MAT 124: Midterm I.

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1 Background

The CDC documents, that the first written account of measles was documented in the 9th century by an unknown Persian doctor. During the early 1900s, before vaccines, the United States was documenting 6000 measles related deaths per year. In the early 1960s, nearly all children contracted measles by the age of 15 and estimated 3 to 4 million US citizens were infected each year making it one of the most infectious diseases of all time. Hospitalization rate was quite low compared to the number of infected with on average 48,000 Americans being hospitalized with 400-500 reported deaths per year. [1]

This is not to presume measles that hospitalization is injective with symptoms as vaccines were discovered the decade after. It is fair to assume many Americans who were not hospitalized suffered from side effects as well.

In 1963, a group of scientists lead by John Enders discovered a method to separate measles from the blood of an infected 13 year old named David Edmonston. The vaccine developed from separating this strain was named Edmonston-Enders and would later be used to in addition with mumps and rubella to develop the (MMR) vaccine. Since the development and distribution of (MMR) the number of cases in America in 1981 dropped by 80 percent since the previous year. Measles would later have an outbreak in 1989 with a second dose of (MMR) this outbreak would quickly be contained and decline. In 2000, Measles was declared eliminated in the United States. [1]

The SEIR, Susceptible-Exposed-Infected-Recovered, models analyzing measles help translate strategies with math to invest in future disease prevention. In this particular article, we look at the spread of measles using a reduced SEIR model and analyze the mathematics behind it.

2 Linearization

An important way to display the spread of disease is by using a system of differential equations. The following model defines the following linear constants

and the rate of changes from compartment to compartment. Note the sum of all compartments is equal to N which we assume to be known. In this model, μ is the number of natural deaths that occur without any relation to measles, whereas measles related deaths are denoted by δ. ν is the proportion of Susceptible individuals that decide to receive their first vaccine. The population that moves from the V_1 compartment back to the susceptible compartment is indicated by ρ. The people that move from the V_1 to V_2 compartment is σ. The population that moves from V_2 to R is ω. β is the transmission rate between the susceptible and infected population. α denotes the population moving from the E to the I compartment. γ is the population that moves from I to R.

$$\mu : 1/70, \beta : 7.45 * 10^{-}7, \nu : 0.94, \rho : 0.60$$

$$\sigma : 0.93, \alpha : 0.018, \gamma : 0.60, \delta : 0.125, N : 163,046,161$$

$$\omega* = 0.8$$

*

First Order Derivatives:

$$S' = \mu N + \beta SI - \nu S - \mu S + \rho V_1$$

$$V_1' = \nu S - \rho V_1 - \sigma V_1 - \mu V_1$$

$$V_2' = \sigma V_1 - \omega V_2 - \mu V_2$$

$$E' = \beta SI - \alpha E - \mu E$$

$$I' = \alpha E - \gamma I - \delta I - \mu I$$

$$R' = \gamma I + \omega V_2 - \mu R$$

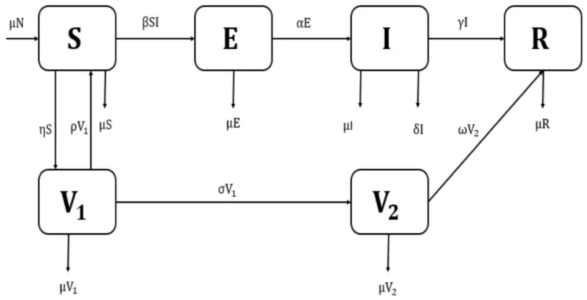

Figure 1: SEIR Flowchart

The equilibrium points for E and I can be calculated by setting the first order derivative equations of E and I to zero. This makes both the equations equivalent to one another. The following are the equations that represent the equilibrium point.

$$I' = \alpha E - \gamma = 0$$
$$E' = \beta SI - \alpha E = 0$$

Then, we must solve for E in the I' equation and I in the E' equation. This yields the following:

$$E = [\gamma I]/\alpha$$
$$\beta SI = \gamma I$$

However, this solution is not viable because I can not be solved for. Instead, we are given a relationship between the transmission rates of β and γ.
By solving for the eigenvalues for the characteristic matrix, we are able to find the general shape of the directional field. We're provided the partial derivatives of each and are able to construct Matrix A.

