Epidemiology Through the Lens of Differential Equations

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Abstract

The spread of a disease can be modelled through systems of differential equations, specifically, epidemiological models. Given the properties of differential equations, we are able to find the equilibria of these systems and perform an analysis using Jacobian matrices to determine how disease transmission will behave. In this paper, we will examine a few epidemiological models. They vary because of inherent differences in how certain pathogens affect the human body.

1 Introduction

Differential equations are the basis of our analysis. They can be used to model almost everything that changes continuously. More technically, they are any "equation that relates the derivatives of an unknown function, the function itself, the variables by which the function is defined, and constants" (Farlow 10). Any differential equation that only depends on one variable is called and "ordinary differential equation."

DEFINITION 1.1. *A system of differential equations,* $\frac{dH}{dt}$*, is represented by:*

$$\frac{dH}{dt} = \begin{cases} \frac{dx}{dt} = f(x,y) \\ \\ \frac{dy}{dt} = g(x,y) \end{cases}$$

Many epidemiological models can only be represented by systems of differential equation. These involve two variables for the number of susceptible individuals in the population and the number of infected individuals in the population. They are not unlike a system of linear equations where we must solve both simultaneously. However, it becomes more complex when we introduce how immunity affects the spread of certain diseases, how infectious a disease might be, or if there are external factors isolating different segments of the population being effected. Given these systems, our main goal is to find the points where the system reaches an equilibrium.

DEFINITION 1.2. *Suppose the differential system,* $\frac{dH}{dt} = F(X)$*. An equilibrium solution of* $\frac{dH}{dt}$ *is a constant solution* $\overline{X}$ *satisfying* $F(\overline{X}) = 0$*.*

When dealing with systems of differential equations, we can analyze the stability of equilibria using linear algebra, specifically Jacobian matrices and their trace and determinant.

DEFINITION 1.3. *A Jacobian matrix is defined by:*

$$J = \begin{bmatrix} f_x(x,y) & f_y(x,y) \\ \\ g_x(x,y) & g_y(x,y) \end{bmatrix} \begin{bmatrix} u \\ \\ v \end{bmatrix}$$

where f_{xy} *and* g_{xy} *are the first-order derivatives of a system of differential equations.*

There are a few different types of equilibria that a system can have. A node is a single isolated point $(\overline{x}, \overline{y})$ such that $f(\overline{x}, \overline{y}) = 0$. They can be categorized as stable or unstable. A stable node, or sink node, can be

identified when all solutions tend toward $(\overline{x}, \overline{y})$, $\lim_{t\to\infty} f(x(t), y(t)) = (\overline{x}, \overline{y})$. An unstable node, or source node, can be identified when all solutions tend away from $(\overline{x}, \overline{y})$. We have a saddle point when there is only one distinct solution that passes through $(\overline{x}, \overline{y})$. They are always classified as unstable. The third type is a focus point. A stable focus is where solutions spiral toward $(\overline{x}, \overline{y})$. An unstable focus is where solutions spiral away from $(\overline{x}, \overline{y})$.

In this paper, we will study epidemiological models and how to analyze them. In section 2, we will cover logistic growth. In section 3, we will look at our first system, the SI epidemic model. In section 4, we add some compexity to our analysis with the SIS epidemic model. In section 5, we discuss some general theory and methodology of more complex systems. In sections 6 and 7, we apply the theorems from section 5 after finding the trace and determinant of the Jacobian matrices associated with the SIR and SIRS epidemic models. In section 8, we apply our findings from section 7 to a real world example using the influenza virus.

2 Verhulst Model for Logistic Growth

We will start with an equation that relates population growth to the population size. This model of logistic growth is called the Verhulst Model, named after Pierre Verhulst (1804-1849). While the model can be solved for an exact value, we will focus mainly on analyzing the equilibrium. The model is given by the equation:

$$\frac{dx}{dt} = r\left(1 - \frac{x}{K}\right)x,$$

where r is the intrinsic growth rate, or rate that a population is able to reproduce, and K is the carrying-capacity of the population. When we solve for x, we find that the equation has 2 equilibria: $x = 0$ and $x = K$. Since x must be non-negative, this leaves us with 2 cases to look at:

1. $0 < x < K$:

   When $0 < x < K$, we see that $r(1 - \frac{x}{K}) > 0$, thus $\frac{dx}{dt} = r(1 - \frac{x}{K})x > 0$.

