7y \\ \frac{dy}{dt} &= x - 2y \end{cases}$$

with solutions

$$x(t) = 7c_1e^{5t} - c_2e^{-3t}$$

and

$$y(t) = c_1e^{5t} + c_2e^{-3t}.$$

We can re-write this system in $X' = AX$ form as follows:

$$\begin{bmatrix} x' \\ y' \end{bmatrix} = A \begin{bmatrix} x \\ y \end{bmatrix}$$

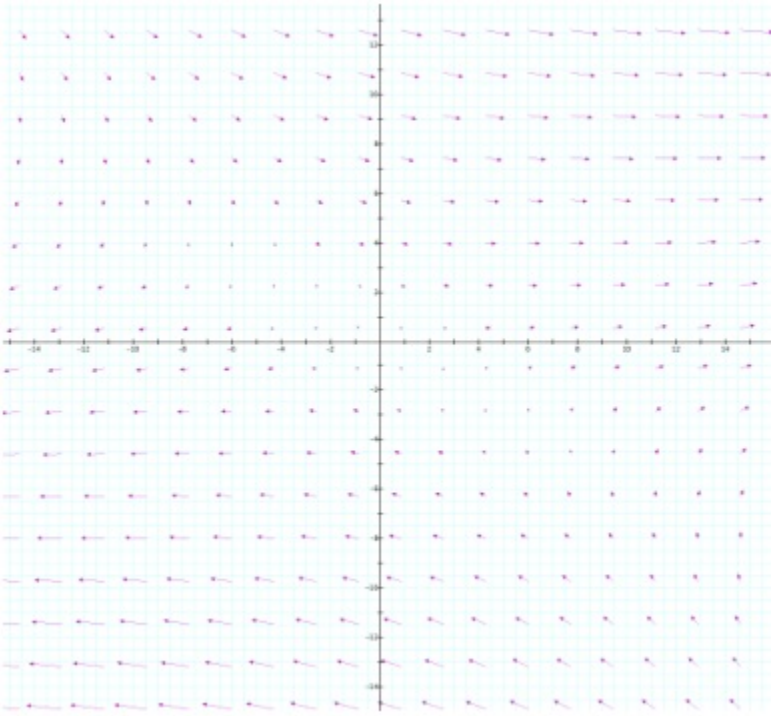
where

$$A = \begin{bmatrix} 4 & 7 \\ 1 & -2 \end{bmatrix}$$

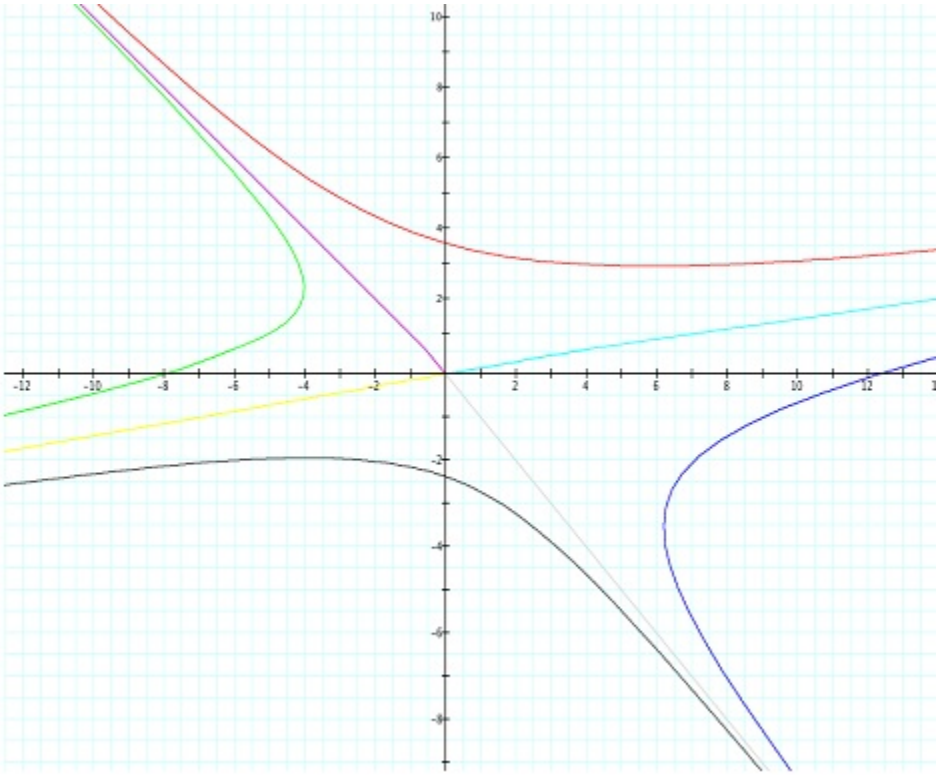
The Cartesian plane where the phase portrait for this system resides is called the phase plane. The parametric curves traced by the solutions are sometimes also called their trajectories.

Graphing the phase portrait for a given system is rather labor intensive, but it is possible to do by hand even without solving the system first. To do so we draw a grid on the phase plane, then at each grid point $x = (a, b)$ we calculate the solution trajectory's instantaneous direction of motion at that point by using the given system of equations to compute the tangent/velocity vector, x'. In short this says we can plug in $x = (a, b)$ to compute $x' = Ax$. This allows us to create a vector field or direction field. The image below shows the vector field associated with the system

$$\begin{cases} \frac{dx}{dt} &= 4x + 7y \\ \frac{dy}{dt} &= x - 2y \end{cases}$$



To find the phase portrait of this system we choose a starting point and trace curves by following the vectors shown. This is possible to do by hand, but computer algorithms have made this process much easier. The following image represents possible phase portraits for the system.



The curves in this phase portrait are graphed using computer software following the trajectories found from the vector field associated with the system. The curves represent possible solution curves for the system with varied constants c_1 and c_2 from the solutions

$$x(t) = 7c_1e^{5t} - c_2e^{-3t}$$

and

$$y(t) = c_1e^{5t} + c_2e^{-3t}$$

already found. Note that in this phase portrait, if $c_1 = 0$, the function exists only for negative x-values and further takes the shape of a line from the origin with slope -1, as depicted by the lines in purple and gray. If $c_2 = 0$ then the graph exists for only positive x-values and has a slope of $\frac{1}{7}$ from the origin as we can see from the light blue and yellow lines. Further we note that in

general if $c_1 > c_2$ the influence of e^{5t} is stronger as seen in the the red curve where $c_1 = 3 > c_2 = 1$. Whereas if $c_2 > c_1$ the influence of e^{-3t} is stronger, which can be seen in the graphs of the green and dark blue curves.

Now that we have an understanding for what phase portraits are and how they can be calculated we are ready to move into a discussion of equilibia points. Note however, phase portraits will appear throughout this thesis as tools for understanding and visualizing relationships in complicated systems. Phase portraits will also be used in 3-dimensional spaces in a similar way in the chapters to follow.

2.5 Equilibria and Stability

Equilibria, also known as stationary points, are points where there is no movement in the system. Throughout the remaining chapters we will determine stability of different equilibrium points in order to determine how certain systems behave near a particular point. It will be helpful to get a thorough understanding the the terminology surrounding these concepts before we move on to the remaining chapters thus, this is what we will aim to do in the next several pages.

Intuitively, an equilibrium is stable if the system returns to the equilibrium when perturbed and unstable otherwise. More precisely, a system is locally stable if for an arbitrary perturbation away from the equilibrium, the systems stays near the equilibrium. If additionally, the system approaches the equilibrium through time, it is said to be locally asymptotically stable. One way to think about a stable point is to think about a marble in the bottom of a bowl; if we tap the marble it will return to the bottom of the bowl. Unstable on the other hand is like balancing a pencil on a table; a small tap will knock

this pencil away, not to return to it's original location.

The concept of global stability will also come up since this allows us to consider perturbations of an arbitrary size within the confines of a particular model, unlike local stability. This is useful when we do not want to restrict ourselves to arbitrary small perturbations. Note though, that we still need to stay within the confines of the particular model or system in which we are working. This means we cannot introduce anything new into our model or remove anything that is not present in the beginning. Biologically, in the models we will explore in Chapter 3 for example, this implies no introduction of new species or extinction of species in the model, as well as no negative populations.

Before we can begin to understand stability analysis we first must define eigenvalues and eigenvectors which will help us to algebraically determine the stability of each equilibria point.

2.6 Eigenvalues, Eigenvectors and Jacobian Matrices

Eigenvalues are a special set of scalars associated with a linear system of equations, sometimes called characteristic roots or characteristic values. Determination of eigenvalues and their corresponding eigenvectors for a particular system arise in common applications such as stability analysis, the physics of rotating bodies and small oscillations of vibrating systems.

The study of eigenvalues and eigenvectors is linked to the study of matrices. Several times throughout this thesis we will consider the Jacobian matrix of a system which is formed by the partial derivatives of the system as

we can see in the following example.

Example 2.16 *Given the linear system*

$$\begin{cases} f(x) &= x_1 + 2x_2 + x_3 \\ g(x) &= 6x_1 - x_2 \\ h(x) &= -x_1 - 2x_2 - x_3 \end{cases}$$

we can find the Jacobian matrix of this system by considering

$$\begin{bmatrix} \frac{df}{dx_1} & \frac{df}{dx_2} & \frac{df}{dx_3} \\ \frac{dg}{dx_1} & \frac{dg}{dx_2} & \frac{dg}{dx_3} \\ \frac{dh}{dx_1} & \frac{dh}{dx_2} & \frac{dh}{dx_3} \end{bmatrix} = \begin{bmatrix} 1 & 2 & 1 \\ 6 & -1 & 0 \\ -1 & -2 & -1 \end{bmatrix}.$$

Re-writing a system of linear equations as a Jacobian matrix, will be helpful in determining valuable information for our ODE systems as we progress. We say that an eigenvector of a square matrix $\mathbf{A}$ is a non-zero vector $\mathbf{V}$ that, when multiplied by $\mathbf{A}$, yields the original vector multiplied by a single number λ, where λ is called an eigenvalue.

Definition 2.17 *Eigenvalues and Eigenvectors: Let* $\mathbf{A}$ *be an* $n \times n$ *matrix. A number* λ *is said to be an eigenvalue of* $\mathbf{A}$ *if there exists a nonzero solution vector* $\mathbf{V}$ *of the linear system* $\mathbf{AV} = \lambda\mathbf{V}$*. The solution vector* $\mathbf{V}$ *is said to be an eigenvector corresponding to the eigenvalue* λ *[16].*

Example 2.18 *To find the eigenvector* $\mathbf{V}$ *we begin by looking at*

$$\det(\mathbf{A} - \lambda I) = 0.$$

Let $\mathbf{A}$ *be defined from the system in Ex 2.16 so that the Jacobian matrix*

$$\mathbf{A} = \begin{bmatrix} 1 & 2 & 1 \\ 6 & -1 & 0 \\ -1 & -2 & -1 \end{bmatrix}.$$

The determinant can be found

$$\det(\mathbf{A} - \lambda I) = \begin{bmatrix} 1-\lambda & 2 & 1 \\ 6 & -1-\lambda & 0 \\ -1 & -2 & -1-\lambda \end{bmatrix}$$

$$\begin{aligned}
&= (1-\lambda)[(-1-\lambda)(-1-\lambda) - (-2\cdot 0)] - 2[(6\cdot(-1-\lambda) - (-1\cdot 0)] + 1[(6\cdot -2) + (-1-\lambda)] \\
&= (1-\lambda)[1+2\lambda+\lambda^2] - 2[-6-6\lambda] + 1[-12-1-\lambda] \\
&= 1+2\lambda+\lambda^2-\lambda-2\lambda^2-\lambda^3+12+12\lambda-13-\lambda \\
&= -\lambda^3-\lambda^2+12\lambda \\
&= -\lambda(\lambda^2-\lambda-12) \\
&= -\lambda(\lambda-4)(\lambda+3) \\
&= 0
\end{aligned}$$

$$\textit{So} \quad \lambda_1 = 0, \quad \lambda_2 = 3 \quad \textit{and} \quad \lambda_3 = -4.$$

These three numbers are the respective eigenvalues of $\mathbf{A}$*. Each eigenvalue has its own corresponding eigenvector. The eigenvector corresponding to each can be found as follows by substituting the particular* λ*'s in and row-reducing using Gauss-Jordan elimination:*

- *For* $\lambda_1 = 0$ *we get*

$$(\mathbf{A} - 0I) = \left[\begin{array}{ccc|c} 1 & 2 & 1 & 0 \\ 6 & -1 & 0 & 0 \\ -1 & -2 & -1 & 0 \end{array}\right] = \begin{array}{r} R_1 \\ -6R_1 + R_2 \\ R_1 + R_3 \end{array} \left[\begin{array}{ccc|c} 1 & 2 & 1 & 0 \\ 0 & -13 & -6 & 0 \\ 0 & 0 & 0 & 0 \end{array}\right]$$

$$= \begin{matrix} \frac{1}{-13}R_2 \\ \\ \end{matrix} \left[\begin{array}{ccc|c} 1 & 2 & 1 & 0 \\ 0 & 1 & \frac{6}{13} & 0 \\ 0 & 0 & 0 & 0 \end{array}\right] = \begin{matrix} -2R_2 + R_1 \\ \\ \end{matrix} \left[\begin{array}{ccc|c} 1 & 0 & \frac{1}{13} & 0 \\ 0 & 1 & \frac{6}{13} & 0 \\ 0 & 0 & 0 & 0 \end{array}\right]$$

Therefore,

$$v_1 = \frac{-1}{13}v_3 \quad v_2 = \frac{-6}{13}v_3 \quad v_3 = t$$

where t is some parameter. If we choose $t = 13$ then the eigenvector we get corresponding to $\lambda_1 = 0$ is

$$V_1 = \begin{bmatrix} -1 \\ -6 \\ 13 \end{bmatrix}$$

- *For $\lambda_2 = 3$ we can solve in a similar fashion to yield*

$$v_1 = -v_3 \quad v_2 = \frac{-3}{2} \quad v_3 = t$$

where t is some parameter. Therefore, if we choose $t = 2$ the eigenvector we get corresponding to $\lambda_2 = 3$ is

$$V_2 = \begin{bmatrix} -2 \\ -3 \\ 2 \end{bmatrix}$$

- *For $\lambda_3 = -4$ we can solve to get the third eigenvector*

$$V_3 = \begin{bmatrix} -1 \\ 2 \\ 0 \end{bmatrix}.$$

This was a simple example designed to give us an idea of how eigenvalues and eigenvectors are found. Next we will see a more complicated example in which we calculate eigenvalues and eigenvectors, that will be used in our study of Lotka-Volterra predator-prey models.

Example 2.19 *Suppose we have the Jacobian matrix at a particular point:*

$$\mathbf{J}\left(\frac{j}{r},\frac{q}{a},0\right)=\begin{bmatrix}0 & -a\frac{j}{r} & 0\\ r\frac{q}{a} & 0 & -b\frac{q}{a}\\ 0 & 0 & -k+c\frac{q}{a}\end{bmatrix},$$

$$\det(\mathbf{J}-\lambda I)=\begin{bmatrix}-\lambda & -a\frac{j}{r} & 0\\ r\frac{q}{a} & -\lambda & -b\frac{q}{a}\\ 0 & 0 & -k+c\frac{q}{a}-\lambda\end{bmatrix}$$

$$=(-k+c\frac{q}{a}-\lambda)\det\begin{bmatrix}-\lambda & -a\frac{j}{r}\\ r\frac{q}{a} & -\lambda\end{bmatrix}$$

$$=\left(\frac{-ka+cq}{a}-\lambda\right)\left(\lambda^2+jq\right)=0$$

Thus,

$$\lambda=\frac{-ka+cq}{a}$$

and

$$\lambda^2=-jg.$$

Finally solving for λ we get

$$\lambda=\pm i\sqrt{qj}.$$

Therefore, the eigenvalues of this matrix are $\lambda=\frac{cq-ka}{a}$ and the purely imaginary numbers $\lambda=\pm i\sqrt{qj}$.

We can find the eigenvectors using the same techniques as we did in the previous example to conclude that an eigenvector corresponding with

$$\lambda = \frac{cq - ka}{a}$$

is

$$\left\langle 1, \frac{r(cq-ka)}{ja^2}, \frac{r}{j} + \frac{r(cq-ka)^2}{qja^2} \right\rangle$$

and eigenvectors corresponding to

$$\lambda = \pm i\sqrt{qj}$$

are

$$\left\langle \frac{b}{2r}, \frac{bi\sqrt{qj}}{a}, 1 \right\rangle \quad \textit{and} \quad \left\langle \frac{i\sqrt{qj}}{rq}, 0, 1 \right\rangle.$$

In most of what follows in the remaining chapters we will be primarily concerned with eigenvalues rather than their corresponding eigenvectors, but it is good to get a feel for them anyways. Now that we have an understanding of eigenvalues we are read to move into stability analysis.

2.6.1 Stability Analysis

Linear systems can be classified in a number of ways. The behavior of the points around each equilibria, or stationary point, give us a way to understand a particular system. We use eigenvalues to help us understand what is happening at each equilibrium point so that we can deduce stability properties. For example, if we have complex eigenvalues, in general, we can expect to see rotational motion around the stationary point. Real eigenvalues on the other hand tend to show direct motion. Before we get into the classifications

for stable and unstable it's important to make note of how the signs of the eigenvalues relate to the systems. In the following general matrix A we can explore the eigenvalues and discuss stability.

Let

$$A = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

The characteristic polynomial

$$P(x) = \lambda^2 - (a+d)\lambda + (ad - bc)$$

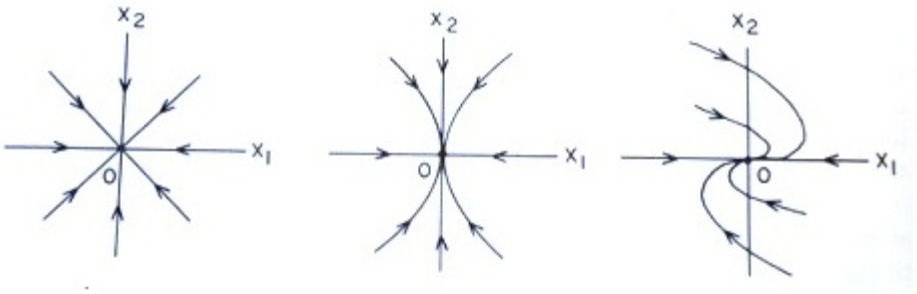
with solutions:

$$\lambda = \frac{\tau \pm \sqrt{\tau^2 - 4\delta}}{2}$$

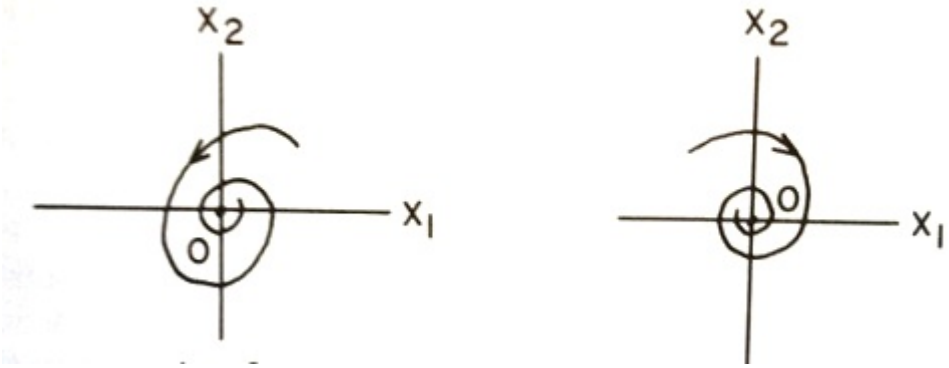
where $\tau = a + d$ and $\delta = ad - bc$.

Notice this results in two solutions for each degree two characteristic polynomial. The following classifications in $\mathbb{R}^2$ give us a way to understand these eigenvalues as they relate to stability.

- If both of the real parts of eigenvalues, are negative, the equilibrium point is stable. We can see this graphically by examining the points around the equilibrium and noticing that they will be attracted towards the stationary point as we will see in the phase portraits to follow. We can further classify the stable equilibrium in the following ways:
  - If both of eigenvalues are real and negative, the equilibrium is called a stable node.

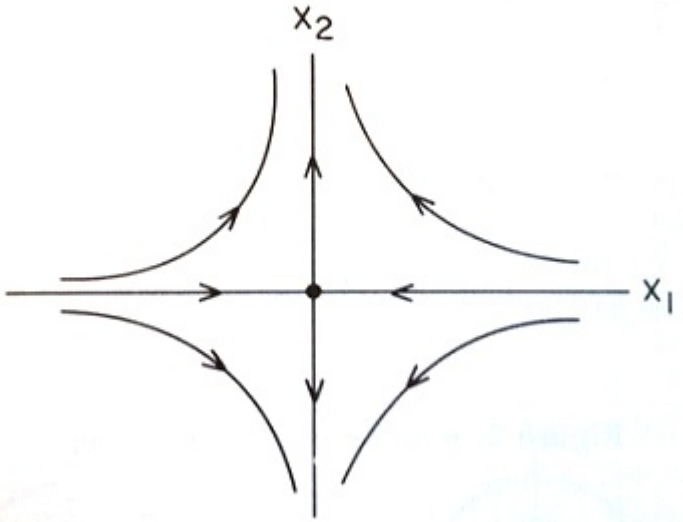


– If the eigenvalues are complex conjugates with negative real parts, the equilibrium is called a stable focus and the system approaches the stationary point in a rotational manor.

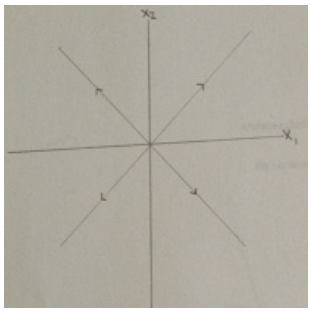
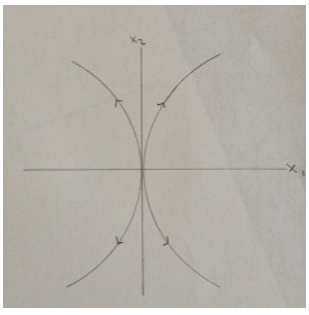
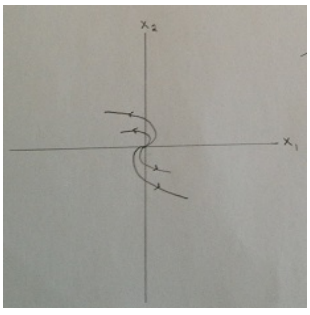


As an aside, we say that an equilibrium point is asymptotically stable if and only if the real part of each eigenvalue is negative and if the equilibrium point is a sink. An equilibrium point is called a sink if any solution with initial conditions sufficiently close to the equilibrium approaches the equilibrium asymptotically as $t \to \infty$. Asymptotically approaching means that for point near the equilibrium, the difference between the point and the equilibrium point approaches zero as $t \to \infty$. Stable nodes and stable focuses are classified as asymptotically stable. Now that we have discussed asymptotically stable points we will move to a discussion of unstable points. Unstable points arise when one of the real parts of the eigenvalues is positive.

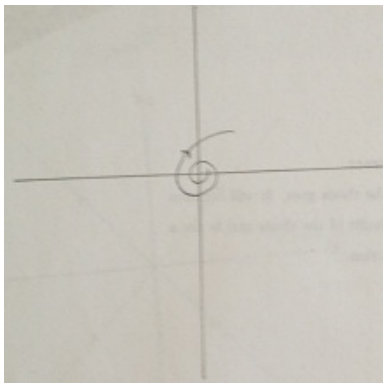
- If one of the real parts of the eigenvalues is positive the equilibrium is unstable, this means that the points surrounding the equilibrium will be repelled from the stationary point. We can further classify unstable equilibria points in the following ways:
  - If both eigenvalues are real with opposite signs, one negative and one positive, the equilibrium is called a saddle.

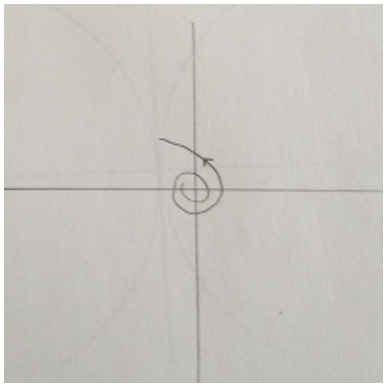


  - If both eigenvalues are real and positive, the equilibrium is called an unstable node. They look like stable nodes, just with direction away from the origin.