2. $x > K$:

   When $x > K$, we see that $r(1 - \frac{x}{K}) < 0$, thus $\frac{dx}{dt} = r(1 - \frac{x}{K})x < 0$.

Thus, we see that when $x > 0$, the population size approaches K. We can apply a similar method to the SI epidemic model.

3 Stability Analysis of SI Epidemic Model

Let's look at the stability of an SI (Susceptible-Infected) epidemic model. In this model, an individual cannot become uninfected. The model takes the form:

$$\frac{dS}{dt} = -\frac{\beta}{N}SI,$$

$$\frac{dI}{dt} = \frac{\beta}{N}SI,$$

where $N =$ the population size and $\beta =$ the average number of adequate contacts made by an infected individual, with $N, \beta > 0$. Since the number of susceptible and infected must add up to total population, we have $N = S+I$. We can rearrange the equation and find $S = N - I$. When we plug in for S in $\frac{dI}{dt}$, we find that:

$$\frac{dI}{dt} = \beta I\left(1 - \frac{I}{N}\right).$$

With some algebra, we simplified the system into a logistic growth model. We can apply the same methods to analyze how the system will behave.

3.1 Logistic Analysis of SI

Let's begin by setting the equation equal to 0. Thus:

$$\frac{dI}{dt} = \beta I\left(1 - \frac{I}{N}\right) = 0$$

Now, Let's solve for I to find the equilibria. We see that:

$$\beta I = 0 \text{ and } \left(1 - \frac{I}{N}\right) = 0$$

implies

$$I = 0 \text{ and } I = N.$$

Again, since I must be non-negative, we have 2 cases to look at:

1. $0 < I < N$: We see that $\beta(1 - \frac{I}{N}) > 0,$ thus $\frac{dI}{dt} = \beta I(1 - \frac{I}{N}) > 0$, and is increasing to the equilibrium $I = K$.

2. $I > N$: We see that $\beta(1 - \frac{I}{N}) < 0,$ thus $\frac{dI}{dt} = \beta I(1 - \frac{I}{N}) < 0$, and is decreasing to the equilibrium $I = K$.

Thus, we see that when $I(0) > 0$, the number of infected individuals approaches N.

4 Stability Analysis of SIS Epidemic Model

Let's look at the stability of an SIS (Susceptible-Infected-Susceptible) epidemic model. In this model, an individual can be infected more than once. The model takes the form:

$$\frac{dS}{dt} = -\frac{\beta}{N}SI + \gamma I,$$
$$\frac{dI}{dt} = \frac{\beta}{N}SI - \gamma I,$$

where $N =$ the population size, $\beta =$ the average number of adequate contacts made by an infected individual, and $\gamma =$ the average recovery rate, with $N, \beta, \gamma > 0$. We can, again, replace S in $\frac{dI}{dt}$ with $N - I$. Thus, we get:

$$\frac{dI}{dt} = I(\beta - \gamma)(1 - \frac{\beta}{(\beta - \gamma)N}I)$$

for $\beta \neq \gamma$. Since we know that I must be non-negative, we are left with 2 cases:

1. $\beta > \gamma$: By setting $\frac{dI}{dt} = 0$ and solving for I, we find that $I = (\beta - \gamma)\frac{N}{\beta}$. When we plug our value for I into $\frac{dS}{dt}$ and solve for S, we find that $S = \frac{\gamma N}{\beta}$. Thus, the infected population approaches $(\beta - \gamma)\frac{N}{\beta}$ and the susceptible population approaches $\frac{\gamma N}{\beta}$. Thus, we have an equilibrium that does not lie on an axis, and the disease becomes endemic.

2. $\beta \leq \gamma$: the infected population approaches 0. Thus, the disease will not survive.

This leads to a very interesting observation on the relationship between β and γ.

4.1 Basic Reproductive Rate

The relationship between β and γ is called the basic reproductive rate, represented R_0. It is the ratio:

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

where β is the average number of adequate contacts made by an infected individual and $1/\gamma$ is the average infectious period. It is used to describe the contagiousness or transmissibility of infectious agents. It is affected by many environmental, sociobehavioral, and biological factors. Therefore, it can be very tricky to model. It also is not a perfect estimate for modeling the spread of a disease. Generally, when $R_0 > 1$, diseases tend to become endemic and when $0 < R_0 \leq 1$, diseases tend to die out.

5 General Analysis of Equilibria

When dealing with systems of differential equations, we can analyze the stability of equilibria using linear algebra, specifically Jacobian matrices.

Let's look at the system, $\frac{dH}{dt}$. The equilibria, $\overline{X}$, of the system are solutions $(\overline{x}, \overline{y})$ so that $f(\overline{x}, \overline{y}) = 0$, and $g(\overline{x}, \overline{y}) = 0$. We must find the trace and determinant of the resulting Jacobian matrix to determine the type of equilibrium we have. By taking the first-order partial derivatives of the system, we get a Jacobian matrix, J, such that

$$J = \begin{bmatrix} f_x(\overline{x}, \overline{y}) & f_y(\overline{x}, \overline{y}) \\ g_x(\overline{x}, \overline{y}) & g_y(\overline{x}, \overline{y}) \end{bmatrix} \begin{bmatrix} u \\ v \end{bmatrix}$$

and we find that:

$$Tr(J) = f_x(\overline{x}, \overline{y}) + g_y(\overline{x}, \overline{y}),$$

$$det(J) = f_x(\overline{x}, \overline{y}) \times g_y(\overline{x}, \overline{y}) - g_x(\overline{x}, \overline{y}) \times f_y(\overline{x}, \overline{y}).$$

From Allen (189-190) we are told, "the stability criteria depend on the eigenvalues of the Jacobian matrix evaluated at $\overline{X}, J(\overline{X})$. If all the eigenvalues have negative real part, then the equilibrium is locally asymptotically stable."

THEOREM 5.1. *Assume the first-order partial derivatives of f and g are continuous in some open set containing the equilibrium* $(\overline{x}, \overline{y})$. *Then the equilibrium is locally asymptotically stable if*

$$Tr(J) < 0 \text{ and } det(J) > 0,$$

where J is the Jacobian matrix evaluated at the equilibrium. In addition, the equilibrium is unstable if either $Tr(J) > 0$ *or* $det(J) < 0$.

Proof. Take the characteristic polynomial of J evaluated at $(\overline{x}, \overline{y})$:

$$\lambda^2 - Tr(J)\lambda + det(J) = 0.$$

It follows that the eigenvalues satisfy:

$$\lambda_{\pm} = \frac{Tr(J) \pm \sqrt{(-Tr(J))^2 - 4det(J)}}{2}.$$

Assume $Tr(J) < 0$ and $det(J) > 0$. We proceed with proof by cases:

1. $(-Tr(J))^2 - 4det(J) < 0$. It follows that $\sqrt{(-Tr(J))^2 - 4det(J)}$ implies $\lambda_{\pm} \in \mathbb{C}$. Thus $Re(\lambda_-) = \frac{p}{2} < 0$.

2. $(-Tr(J))^2 - 4det(J) > 0$. It follows that $\lambda_{\pm} \in \mathbb{R}$. Thus:

   (a) $\lambda_- = \frac{Tr(J) - \sqrt{(-Tr(J))^2 - 4det(J)}}{2} < 0$

   (b) $\lambda_+ = \frac{Tr(J) + \sqrt{(-Tr(J))^2 - 4det(J)}}{2} < \frac{Tr(J) + \sqrt{(-Tr(J))^2}}{2} = \frac{Tr(J) - Tr(J)}{2} = 0$

Therefore, when $Tr(J) < 0$ and $det(J) > 0$, the eigenvalues $\lambda_{\pm} < 0$ and the equilibrium is locally asymptotically stable. □

6 Stability Analysis of SIR Epidemic Model

Let's look at the stability of an SIR epidemic model. This type of model takes the form:

$$\frac{dS}{dt} = -\frac{\beta}{N} SI,$$

$$\frac{dI}{dt} = \frac{\beta}{N} SI - \gamma I,$$

$$\frac{dR}{dt} = \gamma I,$$

where $N =$ the population size, $\beta =$ the average number of adequate contacts made by an infected individual, $\gamma =$ the average recovery rate, with $N, \beta, \gamma > 0$. There are two ways we can analyze the behavior of this model.