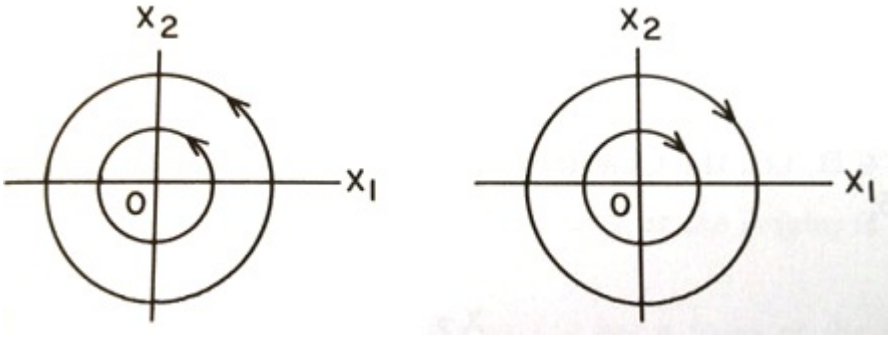
  - If the eigenvalues are complex conjugates with positive real parts, the equilibrium is called an unstable focus. Similar to the stable focus just with direction moving away from the origin.





Again as an aside, we say that an equilibrium point is a source if all solutions that start sufficiently close to the point move away from it as $t \to \infty$. Unstable nodes and unstable focuses are classified as sources. Sources appear to spiral outwards. The last case to consider for equilibria is when both the the real parts of the eigenvalues are zero.

- If both of the real parts of the eigenvalues are zero, the equilibrium is called a center. If an eigenvalue has zero as a real part and eigenvalues that appear as complex conjugate pairs, this means that the points surrounding the equilibrium will oscillate around the stationary point.



A center is an equilibrium point which is stable, but is not asymptotically stable since it never approaches the equilibrium point.

Now that we have defined all possible stability classifications in $\mathbb{R}^2$ we are ready to explore some examples to give us a feel for how we will use

eigenvalues and eigenvectors in stability analysis.

Example 2.20 *Given the system*

$$\begin{cases} \frac{dx_1}{dt} &= -x_1 - x_2 \\ \frac{dx_2}{dt} &= x_1 - 2x_2 \end{cases}$$

The Jacobian matrix for the system is

$$A = \begin{bmatrix} -1 & -1 \\ 1 & -2 \end{bmatrix}$$

with eigenvalues

$$\lambda = -2 \pm i.$$

We can find real solutions to this system corresponding to the complex eigenvalues according to the following theorem:

Theorem 2.21 *Let $\lambda_1 = \alpha + i\beta$ be a complex eigenvalue of the real valued coefficient matrix A and let $B_1 = Re(V_1)$ and $B_2 = Im(V_1)$, where V_1 is the eigenvector corresponding to λ_1, then*

$$x_1 = (B_1 \cos \beta t - B_2 \sin \beta t)e^{\alpha t}$$

$$x_2 = (B_2 \cos \beta t - B_1 \sin \beta t)e^{\alpha t}.$$

are linearly independent solutions of the corresponding system [16].

Note $\lambda_2 = \alpha - i\beta$ is also an eigenvalue and we could have chosen this value instead to yield essentially the same results.

Thus, for $\lambda = -2+i$ in the example in which we are working, we have $\alpha = -2$, $\beta = 1$ and corresponding eigenvector

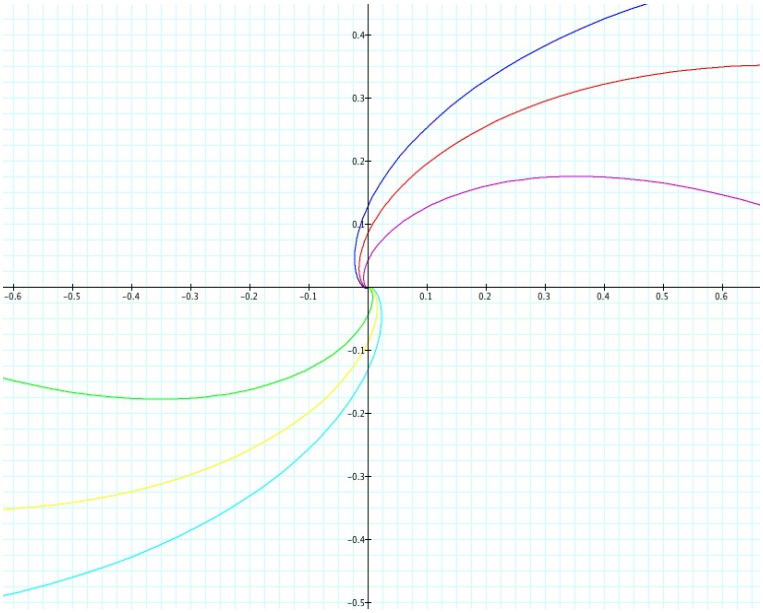
$$V_1 = \begin{pmatrix} i \\ 1 \end{pmatrix}$$

which gives $B_1 = Re(V_1) = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$ *and* $B_2 = Im(V_1) = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$. *Thus we get a particular solution given by*

$$x_i = \left(\begin{pmatrix} 0 \\ 1 \end{pmatrix} \cos t - \begin{pmatrix} 1 \\ 0 \end{pmatrix} \sin t \right) e^{-2t}$$

or more simply,

$$\begin{cases} x_1(t) &= -e^{-2t} \sin t \\ x_2(t) &= e^{-2t} \cos t \end{cases}$$

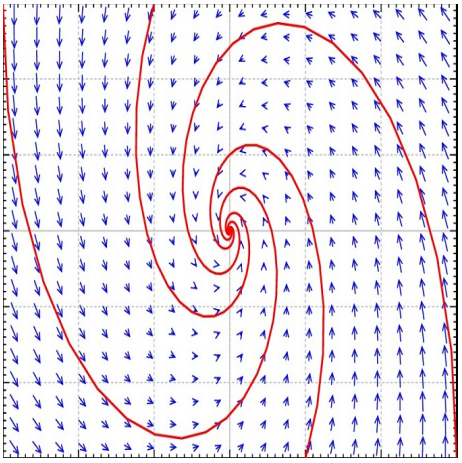


The family of solution curves has a stable focus at the origin which is what we would expect, since the eigenvalues are complex conjugates with negative real parts.

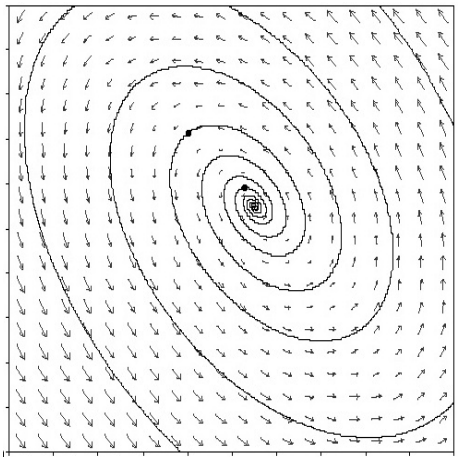
2.6.2 Linear Systems in $\mathbb{R}^3$

Now that we have explored stability in $\mathbb{R}^2$, let's see what happens when we introduce a third variable into our system and a third eigenvalue. This is an important area to discuss now since many of the systems we will study in the coming chapters are systems in three variables. Stability definitions for systems in three variables follow similarly as they do in two variables just now we are talking about three-dimensional stability.

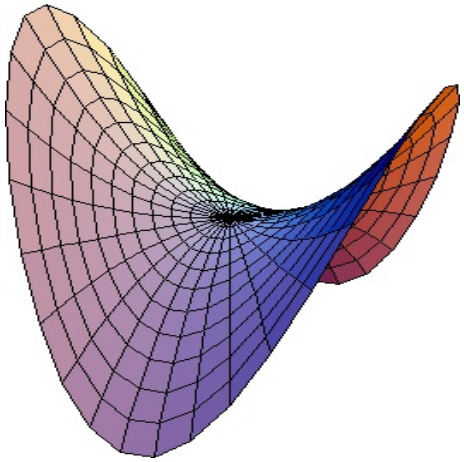
- If all of the eigenvalues have negative real parts the equilibrium point is called a sink and the system spirals inward towards the equilibrium as depicted in the following image:



- If all of the eigenvalues have positive real parts the equilibrium point is called a source and the system spirals outward away from the equilibrium as depicted in the following image:



- If at least one of the real parts of the eigenvalues is positive and at least one of the real parts is negative then the equilibrium point is called a saddle as depicted in the following image:



Stability analysis is a key idea in understanding how different biological models work and in testing their applicability. Thus, it is crucial to have a comprehensive understanding of the classifications discussed in this section. Still, one more concept remains to be discussed before we are ready to move on to the applications in the chapters to follow, the topic of invariance.

2.7 Invariance

A surface S is called invariant with respect to a system of differential equations, if every solution that starts on S does not escape S. This is desirable from a biological standpoint because it implies that if a species becomes extinct then it will not reappear in the system.

To get an understanding of invariant surfaces let's first consider a function $F(x, y, z)$ such that $F(x, y, z) = k$ is a surface S. Let $r(t) = \langle x(t), y(t), z(t) \rangle$ be a curve C of surface S.

Then by the chain rule, the derivative of $F(x, y, z) = k$ is

$$\frac{\partial F}{\partial x} \cdot \frac{dx}{dt} + \frac{\partial F}{\partial y} \cdot \frac{dy}{dt} + \frac{\partial F}{\partial z} \cdot \frac{dz}{dt} = 0.$$

The gradient of F is

$$\bigtriangledown F = \left\langle \frac{\partial F}{\partial x}, \frac{\partial F}{\partial y}, \frac{\partial F}{\partial z} \right\rangle$$

and the tangent vector to $r(t)$ is

$$r'(t) = \left\langle \frac{dx}{dt}, \frac{dy}{dt}, \frac{dz}{dt} \right\rangle.$$

For use in later work we label $r'(t) = \eta$, so that

$$\frac{\partial F}{\partial x} \cdot \frac{dx}{dt} + \frac{\partial F}{\partial y} \cdot \frac{dy}{dt} + \frac{\partial F}{\partial z} \cdot \frac{dz}{dt} = 0$$

which can be re-written as

$$\bigtriangledown F \cdot \eta = 0.$$

We can interpret this as saying that $\bigtriangledown F$ is perpendicular to η at every point on S. To develop an understanding of this idea, let's revisit a previous example.

Example 2.22 *Example 2.15 Revisited*

Given the system

$$\begin{cases} \frac{dx}{dt} &= 4x + 7y \\ \frac{dy}{dt} &= x - 2y \end{cases}$$

with solutions

$$\begin{aligned} x(t) &= 7c_1e^{5t} - c_2e^{-3t} \\ y(t) &= c_1e^{5t} + c_2e^{-3t} \end{aligned}$$

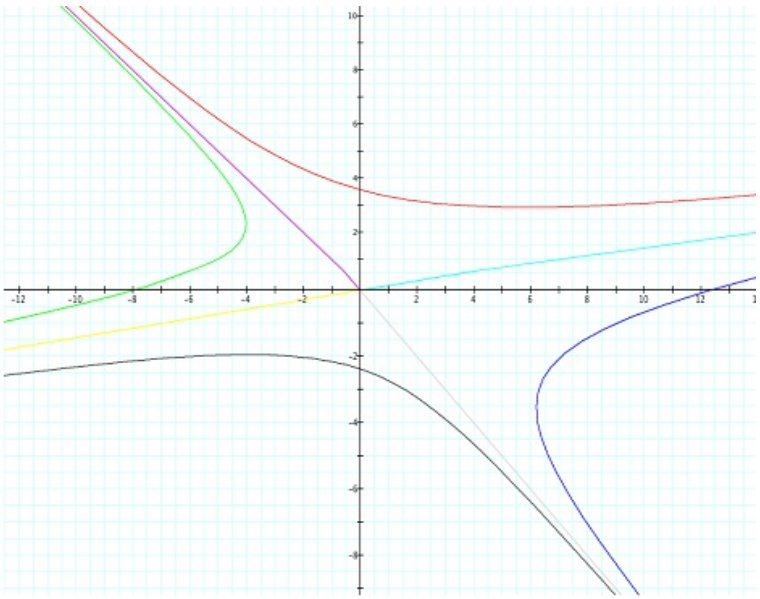
The Jacobian matrix corresponding to this system being

$$J = \begin{bmatrix} 4 & 7 \\ 1 & -2 \end{bmatrix}$$

with eigenvalues 5 and -3 and eigenvectors

$$V_5 = \langle 7, 1 \rangle \quad \textit{and} \quad V_{-3} = \langle -1, 1 \rangle$$

We can see the eigenvalues are both real, one negative and the other positive, therefore the system creates a saddle point at the origin.



We claim that these eigenvectors represent invariant subspaces. We can verify this by looking at the eigenvectors one at a time. The eigenvector

$$V_5 = \langle 7, 1 \rangle$$

at the origin corresponds to the equation

$$y = \frac{1}{7}x$$

which we can write as the invariant surface

$$F(x, y) = y - \frac{1}{7}x$$

with curve

$$F(x, y) = 0.$$

We find

$$\bigtriangledown F = \left\langle -\frac{1}{7}, 1 \right\rangle$$

and

$$\eta = \left\langle \frac{dx}{dt}, \frac{dy}{dt} \right\rangle = \langle 4x + 7y, x - 2y \rangle$$

Thus,

$$\begin{aligned} \bigtriangledown F \cdot \eta &= -\tfrac{1}{7}(4x + 7y) + 1(x - 2y) \\ &= -\tfrac{4}{7}x - y + x - 2y \\ &= \tfrac{3}{7}x - 3y \end{aligned}$$

but since we defined $y = \frac{1}{7}x$*, this gives*

$$\begin{aligned} &= \tfrac{3}{7}x - 3\tfrac{1}{7}x \\ &= 0. \end{aligned}$$

Thus $\bigtriangledown F \cdot \eta = 0$*. This gives us a way to calculate invariance for a system in* $\mathbb{R}^2$ *at the origin* $(0, 0)$*. We can use similar techniques for more difficult systems and for points centered around equilibria points away from the origin as well.*

Theorem 2.23 *Let* S *be a smooth surface in* $\mathbb{R}^3$ *and*

$$\begin{cases} \frac{dx_1}{dt} &= F(x_1, x_2, x_3) \\ \frac{dx_2}{dt} &= G(x_1, x_2, x_3) \\ \frac{dx_3}{dt} &= H(x_1, x_2, x_3) \end{cases}$$

Suppose that for all $(x_1, x_2, x_3) \in S$ *we have that*

$$\eta \cdot \left\langle \frac{dx_1}{dt}, \frac{dx_2}{dt}, \frac{dx_3}{dt} \right\rangle = 0$$

where η *is a normal vector to the surface* S *at* (x_1, x_2, x_3)*. Then* S *is invariant with respect to the system above [7].*

We will use the ideas from this theorem when we explore the three-variable Lotka-Volterra model, but it would be good to get a feel for how this theorem works.

Example 2.24 *Given*

$$\begin{cases} \frac{dx_1}{dt} &= 2x_1 \\ \frac{dx_2}{dt} &= x_2 - x_3 \\ \frac{dx_3}{dt} &= x_2 + x_3 \end{cases}$$

The corresponding Jacobian matrix is

$$J = \begin{bmatrix} 2 & 0 & 0 \\ 0 & 1 & -1 \\ 0 & 1 & 1 \end{bmatrix}$$

yielding

Eigenvalues	*Eigenvectors*
2	$V_2 = [1, 0, 0]$
$1 + i$	$V_{i+1} = [0, i, 1]$
$1 - i$	$V_{1-i} = [0, -i, 1]$

Notice that the differential equation $\frac{dx_1}{dt}$ is independent of x_2 and x_3, thus it is clear that the x_1-axis is invariant. Also this independence allows us to solve the equation $\frac{dx_1}{dt} = 2x_1$ as in Section 2.4 to yield $x_1 = c_1e^{2t}$.

Additionally, we have $\frac{dx_2}{dt}$ and $\frac{dx_3}{dt}$ both independent of x_1 with eigenvalues that are complex conjugates. Thus, for $\lambda = 1 + i$ and corresponding eigenvector $[i, 1]$ (ignoring the x_1 portion), according to Theorem 2.21, we have generic solutions

$$x_i = \left(\begin{pmatrix} 0 \\ 1 \end{pmatrix} \cos t - \begin{pmatrix} 1 \\ 0 \end{pmatrix} \sin t \right) c_i e^t$$

for $i = 2, 3$. Therefore yielding solutions $x_2 = c_2e^t \sin t$ and $x_3 = c_3e^t \cos t$. We can also verify the x_2x_3 -plane is invariant, as we will see in the following exploration.

- *Let*

  $$F(x_1, x_2, x_3) = x_1.$$

  Notice that the surface

  $$F(x_1, x_2, x_3) = 0$$

  is the x_2x_3-plane so with

  $$\eta = \langle 0, x_2 - x_3, x_2 + x_3 \rangle$$

  and

  $$\bigtriangledown F = \langle 1, 0, 0 \rangle$$

  we get

  $$\eta \cdot \bigtriangledown F = 0.$$

  Thus the x_2x_3-plane is invariant.

Putting everything together we have that a generic solution to this system is

$$\begin{cases} x_1 &= c_1 e^{2t} \\ x_2 &= c_2 e^t \sin t \\ x_3 &= c_3 e^t \cos t \end{cases}$$

Now that we have had a chance to explore some of the ODE basics and dynamical system interactions to be used in later work, we are ready to apply our techniques to biological models. The first we explore is the Lotka-Volterra predator prey model established in the early 20th century.

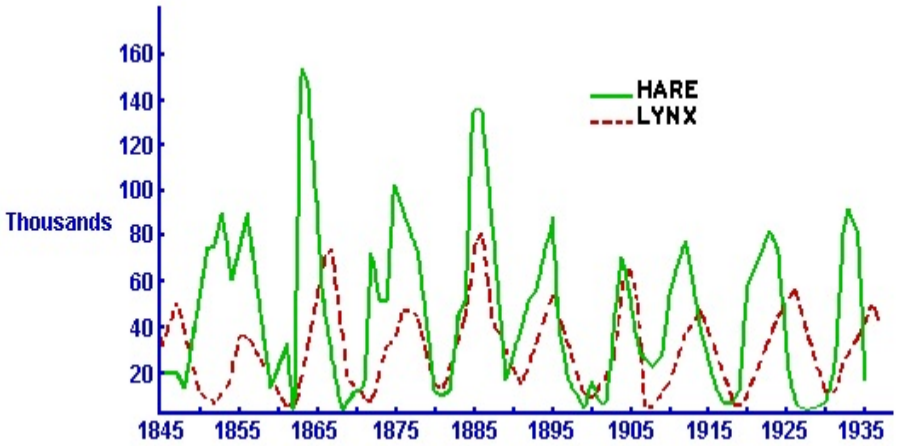
Chapter 3

Predator-Prey Relationships

3.1 Hudson's Bay Company

To begin the study of predator-prey models we are going to examine data regarding snowshoe hares found by the Hudson Bay Company in Northern

Ontario Canada between 1845 and 1935. The Hudson Bay Company, a fur trading company involved in purchasing pelts from trappers and selling them to furriers, kept meticulous records of the number of furs traded from across Canada. For our study we are specifically interested in the number of lynx and snowshoe hare pelts traded. It is reasonable to assume that the success of trapping each species was roughly proportional to the number of species in the wild at any given time, thus we have significant set of data regarding the fluctuations in populations of lynx and hares in this time period.



Some of the interesting observations made from the data:

1. The population of the snowshoe hare tends to vary on a 10-year oscillating cycle.

2. The lynx, a known specialist predator of the snowshoe hare, has a rise and fall in population numbers that mirrors the rise and fall of the snowshoe hare populations, with a slight lag time.

Also, it was determined that the 10-year hare cycles seems to occur in synchrony across broad regions, thus immigration or emigration does not explain the population changes.

The oscillating population densities of the hare and lynx populations have intrigued scientists for years and since the scientific community often looks for ways to quantitatively understand the world, focus fell on the Lotka-Volterra Predator-Prey model to provide a possible explanation for the oscillations discovered by the Hudson Bay Company. Our goal in exploring this theoretical model is to test it's generality and to determine the correlation between the model and the data in an attempt to analyze it's usefulness. Of course we would need to test this model on several different scenarios to establish generality, but for now let's try to determine if the Lotka-Volterra model can be used to make sense of the Hudson Bay data. If the model appears to fit the data and if the parameters have a plausible biological interpretation, then the model may be useful for similar ecological systems and further, for experimenting with manipulations to the system.

3.2 Lotka-Volterra Models

The Lotka-Volterra predator-prey equations were established separately by Alfred Lotka in 1925 and Vito Volterra in 1926. The Lotka-Volterra model is the earliest known model proposed for a predator-prey system, thus many consider Lotka and Volterra to be the instigators of theoretical ecology [4]. The model we are about to explore is intended to aid in understanding the global features of the system studied rather than make qualitative predictions for the future.

In our exploration of the Lotka-Volterra model we will be using differential equations and dynamical systems, both of which were discussed in Chapter 2. Before we can dive too deep into the systems we will be modeling, we must consider the set of assumptions that Lotka and Volterra worked under:

1. The prey is limited only by the predator. This implies that without predation, the prey population grows exponentially.

2. In the absence of prey, the predator dies off exponentially.

3. The "per predator rate," the rate at which the prey are killed, is a linear function of the number of prey.

4. Every prey death contributes identically to the growth of the predator population.

With these assumptions we are ready to move forward in our exploration.

Let the number of prey be denoted by H, since we will consider the example with hare as the prey, and the number of predators be denoted by L for the predatory lynx. Then in words, {rate of change of H} = {net rate of growth of H without predation} - {rate of loss of H due to predation} and {rate of change of L} = {net rate of growth of L due to predation} - {net rate of loss of L without prey}.

$$\begin{cases} \frac{dH}{dt} &= rH - bHL \\ \frac{dL}{dt} &= cHL - kL \end{cases} \tag{3.1}$$

where r represents the intrinsic rate of increase of the prey in absence of the predator, k denotes the rate of decline of the predator in the absence of prey and b and c are constants of proportionality.

Going back to our assumptions:

1. The first assumption means that if the predator population is zero, corresponding to $L = 0$ then, $\frac{dH}{dt} = rH$ so $H = C_H e^{rt}$ for some constant

C_H. This means that without the lynx, the hare population would grow exponentially.

2. The second assumption implies that if prey is absent, $H = 0$, then we have $\frac{dL}{dt} = -kL$ so $L = -C_L e^{kt}$ for some constant C_L. This would imply that the lynx population would die off exponentially without their food source.

3. The third assumption says that the death rate of the prey from predation is proportional to the product of the prey and predator populations. Therefore, we write bHL in our system with b a constant of proportionality representing the effect of predation on the prey population. Note that since b represents the effect of predation on the prey population, bH represents the number of hare eaten by an individual lynx during a brief period of time. Thus subtracting bHL in the first equation accounts for the rate at which the number of hare is being removed from the hare population as the result of predation by the lynx population.

4. Similarly, the forth assumption says that the contribution of predation to the growth rate of the predator population is given by cHL, where c is a constant of proportionality representing the efficiency and propagation rate of the predator in the presence of prey. Here we have c representing a growth rate for the predator population dependent upon the prey, thus cH shows the growth rate of one lynx in the presence of hare during a brief period of time and cHL contributes to the growth rate for the entire lynx population in that brief period. Thus, adding cHL in the second equation shows the increase in the lynx population due to successful predation on the hare.

Now we are ready to explore the dynamics of this system. For clarity we re-state the parameters.

Parameters	Use in the 2-Variable Lotka-Volterra Equations
r	intrinsic rate of increase of the hare in the absence of the lynx
k	rate of decline of the lynx in the absence of the hare population
b	effect of predation by the lynx on the hare population
c	efficiency and propagation rate of the lynx in the presence of the hare

3.2.1 Dynamics of the two equation Lotka-Volterra model

First let's analyze this system graphically. To do this we are going to need to find the equilibria or stationary points of the model. Let $F(H, L) = \frac{dH}{dt}$ be the growth rate of the hare population and let $G(H, L) = \frac{dL}{dt}$ be the growth rate of the lynx population. We can find stationary points by setting both $F = 0$ and $G = 0$, since this means both the hare an lynx populations, H and L, are no longer changing. When $F = 0$ we have

$$rH - bHL = 0 \quad \text{or equivalently} \quad H(r - bL) = 0$$

Thus we conclude trivially $H = 0$ or non-trivially $L = \frac{r}{b}$.
Similarly, for $G = 0$ we have

$$cHL - kL = 0 \quad \text{or equivalently} \quad L(cH - k) = 0$$

Thus we conclude trivially $L = 0$ or non-trivially $H = \frac{k}{c}$.

Therefore, there are two stationary points for the model; one with both species zero, and one in which both the lynx and hare populations are nonzero, namely

$$(0, 0) \quad \text{and} \quad \left(\frac{k}{c}, \frac{r}{b}\right).$$

In order to determine the stability of the two equilibria we can either explore graphically or we can use eigenvalues to make an algebraic case. We will consider eigenvalues here.