6.1 Integrating

We will start by using a similar method as the logistic models and integrating to get a solution. It is sufficient to look at only $\frac{dS}{dt}$ and $\frac{dI}{dt}$ since we know $N = S + I + R$ and $\frac{dR}{dt}$ depends only on I. Thus, we obtain the model

$$\frac{dS}{dt} = -\frac{\beta}{N}SI,$$

$$\frac{dI}{dt} = \frac{\beta}{N}SI - \gamma I.$$

Notice that

$$\frac{\frac{dI}{dt}}{\frac{dS}{dt}} = \frac{\frac{\beta}{N}SI - \gamma I}{-\frac{\beta}{N}SI},$$

simplifies to

$$\frac{dI}{dS} = \frac{\frac{\beta}{N}SI - \gamma I}{-\frac{\beta}{N}SI} = -1 + \frac{\gamma N}{\beta S},$$

Since we have a single variable, we can integrate to find a solution. We can rearrange the equation and we get:

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

Then we integrate:

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

$$I(t) = -S(t) + \frac{\gamma N}{\beta} \ln S(t) + C$$

We then solve for C and find:

$$C = I(0) + S(0) - \frac{\gamma N}{\beta} \ln S(0) = N - R(0) - \frac{\gamma N}{\beta} \ln S(0)$$

Thus:

$$I(t) = -S(t) + \frac{\gamma N}{\beta} \ln S(t) + N - R(0) - \frac{\gamma N}{\beta} \ln S(0)$$

$$I(t) = N - R(0) - S(t) + \frac{\gamma N}{\beta} \ln \left(\frac{S(t)}{S(0)}\right).$$

Note that $S(t)$ is a decreasing funtion of t. Also note that if we set $\frac{dI}{dt} = 0$ and solve for S, we find that $S = \frac{\gamma N}{\beta}$. Thus, if $S(0) > \frac{\gamma N}{\beta}$, then $I(t)$ will increase to a maximum where an epidemic occurs and then decrease to 0. Also note that if $S(0) \leq \frac{\gamma N}{\beta}$, then $I(t)$, will decrease to 0. The epidemic always dies out.

6.2 Jacobian Analysis

The second method is by utilizing Jacobian matrices and analyzing the trace and determinant. Recall that the epidemic will always die out in this model. When we set each equation equal to 0 and solve for S and I, we find that we get 2 unique equilibria:

1. $(0, 0)$
2. $\left(\frac{\gamma N}{\beta}, 0\right)$

6.3 (0,0)

Let's analyze the equilibrium (0,0). After taking the partial derivatives of $\frac{dS}{dt}$ and $\frac{dI}{dt}$ with respect to S and I, we get the following Jacobian matrix, J:

$$J = \begin{bmatrix} \frac{-\beta}{N}I & \frac{-\beta}{N}S \\ \frac{\beta}{N}I & \frac{\beta}{N}S - \gamma \end{bmatrix}$$

When we plug in the equilibria, we get that J becomes:

$$J = \begin{bmatrix} \frac{-\beta}{N}(0) & \frac{-\beta}{N}(0) \\ \frac{\beta}{N}(0) & \frac{\beta}{N}(0) - \gamma \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & -\gamma \end{bmatrix}$$

Given the matrix J, we find that $Tr(J) = -\gamma < 0$ and $det(J) = 0$. Thus, we find the origin is stable.