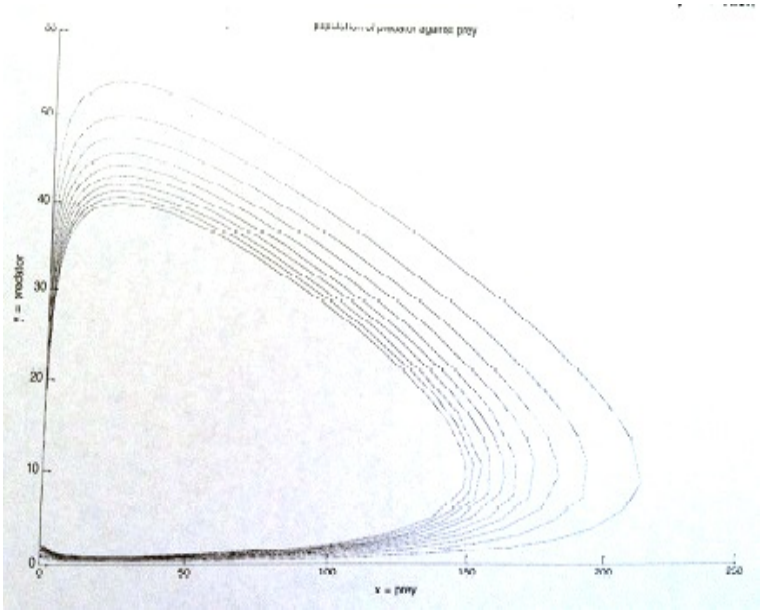
In two dimensional systems the eigenvalues of the Jacobian matrix are related to the local change at a point. If we consider complex eigenvalues, the sign of the real parts of the eigenvalues will determine the behaviors points surrounding each equilibria point. We can determine equlibria stability by considering the Jacobian matrix formed by the partial derivatives of the ODE functions. For the two-variable Lotka-Volterra model the Jacobian matrix follows:

$$J = \begin{bmatrix} \frac{\partial F}{\partial H} & \frac{\partial F}{\partial L} \\ \frac{\partial G}{\partial H} & \frac{\partial G}{\partial L} \end{bmatrix} = \begin{bmatrix} r - bL & -bH \\ cL & cH - k \end{bmatrix}$$

For the stationary point $(0, 0)$ the Jacobian matrix is

$$J(0,0) = \begin{bmatrix} r & 0 \\ 0 & -k \end{bmatrix}$$

the eigenvalues are r and $-k$, hence it is unstable and further a saddle-point. We can create a phase portrait depicting the solution curves using computer software the same way we discussed in Chapter 2 to see the saddle point.



From the phase portrait we can see that each contour is a periodic oscillation and that any perturbation can drive the oscillation into a different cycle, especially near the origin. Note that this seems logical, since we just showed that equilibrium point $(0, 0)$ is an unstable saddle. When we graph the image with computer software we can see in the x-direction (H-direction) our graph is repelling moving way from the origin, but in the y-direction (L-direction) the graph is attracting, being pulled toward the origin again. The biological interpretation of this diagram is that when the lynx population is low the hare population increases over time. Then, in the presence of hare, the lynx population has a large food source so it can begin to increase, which slowly lowers the hare population. Eventually the system ends up with more lynx than the hare population can support which causes a crash in both species, bringing the system back to near equilibrium.

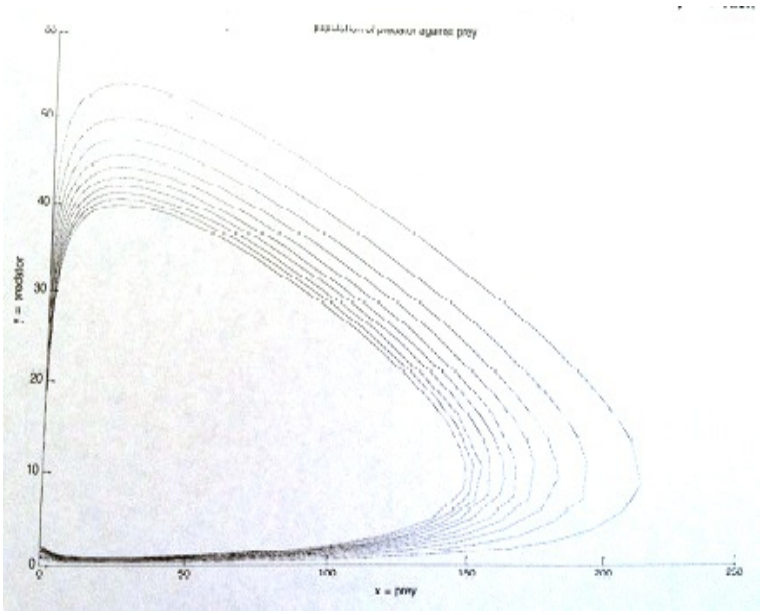
For the stationary point $(H, L) = \left(\frac{k}{c}, \frac{r}{b}\right)$ the Jacobian matrix is

$$J\left(\frac{k}{c}, \frac{r}{b}\right) = \begin{bmatrix} r - b\frac{r}{b} & -b\frac{k}{c} \\ c\frac{r}{b} & c\frac{k}{c} - k \end{bmatrix} = \begin{bmatrix} 0 & -b\frac{k}{c} \\ c\frac{r}{b} & 0 \end{bmatrix}$$

The eigenvalues in this case are not as obvious so we will need to do some work to find them. We set the determinant of $J - \lambda I$ to be zero, then solve for λ.

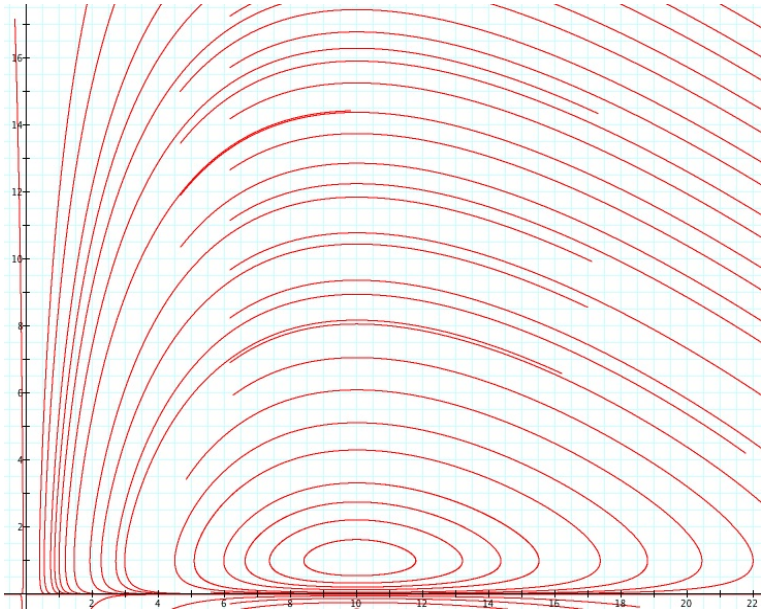
$$\text{Det}(J - \lambda I) = \begin{vmatrix} -\lambda & -b\frac{k}{c} \\ c\frac{r}{b} & -\lambda \end{vmatrix} = \lambda^2 + rk = 0$$

The polynomial $\lambda^2 + rk$ is the characteristic polynomial whose roots are the eigenvalues, $\lambda = \pm i\sqrt{rk}$. Thus, since the eigenvalues have no real parts, only imaginary, in the Lotka-Volterra model the equilibrium point $(H, L) = (\frac{k}{c}, \frac{r}{b})$ is a center. Graphically this means that the system is stable, but not asymptotically stable about the equilibrium. This means that the graph is centered around $(H, L) = (\frac{k}{c}, \frac{r}{b})$ but over time does not approach or move away from the point.

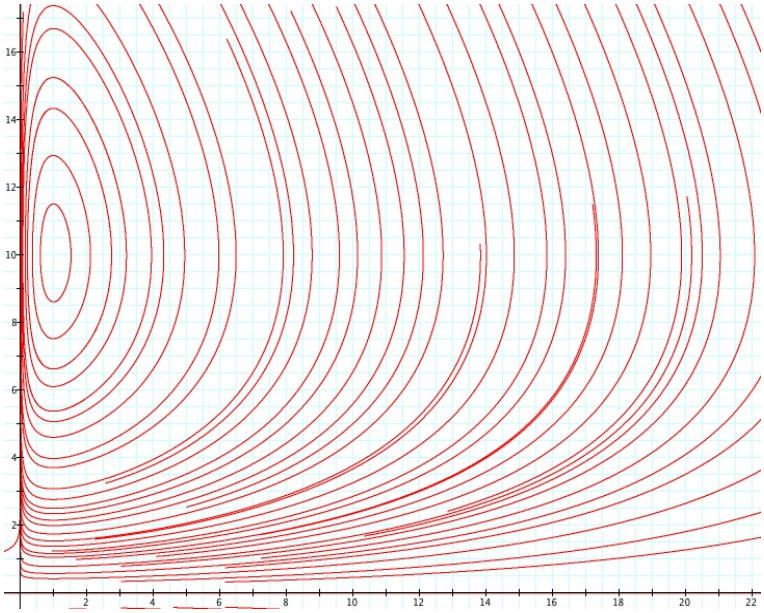


Looking again at the phase portrait we can imagine a center in all of the curves. All cycles oscillate around this center, specifically the equilibrium point $\left(\frac{k}{c}, \frac{r}{b}\right)$ but never approach the point. Depending on the picks for constants k, c, r, b the center may shift, but still remains a center point in the system, as

seen in the following phase portraits with varied parameters:



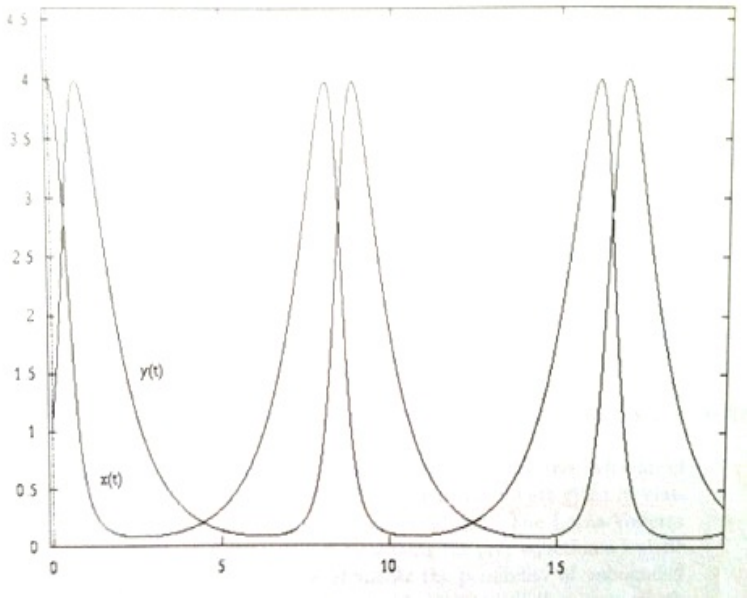
where the center shifts right on the horizontal axis.



where the center shifts up the vertical axis.

3.2.2 Application to Hudson's Bay Data

Now that we have explored the stability of the system we can explore a graph of the model to see how well it aligns with the data. Graphing the same information as in the previous phase diagram displayed a little differently, with the cycles of both the hare and lynx shown with respect to time, we get the the following image.



The model predicts a phase shifted periodic behavior in the populations of both species with a common period. Each species exhibits peaks then drops, with the peaks of the hare population occurring slightly before the lynx. This behavior definitely looks close to what we saw for when we looked at the Hudson Bay data however, an argument can be made that it neglects some key players. The hares require a food source! To examine what happens if we include a third species in our system, this will require exploration of a three-variable Lotka-Volterra model. In the three-variable system we will have two levels of predator-prey relationships. The first between the hare the vegetation in which they feed and the next between the hare and the lynx.

3.3 Three Species Lotka-Volterra Model

To begin examining the three species model, let V represent the vegetation, the first level of prey, and for consistency let's stick with H for the hare population and L for the lynx population. For clarity let's restate our variables as well as introduce some new ones:

- Let q represent the natural growth rate of the vegetation in the absence of hares.
- Let a represent the effect of predation by the hares on the vegetation.
- Let j represent the natural death rate of the hares in the absence of vegetation.
- Let r represent the efficiency and propagation rate of the hares in the presence of the vegetation
- Let b represent the effect of predation on the hare population by the lynx population.
- Let k represent the natural death rate of the lynx in the absence of prey, in this case the hare.
- Let c represent the efficiency and propagation rate of the lynx in the presence of the hare.

3.3.1 Assumptions for 3-Variable System

Many of the assumptions used in the two-variable model hold for the three-variable model as well; we will revisit those that still hold and discuss any additions and/or adaptations.

1. The vegetation population is limited only by the hare, thus without predation will grow exponentially.

2. In the absence of the hare population, the lynx population will die off exponentially.

3. The "per predator rate," the rate at which the prey are killed, at both levels (vegetation-hare; hare-lynx), is a linear function of the number of prey.

4. Every prey death contributes identically to the growth of the predator population.

5. The hare population is impacted by both the vegetation population and the lynx population.

This gives us a system of three differential equations as follows:

$$\begin{cases} \frac{dV}{dt} &= qV - aVH \\ \frac{dH}{dt} &= -jH + rVH - bHL \\ \frac{dL}{dt} &= -kL + cHL \end{cases} \tag{3.2}$$

Going back to our assumptions in an attempt to make sense of the system:

1. The first assumption means that if the hare population is zero, $H = 0$, we get $\frac{dV}{dt} = qV$, so $V = C_V e^{qt}$ for some constant C_V. Thus, the vegetation population will grow exponentially.

2. The second assumption implies that if the hare population is absent $H = 0$, then $\frac{dL}{dt} = -kL$ so $L = C_L e^{-kt}$ for some constant C_L. Thus, the lynx population dies off exponentially without food.

3. The third assumption means that the death rate of the prey from predation is proportional to the product of the prey and predator populations. This assumption holds both with the vegetation-hare relationship and the hare-lynx population. Therefore we write a as the effect of predation on the vegetation population and b as the effect of predation on the hare population. We subtract aVH from the first equation since for a brief period each hare eats a quantity of aV vegetation. Similarly, we subtract bHL from the second equation since each lynx contributes bH hare.

4. Similarly, the forth assumption implies that the contribution of predation to the growth rate of the predator population is proportional to the product of the prey and predator populations. Therefore we write r as the growth rate of hare population in the presence of the vegetation population and c as the growth rate of the lynx population in the presence of the hare population. We see rVH as a gain term for the hares since in the presence of vegetation the hare population grows and we see cHL as a gain term for the lynx since successful propogation of the lynx happens when they have each cH hares to feed upon.

5. The final assumption says that both the growth of the vegetation and the effect of predation by the lynx play a role in the hare population.

Since populations are non-negative we can restrict our domain to the non-negative region $\{(V, H, L)|V \geq 0, H \geq 0, L \geq 0\} \subset \mathbb{R}^3$, and without extinction we could restrict it further to only positive values for V, H and L, denoted $\mathbb{R}^3_+$.

3.3.2 Analysis of the Model

First, let's begin by showing that each coordinate plane is invariant with respect to the system described. Recall that a surface S is called invariant with respect to a system of differential equations if every solution that starts on S does not escape S. This is desirable from a biological aspect because it implies that if some species becomes extinct, it will not reappear.

- If $F_1(V, H, L) = L$ with the surface $L = 0$ corresponding to a lynx population of zero, the system reduces to

$$\begin{cases} \frac{dV}{dt} &= qV - aVH \\ \frac{dH}{dt} &= -jH + rVH \\ \frac{dL}{dt} &= 0 \end{cases}$$

  The gradient $\bigtriangledown F_1 = \langle 0, 0, 1 \rangle$ is normal to S and at a point $(V, H, 0)$ we have

$$\eta = \left\langle \frac{dV}{dt}, \frac{dH}{dt}, \frac{dL}{dt} \right\rangle = \langle qV - aVH, -jH + rVH, 0 \rangle.$$

  Clearly,

$$\bigtriangledown F_1 \cdot \eta = \langle 0, 0, 1 \rangle \cdot \langle qV - aVH, -jH + rVH, 0 \rangle = 0.$$

  Therefore, the VH plane is invariant.

- If $F_2(V, H, L) = H$ with the surface $H = 0$ corresponding to a hare population of zero, the system reduces to

$$\begin{cases} \frac{dV}{dt} &= qV \\ \frac{dH}{dt} &= 0 \\ \frac{dL}{dt} &= -kL \end{cases}$$

The gradient $\bigtriangledown F_2 = \langle 0, 1, 0 \rangle$ is normal to S and at a point $(V, 0, L)$ we have

$$\eta = \langle qV, 0, -kL \rangle.$$

Clearly,

$$\bigtriangledown F_2 \cdot \eta = \langle 0, 1, 0 \rangle \cdot \langle qV, 0, -kL \rangle = 0.$$

Therefore, the VL plane is invariant.

- If $F_3(V, H, L) = V$ with the surface $V = 0$ corresponding to vegetation population of zero, the system reduces to

$$\begin{cases} \frac{dV}{dt} &= 0 \\ \frac{dH}{dt} &= -jH - bHL \\ \frac{dL}{dt} &= -kL + cHL \end{cases}$$

The gradient $\bigtriangledown F_3 = \langle 1, 0, 0 \rangle$ is normal to S and at a point $(0, H, L)$ we have

$$\eta = \langle 0, -jH - bHL, -kL + bHL \rangle.$$

Clearly,

$$\bigtriangledown F_3 \cdot \eta = \langle 1, 0, 0 \rangle \cdot \langle 0, -jH - bHL, -kL + cHL \rangle = 0.$$

Therefore, the HL plane is invariant.

Now that we have shown invariance in the absence of any species, thus showing that if any population becomes extinct it does not reappear, we are ready to take it further to examine the impact extinction of any one species has on the remaining species in the system. To do this we will solve each of the three corresponding planar (2-variable) systems in their respective coordinate planes.

3.3.3 Absence of the Hare

First, we notice that in the absence of the hare, the system reduces to

$$\begin{cases} \frac{dV}{dt} &= qV \\ \frac{dH}{dt} &= 0 \\ \frac{dL}{dt} &= -kL \end{cases} \tag{3.3}$$

The equation $\frac{dL}{dt} = -kL$ yields

$$L = C_L e^{-kt}$$

for some constant C_L. This implies that the lynx population decreases exponentially as time increases (i.e. $L(t) \to 0$ as $t \to \infty$). Also, $\frac{dV}{dt} = qV$ yields

$$V = C_V e^{qt}$$

for some constant C_V, This implies that the vegetation population grows exponentially as $t \to \infty$.

This seems to fit biologically since if the hare population dies out, the vegetation will exhibit unbounded growth without predation. Meanwhile, the lynx population will die out without a food source. The trajectories in the VL-plane can be directly computed from the separable equation:

$$\frac{dL}{dV} = \frac{\frac{dL}{dt}}{\frac{dV}{dt}} = \frac{-kL}{qV}$$

Through a process of separating variables, first by moving both of the terms with the variable L on one side and the two terms with variable V on the other side

$$\frac{dL}{-kL} = \frac{dV}{qV}.$$

Integrating with respective variables yields

$$\frac{-\ln L}{k} = \frac{\ln V}{q} + C.$$

Multiplying both sides by $-k$ in an effort to isolate L gives

$$\ln L = \frac{-k}{q} \ln V + C.$$

Finally, exponentiating both sides we get

$$L = CV^{-k/q}$$

where C is just an arbitrary constant and any solution to the system must satisfy this equation. Notice that plugging in the solutions we found earlier, namely $L = C_L e^{-kt}$ and $V = C_V e^{qt}$,

$$L = CV^{-k/q}$$

becomes

$$C_L e^{-kt} = C\left(C_V e^{qt}\right)^{-k/q}.$$

Simplifying exponents yields

$$C_L e^{-kt} = C C_V^{-k/q} e^{-kt}$$

and from this we can see equality with

$$C = \frac{C_L}{C_V^{-k/q}}.$$

This tells us that

$$L = C V^{-k/q}$$

is a solution curve containing the solutions already found. Thus, we can be confident that the solution curves can be represented by equations found using the above technique of separating variables. Seeing this relationship will be helpful when looking at the absence of lynx and absence of vegetation models when the solution curves are not as simple.

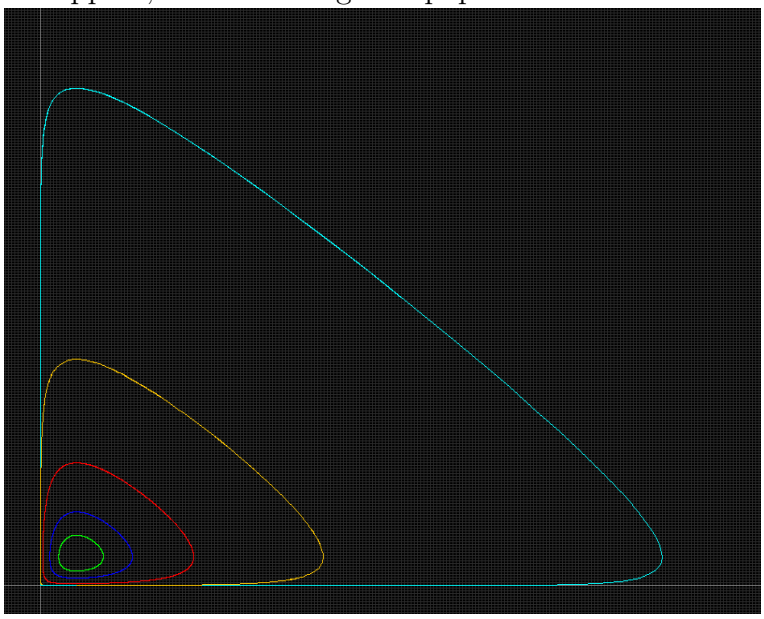
3.3.4 Absence of the Lynx

Now we can examine what happens in the absence of the top predator, the lynx. Notice the system reduces to

$$\begin{cases} \frac{dV}{dt} &= qV - aVH \\ \frac{dH}{dt} &= -jH + rVH \end{cases} \tag{3.4}$$

which is just the classic Lotka-Volterra equations, now for the hare and vegetation relationship. This system is centered at the equilibrium point $\left(\frac{j}{r}, \frac{q}{a}\right)$ which is calculated identically as it was in the previous section using the Jacobian matrix. The following phase portrait shows the dynamics of the system. We have an unstable saddle at the origin and a center at $\left(\frac{j}{r}, \frac{q}{a}\right)$. The vegetation grows along the x-axis, then the hare population increases, slowly lowering the

vegetation population until eventually there are more hares present than the vegetation can support, thus resulting in a population crash for both species.



In the next subsection, we will show how to calculate the equilibrium points for the entire three-variable model and further explore the dynamics, but for now we will focus our attention on finding the solutions to the equations in the absence of the lynx. Solutions to the equations in 3.4 can be calculated by separating variables and integrating and are of the form:

$$\frac{dV}{dH} = \frac{qV - aVH}{-jH + rVH} = \frac{V(q - aH)}{H(-j - rV)}$$

Separating yields

$$dH\left(\frac{q}{H} - a\right) = \left(\frac{-j}{V} + r\right) dV$$

then integrating with respect to respective variables on each side gives

$$q \ln H - aH = -j \ln V + rV + C.$$

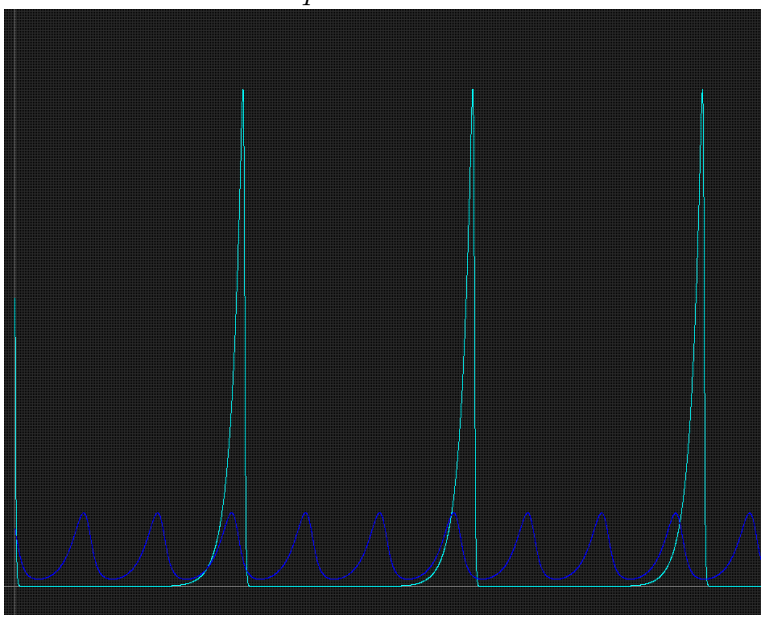
Thus, for some constant C, the solutions are of the form

$$C = q \ln H - aH + j \ln V - rV \tag{3.5}$$

.

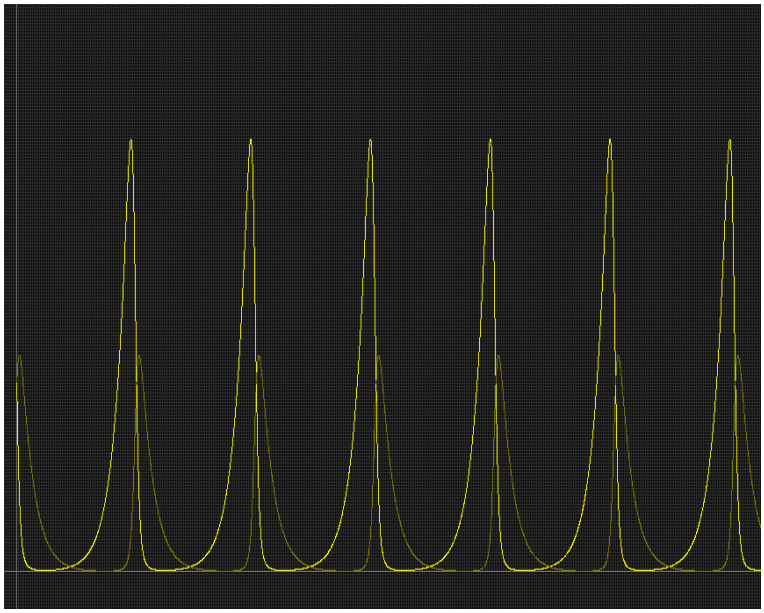
This means that any solution must satisfy this equation or lie on this surface. Notice q, a, j, r will all play an important role in deciding what happens in the system. For example if $q \to 0$ in the above equation the hare population will die out, which makes sense, considering q represents the growth rate of the vegetation. Similarly, we can see the role limiting any of the parameters will play from this solution.

In the following image we see what happens to the vegetation population when we increase the q value. The light blue shows $q = 5$ where the dark blue leaves $q = 1$. We can see that the vegetation grows to a much higher population, but also crashes a lot harder and takes significantly longer to rebuild it's population as we increase the q value.



For reasonable parameters, the system in the absence of lynx looks just as it did in the two variable model we studied earlier; now with the vegetation

as the prey, peaking first followed by the hare population.



The final case to consider is what happens in the absence of vegetation.

3.3.5 Absence of the Vegetation

Finally, let's consider when $V = 0$, no vegetation present

$$\begin{cases} \frac{dV}{dt} &= 0 \\ \frac{dH}{dt} &= -jH - bHL \\ \frac{dL}{dt} &= -kL + cHL \end{cases} \tag{3.6}$$

since $\frac{dH}{dt} \leq -jH$ and we know that $b, H, L > 0$, then as $t \to \infty$ it's evident $H(t) \to 0$, since the rate of change is negative. This will in turn cause $L(t) \to 0$ as well since $\frac{dL}{dt} = -kL + cHL \to 0$ when $H \to 0$ since $k, L > 0$. Thus, in the absence of vegetation both the hare and lynx populations will die out, which is what we would expect to happen biologically if the lowest level food source dies out. If the bottom level prey dies out, all higher level predators

will follow.

Note that $\frac{dL}{dH}$ is also separable with solutions of the form:

$$\frac{dL}{dH} = \frac{-kL + cHL}{-jH - bHL} = \frac{L(-k + cH)}{H(-j - bL)}$$

Separating yields

$$dH\left(\frac{-k}{H} + c\right) = \left(\frac{-j}{L} - b\right) dL.$$

Integrating by respective variables then yields

$$-k \ln H + cH = -j \ln L - bL + C$$

for some arbitrary integration constant C. Thus, any solution must satisfy the equation

$$C = -k \ln H + cH + j \ln L + bL.$$

Again, this equation determines all possible surfaces the solutions lie on. For clarity, let's revisit how our parameters so that we can refer to them in the next subsection.

Parameters	Use in the 3-Variable Lokta-Volterra Equations
q	natural growth rate of the vegetation in the absence of hares
a	effect of predation by the hares on the vegetation
j	natural death rate of the hares in the absence of vegetation
r	efficiency and propagation rate of the hares in the presence of vegetation
k	natural death rate of the lynx in the absence of the hare
b	effect of predation on the hare population by the lynx population
c	efficiency and propagation rate of the lynx in the presence of hare

3.3.6 Dynamics of the three equation Lotka-Volterra Model

Using the same method as before we can calculate the equilibria for this model by solving

$$\frac{dV}{dt} = 0, \quad \frac{dH}{dt} = 0, \quad \text{and} \quad \frac{dL}{dt} = 0.$$

- From the first equation $\frac{dV}{dt} = qV - aVH = V(q - aH) = 0$ implies $V = 0$ or $H = \frac{q}{a}$.
- The third equation $\frac{dL}{dt} = -kL + cHL = L(-k + cH) = 0$ implies $L = 0$ or $H = \frac{k}{c}$.
- The second equation $\frac{dH}{dt} = -jH + rVH - bHL = H(-j + rV - bL) = 0$ implies $H = 0$ or $-j + rV - bL = 0$. Now depending on which variable we solve for in the second equation, we have $V = \frac{bL+j}{r}$ or $L = \frac{rV-j}{b}$.

From this we are able to find and analyze the equilibria points. We have:

- The trivial fixed point
$$(0, 0, 0).$$
- When $L = 0$ we find that another point obtained for the two equation system at
$$\left(\frac{j}{r}, \frac{q}{a}, 0\right)$$
since $V = \frac{bL+j}{r} = \frac{j}{r}$ when $L = 0$.
- Additionally, from the calculations we made we see that since $H = \frac{q}{a}$ and $H = \frac{k}{c}$, this implies $\frac{q}{a} = \frac{k}{c}$. This yields an invariant ray of fix points parameterized by:
$$\left(s, \frac{q}{a}, \frac{rs - j}{b}\right)$$

where s represents a particular population of vegetation, $H = \frac{q}{a}$ and $L = \frac{rV-j}{b} = \frac{rs-j}{b}$ for $V = s$. Also, from the equation $V = \frac{bL+j}{r}$ calculated above we know that $V = s = \frac{bL+j}{r} = \frac{bL}{r} + \frac{j}{r} \geq \frac{j}{r}$, so $s \geq \frac{j}{r}$ regardless of the population of L, a fact we will use shortly.

Now to determine the stability of the equlibria we explore what happens near each of the fixed points using Jacobian analysis.

$$J = \begin{bmatrix} \frac{\partial f}{\partial V} & \frac{\partial f}{\partial H} & \frac{\partial f}{\partial L} \\ \frac{\partial g}{\partial V} & \frac{\partial g}{\partial H} & \frac{\partial g}{\partial L} \\ \frac{\partial h}{\partial V} & \frac{\partial h}{\partial H} & \frac{\partial h}{\partial L} \end{bmatrix} = \begin{bmatrix} q & -aV & 0 \\ rH & -j & -bH \\ 0 & cL & -k \end{bmatrix}$$

The origin is an unstable saddle point since

$$J(0,0,0) = \begin{bmatrix} q & 0 & 0 \\ 0 & -j & 0 \\ 0 & 0 & -k \end{bmatrix}.$$

with eigenvalues q, $-j$ and $-k$. Recalling that q represents the growth rate of the vegetation where j and k are death rates of the predator species, this seems to agree nicely with our findings in the coordinate planes where we discovered that all solutions on the HL-plane approach zero, while solutions on the V-axis grow exponentially.

Now for point $\left(\frac{j}{r}, \frac{q}{a}, 0\right)$ we have

$$J\left(\frac{j}{r}, \frac{q}{a}, 0\right) = \begin{bmatrix} 0 & -a\frac{j}{r} & 0 \\ r\frac{q}{a} & 0 & -b\frac{q}{a} \\ 0 & 0 & -k + c\frac{q}{a} \end{bmatrix}.$$

The eigenvalues of this matrix, calculated in Chapter 2, are $\frac{cq-ka}{a}$ and the purely imaginary numbers $\pm i\sqrt{qj}$. The eigenvalues $\pm i\sqrt{qj}$ with no real parts

correspond with our previous analysis that when the lynx population is zero, the equilibria point $\left(\frac{j}{r}, \frac{q}{a}, 0\right)$ is a center on the VH-plane. This means that the hare and vegetation populations co-exist on an 2-variable oscillating Lokta-Volterra cycle.

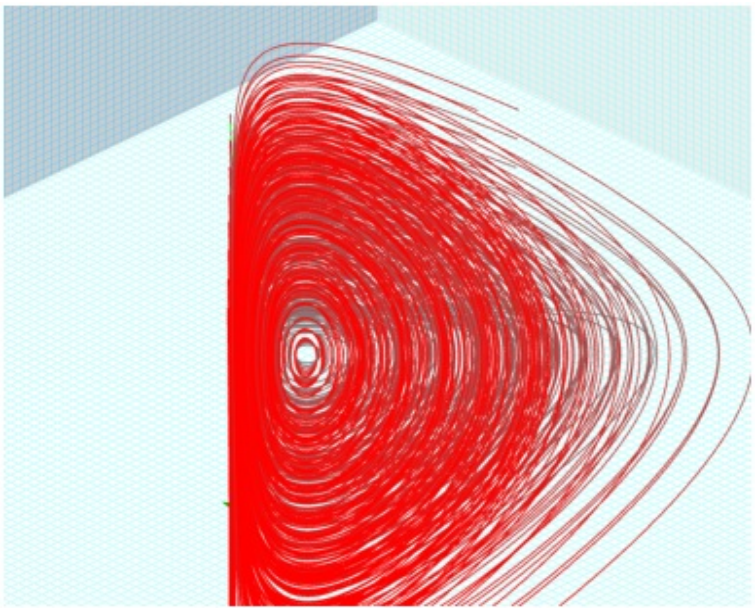
The stability associated with the eigenvalue $\frac{cq-ka}{a}$ is dependent on the sign of of eigenvalue $\lambda = \frac{cq-ka}{a}$, which we can reduce to examining the sign of $cq-ka$ since a represents the effect of predation by the hares on the vegetation population and thus $a > 0$.

Recall that c represents the the efficiency and propagation rate of the lynx in the presence of the hare and q represents the growth rate of the vegetation without the hare; both exponential. Also, k and a both represent death rates; k represents the death rate of lynx in the absence of hare and a represents the death rate of vegetation in the presence of the hare. So if we consider the case $cq = ka$, this means that product of the growth rates is equivalent to the product of the death rates. In the case $cq - ka < 0$ we have that the death rates exceed the growth rates. And if $cq - ka > 0$ we have that the growth rates exceed the death rates. To further explore the impact that the sign of $cq - ka$ has on the stability of the system we will need to consider each case separately.

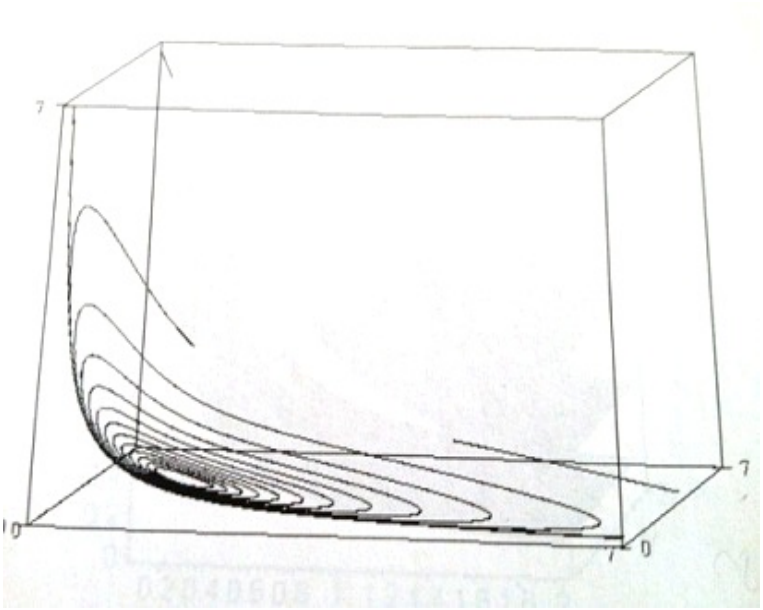
In the case $cq = ka$, we obtain a continuum of fixed points $\left(s, \frac{q}{a}, \frac{rs-j}{b}\right)$, with $s \geq \frac{j}{r}$, which is something different than what he have seen in the two system model. Thus, we need to consider a new method for determining stability of the equilibria. If we can show what happens in each case graphically and justify it algebraically, we can determine stability of the fixed points.

3.3.7 The case $cq - ka = 0$.

In this case, solutions are modeled with invariant surfaces or sheets filled with periodic orbits enclosing the ray of fixed points $(s, \frac{q}{a}, \frac{rs-j}{b})$, with $s \geq \frac{j}{r}$. The following image you can see the sheets surrounding the enclosed ray in the center, like the eye of a tornado.



Because there is so much going on the this picture we will simplify it by looking at only one particular sheet in the next picture so it is a little easier to see what the orbits look like.



In this picture we can see a family of closed orbits on a particular sheet corresponding to $L = CV^{\frac{-k}{q}}$ with all parameters equal to 1. We can find the equations of these surfaces rather easily after noticing that the projection of any particular solution onto the plane $H = 0$ is precisely contained in one of the trajectories $L = CV^{\frac{-k}{q}}$ in the VL-plane as demonstrated in the corollary below.

Corollary 3.3.7.1 Let $cq = ka$. The surfaces defined by $L = CV^{\frac{-k}{q}}$ which we will write and re-label as $F(V, H, L) = L - CV^{\frac{-k}{q}}$ are invariant with respect to

$$\begin{cases} \frac{dV}{dt} &= qV - aVH \\ \frac{dH}{dt} &= -jH + rVH - bHL \\ \frac{dL}{dt} &= -kL + cHL \end{cases}$$

.

Proof: :

The gradient $\bigtriangledown F = \left\langle C\frac{k}{q}V^{\frac{-k}{q}-1}, 0, 1 \right\rangle$ is always normal to $L - CV^{\frac{-k}{q}} = 0$. Consider,

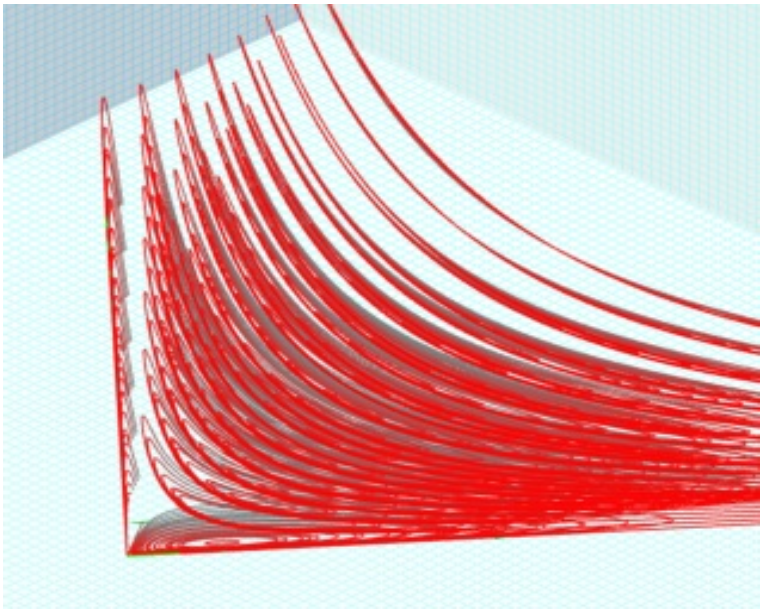
$$
\begin{aligned}
\bigtriangledown F \cdot \eta &= \left\langle C\tfrac{k}{q}V^{\frac{-k}{q}-1}, 0, 1 \right\rangle \cdot \langle qV - aVH, -jH + rVH - bHL, -kL + cHL \rangle \\
&= (qV - aVH)\left(C\tfrac{k}{q}V^{\frac{-k}{q}-1}\right) - kL + cHL \\
&= kCV^{\frac{-k}{q}} - \tfrac{kaCH}{q}V^{\frac{-k}{q}} - kCV^{\frac{-k}{q}} + cCHV^{\frac{-k}{q}} \\
&= kCV^{\frac{-k}{q}} - cCHV^{\frac{-k}{q}} - kCV^{\frac{-k}{q}} + cCHV^{\frac{-k}{q}} \\
&= 0
\end{aligned}
$$

since we supposed that $cq = ka$ and $L = CV^{\frac{-k}{q}}$. Thus, we have the surface $L = CV^{\frac{-k}{q}}$ is invariant with respect to

$$
\begin{cases}
\frac{dV}{dt} &= qV - aVH \\
\frac{dH}{dt} &= -jH + rVH - bHL \\
\frac{dL}{dt} &= -kL + cHL
\end{cases} \cdot
$$

□

The following image shows the invariant surfaces or sheets in which the solutions lie. They correspond to the surfaces $L = CV^{\frac{-k}{q}}$ with $k = q = 1$.



Now that we have shown invariance for the system and $L = CV^{\frac{-k}{q}}$ we can solve the system subject to this condition in order to characterize it's behavior. Solving the differential equation for fixed C with $L = CV^{\frac{-k}{q}}$, the system becomes

$$\begin{cases} \frac{dV}{dt} &= qV - aVH \\ \frac{dH}{dt} &= -jH + rVH - bHCV^{\frac{-k}{q}} \end{cases}$$

Since this differential equation is separable we can integrate to obtain:

$$\frac{dH}{dV} = \frac{\frac{dH}{dt}}{\frac{dV}{dt}} = \frac{H(-j + rV - bCV^{\frac{-k}{q}})}{V(q - aH)}$$

Or more simply

$$\frac{dH}{dV} = \frac{H(-j + rV - bCV^{\frac{-k}{q}})}{V(q - aH)}.$$

Multiplying to clear fractions yields

$$dH(V(q - aH)) = dV(H(-j + rV - bCV^{\frac{-k}{q}})$$

then dividing both sides by V and by H gives

$$dH\left(\frac{q}{H} - a\right) = dV\left(\frac{-j}{V} + r - bCV^{\frac{-k}{q}-1}\right).$$

Integrating both sides with respect to their respective variables produces

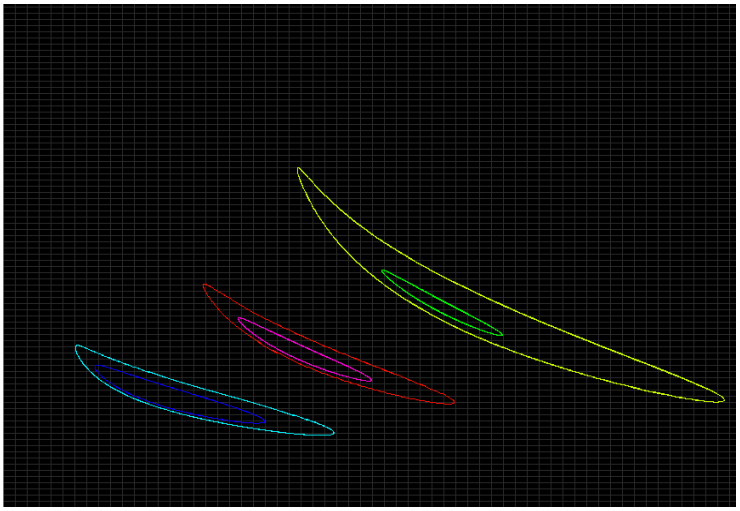
$$q \ln H - aH = -j \ln V + rV + \frac{bqC}{k}V^{\frac{-k}{q}} + K.$$

Finally solving for K yields

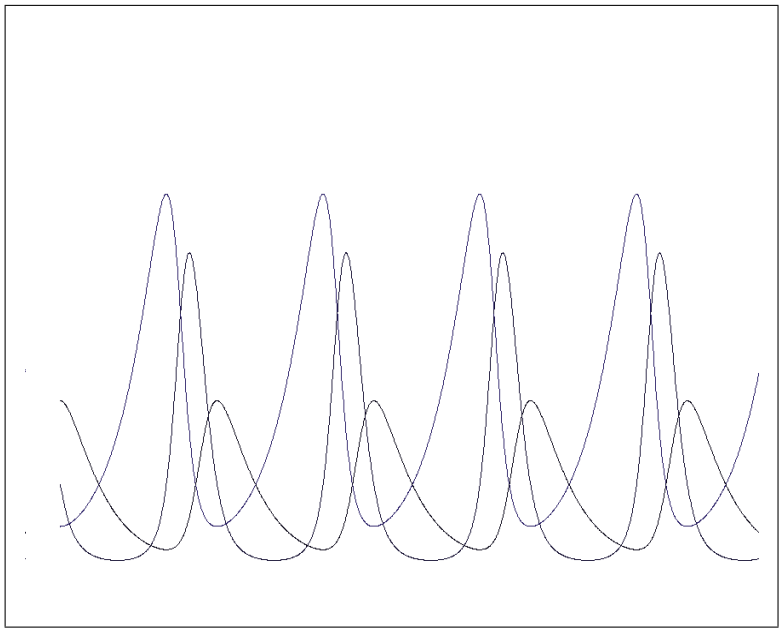
$$q \ln H - aH + j \ln V - rV - \frac{bqC}{k}V^{\frac{-k}{q}} = K.$$

Thus, any solution subject to the condition $L = CV^{\frac{-k}{q}}$ must satisfy this equation. Note that the parameter K above matches exactly the parameter C for $\frac{dH}{dV}$ on the surface $L = CV^{\frac{-k}{q}}$ when $L = 0$ in the VH -plane. The image to

follow shows the trajectories on the sheets determined by $L = V$ and varying H; closed trajectories with all parameters equal to 1.

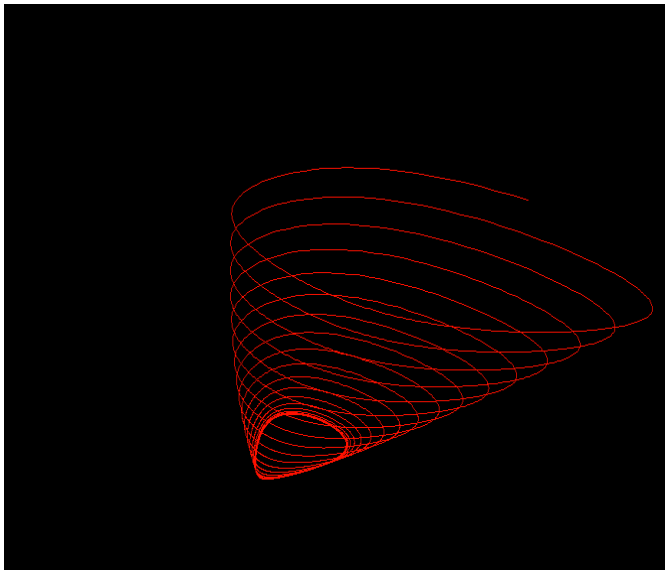


This completely characterizes the behavior of the special case $cq = ka$. Biologically, all three species persist and have populations that vary periodically over time. The following image with the highest peaks to the vegetation population, the middle to the hare and the lowest to the lynx shows this periodic behavior. Notice it makes sense that the vegetation peaks first with the predators to follow in sequence.



3.3.8 The case $cq < ka$

The case $cq < ka$. Plots of solutions using computer animation suggest that all solutions spiral down to the VH-plane and limit to a periodic solution. The solutions move down sheets $L = CV^{\frac{-k}{q}}$ from higher values of C to lower values of C as seen in the following corollary and corresponding picture.



A trajectory with initial conditions $(V, H, L) = (.5, 1, 2), c = 0.88$ and all other parameters equal to 1.

Corollary 3.3.8.1 *Let $cq < ka$ and $F(V, H, L) = LV^{\frac{k}{q}}$ be the respective invariant surface. Then for any solution $(V(t), H(t), L(t))$ of 3.2 in $\mathbb{R}^3_+$ we have*

$$\bigtriangledown F \cdot \eta < 0.$$

Proof:

First note that $F(V, H, L) = LV^{\frac{k}{q}}$ can be found by taking our previous invariance surface $L = CV^{\frac{-k}{q}}$ and solving this equation for C.

$$\begin{aligned}
\bigtriangledown F \cdot \eta &= \left(\tfrac{k}{q} LV^{\frac{k}{q}-1}, 0, V^{\frac{k}{q}}\right) \cdot \left\langle qV - aVH, -jH + rVH - bHL, -kL + cHL \right\rangle \\
&= kLV^{\frac{k}{q}} - \tfrac{ak}{q} LHV^{\frac{k}{q}} - kLV^{\frac{k}{q}} + cHLV^{\frac{k}{q}} \\
&= -\tfrac{ak}{q} LHV^{\frac{k}{q}} + cHLV^{\frac{k}{q}} \\
&= LHV^{\frac{k}{q}} \left(\tfrac{-ak}{q} + c\right) \\
&< 0
\end{aligned}$$

since we supposed that $cq < ka$ which implies that $\frac{-ak}{q} + c < 0$.

□

This corollary shows that when $cq < ka$ solutions travel down the level surfaces of the function F, which are precisely $C = LV^{\frac{k}{q}}$.

3.3.9 The case $cq > ka$

Now to explore that happens when $cq > ka$.

The following corollary implies that when $cq > ka$ the solutions travel down the level surfaces of $G = \left(aH - q\ln H + rV - j\ln V + \frac{bq}{k}L\right)$ as time increases. In particular, a solution starting with initial condition (V_0, H_0, L_0) at time t_0 can never travel to a region in $\mathbb{R}^3_+$ where $G(V, H, L) \geq G(V_0, H_0, L_0)$. Further, since the VH-plane is invariant, the solution will be trapped in the region bounded above by the VH-plane and below by the surface $G(V_0, H_0, L_0)$ for all $t > t_0$.