6.4 $\left(\frac{\gamma N}{\beta}, 0\right)$

Let's analyze the equilibrium $\left(\frac{\gamma N}{\beta}, 0\right)$. After taking the partial derivatives of $\frac{dS}{dt}$ and $\frac{dI}{dt}$ with respect to S and I, we get the following Jacobian matrix, J:

$$J = \begin{bmatrix} \frac{-\beta}{N}I & \frac{-\beta}{N}S \\ \frac{\beta}{N}I & \frac{\beta}{N}S - \gamma \end{bmatrix}$$

When we plug in the equilibria, we find that:

$$J = \begin{bmatrix} \frac{-\beta}{N}(0) & \frac{-\beta}{N}(\frac{\gamma N}{\beta}) \\ \frac{\beta}{N}(0) & \frac{\beta}{N}(\frac{\gamma N}{\beta}) - \gamma \end{bmatrix} = \begin{bmatrix} 0 & -\gamma \\ 0 & 0 \end{bmatrix}$$

Given the matrix J, we find that $Tr(J) = 0$ and $det(J) = 0$. Thus, the equilibria is not locally asymptotically stable.

7 Stability Analysis of SIRS Epidemic Model

Let's look at the stability of an SIRS (Susceptible-Infected-Recovered-Susceptible) epidemic model. This model allows an individual to be reinfected after a recovery period. The model takes the form:

$$\frac{dS}{dt} = -\frac{\beta}{N}SI + \nu R,$$
$$\frac{dI}{dt} = \frac{\beta}{N}SI - \gamma I,$$
$$\frac{dR}{dt} = \gamma I - \nu R,$$

where N = the population size, β = the average number of adequate contacts made by an infected individual, γ = the average recovery rate, ν = rate of loss of immunity, with $N, \beta, \gamma, \nu > 0$.

Since R can be obtained from S, I, and N, the system can be written in terms of S and I:

$$\frac{dS}{dt} = -\frac{\beta}{N}SI + \nu(N - S - I),$$
$$\frac{dI}{dt} = \frac{\beta}{N}SI - \gamma I,$$

When we set each equation equal to 0 and solve for S and I, we find that there are 2 equilibria of interest:

1. $\left(\frac{\gamma N}{\beta}, \frac{\nu N(\beta-\gamma)}{\beta(\nu+\gamma)}\right)$
2. $(N, 0)$

7.1 $\left(\frac{\gamma N}{\beta}, \frac{\nu N(\beta-\gamma)}{\beta(\nu+\gamma)}\right)$

This is a very unique equilibrium. If the initial conditions are right, the disease will become endemic, meaning it will never die out. Let's look at the resulting Jacobian matrix:

$$J = \begin{bmatrix} \frac{-\beta}{N}I - \nu & \frac{-\beta}{N}S - \nu \\ \frac{\beta}{N}I & \frac{\beta}{N}S - \gamma \end{bmatrix} = \begin{bmatrix} \frac{-\beta}{N}(\frac{\nu N(\beta-\gamma)}{\beta(\nu+\gamma)}) - \nu & \frac{-\beta}{N}(\frac{\gamma N}{\beta}) - \nu \\ \frac{\beta}{N}(\frac{\nu N(\beta-\gamma\beta)}{\beta(\nu+\gamma)}) & \frac{\beta}{N}(\frac{\gamma N}{\beta}) - \gamma \end{bmatrix}$$

which can simplified further to:

$$\begin{bmatrix} -\beta(\frac{\nu(\beta-\gamma)}{\beta(\nu+\gamma)}) - \nu & -\gamma - \nu \\ \beta(\frac{\nu(\beta-\gamma)}{\beta(\nu+\gamma)}) + \nu & 0 \end{bmatrix}$$

we find that $Tr(J) = -\left(\frac{\nu(\beta-\gamma)}{\nu+\gamma}\right) - \nu$ and $det(J) = \nu(\beta - \gamma)$. From here, we find that we have two cases:

1. $\beta > \gamma$

$$Tr(J) = -\left(\frac{\nu(\beta-\gamma)}{\nu+\gamma}\right) - \nu < 0$$

$$det(J) = \nu(\beta-\gamma) > 0$$

2. $\beta < \gamma$

$$I = \frac{\nu N(\beta-\gamma)}{\beta(\nu+\gamma)} < 0$$

thus, when $\beta < \gamma$, $I < 0$ and the equilibrium has no practical meaning.