Corollary 3.3.9.1 *Let $cq > ka$ and*

$$G(V, H, L) = \left(aH - q\ln H + rV - j\ln V + \frac{bq}{k}L\right).$$

Then for any solution $(V(t), H(t), L(t))$ of 3.2 in $\mathbb{R}^3_+$ we have

$$\bigtriangledown G \cdot \eta < 0.$$

Proof: :

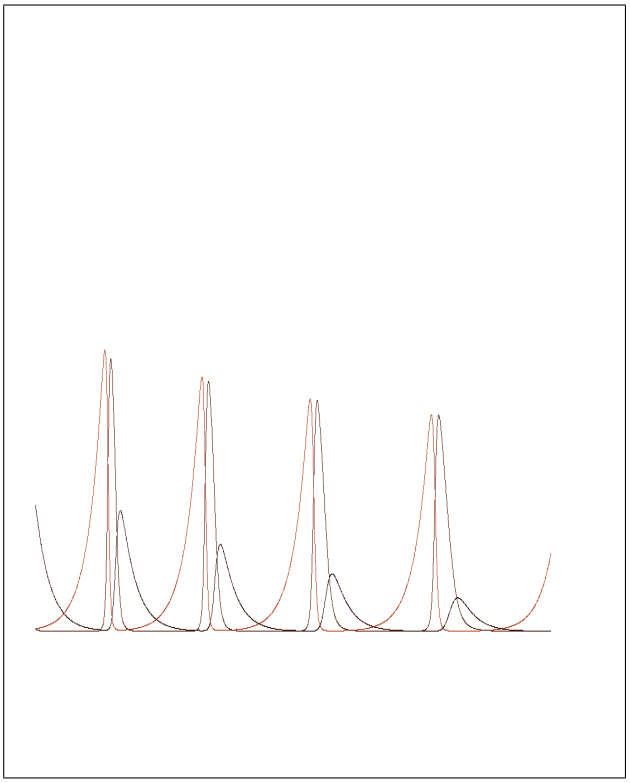
Consider

$$
\begin{aligned}
\bigtriangledown G \cdot \eta &= \left(\tfrac{j}{V} - r, \tfrac{q}{H} - a, -\tfrac{bq}{k}\right) \cdot \left\langle qV - aVH, -jH + rVH - bHL, -kL + cHL \right\rangle \\
&= -rqV + raVH + jq - ajH + ajH - arVH + abHL - qj + qrV - bqL + bqL - \tfrac{cHLbq}{k} \\
&= abHL - \tfrac{cHLbq}{k} \\
&= HLb\left(a - \tfrac{cq}{k}\right) \\
&< 0
\end{aligned}
$$

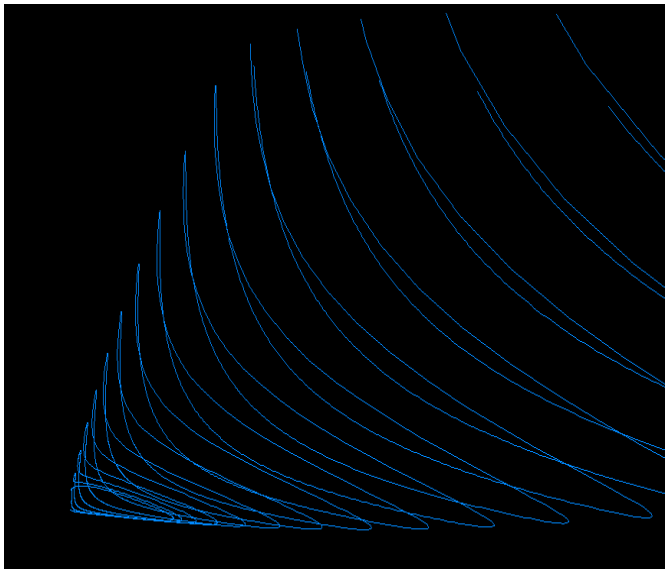
since we supposed that $cq > ka$.

□

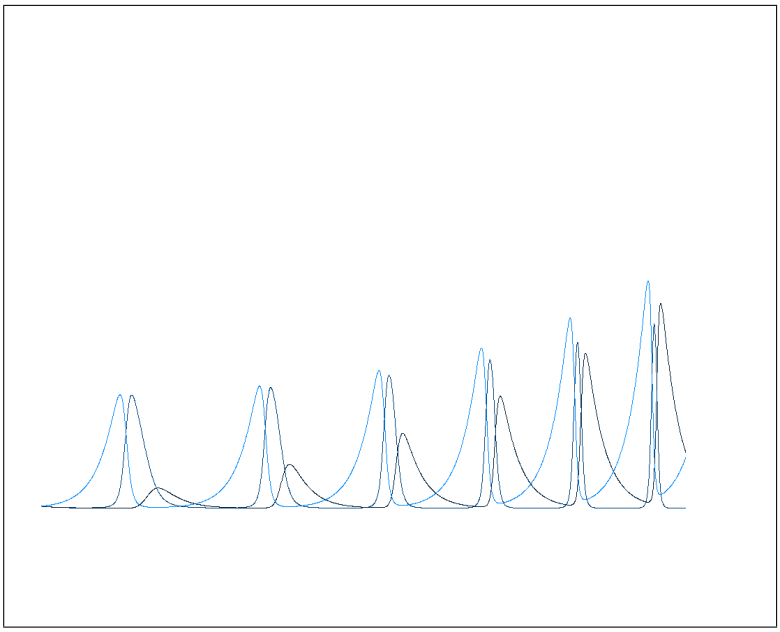
The corollaries show that for $cq < ka$, all trajectories beginning in $\mathbb{R}^3_+$ tend to the plane $L = 0$ and further that all such solutions approach a periodic solution in the VH - plane. From a biological standpoint this means that if the top predator, the lynx tends to extinction, the population distribution of the hare and vegetation will follow the traditional Lotka-Volterra oscillations.



The case $cq > ka$ implies that all trajectories starting in $\mathbb{R}^3_+$ travel up the sheets $L = CV^{\frac{-k}{q}}$, i.e. $L(t) \to \infty$ as $t \to \infty$. This implies that the lynx population tends to ∞, non-monotonically, while the populations of the hares and vegetation overtime experience larger and larger fluctuations, having both 0 and $+\infty$ as limit points as seen in the following phase portrait.



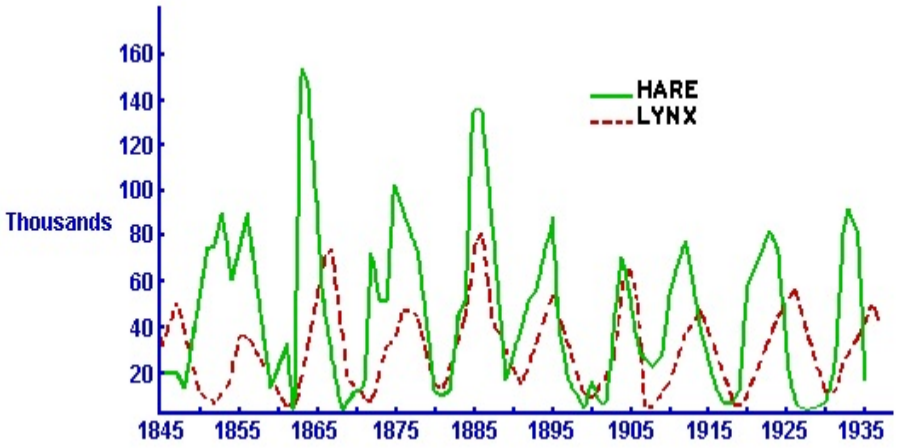
For this situation all species exist on oscillating cycles with the lynx population tending to infinity and all of the species populations having increasingly larger oscillations. The following image represents this situation with initial conditions $(.5, .5, 2)$ with $c = 0.88$ and the rest of the parameters 1.



In conclusion, it seems that the lynx population in the long term hinges on the parameters q, a, k and c. If $cq < ka$, then the lynx population dies out, while if $cq > ka$, the lynx population survives and grows without bound. This coincides with our intuition as larger values of q and c are explicitly beneficial to the lynx population, larger values of a and k are inhibitory. Interestingly, the parameters most directly related to the hare population, namely j, r and b have very little if any influence on whether the lynx population will become extinct in our model. In short, the mid-level predator simply acts as a conduit between the top and bottom species. Also, it's interesting to note that all species in the model are co-dependent. If either of the lower level species become extinct it causes extinction of any of the predators in the higher trophic levels (i.e. extinction of vegetation, results in complete extinction, but extinction of the hare only results in lynx extinction leaving the vegetation population to grow without bound).

Thus, after analyzing both the two and the three species Lokta-Volterra predator-prey models, it it appears more logical that the hare cycle is produced

by an interaction between both predation and food supplies. After 70 years of research, time series analyses, and field experiments, scientists finally have a good understanding of the dynamics behind the 10-year snowshoe hare cycle and the importance of predation and food supplies in regulating that cycle.



3.4 Summary

- First we explored the two species Lotka-Volterra model.
- We calculated equilibria values and determined their stability in an attempt to understand the relationships between the interacting species.
- We concluded that the Lotka-Volterra models are usable tools for developing understanding of species interactions but decided to explore whether a modification to this model would be more reasonable to describe the data collected by the Hudson Bay Company.
- We explored the three species Lotka-Volterra model and showed the system was invariant (thus if once species became extinct it would not reappear in the model).

- Calculating equilibria values and determining stability was a bit more complicated for this system, but eventually we were able to get a feel for the stability of the system.

- Finally, we were able to conclude that the 10-year oscillating hare cycle is more likely the result of a three-tropic level interaction between the hare, lynx and the hares prey.

3.5 Problems with the Lotka-Volterra Model

- Minimum sustainable population size for each species is not taken into account.

- Predators have an unlimited consumption rate, the model does not take into account saturation.

- The rate of prey consumption is proportional to prey density.

- The model does not consider any competition among predators and prey. The Lotka-Volterra model does not give accurate results if the predator and prey are competing for some resource (i.e. space). We will revisit this concept of carrying capacity in later chapters.

Now that we have spent some time getting a feel for simple predator-prey relationships we can begin to work with mathematical models designed to study infectious diseases. Parallel's to the Lotka-Volterra systems are evident as we will be able to see in the next exploration.

Chapter 4

Infectious Diseases

4.1 Introduction

Infectious diseases come in many different varieties, thus we must have several different models to work from to try to understand them. In the models we will explore we will consider populations of susceptible, infectious and recovered persons. When studying infectious diseases there are many questions we need to ask ourselves. We need to think about the size of the population affected; whether the population is constant, growing or shrinking. Also, whether age and/or sex are factors to contracting and surviving the disease. Additionally, we need to think about how the disease is spread. Is it spread though insects? Contact with an infected individual? Is there an incubation period in which a person is infectious before symptoms appear? Can some individuals carry the disease without being impacted personally? If infected individuals recover is it possible for them to be infected again? Is the disease micro-parasitic or macro-parasitic? Is it an epidemic or endemic? We will attempt to answer several of these questions while exploring different infectious disease models.

We will begin with simple models assuming closed population sizes then move to more complicated systems, while leaving other questions open for further research.

In the sections to follow we will examine models for different types of infectious diseases. We will discuss the models in the context of a few actual disease situations and work to understand how the systems interact.

4.2 Simple Epidemic

The most basic model we are going to explore is called a simple epidemic model. In a simple epidemic the population consists only of two non-intersecting groups, susceptibles and infectives. These groups are often called classes or compartments. The susceptible class is usually denoted by S and represents the portion of the population who can contract the disease under appropriate conditions. The class of infectives, denoted by I, consists of the portion of the population that have contracted the disease and that can transmit the disease to a susceptible though contact of some form; I is also referred to as the prevalence of the disease. A disease is contagious if it is spread by contact between a susceptible and an infective. Simple epidemic models assume that a susceptible, once infected, becomes infectious immediately and remains so indefinitely. In the latter scenarios we will explore, we will look at models that exist under different assumptions.

Simple models or SI models, as they are called, an acronym standing for susceptible-infectious models, are reasonable approximations to the initial stages of many diseases. They work to explain how disease transmission impacts a particular population. However, because they do not account for what happens after infection, we will need to add some extra variables to explore

outcomes in the sections to follow. For the SI model we will assume that the population is closed, which means that there is no population change due to death and/or birth since we are only talking about a short time period for this model. Let $S(\tau)$ and $I(\tau)$, represent the number of susceptible and infectious individuals at time τ, so that $S(\tau) + I(\tau) = N$, where N is a constant population size. The differential equations satisfied by S and I are given by

$$\frac{dS}{d\tau} = -f(S, I), \quad \frac{dI}{d\tau} = f(S, I),$$

where $f(S, I)$ represents incidence of the disease or rather the rate at which infections occur. Clearly, f is an increasing function of both S and I as defined since it is early in the spread of the disease, and the simplest model which we will use is

$$f(S, I) = \lambda(I)S = \beta IS.$$

The function $\lambda(I)$ is called the force of infection and is defined as the probability density or the probability that a given susceptible will contract the disease in the next small interval of time. Defining $\lambda(I) = \beta I$, the parameter β is called the pairwise infectious contact rate or the rate of infection per susceptible and per infective. This yields the system

$$\begin{cases} \frac{dS}{d\tau} &= -\beta IS \\ \frac{dI}{d\tau} &= \beta IS \end{cases}$$

If we suppose that $\frac{dI}{d\tau} = f(S, I) = \beta IS$ and $S + I = N$, then we can re-write $\frac{dI}{d\tau} = \beta I(N - I)$, eliminating the S in the second equation, the system becomes

$$\begin{cases} \frac{dS}{d\tau} &= -\beta IS \\ \frac{dI}{d\tau} &= \beta I(N - I) \end{cases}$$

Re-writing the system in this way allows us to solve the system as a single differential equation

$$\frac{dI}{d\tau} = \beta I(N - I)$$

since it seperates into

$$\frac{dI}{I(N - I)} = \beta d\tau.$$

We will not solve this equation at this point, but it is good to understand this relationship as it will allow us in later sections to be able to reduce systems of three equations to two, for ease of analysis. To get a feel for the parameters of this system we will consider the following brief example.

Example 4.1 *Suppose that in a small community a family goes on a trip and contracts a tropical virus. When they return home to their community, they begin infecting their community members. The β value associated with the disease contracted determines how fast the disease spreads. If the particular disease carries a infection rate with a small β value this means the disease spreads at a relatively low rate. As β increases the rate of infection increases.*

This is the most basic model, which is wonderful for getting a feel for how different parameters influence the model, but it does not take us to what happens next, which is key to understanding real life infectious diseases. The following two models explore what happens after infection, recovery and immunity or recovery with susceptibility and/or death. Consider the following exploration of the disease chancroid as it relates to a modification of the SI model.

4.3 Disease Example: S-I-S

Chancroid is a highly contagious yet curable sexually transmitted disease caused by the bacteria Haemophilus Ducreyi. It is very common in Africa, and has begun to make a presence in the United States as well. Chancroid causes ulcers, usually in the genitals, and is typically accompanied by swollen and painful lymph glands. The ulcers begin as tender, elevated bumps or papules that become pus-filled open sores with eroded or ragged edges. They are typically soft to the touch and can be very painful, especially in men. Women on the other hand can be asymptomatic and unaware of that they are infected with the disease. Chancroid is transmitted sexually though skin-to-skin contact with open sores and sometimes non-sexually though contact with the pus-like fluid from ulcers on other parts of the body.

A person is considered infectious when ulcers are present with symptoms developing within 4-10 days. Chancroid can be treated with antibiotics, usually azithromycin, ceftriaxone, ciprofloxacin and erythromycin, all of which cure the infection, eliminate symptoms and prevent transmission to others. If the treatment is successful the ulcers typically improve within 3-7 days, though the time of complete healing is dependent on the size of the ulcers; large ulcers may require two weeks or more to heal. After the infection has cleared the individual is again susceptible to infection from the same bacterium, which means no immunity is developed.

In addition to the immediate symptoms chancroid also has some scary complications. In 50% of cases, the lymph node glands in the groin become infected and sometimes enlarged, hard and painful. These lymph nodes can even fuse together to form bubo's and require drainage surgery. These buboes are also susceptible to secondary infections. Additional complications can

be introduced for uncircumcised males and what is even more frightening, chancroid has been well established as a cofactor for HIV transmission.

Since individuals that contract chancroid return to the susceptible class after infection we need to alter our SI model to a SIS model, which means a person that contracts the disease is categorized as susceptible, then infectious, then susceptible again. We will explore this new model in the next section and refer back to this case to get a feel for how it works in a particular disease example.

4.3.1 S-I-S Models

The S-I-S model consists of a susceptible becoming infective, then becoming susceptible again. Some well known diseases that may follow this type of model are bacterial infections such as chancroid, viral infections such as hemorrhagic conjunctivitis, and the common cold. If we assume that the modeling time scale is short compared to the lifetime of its hosts, so that we can neglect birth and death, we again have a closed population.

$$S(\tau) + I(\tau) = N$$

with

$$\frac{dS}{d\tau} = -f(S,I) + g(I) \quad \text{and} \quad \frac{dI}{d\tau} = f(S,I) - g(I).$$

Now we introduce a new term, $g(I)$, representing recovery from the disease. The simplest recovery function is $g(I) = \gamma I$, where γ is called the rate of recovery.

$$\begin{cases} \frac{dS}{d\tau} &= -\beta IS + \gamma I \\ \frac{dI}{d\tau} &= \beta IS - \gamma I \end{cases}$$

In this model we again have a closed and invariant system. We also see that this system is very interdependent. Note that if

$$\frac{dS}{d\tau} = 0$$

then

$$I(-\beta S + \gamma) = 0.$$

Therefore either

$$I = 0$$

or

$$-\beta S + \gamma = 0$$

which gives that

$$S = \frac{\gamma}{\beta}.$$

And since $N = I + S$

- when $I = 0$ this implies

$$S = N$$

- when $S = \frac{\gamma}{\beta}$ this implies

$$I = N - \frac{\gamma}{\beta}$$

.

Therefore, we have equilibria points

$$(N, 0) \quad \text{and} \quad \left(\frac{\gamma}{\beta}, N - \frac{\gamma}{\beta}\right).$$

If $I = 0$, this means that there are no infectives which implies the entire population exists in the susceptible class. Biologically this means that there is no change in the number of susceptibles nor in the number of infectives, which

makes sense if there are no infectives anyways. And if $S = \frac{\gamma}{\beta}$ this means the remaining total population $N - \frac{\gamma}{\beta}$ must be contained in the infectious class. Therefore, as the ratio of $\frac{\gamma}{\beta}$ decreases, corresponding to a larger β value or a smaller γ value, $I = N - S$ is getting larger, which means the infectious class is growing.

To get a better feel for these parameters, let's refer back to the chancroid example. Since a person that contracts chancroid has an expected length of time infected of 3-7 days, we will consider an average infected time of 5 days. This means that $\gamma = 5$ days or $\gamma = \frac{5}{7}$ weeks, if γ is measured in weeks. Also, since chancroid is an SIS disease we have the following system with $\gamma = \frac{5}{7}$,

$$\begin{cases} \frac{dS}{d\tau} &= -\beta IS + \frac{5}{7}I \\ \frac{dI}{d\tau} &= \beta IS - \frac{5}{7}I \end{cases}$$

As we discussed earlier the larger the β value the faster the disease spreads. Since γ represents the rate of recovery, the larger the γ value, the quicker the individuals will recover from the disease. Thus if β is large and γ is small the infectious class will be large whereas if β is small and γ is large, the majority of the total population will be contained in the susceptible class.

The phase portraits depicting these parameter changes are rather uninteresting to look at since both β and γ represent speed. Graphing them on computer software you can see the rate in which the phase portrait is created, thus making it interesting, but without live animation it is relatively useless to show the phase portraits with differing β and γ values.

4.3.2 Further Analysis

To further understand the dynamics of this model we can non-dimensionalize the variables which is equivalent to considering the change in the overall population by defining,

$$s = \frac{S}{N}, \quad i = \frac{I}{N}, \quad t = \gamma\tau.$$

Now we will work to define $\frac{ds}{dt}$ and $\frac{di}{dt}$. First we will start with what we know from before

$$\frac{dS}{d\tau} = -\beta IS + \gamma I.$$

Substituting sN for S and iN for I as in the previous definition we obtain

$$\frac{dS}{d\tau} = -\beta siN^2 + \gamma iN.$$

Since $s = \frac{S}{N}$ and $ds = \frac{dS}{N}$, this implies $dS = Nds$. Replacing dS and dividing by N gives,

$$\frac{ds}{d\tau} = -\beta siN + \gamma i.$$

Our goal is to find $\frac{ds}{dt}$, noting that

$$\frac{ds}{dt} = \frac{ds}{d\tau} \cdot \frac{d\tau}{dt}.$$

As defined we know that $t = \gamma\tau$, thus $\tau = \frac{t}{\gamma}$. Therefore, if we take the derivative

$$\frac{d\tau}{dt} = \frac{1}{\gamma}.$$

Together we can write

$$\begin{aligned} \tfrac{ds}{dt} &= (-\beta siN + \gamma i) \cdot \left(\tfrac{1}{\gamma}\right) \\ &= \tfrac{-\beta siN}{\gamma} + i \\ &= -\left(\tfrac{\beta Ns}{\gamma} - 1\right) i \end{aligned}$$

Defining R_0 as follows

$$R_0 = \frac{\beta N}{\gamma}$$

we finally obtain

$$\frac{ds}{dt} = -(R_0 s - 1)i.$$

Now to explore find $\frac{di}{dt}$. Starting with what we know

$$\frac{dI}{d\tau} = \beta IS - \gamma I.$$

Substituting sN for S and iN for I as in the definition above we obtain

$$\frac{dI}{d\tau} = \beta siN^2 - \gamma iN.$$

Since $i = \frac{I}{N}$ and $di = \frac{dI}{N}$, this implies $dI = Ndi$. Replacing dI and dividing by N gives,

$$\frac{di}{d\tau} = \beta siN - \gamma i.$$

Then to find $\frac{di}{dt}$, rewrite

$$\frac{di}{dt} = \frac{di}{d\tau} \cdot \frac{d\tau}{dt}$$

and we know

$$\frac{d\tau}{dt} = \frac{1}{\gamma}$$

Thus, together we can write

$$\begin{aligned} \tfrac{di}{dt} &= (\beta siN - \gamma i) \cdot \left(\tfrac{1}{\gamma}\right) \\ &= \tfrac{\beta siN}{\gamma} - i \\ &= \left(\tfrac{\beta Ns}{\gamma} - 1\right) i \end{aligned}$$

Again letting

$$R_0 = \frac{\beta N}{\gamma},$$

we have

$$\frac{di}{dt} = (R_0 s - 1)i$$

Thus,

$$\frac{ds}{dt} = -(R_0 s - 1)i, \quad \frac{di}{dt} = (R_0 s - 1)i$$

and we note that

$$\frac{ds}{dt} + \frac{di}{dt} = 0.$$

The equations are to be solved on the one-dimensional simplex, or line segment, $S_1 = \{(s, i) | 0 \leq s \leq 1, 0 \leq i \leq 1, s + i = 1\}$. We can see that since $S + I = N$, that we have $\frac{S}{N} + \frac{I}{N} = \frac{N}{N}$, which is the same as saying $s + i = 1$. From this we also get that $\frac{ds}{dt} + \frac{di}{dt} = 0$, so $\frac{ds}{dt} = -\frac{di}{dt}$, which is exactly what we found above.

R_0 is called the basic reproductive ratio and in the equations found is defined to be $R_0 = \frac{\beta N}{\gamma}$, where βN is the rate at which a single infective introduced into a susceptible population of size N makes infectious contacts and $\frac{1}{\gamma}$ is the expected length of time such an infective remains infectious. Thus, R_0 is the expected number of infectious contacts made by such an infective. This is a key component in each of the models to follow since we consider $R_0 < 1$ to be indicative of a disease die out and $R_0 > 1$ implies that a particular disease remains endemic in the population. It is interesting to note the R_0 values of some well know diseases:

Disease	R_0
AIDS	2-5
Chickenpox	9-10
Diphtheria	4-6
German Measles	6
Influenza, H1N1	1.1-2
Measles	12-13
Mumps	4-7
Poliomyelitis	6
Scarlet Fever	5-7
Smallpox	3-5
Whooping Cough (Pertussis)	13 - 17

4.3.3 Equilibria and Stability

For the system

$$\frac{ds}{dt} = -(R_0 s - 1)i, \quad \frac{di}{dt} = (R_0 s - 1)i$$

since $s+i = 1$, we have $i = 1-s$, so solving to find equilibria in either equation we have

$$0 = (R_0 s - 1)(1 - s)$$

thus

$$s = 1 \quad \text{or} \quad s = \frac{1}{R_0}.$$

When $s = 1$ we must have the value $i = 0$, which results in a disease free steady-state. We can explore the stability properties of the disease-free steady state $(s, i) = (1, 0)$ by examining the Jacobian matrix at this point

$$J = \left(\begin{array}{cc} -R_0 i & -R_0 s + 1 \\ R_0 i & R_0 s - 1 \end{array} \right) \Bigg|_{(1,0)} = \left(\begin{array}{cc} 0 & -R_0 + 1 \\ 0 & R_0 - 1 \end{array} \right)$$

which has eigenvalues 0 and $R_0 - 1$.

The equilibrium corresponding to these eigenvalues is dependent on the value of $R_0 - 1$. If $R_0 < 1$ this expression is negative which corresponds to a stable equilibrium since neither eigenvalue is positive, but if $R_0 > 1$ this results in a positive eigenvalue which corresponds to an unstable equilibrium point since one of the real parts of the eigenvalues is positive.

The value $s = \frac{1}{R_0}$, corresponds to $i = 1 - \frac{1}{R_0}$, since we are considering a rate change with introduction to some number of infectious individuals that must relate to $N = S + I$. This implies $1 = s + i$ when we non-dimensionalize, so $i = 1 - s$ and since $s = \frac{1}{R_0}$ we have $i = 1 - \frac{1}{R_0}$. Therefore the Jacobian

$$J = \left(\begin{array}{cc} -R_0 i & -R_0 s + 1 \\ R_0 i & R_0 s - 1 \end{array} \right) \Bigg|_{\left(\frac{1}{R_0}, 1 - \frac{1}{R_0}\right)} = \left(\begin{array}{cc} -R_0 + 1 & 0 \\ R_0 - 1 & 0 \end{array} \right)$$

Thus the eigenvalues are $-R_0 + 1$ and 0. Similarly to the previous equilibrium analysis if $-R_0 + 1 > 1$, implying $R_0 < 0$ we have an unstable equilibrium, but if $R_0 > 0$ we have a stable equilibrium point.

Notice that when we non-dimensionalized our system we came up with steady states

$$(s, i) = (1, 0) \quad \text{and} \quad (s, i) = \left(\frac{1}{R_0}, 1 - \frac{1}{R_0} \right)$$

and before we non-dimensionalized we found equilibria at

$$(S, I) = (N, 0) \quad \text{and} \quad (S, I) = \left(\frac{\gamma}{\beta}, N - \frac{\gamma}{\beta} \right)$$

Simple division by N changes (S, I) to (s, i) thus,

$$(s, i) = \left(\frac{N}{N}, 0 \right) = (1, 0)$$

and

$$(s,i) = \left(\frac{\frac{\gamma}{\beta}}{N}, \frac{N-\frac{\gamma}{\beta}}{N}\right) = \left(\frac{\gamma}{\beta N}, 1-\frac{\gamma}{\beta N}\right) = \left(\frac{1}{R_0}, 1-\frac{1}{R_0}\right).$$

This concludes our study of SIS models. We find two equilbira points with stability dependent on the parameters γ and β or R_0.

4.4 S-I-R Models

The next epidemic model to explore is the SIR model, which consists of susceptibles, infectives and now a new class which we called removed. The removed class consists of those individuals which play no further role in the disease. They may be dead, recovered and immune, removed by an isolation policy or otherwise. The majority of infectious diseases, such as measles, mumps, smallpox, different plagues and more have such a removed class R.

$$S \to I \to R$$

The first model introduced to understand SIR diseases was developed by Kermack and McKendrick [4] and looked similar to what follows. To begin let's assume that the duration of the epidemic is short compared to the lifetime of its host so that we can neglect birth and non-disease related death rates and work within the closed population of constant size $N = S(\tau) + I(\tau) + R(\tau)$. The following system models the movement between population classes.

$$\begin{cases} \frac{dS}{d\tau} &= -\beta IS \\ \frac{dI}{d\tau} &= \beta IS - \gamma I \\ \frac{dR}{d\tau} &= \gamma I \end{cases}$$

Where βIS represents the number of susceptibles who become infective

and γ represents the rate at which individuals leave the infectious class, called the recovery rate. Notice that the difference between this model and the SIS model is that the γI term moves into the removed class rather than back into the susceptible class because we are assuming that the individuals are no longer susceptible after infection.

The SIR model, like it's friends the SI and SIS models, is called a compartmental model because each individual in the total population can only reside in one compartment at a time. The total population is given by the sum of each compartment

$$N(\tau) = S(\tau) + I(\tau) + R(\tau).$$

Since we assume the population does not change, it is constant and we have

$$N'(\tau) = S'(\tau) + I'(\tau) + R'(\tau) = -\beta IS + \beta IS - \gamma I + \gamma I = 0.$$

In this section our goal is to be able to use these equations and parameters to explore how well these models relate to the real world. First, let's examine what happens when there is no influx into the infective class. This would imply no movement from the susceptible class to the infectious class, which limits movement strictly between infectious and recovery classes. Thus, $\frac{dI}{d\tau}$ becomes

$$\frac{dI}{d\tau} = -\gamma I,$$

with initial condition $I(0) = I_0$. This is exponential decay and gives the number of people in the infectious class at time τ given by

$$I(\tau) = I_0 e^{-\gamma\tau}.$$

Hence for $\tau \neq 0$,

$$\frac{I(\tau)}{I_0} = e^{-\gamma\tau}$$

represents the proportion of people who are still infectious at time τ. Letting

$$F(\tau) = 1 - e^{-\gamma\tau}, \quad \tau \neq 0$$

then this equation represents the probability of recovering and/or leaving the infectious class in the interval $[0, \tau)$. Thus, if we define $f(\tau) = \frac{dF}{d\tau}$ we have

$$f(\tau) = \gamma e^{-\gamma\tau}.$$

Since τ represents a measure of time, we will define $f(\tau) = 0$ for $\tau < 0$. The average time spent in the infective class varies based on the particular disease, thus we need to find some way to account for this in our model. Let X denote the time for exiting the infectious class and represent the mean time spent in the infectious class then the "Expected Value" defined to be

$$E[X] = \int_{-\infty}^{\infty} \tau f(\tau) d\tau$$

can be used to determine how long the average person is infective. [11], [27]. Evaluating this integral for $f(\tau)$ defined above and integrating gives

$$\int_{-\infty}^{\infty} \tau f(\tau) d\tau = \int_{0}^{\infty} \tau\gamma e^{-\gamma\tau} d\tau = \frac{1}{\gamma},$$

by way of integration by parts. This implies that the mean time spent in the infectious class is $\frac{1}{\gamma}$ which matches the previous model.

Briefly this means that for a common disease such as influenza which typically lasts from 3 to 7 days, the mean time spent infectious is approximately 5 days. Therefore, the recovery rate γ measured in days is $\frac{1}{5}$, which implies that each person is recovering at a rate of $\frac{1}{5^{th}}$ recovery per day.

Now that we have some understanding on the role of the parameters, let's focus on solving the system. To begin, first notice that the variable R

does not participate in the first two equations, thus we can consider only the equations for S and I, which are coupled, and leave out the equation of R. Notice that since we know

$$N = S + I + R$$

we can find R by solving

$$R = N - S - I.$$

From the system

$$\begin{cases} \frac{dS}{d\tau} &= -\beta IS \\ \frac{dI}{d\tau} &= \beta IS - \gamma I \\ \frac{dR}{d\tau} &= \gamma I \end{cases}$$

we can divide the first two equations to yield,

$$\frac{\frac{dI}{d\tau}}{\frac{dS}{d\tau}} = \frac{\beta IS - \gamma I}{-\beta IS} = -1 + \frac{\gamma}{\beta S}$$

Now by separating variables,

$$dI = \left(-1 + \frac{\gamma}{\beta S}\right) dS.$$

Then integrating gives

$$I = -S + \frac{\gamma}{\beta} \ln S + C,$$

where C is an arbitrary constant. Thus we can say that,

$$I + S - \frac{\gamma}{\beta} \ln S = C$$

with initial conditions $S(0) = S_0$ and $I(0) = I_0$ given. Assume the that $\lim_{\tau \to \infty} I(\tau) = 0$ so that the number of infectious individuals goes to zero eventually, while $S_\infty = \lim_{\tau \to \infty} S(\tau)$ gives the final number of susceptible individuals after the epidemic is over.

- For the initial value (S_0, I_0), this equation becomes

$$I_0 + S_0 - \frac{\gamma}{\beta} \ln S_0 = C.$$

- And when $\tau \to \infty$ we have $(S_\infty, 0)$, so the equation becomes

$$S_\infty - \frac{\gamma}{\beta} \ln S_\infty = C.$$

Next we will work to find the maximum number of infectious individuals possible. This maximum is closely related to the concept of carrying capacity which we will discuss in the next chapter. First we will solve for $\frac{\beta}{\gamma}$ by setting the equations for $\tau = 0$ and $\tau \to \infty$ equal to one another.

Notice first that $\frac{\gamma}{\beta}$ is the S value for the one of the equilibria of the system, found when we set $\frac{dI}{d\tau} = 0$. When $\frac{dI}{d\tau} = 0$ this imples

$$-1 + \frac{\gamma}{\beta S} = 0$$

which gives

$$S = \frac{\gamma}{\beta}.$$

This is interesting to note as it gives us some context for what $\frac{\gamma}{\beta}$ is. Using the equation discussed we get

$$I_0 + S_0 - \frac{\gamma}{\beta} \ln S_0 = S_\infty - \frac{\gamma}{\beta} \ln S_\infty.$$

so

$$\frac{\beta}{\gamma} = \frac{\ln \frac{S_0}{S_\infty}}{S_0 + I_0 - S_\infty}.$$

Note that since the population is constant, $S_\infty < S_0 + I_0$. Therefore this solution allows us to compute the maximum number infected individuals possible. This number occurs when $\frac{dI}{d\tau} = 0$, that is when $S = \frac{\gamma}{\beta}$ since $\frac{dI}{d\tau} = \beta IS - \gamma I$ at $S = \frac{\gamma}{\beta}$ the differential equation becomes

$$\frac{dI}{dt} = \beta I\left(\frac{\gamma}{\beta}\right) - \gamma I = \gamma I - \gamma I = 0.$$

To find the maximum infectious population we have

$$I + S - \frac{\gamma}{\beta}\ln S = I_0 + S_0 - \frac{\gamma}{\beta}\ln S_0.$$

Substituting the expression for S and moving all terms except I to the right-hand side leads to

$$I_{max} = -\frac{\gamma}{\beta} + \frac{\gamma}{\beta}\ln\frac{\gamma}{\beta} + S_0 + I_0 - \frac{\gamma}{\beta}\ln S_0.$$

This means that the maximum number of people infected is related to the parameters β and γ as well as to the initial amount of people susceptible and infectious. This makes sense, because we are dealing with a closed population. Thus, the maximum number of people infected must not exceed the total population size. This gets at the idea of carrying capacity which we will revisit in a later chapter. Before we move on to some further analysis of the system we will explore an example studying the Great Plague of Eyam to estimate how the parameter values relate.

4.4.1 Great Plague of Eyam

Eyam, a small village in England, suffered an outbreak of bubonic plague in 1666. The source was believed to be the Great Plague of London. In order to contain the spread the village was quarantined. The initial population of Eyam was 350. In mid-may 1666 there were 254 susceptibles and 7 infectives. Detailed records were recorded and preserved and are as follows:

Date 1666	Susceptibles	Infectives
Mid-May	254	7
July 3/4	235	14.5
July 19	201	22
August 3/4	153.5	29
August 19	121	21
September 3/4	108	8
September 19	97	8
October 3/4	Unknown	Unknown
October 20	83	0

From the data we have initial population sizes $S_0 = 254$ and $I_0 = 7$ and final susceptible population $S_\infty = 83$ and $I_\infty = 0$. Also, from the earlier computations we have

$$\frac{\beta}{\gamma} = \frac{\ln \frac{S_0}{S_\infty}}{S_0 + I_0 - S_\infty} = \frac{\ln \frac{254}{83}}{254 + 7 - 83} = 0.00628.$$

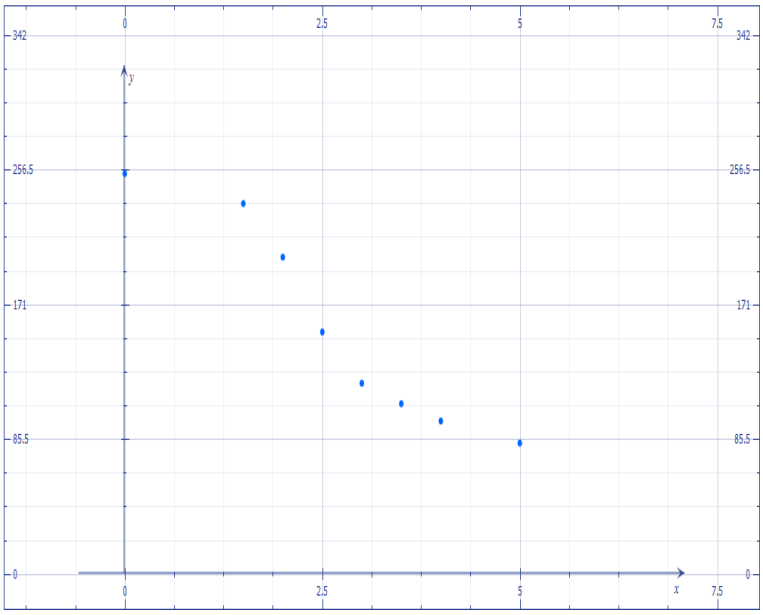
so

$$\frac{\gamma}{\beta} = \frac{1}{0.00628} = 159.322$$

.

Note that if we let $\tau_0 = 0$ represent time zero. The die-out of the disease appears to occur in mid-October of 1666 according to this data so $\tau_{end} = 5$ is the ending time measured in months.

Graphing the number of susceptibles with respect to time, it is easy to see a curve forming starting high and ending low.



The infective period of the bubonic plaque is roughly 11 days, thus converting to months supposing a 31 day month, 11 days $= \frac{11}{31} = 0.35483871$ months. Now we can estimate γ as the reciprocal of the average time spent as an infectious individual,

$$\gamma = \frac{1}{0.35483871} \approx 2.82.$$

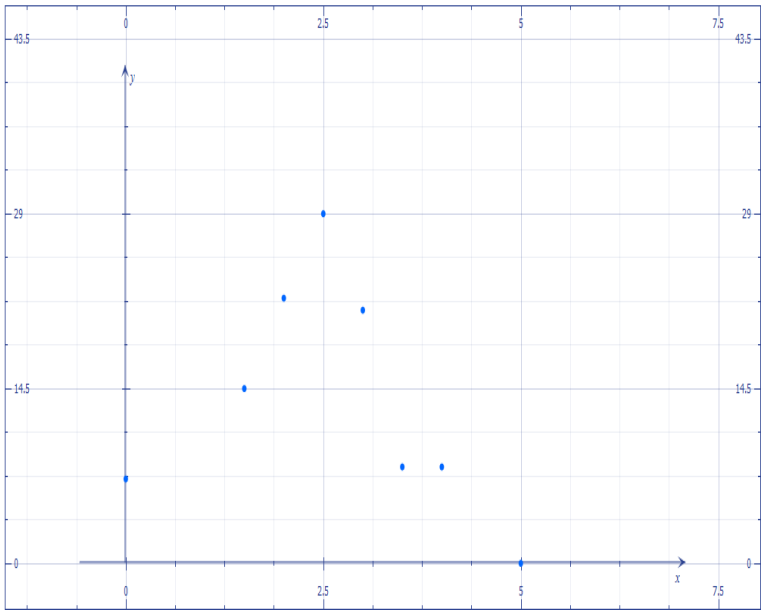
From above we have $\frac{\beta}{\gamma} \approx 0.00628$ so we can calculate β as follows

$$\beta = 0.00628 \times \gamma = 0.00628 \times 2.82 \approx 0.0177.$$

Finally, from the equation for I_{max} we can estimate the maximum number of infectives during the epidemic. Thus,

$$I_{\max} = -159 + 159 \ln 159 + 254 + 7 - 159 \ln 254 \approx 27.51962$$

Notice that the data given shows the maximum number of infective individuals as 29 which is relatively close to the maximum approximation from the model when we look at a scatter plot of the infectives (y-axis) with respect to time (x-axis).



4.4.2 Further Analysis

Now that we have a feel for how these models work in common diseases, we can further analyze the inter-workings of the mathematical system. As in the SIS model we can non-dimensionalize the equations in the SIR model by defining

$$s = \frac{S}{N}, \quad i = \frac{I}{N}, \quad r = \frac{R}{N}, \quad t = \gamma\tau.$$

Notice that $\frac{dI}{d\tau}$ is defined identically as in the SIS case, thus non-dimensionalizing yields $\frac{di}{dt} = (R_0 s - 1)i$. Now we need to find the other two equations.

$$\begin{aligned} \tfrac{ds}{dt} &= \tfrac{ds}{d\tau} \cdot \tfrac{d\tau}{dt} \\ &= -\beta s i N \tfrac{1}{\gamma} \\ &= -\tfrac{\beta N}{\gamma} s i \\ &= -R_0 s i \end{aligned}$$

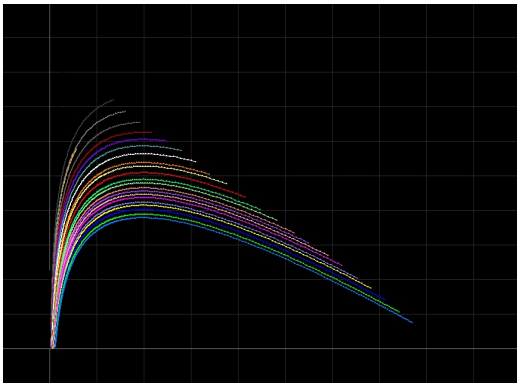
And

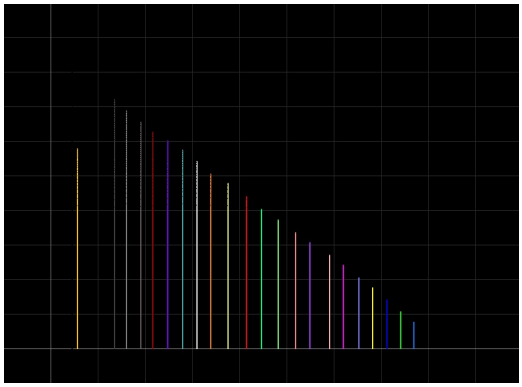
$$\begin{aligned}\frac{dr}{dt} &= \frac{dr}{d\tau} \cdot \frac{d\tau}{dt} \\ &= \gamma i \cdot \frac{1}{\gamma} \\ &= i\end{aligned}$$

where R_0 is defined in the same was as it was in the SIS model; the basic reproductive ratio $R_0 = \frac{\beta N}{\gamma}$. Therefore the equations become

$$\frac{ds}{dt} = -R_0 si, \quad \frac{di}{dt} = (R_0 s - 1)i, \quad \frac{dr}{dt} = i.$$

This system is to be solved on the two-dimensional simplex or triangle $T = \{(s, i, r) |\ 0 \leq s \leq 1,\ 0 \leq i \leq 1,\ 0 \leq r \leq 1,\ s + i + r = 1\}$. Since the first two equations do not involve r we can look at them with the projection onto the (s, i)-plane bounded by the line $s + i = 1$, the s-axis and the i-axis. Any point on the s-axis is a steady state. The phase portraits to follow show what happens for $R_0 > 1$ and $R_0 < 1$.





The first image shows when $R_0 = 5$, so $R_0 > 1$. In this image the system is approaching the origin. The second image shows when $R_0 = 0.001$, so $R_0 < 1$ that all the curve collapse straight down to the s-axis, where every point is a stable point.

Stability properties of the disease-free state (s, i)=(1,0) are suggested by the phase diagram we explored earlier, but as in the previous chapter we can also explore stability by finding the eigenvalues of the Jacobian matrix

associated with the system.

The Jacobian at (1,0) is given by

$$J = \left(\begin{array}{cc} -R_0 i & -R_0 s \\ R_0 i & R_0 s - 1 \end{array} \right) \Bigg|_{(1,0)} = \left(\begin{array}{cc} 0 & -R_0 \\ 0 & R_0 - 1 \end{array} \right),$$

which has eigenvalues 0 and $R_0 - 1$. From this we have

- The disease-free steady state is stable, but not asymptotically stable, if $R_0 < 1$ so that the diseases dies out since this would result in eigenvalues with non-positive real parts.

- The disease-free steady state is unstable if $R_0 > 1$, so that an epidemic may potentially occur since this would result in a one positive eigenvalue.

- Interestingly, basic reproductive ratio $R_0 = \frac{\beta N}{\gamma}$, is the same as our previous model and represents the average number of new cases produced by a single infective introduced into a purely susceptible population of size N.

- Additionally, the initial per capita growth rate of the infectives is given by $\gamma(R_0 - 1)$ in dimensional terms.

It is important to find the size of the epidemic, the total number who will suffer from the disease. This is given by the number who are eventually in the removed class. We can find this by noting that the system

$$\begin{cases} \frac{ds}{dt} &= -R_0 si \\ \frac{di}{dt} &= (R_0 s - 1)i \\ \frac{dr}{dt} &= i \end{cases}$$

is separable in (s, i, r)-space. Examining interrelationships we have

$$\frac{dr}{ds} = \frac{i}{-R_0 si} = \frac{1}{-R_0 s}$$

and

$$\frac{di}{ds} = \frac{(R_0 s - 1)i}{-R_0 si} = -1 + \frac{1}{R_0 s}.$$

Trajectories for the simplex T in (s, i, r)-space are found by integrating these equations. First consider the trajectory T which starts at the disease-free steady state (1,0,0); the goal is to see where T ends up.

Integrating,

$$\frac{dr}{ds} = \frac{1}{-R_0 s}$$

we get

$$\int dr = \int \frac{1}{-R_0 s} ds$$

thus

$$r = \frac{-\ln |s|}{R_0}.$$

Solving for s yields

$$s = e^{-R_0 r}.$$

This equation is satisfied everywhere on T, since s and r are defined as monotonic bounded functions of t. We can therefore say that the functions tend to limits

$$s(t) \to s_1 \quad \text{and} \quad r(t) \to r_1 \quad \text{as} \quad t \to \infty$$

and

$$\frac{dr}{dt}(t) \to 0.$$

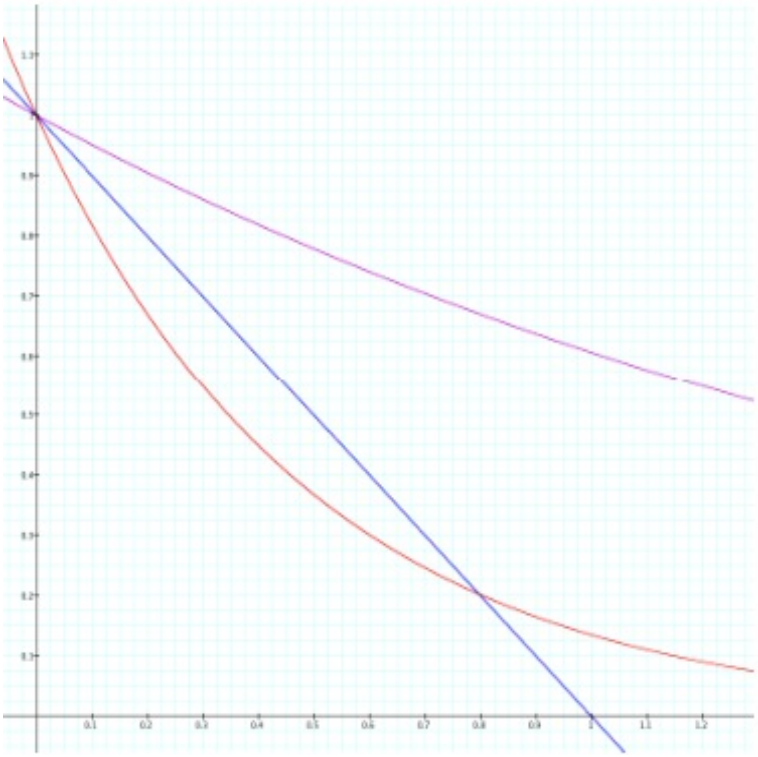
Therefore as defined,

$$i(t) \to 0 \quad \text{as} \quad t \to \infty.$$

Hence, $(s(t), i(t), r(t)) \to (s_1, 0, r_1) = (1 - r_1, 0, r_1)$ as $t \to \infty$. Finally, taking the limit of $s = e^{-R_0 r}$, we have

$$1 - r_1 = e^{-R_0 r_1}.$$

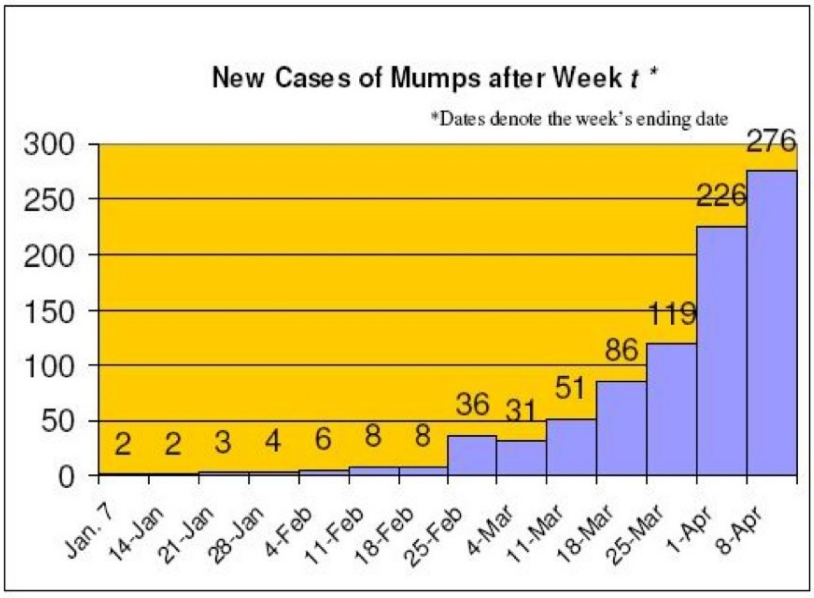
In the following we can see pictorially the relationships between the functions $1 - r$ which is graphed in blue and $e^{-R_0 r}$ for $R_0 < 1$ which is the purple line and $R_0 > 1$, the red line.