7.2 $(N, 0)$

Let's look at the Jacobian:

$$J = \begin{bmatrix} \frac{-\beta}{N}I - \nu & \frac{-\beta}{N}S - \nu \\ \frac{\beta}{N}I & \frac{\beta}{N}S - \gamma \end{bmatrix} = \begin{bmatrix} \frac{-\beta}{N}(0) - \nu & \frac{-\beta}{N}(N) - \nu \\ \frac{\beta}{N}(0) & \frac{\beta}{N}(N) - \gamma \end{bmatrix}$$

which can be simplified further to:

$$\begin{bmatrix} -\nu & \beta - \nu \\ 0 & \beta - \gamma \end{bmatrix}$$

we find that $Tr(J) = -\nu + (\beta - \gamma)$ and $det(J) = -\nu(\beta - \gamma)$. From here, we find that we have two cases:

1. $\beta > \gamma$:

$$det(J) = -\nu(\beta-\gamma) < 0,$$

thus, it is unstable.

2. $\beta < \gamma$

$$Tr(J) = -\nu + (\beta-\gamma) < 0$$

$$det(J) = -\nu(\beta-\gamma) > 0$$

thus, when $\beta < \gamma$, the equilibrium is locally asymptotically stable.

8 Application to Influenza

We can apply the results from the SIRS model to the Influenza virus. By being able to visualize how the virus spreads, we can provide data to help develop better sanitary habits and policies. The CDC provides some parameters for the Influenza virus:

- The average infectious period for the virus is 4 days $= 1/\gamma$, thus $\gamma = \frac{1}{4} = .25$.
- The average length of immunity is 6 months = 180 days $= \frac{1}{\nu}$, thus $\nu = \frac{1}{180} = .00556$.

With this information, we can look at the equilibrium $\left(\frac{\gamma N}{\beta}, \frac{\nu N(\beta-\gamma)}{\beta(\nu+\gamma)}\right)$.

8.1 Calculating Trace and Determinant

Recall, the Jacobian matrix for the SIRS model at the equilibrium $\left(\frac{\gamma N}{\beta}, \frac{\nu N(\beta-\gamma)}{\beta(\nu+\gamma)}\right)$ is:

$$\begin{bmatrix} \frac{-\beta}{N}(\frac{\nu N(\beta-\gamma)}{\beta(\nu+\gamma}))-\nu & \frac{-\beta}{N}(\frac{\gamma N}{\beta})-\nu \\ \frac{\beta}{N}(\frac{\nu N(\beta-\gamma\beta)}{\beta(\nu+\gamma}))) & \frac{\beta}{N}(\frac{\gamma N}{\beta})-\gamma \end{bmatrix} = \begin{bmatrix} \frac{-\beta}{N}\frac{(.00556N(\beta-.25)}{\beta(.00556+.025}))-.00556 & \frac{-\beta}{N}(\frac{.25N}{\beta})-.00556 \\ \frac{\beta}{N}(\frac{.00556N(\beta-.25\beta)}{\beta(.00556+.25}))) & \frac{\beta}{N}(\frac{.25N}{\beta})-.25 \end{bmatrix}$$

which can simplified further to:

$$\begin{bmatrix} -(\frac{.00556(\beta-.25)}{(.00556+.25)})-.00556 & -.25-.00556 \\ (\frac{.00556(\beta-.25)}{\beta(.00556+.25)}) & 0 \end{bmatrix} = \begin{bmatrix} -(\frac{.00556(\beta-.25)}{(.00556+.25)})-.00556 & -.25-.00556 \\ (\frac{.00556(\beta-.25)}{(.00556+.25)}) & 0 \end{bmatrix}$$

Since $\beta > \gamma = .25$, then:

$$Tr(J) = \frac{.00556(\beta-.25)}{.25556} - .00556 < 0,$$

$$det(J) = .00556(\beta-.25) + .00556 > 0,$$

and thus, is locally asymptotically stable.

8.2 Interpreting the Results

In order to keep influenza as tame as possible, we must try to keep β as close to .25 as possible. This can mean many different things in the real world. For example, a few ways to avoid catching and spreading the virus are to:

1. Wash our hands frequently
2. Avoid other when we are sick
3. Get the flu vaccine each year
4. etc.

9 References

References

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