When $R_0 > 1$ it is clear that there is a distinct intersection point between the two functions; this intersection determines the final size of the epidemic, whereas when $R_0 < 1$ this intersection point does not exist. Before we draw this chapter to an end we will consider one more example; that of the Iowa Mumps outbreak of 2006.

4.4.3 Iowa Mumps Outbreak

Mumps is an infectious disease caused by the Infectious Parotitis Virus. Common symptoms include fever, headache, and swollen glands under the jaw, but it can also lead to hearing loss and aseptic meningitis. In 2006, Iowa experienced a mumps outbreak that is believed to have begun with two single cases that showed up in the beginning of January 2006 after the couple traveled to England where an outbreak was present. Even though the population of Iowa in 2006 was roughly 2.97 million, there were only an estimated 200,000 people in Iowa susceptible at this time, because 15 years prior all school-aged students were required to be vaccinated against this and other infectious diseases. However, the vaccine is only about 95% effective and it is believed only about 98% of school age students actually received the vaccine. The following image shows the number of new cases of mumps reported per week in Iowa from January to April.



A person infected with mumps is typically able to transmit the disease from two days before the onset of symptoms to 5 days after. Therefore, the

average time spent infective is 7 days, or 1 week keeping with our scale of weeks from the data. Using weeks as our unit of time we can say $\gamma = 1$.

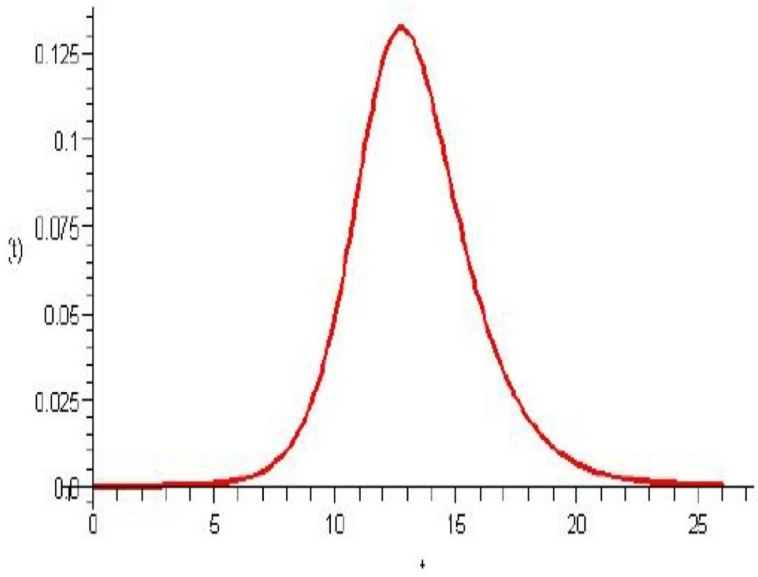
Looking at the data by curve fitting we can estimate $\beta = 0.0188$ [28]. Also taking our initial conditions as percentages we have

$$S(0) = 0.99999, I(0) = 0.00001 \text{ and } R(0) = 0.$$

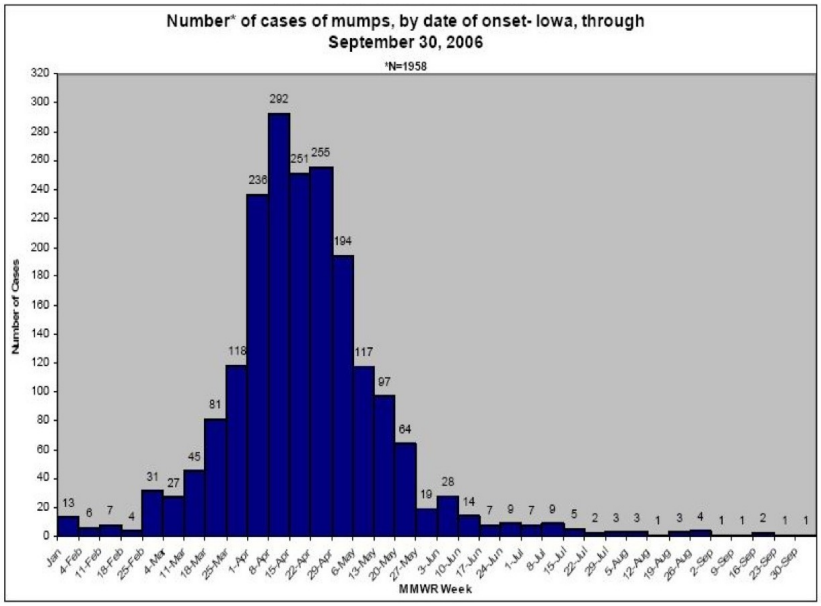
Choosing $\gamma = 1$ for the system

$$\begin{cases} \frac{dS}{d\tau} &= -\beta IS \\ \frac{dI}{d\tau} &= \beta IS - \gamma I \\ \frac{dR}{d\tau} &= \gamma I \end{cases}$$

the graph of $I(\tau)$ from January 2006 to August 2006 from the SIR model follows:



Now to compare this with what really happened in Iowa in 2006 with the final case reported September 30,2006.



The peak in from the model shows a maximum infection of 0.125% of the population. The data on the other hand has a maximum infective percentage, assuming 200,000 people susceptible, of 0.146% which is relatively close. More importantly though we see a similar rise and fall pattern in the overall shape of the graphs. Thus we can conclude the SIR model is a decent model for predicting the rise and fall patterns associated with the Iowa Mumps outbreak of 2006.

This model, and those we have explored thus far are examples of epidemics without explicit demography, which means models that do not consider non-disease related birth and death rates. These types of model are useful for epidemic modeling on a short time scale, such as the plague of Eyam and influenza, mumps, measles and those others we have discussed, but do not include those diseases which transition from compartment to compartment more slowly. Slow diseases require models with explicit demography, adding in the parameters for birth and death rates. Diseases of this nature include HIV, tuberculosis and hepatitis, which develop very slowly and spread slowly

as well. When studying diseases such as these we no longer have the luxury of supposing a constant total population size.

4.5 Summary

- First we explored simple epidemic models to get a feel for how the parameter β impacts a system of ODE's.
- After exploring SI models we explored SIS and SIR models and the additional parameter γ.
- We also examined stability of the models and made sense of them in the context of some known diseases.

There are many more areas to explore which we were not able to explore at this time, such as latency and vaccination in addition to different methods of contracting diseases. It would be interesting to further explore these areas at another time. One more topic we will examine before this thesis is finished regards long-term epidemic models. So far all of the examples we have considered have neglected birth and death rates, in the next chapter we will consider when birth and death play a role.

Chapter 5

Long Term

Before getting too much into long-term models we need to develop the idea of carrying capacity which we have neglected a bit up to this point.

5.1 Logistic Models and Carrying Capacity

As mentioned in the previous chapter, carrying capacity is considered a limiting agent in many mathematical models. Carrying capacity in a system of differential equations represents the value of the population density at which the per capita growth rate is zero. For example, in the Lokta-Volterra system competition for space between the lynx and hare could have been a limiting agent leading to a maximum amount of population, but was not accounted for in the model. In the infectious disease modeling chapter we saw some limiting factors as well when we explored I_{max} which represented the maximum number of infectives at any given time. We also had N as a limiting factor since we were dealing with a closed population. In the sections to follow we will be studying the framework of models that show how carrying capacity impacts systems such as cell-to-cell spread of particular diseases, such as HIV.

We will examine logistic models in general, then look at some modifications and specific cases. Since we are going to eventually discuss cell-to-cell spread, we will examine these models with interacting cell populations rather than interacting human populations.

5.2 Logistic Model Example A

Suppose a particular total population of infectious, susceptible and removed cells changes over time according to the simplest demographic model which describes logistic growth

$$\frac{dN}{d\tau} = \alpha - \mu N.$$

We know that the total cell population change equals the sum of the changes in each compartment since we are dealing with a closed system, thus

$$S' + I' + R' = N'.$$

A general model for long term infectious disease spread in the body follows:

$$\begin{cases} \frac{dS}{d\tau} &= \alpha - \beta IS - \mu S \\ \frac{dI}{d\tau} &= \beta IS - \gamma I - \mu I \\ \frac{dR}{d\tau} &= \gamma I - \mu R \end{cases}$$

Note that since N is no longer constant, $N' \neq 0$. In fact

$$N' = (\alpha - \beta IS - \mu S) + (\beta IS - \gamma I - \mu I) + (\gamma I - \mu R) = \alpha - \mu(S + I + R) = \alpha - \mu N,$$

which is exactly the logistic growth equation seen earlier where:

- α is the total birth rate of new cells measured in births per unit of time.
- μ is the per capita natural death rate of cells, thus μN is the total amount of dead cells and μS represents the number of cells in the susceptible class dieing per unit of time.

- β is the transmission coefficient, thus βI is the per capita rate of infection.

Taking the equation

$$\frac{dN}{d\tau} + \mu N = \alpha$$

and multiplying by $e^{\mu\tau}$ gives

$$\frac{dN}{d\tau}e^{\mu\tau} + e^{\mu\tau}\mu N = e^{\mu\tau}\alpha.$$

So

$$\frac{d(Ne^{\mu\tau})}{d\tau} = e^{\mu\tau}\alpha.$$

Integrating yields

$$Ne^{\mu\tau} = \alpha \int e^{\mu\tau} d\tau$$

so

$$N = \alpha e^{-\mu\tau} \int e^{\mu\tau}\tau.$$

Integrating gives

$$N = \alpha e^{-\mu\tau}\left(\frac{1}{\mu}e^{\mu\tau} + C\right)$$

so

$$\frac{\alpha}{\mu} + C\alpha e^{-\mu\tau}.$$

Now when $t = 0$, we have

$$N_0 = \frac{\alpha}{\mu} + C$$

so

$$C = N_0 - \frac{\alpha}{\mu}.$$

Thus substituting C,

$$N = \frac{\alpha}{\mu} + \left(N_0 - \frac{\alpha}{\mu}\right)e^{-\mu\tau}.$$

This logistic growth equation represents the change in the total population.

We can estimate the value of μ by considering the natural death rate of the cells. The average life span of a cell depends on the type of cell it is. For example most blood cells live only a few hours, whereas taste receptor cells live closer to 10 days, skin cells live roughly a month, muscle cells live roughly 15 years and nerve cells may last a lifetime [34].

Since the examples we are going to look at will be blood related diseases, we are going to focus on blood cells for now (though HIV deals primarily with T-cells). If we suppose that the average cell lives 3 hours, the natural mortality rate is $\frac{1}{3}$ so $\mu = \frac{1}{3}$ hours. In general, we say that if T is the time spent in a class or compartment in our model, then the per capita rate at which the individuals leave that compartment is given by $\frac{1}{T}$. So if γ is the per capita rate spent infective then $\gamma = \frac{1}{T}$ or equivalently, $T = \frac{1}{\gamma}$ is the time spent in that compartment.

5.2.1 Equilibria Analysis

To truly understand what a particular disease will do long term, whether it will die out completely or become endemic, present in the body long term, we need to study equilibrium points which are independent of time. Proceeding in a familiar way to calculate the equilibria points we can set

$$\frac{dS}{d\tau} = 0 \quad \frac{dI}{d\tau} = 0 \quad \text{and} \quad \frac{dR}{d\tau} = 0,$$

so our system becomes

$$\begin{cases} 0 &= \alpha - \beta IS - \mu S \\ 0 &= \beta IS - \gamma I - \mu I \\ 0 &= \gamma I - \mu R \end{cases}$$

Solving for R in the last equation we obtain

$$R = \frac{\gamma}{\mu} I$$

Then solving for I in equation two, $0 = I(\beta S - \gamma - \mu)$, we see that either

$$I = 0$$

or

$$\beta S - \gamma - \mu = 0.$$

- If $I = 0$ then by how R is defined, $R = 0$ as well, and the first equation becomes $0 = \alpha - \mu S$ so $S = \frac{\alpha}{\mu}$. This means that if there are no infective or removed cells, S is equal to a ratio of the birth and death rates for the total cell population. Notice we see this term $S = \frac{\alpha}{\mu}$ show up in our definition of $N(\tau) = N_0 e^{-\mu\tau} + \frac{\alpha}{\mu}(1 - e^{-\mu\tau})$ and can also show that $\frac{dN}{d\tau} = 0$ implies $N = \frac{\alpha}{\mu}$, which makes sense, considering this would mean the entire population is contained in the susceptible class ($N = S$). Therefore, we get the equilibrium value

  $$\left(\frac{\alpha}{\mu}, 0, 0\right).$$

  This equilibrium exists for all values of the parameters supposing positive birth and death rates. Notice that the number of infective cells is zero in this equilibrium state, thus it is called the disease-free equilibrium. Therefore if a system approaches this equilibrium, the number of infective cells $I(\tau)$ will approach 0, so the disease will disappear from the body.

- If we look at the second case, where $I \neq 0$ and $\beta S - \gamma - \mu = 0$ we can solve to get

  $$S = \frac{\gamma + \mu}{\beta}$$

and using this in the first equation gives

$$0 = \alpha - \beta IS - \mu S.$$

Thus

$$\alpha = \beta IS + \mu S$$

and if we divide by S

$$\frac{\alpha}{S} = \beta I + \mu.$$

Now, substitution for S

$$\frac{\alpha}{\left(\frac{\gamma+\mu}{\beta}\right)} = \beta I + \mu$$

so

$$\frac{\alpha\beta}{\gamma+\mu} = \beta I + \mu.$$

Rewriting

$$\beta I = \frac{\alpha\beta}{\gamma+\mu} - \mu$$

Or,

$$\beta I = \frac{\alpha\beta - \mu(\gamma+\mu)}{\gamma+\mu}.$$

Finally solving for I,

$$I = \frac{\alpha\beta - \mu(\gamma+\mu)}{\beta(\gamma+\mu)}.$$

Clearly if $I > 0$ then $\alpha\beta > \mu(\gamma+\mu)$ as defined, thus only if this condition is satisfied does the equilibrium solution below exist

$$\left(\frac{\gamma+\mu}{\beta}, \quad \frac{\alpha\beta - \mu(\gamma+\mu)}{\beta(\gamma+\mu)}, \quad \frac{\gamma}{\mu}\frac{(\alpha\beta - \mu(\gamma+\mu))}{\beta(\gamma+\mu)}\right).$$

In this equilibrium solution we are supposing that I is strictly positive, thus if $I(\tau)$ in a given system approaches this equilibrium as time approaches infinity then the number of infective cells will remain strictly

positive and approach this I value. Therefore the disease remains in the body and becomes an endemic. This equilibrium point is called the endemic equilibrium.

Note that for $I \neq 0 \neq R$ we must have

$$\alpha\beta - \mu(\gamma + \mu) \neq 0.$$

This should be clear since we are dealing with a positive population (> 0). Thus,

$$\frac{\alpha\beta}{\mu(\gamma + \mu)} \neq 1$$

because when we solve the inequality above we get the equation is strictly greater than 1. We call this parameter the reproduction number R_0,

$$R_0 = \frac{\alpha\beta}{\mu(\gamma + \mu)}$$

where $\gamma + \mu$ represents the rate at which individual cells leave the infective class. Thus the average time spent in the infective class is $\frac{1}{\gamma+\mu}$ time units.

The number of transmissions per unit rate of time is given by the incidence rate βSI. If there is only one infective cell, $I = 1$ and all other cells reside in the susceptible class then $S = \frac{\alpha}{\mu}$; thus the number of transmissions by one infective cells is $\frac{\alpha\beta}{\mu}$.

Together we can conclude that the number of infectious transmissions that one cell can make during the entire time infected assuming all other cells are susceptible is

$$\frac{\alpha\beta}{\mu(\gamma + \mu)} = R_0.$$

The condition for existence of an endemic equilibrium can be determined when $R_0 = \frac{\alpha\beta}{\mu(\gamma+\mu)} > 1$. From an epidemiological standpoint, the reproductive number tells us how many secondary cases a particular infective cell

will produce in an entirely susceptible population. Thus we are left to make the following conclusions:

- If $R_0 = 1$ then we get the point $\left(\frac{\alpha}{\mu}, 0, 0\right)$. Recall that from the previous study that a cell population that consists of only susceptible cells, in the long run has a susceptible population of $\frac{\alpha}{\mu}$.
- If $R_0 > 1$ again we get the equilibria $\left(\frac{\alpha}{\mu}, 0, 0\right)$ as well as the endemic equilibrium $\left(\frac{\gamma+\mu}{\beta}, \quad \frac{\alpha\beta-\mu(\gamma+\mu)}{\beta(\gamma+\mu)}, \quad \frac{\gamma}{\mu}\frac{\alpha\beta-\mu(\gamma+\mu)}{\beta(\gamma+\mu)}\right)$. The disease-free equilibrium in this case is not attractive, which can be seen by noticing that the solutions of the system that start very close to this tend to go away from it in the S direction. The endemic equilibrium is attractive so that solutions to the system approach it as time approaches infinity. Thus, the disease remains present in the body.
- If $R_0 < 1$ then there exists only the disease-free equilibrium and we can show that it is attractive so that every solution of the system approaches this equilibrium and the disease will eventually disappear from the population.

5.3 Logistic Model Example B

The following model is another logistic model but now one that takes carrying capacity into consideration. It looks very similar to one in which we will work in the next section when we begin studying cell-to-cell spread of diseases and will be used to make sense of the inner-workings in a more simple setting.

The logistic model begins with a function $f(N)$, that is positive for all $N \in (0, K)$ where K represents the carrying capacity and satisfies the

condition that $f(0) = f(K) = 0$. The simplest equation for this is

$$\frac{dN}{dt} = f(N) = rN\left(1 - \frac{N}{K}\right).$$

This equation is called the logistic equation and it's solution is known as a logistic curve with parameters r and K. The solution to this model can be found explicitly so that we can determine the density N as a function of time. Let's begin by separating variables,

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right).$$

Moving all terms with N to one side of the equation and with all others on the other side of the equation gives

$$\frac{dN}{N\left(1 - \frac{N}{K}\right)} = rdt.$$

Integrating from time $t = 0$ to $t = T$,

$$\int_{N(0)}^{N(T)} \frac{dN}{N\left(1 - \frac{N}{K}\right)} = \int_0^T rdt$$

gives

$$\int_0^T rdt = rt|_0^T = rT$$

when we integrate the right side. Integrating the left side however requires the use of partial fractions. We can re-write

$$\frac{1}{N\left(1 - \frac{N}{K}\right)} = \frac{1}{N} + \frac{\frac{1}{K}}{1 - \frac{N}{K}}$$

So

$$\int_{N(0)}^{N(T)} \frac{1}{N} + \frac{\frac{1}{K}}{1 - \frac{N}{K}} = \left[\ln(N) - \ln\left(1 - \frac{N}{K}\right)\right]_{N(0)}^{N(T)}$$

Therefore we have,

$$\ln(N(T)) - \ln\left(1 - \frac{N(T)}{K}\right) - \ln(N(0)) + \ln\left(1 - \frac{N(0)}{K}\right) = rT.$$

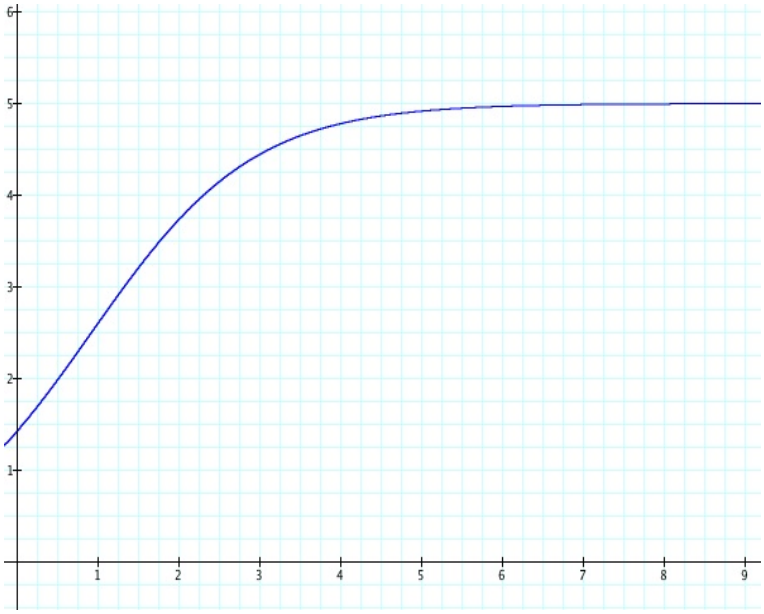
Exponentiating both sides gives

$$\frac{N(T)\left(1-\frac{N(0)}{K}\right)}{\left(1-\frac{N(T)}{K}\right)N(0)} = e^{rT}.$$

Solving for $N(T)$ yields

$$N(T) = \frac{KN(0)e^{rT}}{K - N(0) + N(0)e^{rT}}.$$

Therefore in general we get the result that the population grows rapidly at first then approaches an equilibrium which we can see in the following picture when we graph the logistic function choosing with arbitrary choices for $N(0)$ and K.



In the next section we will use a similar technique to solve a system designed to model cell-to-cell spread of HIV. This model could be modified to model other long term diseases as well as long term population dynamics, though it was specifically designed to study cell-to-cell HIV spread.

5.4 Understanding Cell-to-Cell Spread

Now that we have some understanding about how the introduction of different parameters and compartments can alter our simple model we can begin to try to understand some of the components involved virus transmission through the body. Recall that in this chapter we are exploring cell-to-cell transmission, thus we are dealing with a population of cells rather than people as in the previous chapter. The first model we will explore, we assume that infection spreads directly from infected cells to healthy cells in a bilinear fashion. That is, virus transmission is dependent only on the product of the concentrations of the two cell populations.

Given the system

$$\begin{cases} \frac{dS}{d\tau} &= r_S S(1 - \frac{S+\gamma R}{S_R}) \\ \frac{dR}{d\tau} &= \mu_S S \end{cases}$$

where

- $S(\tau)$ represents the concentration of healthy cells, which we can think of in a way similarly to susceptible cells.
- $R(\tau)$ represents the concentration of dead cells which are a specific case of the removed class explored earlier.
- r_S is the effective reproductive rate of healthy cells which is similar to a birth rate except it also takes into account the non-disease related death rate.
- μ_S is the death rate of healthy cells.
- $1 - \frac{S+\gamma R}{S_R}$ is a control term that prevents the system from exceeding its carrying capacity.

- S_R represents the carrying capacity of the system.
- γ is the relative reduction in carrying capacity due to dead cells and cellular debris.
- Notice
$$\frac{dS}{d\tau} = r_S S\left(1 - \frac{S + \gamma R}{S_R}\right)$$
is a logistic growth function for population. So that if $S + R = N$ then for $R = 0$, $\frac{dS}{d\tau}$ reduces to
$$r_S N\left(1 - \frac{N}{S_R}\right).$$

which just like the logistic function in Example B capturing the carrying capacity. To get a better feel for carrying capacity we will explore this idea in the next subsection.

5.4.1 Carrying Capacity

Note that we are no longer dealing with a closed population $N = S + I + R$, but in the long-term model, N is no longer constant thus $N' \neq 0$. Rather N' is a logistic equation. Let's define a system introducing infected cells, where

- $I(\tau)$ is the concentration of infected cells
- k_I represents the rate constant for infection of healthy cells.

  Just as in the last chapter, this the infectious rate is given as a gain term, for the infectious class and a loss term for the susceptible class or healthy cells in this case, since as healthy cells become infected they leave the susceptible class and become part of the infectious class.

- Additionally we have the parameter μ_I which represents the death rate of infectious cells.

Together this yields the system

$$\begin{cases} \frac{dS}{d\tau} &= -k_I IS + r_S S\left(1 - \frac{S+I+\gamma R}{S_R}\right) \\ \frac{dI}{d\tau} &= k_I IS - \mu_I I \\ \frac{dR}{d\tau} &= \mu_S S + \mu_I I \end{cases}$$

Notice this population is no longer closed as we are introducing non-disease related birth and death rates.

5.4.2 Equilibria

Just as in the last two chapters we can ignore the last equation when first considering the dynamics of the system, since the dead cells and cellular debris play a negligible role in the spread of infection from cell-to-cell. Also, assume that $\gamma = 0$ since γ represents the relative reduction in carrying capacity due to dead cells and cellular debris which is all related to this R variable, thus because all equations are written in terms of only S and I (not R) with $\gamma R = 0$ we can write

$$\begin{cases} \frac{dS}{d\tau} &= -k_I IS + r_S S\left(1 - \frac{S+I}{S_R}\right) \\ \frac{dI}{d\tau} &= k_I IS - \mu_I I \end{cases}$$

Before we find the equilibria notice that when we add

$$\frac{dS}{d\tau} + \frac{dI}{d\tau} = r_S S\left(1 - \frac{S+I}{S_R}\right) - \mu_I I$$

and if all cells are either infectious or susceptible we get $S + I = N$ so

$$N' = r_S S\left(1 - \frac{S+I}{S_R}\right) - \mu_I I = r_S S\left(1 - \frac{N}{S_R}\right) - \mu_I I$$

which is the logistic growth equation with the removal of dead infectious cells which can be seen in the last term $-\mu_I I$. Note that if $I = 0$ we just get the logistic growth equation

$$N' = r_S N \left(1 - \frac{N}{S_R}\right)$$

Now we can find the equilibrium points in the usual way by setting the equations equal to zero.

- $\frac{dS}{d\tau} = 0$ implies $0 = S\left(-k_I I + r_S\left(1 - \frac{S+I}{S_R}\right)\right)$

  Thus,

  $$S = 0$$

  or $-k_I I + r_S\left(1 - \frac{S+I}{S_R}\right) = 0$ yielding

  $$I = \frac{r_S(S_R - S)}{r_S + S_R k_I}$$

  which forces $\frac{dI}{d\tau} = 0$ as well.

- $\frac{dI}{d\tau} = 0$ implies $0 = I(k_I S - \mu_I)$,

  Thus,

  $$I = 0$$

  or $k_I S = \mu_I$ yielding

  $$S = \frac{\mu_I}{k_I}$$

  which forces $\frac{dS}{d\tau} = 0$ as well.

Now

- when $S = 0$ solving for I yields $I = 0$ as well. Thus we get the equilibrium

  $$(0, 0)$$

- when $I = 0$ then for

$$\frac{dS}{d\tau} = -k_I IS + r_S S\left(1 - \frac{S+I}{S_R}\right) = 0$$

we get

$$k_I IS = r_S S\left(1 - \frac{S+I}{S_R}\right)$$

but $I = 0$ implies this becomes

$$0 = r_s S - \frac{r_S S^2}{S_R}$$

moving the last term over

$$r_s S = \frac{r_S S^2}{S_R}$$

divide both sides by $r_S S$ to get

$$1 = \frac{S}{S_R}$$

So finally

$$S = S_R.$$

Thus we get the equilibrium

$$(S_R, 0)$$

so that the maximum population (carrying capacity) is all contained in the susceptible class.

- when $S = \frac{\mu_I}{k_I}$, plugging this into the equation we found for I, when $\frac{dS}{d\tau} = 0$,

$$I = \frac{r_S(S_R - S)}{r_S + S_R k_I}$$

becomes

$$I = \frac{r_S(S_R - \mu)}{k_I(r_S + S_R k_I)}.$$

Finally giving the equilibrium point

$$\left(\frac{\mu_I}{k_I}, \frac{r_S(S_R - \mu_I)}{k_I(k_I S_R + r_S)}\right).$$

Therefore the equilibrium points for this system are

$$(0,0), \quad (S_R, 0) \quad \text{and} \quad \left(\frac{\mu_I}{k_I}, \frac{r_S(S_R - \mu_I)}{k_I(k_I S_R + r_S)}\right).$$

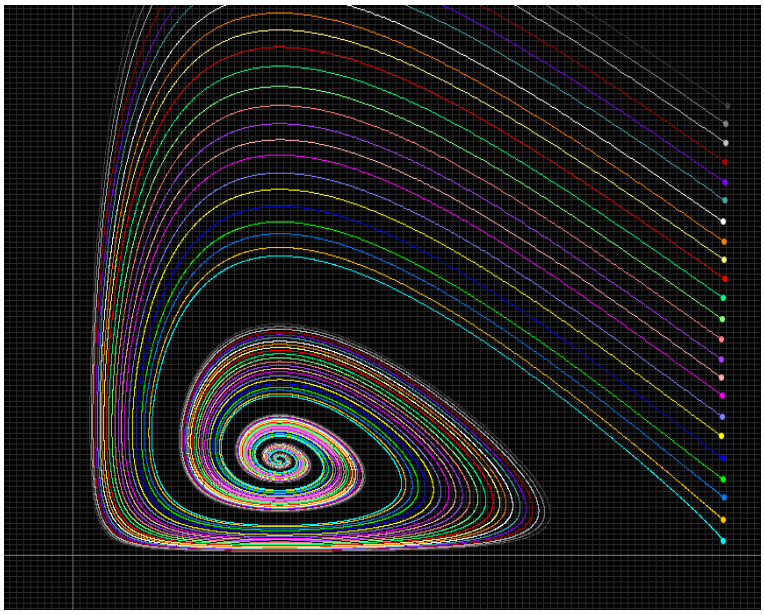
5.4.3 Stability Analysis

Possible scenarios for stability:

- $S < \frac{\mu_I}{k_I}$. In this case healthy cells predominate and infected cells die off exponentially. We have $(0,0)$ is an unstable equilibrium point whereas $(S_R, 0)$ is asymptotically stable.

- $S > \frac{\mu_I}{k_I}$. In this case healthy cells and infected cells co-exist. This means that the infection is present, but does not grow out of control and healthy cells do not crash to zero. We have that $(0,0)$ remains unstable, but $(S_R, 0)$ is unstable now as well.

- $S = \frac{\mu_I}{k_I}$. In this case $\left(\frac{\mu_I}{k_I}, \frac{r_S(S_R - \mu_I)}{k_I(k_I S_R + r_S)}\right)$ is asymptotically stable. The following phase portrait shows this asymptotically stable point in the middle of the spiral.



5.5 Model Modified for a more realistic response function

Now that we have a chance to get a feel for a model incorporating carrying capacity, as well as changes in total population size, we can try to explore a more reasonable cell-to-cell spread model. In the previous model we assumed that infection spread in a bilinear fashion, assuming a system of cells that were well mixed, which showed up in the system in the term $k_I IS$. Spouge et al. questioned the accuracy of the use of the term $k_I IS$ as it is "appropriate in a system if the cells are well-mixed, an assumption deserving some scrutiny...tissue culture systems are generally not well-mixed, and a cell usually maintains contact with its neighbors" [20]; thus an interesting contrast would be to explore a modification for this term. One modification to consider is to replace the $k_I IS$ with potentially a more realistic one, one proposed by the Michaelis-Menten response function

$$k_I = \frac{k}{a+S}$$

where a is the half-saturation constant for the proliferation process. The proliferation process in cells is the process that brings the production of reproductive cells, fertilization and cell growth. It is responsible for healing injured tissues and even for increasing functions of certain organs to compensate for the absence of another organ. In the case of unhealthy cells however, which is the case when studying infectious diseases such as HIV, this process can result in organism death. Since cells divide to reproduce, if unhealthy cells are diving they are producing more unhealthy cells. The a term takes into account the contact rate between infected and healthy cells, the fraction of healthy cells which are activated (going through the proliferation process) thus making them susceptible to infection and the virus which result in productive infected cells. From my understanding a represents half of the maximum speed of virus transmission between cells; for HIV models a is defined specifically based on a saturation function of T-Cells which have a well-defined maximal rate of proliferation [13].

With this modification the system becomes

$$\begin{cases} \frac{dS}{d\tau} &= -k\frac{IS}{a+S} + r_S S(1 - \frac{S+I}{S_R}) \\ \frac{dI}{d\tau} &= k\frac{IS}{a+S} - \mu_I I \end{cases}$$

Since we are still working with a long-term model, including non-disease related birth and death rates, we are still assuming that the total population N varies thus $N' \neq 0$.

5.5.1 Equilibra

First by solving

$$\frac{dI}{d\tau} = k\frac{IS}{a+S} - \mu_I I = 0,$$

Factoring out I gives

$$I(k\frac{S}{a+S} - \mu_I) = 0$$

and by the zero product property this means that either

$$I = 0$$

or

$$k\frac{S}{a+S} - \mu_I = 0.$$

Solving the later equation for S by first moving μ_I gives

$$\frac{ks}{a+S} = \mu_I.$$

Then multiplying by $(a+S)$ yields

$$kS = \mu_I a + \mu_I S.$$

Now getting the S terms to one side

$$kS - \mu_I S = \mu_I a.$$

Factoring the S on the left yields

$$S(k - \mu_I) = \mu_I a$$

and finally dividing to isolate S gives

$$S = \frac{\mu_I a}{k - \mu_I}.$$

Now letting the first equation equal zero

$$\frac{dS}{d\tau} = -k\frac{IS}{a+S} + r_S S\left(1 - \frac{S+I}{S_R}\right) = 0$$

Factoring out S gives

$$S\left(-k\frac{I}{a+S} + r_S\left(1 - \frac{S+I}{S_R}\right)\right) = 0$$

and by the zero product property this means that either $S = 0$ or we have $-k\frac{I}{a+S} + r_S\left(1 - \frac{S+I}{S_R}\right) = 0$. Solving the later equation for I by first distributing gives

$$\frac{-kI}{a+S} + r_S - \frac{r_S S}{S_R} - \frac{r_S I}{S_R} = 0$$

and clearing fractions yields

$$-kIS_R + r_S S_R a + r_S S_R S - r_S S a - r_S S^2 - r_S I a - r_S I S = 0.$$

Then since the goal is to solve for I, moving all I terms to one side of the equation gives

$$kIS_R + r_S I a + r_S I S = r_S S_R a + r_S S_R S - r_S S a - r_S S^2.$$

Factoring out the I yields

$$I(kS_R + r_S a + r_S S) = r_S S_R a + r_S S_R S - r_S S a - r_S S^2$$

and finally dividing to isolate I gives

$$I = \frac{r_S S_R a + r_S S_R S - r_S S a - r_S S^2}{kS_R + r_S a + r_S S} = \frac{r_S(a+S)(S_R - S)}{kS_R + r_S(a+S)}.$$

Now that we have solved both equations for each respective variable we can find the equilibria.

- If $S = 0$ from the equation $\frac{dS}{dt} = 0$ then substituting this value into $\frac{dI}{dt} = 0$ gives

$$-\mu_I I = 0.$$

Solving for I by diving by $-\mu_I$ then results in

$$I = 0$$

so we get the equilibria point

$$(0, 0).$$

- If $I = 0$ from the equation $\frac{dI}{dt} = 0$ then substituting this value into $\frac{dS}{dt} = 0$ gives

$$r_S S - \frac{r_S S^2}{S_R} = 0.$$

Adding the second term to the right side of the equation yields

$$r_S S = \frac{r_S S^2}{S_R}.$$

Multiplying by S_R

$$r_S S S_R = r_S S^2$$

and finally diving by $r_S S$ gives

$$S = S_R$$

so we get the equilibria point

$$(S_R, 0).$$

- Finally, when

$$S = \frac{\mu_I a}{k - \mu_I}$$

substituting S into the equation we found for I earlier, namely

$$I = \frac{r_S S_R a + r_S S_R S - r_S S a - r_S S^2}{k S_R + r_S a + r_S S}$$

we have

$$I = \frac{r_S S_R a + r_S S_R \left(\frac{\mu_I a}{k-\mu_I}\right) - r_S \left(\frac{\mu_I a}{k-\mu_I}\right) a - r_S \left(\frac{\mu_I a}{k-\mu_I}\right)^2}{k S_R + r_S a + r_S \left(\frac{\mu_I a}{k-\mu_I}\right)}.$$

Factoring out an r_S in the numerator

$$I = \frac{r_S \left(S_R a + S_R \left(\frac{\mu_I a}{k-\mu_I}\right) - \left(\frac{\mu_I a}{k-\mu_I}\right) a - \left(\frac{\mu_I a}{k-\mu_I}\right)^2\right)}{k S_R + r_S a + r_S \left(\frac{\mu_I a}{k-\mu_I}\right)}.$$

Multiplying both the numerator and denominator by $k - \mu_I$ yields

$$I = \frac{r_S \left(S_R a k - S_R a \mu_I + S_R \mu_I a - \mu_I a^2 - \frac{\mu_I^2 a^2}{k-\mu_I}\right)}{k^2 S_R - k S_R \mu_I + r_S a k - r_S a \mu_I + r_s \mu_I a}.$$

Simplifying like terms gives

$$I = \frac{r_S \left(S_R a k - \mu_I a^2 - \frac{\mu_I^2 a^2}{k-\mu_I}\right)}{k^2 S_R - k S_R \mu_I + r_S a k}.$$

Now getting a common denominator for the numerator

$$I = \frac{r_S \left(\frac{S_R a k (k-\mu_I) - \mu_I a^2 (k-\mu_I) - \mu_I^2 a^2}{k-\mu_I}\right)}{k^2 S_R - k S_R \mu_I + r_S a k}.$$

Distributing

$$I = \frac{r_S \left(\frac{S_R a k^2 - S_R a k \mu_I - \mu_I a^2 k + \mu_I^2 a^2 - \mu_I^2 a^2}{k-\mu_I}\right)}{k^2 S_R - k S_R \mu_I + r_S a k}.$$

Simplifying like terms

$$I = \frac{r_S \left(\frac{S_R a k^2 - S_R a k \mu_I - \mu_I a^2 k}{k-\mu_I}\right)}{k^2 S_R - k S_R \mu_I + r_S a k}$$

then multiplying by the reciprocal of the denominator to eliminate the compound fraction gives

$$I = r_S \left(\frac{S_R a k^2 - S_R a k \mu_I - \mu_I a^2 k}{k - \mu_I} \right) \cdot \frac{1}{k^2 S_R - k S_R \mu_I + r_S a k}.$$

Factoring the numerator and denominator and multiplying yields

$$I = \frac{r_S a k (S_R k - S_R \mu_I - \mu_I a)}{(k - \mu_I) k (k S_R - S_R \mu_I + r_S a)}.$$

simplifying results it

$$I = \frac{r_S a (S_R k - S_R \mu_I - \mu_I a)}{(k - \mu_I)(k S_R - S_R \mu_I + r_S a)}$$

so

$$I = \frac{r_S a (S_R (k - \mu_I) - \mu_I a)}{(k - \mu_I)(S_R (k - \mu_I) + r_S a)}.$$

Thus, the final equilibra point is

$$\left(\frac{\mu_I a}{k - \mu_I}, \frac{r_S a (S_R (k - \mu_I) - \mu_I a)}{(k - \mu_I)(S_R (k - \mu_I) + r_S a)} \right).$$

Therefore we have equilibria points

$$(0, 0), \quad (S_R, 0) \quad \text{and} \quad \left(\frac{\mu_I a}{k - \mu_I}, \frac{r_S a (S_R (k - \mu_I) - \mu_I a)}{(k - \mu_I)(S_R (k - \mu_I) + r_S a)} \right)$$

5.5.2 Stability

We can find the Jacobian matrix of this system by writing:

$$\begin{cases} F = \frac{dS}{d\tau} = -k \frac{IS}{a+S} + r_S S (1 - \frac{S+I}{S_R}) \\ G = \frac{dI}{d\tau} = k \frac{IS}{a+S} - \mu_I I \end{cases}$$

Then

$$\frac{\partial F}{\partial S} = \frac{-kI(a + S) + kIS}{(a + S)^2} + r_S - \frac{2 r_S S}{S_R} - \frac{r_S I}{S_R}.$$

Simplifying like terms

$$= \frac{-kIa}{(a+S)^2} + r_S - \frac{2r_S S}{S_R} - \frac{r_S I}{S_R}$$

and re-writing

$$= r_S - ak\frac{I}{(a+S)^2} - 2r_S\frac{S}{S_R} - r_S\frac{I}{S_R}.$$

We can equivalently find the remaining partial derivatives therefore yielding

$$\begin{aligned}
\tfrac{\partial F}{\partial S} &= \tfrac{I}{(a+S)^2} - 2r_S\tfrac{S}{S_R} - r_S\tfrac{I}{S_R} \\
\tfrac{\partial F}{\partial I} &= \tfrac{-kS}{a+S} - \tfrac{r_S S}{S_R} \\
\tfrac{\partial G}{\partial S} &= \tfrac{kI(a+S)-kIS}{(a+S)^2} \\
\tfrac{\partial G}{\partial I} &= \tfrac{KI}{a+S} - \mu_I
\end{aligned}$$

and together this gives the Jacobian matrix

$$J = \begin{bmatrix} r_S - ak\frac{I}{(a+S)^2} - 2r_S\frac{S}{S_R} - r_S\frac{I}{S_R} & -k\frac{S}{a+S} - r_S\frac{S}{S_R} \\ ak\frac{I}{(a+S)^2} & k\frac{S}{a+S} - \mu_I \end{bmatrix}.$$

- At $(0,0)$:

$$J = \begin{bmatrix} r_S & 0 \\ 0 & -\mu_I \end{bmatrix}$$

  Then since our eigenvalues are r_S and $-\mu_I$, we see that both eigenvalues are real and one of the real parts of the eigenvalues is positive, thus it is clear that $(0,0)$ will always be an unstable saddle.

- At $(S_R, 0)$:

$$J = \begin{bmatrix} -r_S & -k\frac{S_R}{a+S_R} - r_S \\ 0 & k\frac{S_R}{a+S_R} - \mu_I \end{bmatrix}$$

  The eigenvalues are $-r_S$ and $k\frac{S_R}{a+S_R} - \mu_I$

- If $S_R < \frac{a\mu_I}{k-\mu_I}$ then both eigenvalues are negative and we have an aysomptotically stable point.
- If $S_R > \frac{a\mu_I}{k-\mu_I}$ the one of the eigenvalues is negative and one positive, thus we have an unstable saddle point.
- If $S_R = \frac{a\mu_I}{k-\mu_I}$ then one of the eigenvalues is negative and the other is zero, thus we have an asymptotically stable point.

- At

$$\left(\frac{\mu_I a}{k-\mu_I}, \frac{r_S a(S_R(k-\mu_I)-\mu_I a)}{(k-\mu_I)(S_R(k-\mu_I)+r_S a)}\right)$$

$$J = \begin{bmatrix} a_1 & a_2 \\ a_3 & 0 \end{bmatrix}$$

where each a_i is defined in a particular way

  - First

$$a_1 = r_S - \frac{r_s a(S_R(k-\mu_I)-\mu_I a)}{S_R(k-\mu_I)+r_S a} - \frac{2r_S}{S_R}\left(\frac{\mu_I a}{k-\mu_I}\right) - \frac{r_S}{S_R}\left(\frac{r_s a(S_R(k-\mu_I)-\mu_I a}{(k-\mu_I)(S_R(k-\mu_I)+r_S a)}\right)$$

  - Now

$$a_2 = \frac{-k\left(\frac{\mu_I a}{k-\mu_I}\right)}{a+\left(\frac{\mu_I a}{k-\mu_I}\right)} - \frac{r_S}{S_R}\left(\frac{\mu_I a}{k-\mu_I}\right)$$

$$= \frac{\frac{-k\mu_I a}{k-\mu_I}}{\frac{a(k-\mu_I)+\mu_I a}{k-\mu_I}} - \frac{r_S\mu_I a}{S_R(k-\mu_I)}$$

$$= \frac{\frac{-k\mu_I a}{k-\mu_I}}{\frac{ak}{k-\mu_I}} - \frac{r_S\mu_I a}{S_R(k-\mu_I)}$$

$$= \frac{-k\mu_I a}{ak} - \frac{r_S\mu_I a}{S_R(k-\mu_I)}$$

$$= -\mu_I - \frac{r_S \mu_I a}{S_R(k-\mu_I)}$$

- Finally

$$a_3 = ak \frac{r_S a(S_R(k-\mu_I) - \mu_I a)}{(k-\mu_I)(S_R(k-\mu_I) + r_S a)} \cdot \frac{1}{a + \frac{\mu_I a}{k-\mu_I}}$$

$$= \frac{k r_S a^2 (S_R(k-\mu_I) - \mu_I a)}{(k-\mu_I)(S_R(k-\mu_I) + r_S a)} \cdot \frac{k-\mu_I}{a(k-\mu_I) + \mu_I a}$$

$$= \frac{k r_S a^2 (S_R(k-\mu_I) - \mu_I a)}{(k-\mu_I)(S_R(k-\mu_I) + r_S a)} \cdot \frac{k-\mu_I}{ak}$$

$$= \frac{r_S a(S_R(k-\mu_I) - \mu_I a)}{S_R(k-\mu_I) + r_S a}$$

- Note that the forth entry in the matrix is 0 since we would have

$$\frac{k\left(\frac{\mu_I a}{k-\mu_I}\right)}{a + \left(\frac{\mu_I a}{k-\mu_I}\right)} - \mu_I$$

$$= \frac{\frac{k\mu_I a}{k-\mu_I}}{\frac{a(k-\mu_I)+\mu_I a}{k-\mu_I}} - \mu_I$$

$$= \frac{\frac{k\mu_I a}{k-\mu_I}}{\frac{ak}{k-\mu_I}} - \mu_I$$

$$= \frac{k\mu_I a}{ak} - \mu_I$$

$$= \mu_I - \mu_I$$

$$= 0$$

.

The characteristic equation, we can find by looking at the matrix

$$|J - \lambda I| = 0,$$

$$\lambda^2 - a_1\lambda - a_2a_3 = 0$$

with roots

$$\lambda_{1,2} = \frac{a_1 \pm \sqrt{a_1^2 + 4a_2a_3}}{2}.$$

- This system has real roots if $4a_2a_3 \geq -a_1^2$
  - Both roots are negative when $\sqrt{a_1^2 + 4a_2a_3} < -a_1$ for $a_1 < 0$
  - Both roots are positive when $\sqrt{a_1^2 + 4a_2a_3} < a_1$ for $a_1 > 0$
  - One root is negative and one root is positive if one of the following occur:
    - If $a_1 < 0$ implies $\sqrt{a_1^2 + 4a_2a_3} > -a_1$
    - If $a_1 > 0$ implies $a_2a_3 > 0$
- The system has complex roots if $4a_2a_3 < -a_1^2$ where a_1 represents the real part.

Therefore, we have a means to characterize the equilibria values to determine stability for all three equilibria points in this much more complicated system. With these tools we are able to begin to understand more complicated diseases such as HIV and herpes as well as more complicated population dynamic scenarios.

Chapter 6

Conclusions

Throughout this thesis we have explored the inter-workings of several different models involving differential equations. The first model we explored was the two-variable Lotka-Volterra model which we aimed to relate to the Hudson Bay Company data. Then we decided to expand to a 3-variable Lotka-Volterra model since we it seemed logical that the hare population was dependent on their food source as well and found this model to be more indicative of the data found by the Hudson Bay Company. It seemed that the model worked well with the data however the model does have some limitations. The Lotka-Volterra model does not account for a minimum sustainable population size for each species. Carrying capacity is not accounted for and with interacting species this is likely something that should be. For example, in the models we studied we never took into account what impact competition for space may have on the populations taken into consideration. It would be interesting to try study species interactions with space limitations to see how well the model would fit with these parameters.

The next set of models we studied were infectious disease models. We

examined SI, SIS and SIR models to get a feel for how these relate to different infectious diseases that impact persons currently and throughout history. McKendrick and Kermack developed several models in addition to those that we discussed; others that would be interesting to explore are those that take into account latent stages or incubation periods, i.e. time in which a person is infected but not showing symptoms. Also, models that include time delay, immunity and vaccination would be interesting to study. Additionally models that take into account different methods of disease spread, such as through insects and organisms both macro and micro parasitic are intriguing; Ronald Ross's exploration into the spread of Malaria through mosquitoes for instance. Other interesting yet complicated systems to study would include systems in which particular populations are more affected than others; such as diseases that impact the elderly or young children more than adults. STD's are also an interesting area of study because the spread is much more prominent in adolescents and young adults, likely caused by common lifestyles and lack of monogamy. The epidemic models we explored can be altered in a variety of ways and studied to make sense of changing and more complicated infectious diseases; thus creating several interesting areas for further research.

Finally, we began the study of long-term diseases such as HIV. There is much more to study in this section as we barely scratched the surface of cell-to-cell modeling and haven't even looked at how the disease spreads in different communities. Other areas we could develop are inclusion of time delay, immunity, etc...

Overall wehave seen that several of the relationships that exist in the world around us can be better understood though the study of mathematics. The more accurate our model, the more complicated it gets, but hopefully

this thesis gives a good background and look into how the study of differential equations applies in the biological setting.

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