$$\begin{bmatrix} \beta SI - \alpha E - \mu E & \beta SI - \alpha E - \mu E \\ \alpha E - \gamma I - \delta I - \mu I & \alpha E - \gamma I - \delta I - \mu I \end{bmatrix} \begin{bmatrix} d/dE \\ d/dI \end{bmatrix} \tag{1}$$

Taking the partial derivatives we obtain the Char(A).

$$\begin{bmatrix} \beta SI - \alpha - \mu & \beta S \\ \alpha & -\gamma - \delta - \mu \end{bmatrix} \tag{2}$$

Solving this will yield us our Eigenvalues. Setting I = 0 and evaluating at said constants gives us (3). Note the SEIR model considers the added factors denoted by μ, and δ referring to people within compartments who die and whose cause of death are unrelated and related to measles respectively. To purely measure the rate of change between compartments we omit these constants to simplify the characteristic equation. Although they can be computed for messier lambdas.

$$\begin{bmatrix} 0 - \lambda 1 & \beta S \\ 0.018 & -0.6 - \lambda 2 \end{bmatrix} \tag{3}$$

The desired characteristic equation to solve is: $0 = -\lambda 1(-0.6 - \lambda 2)$

$$\lambda 1 = 0$$

$$\lambda 2 = -0.6$$

Based on the results of the eigenvalues, the graph would be categorized as a sink.
Checking Relative Removal Rate: The Eigenvalue solutions to the characteristic equation confirm that our adjusted relative removal rate is indeed γ. This makes sense as $\gamma$is defined as the rate of survivors exiting the infected compartment and entering the recovery compartment.
When looking at the system as a whole we consider the 5x5 jacobian matrix utilizing: dS, dV1, dV2, dE,dI. Plugging in our constants mentioned in the

beginning as well as our estimated I value we obtain the simplified Jacobian matrix.

$$\begin{bmatrix} -0.9295 & 0.6 & 0 & 0 & -0.64319 \\ 0.94 & -1.5443 & 0 & 0 & 0 \\ 0 & 0.93 & -0.9643 & 0 & 0 \\ 0.02474 & 0 & 0 & -0.0037 & 0.64319 \\ 0 & 0 & 0 & 0.018 & -0.2393 \end{bmatrix} \tag{4}$$

The eigenvalue solutions are:

$$\lambda 1 = -2.0484, \lambda 2 = -0.9643, \lambda 3 = -0.4283, \lambda 4 = -0.2766, \lambda 5 = 0.0365$$

The Eigenvalues describe the stability of the system. With 4 of eigenvalues being negative and λ 5 being positive we can presume the equilibrium points in this set up are asymptotically unstable. It is worth noting the trivial eigenvalue solution is stable simply because disease-free equilibrium point implies the eigenvalues will be equal and opposite to the susceptible population. This is always a positive number.

Solution Curves: Taking the integral of dI/dE yields an equation similar to $I(S)$ from the SIR model.

$$\frac{dI}{dE} = \frac{\alpha E - \gamma I - \delta I - \mu I}{\beta SI - \alpha E - \mu E} \tag{5}$$

$$I(E) = -\alpha(\frac{\beta SI \ln|\mu+\alpha|E - \beta SI}{\mu^2 + 2\alpha\mu + \alpha^2} + \frac{E}{\mu+\alpha}) + I(\gamma+\delta+\mu)\frac{ln(|(\mu+\alpha)E - \beta SI)}{\mu+\alpha} + C \tag{6}$$

Observing this solution we see that we have a negative base population signified by the first term in (5). This is our base infected notably the

$$\beta SIln(|\mu+\alpha|)E - \beta SI$$

term in the numerator adjusted for deaths. The 2nd term indicates the relative removal rate adjusted with death by natural causes and death by disease as signified by:

$$I(\gamma + \delta + \mu)$$

.

Reproduction Rate: The reproduction rate is simply the rate at which primary cases of the disease spread to the susceptible population creating a group of secondary cases. In the instance of the measles outbreak in Bangladesh, the reproduction rate is denoted as:

$$R_0 = \frac{\alpha\beta\mu N(\rho + \sigma\mu)}{(\alpha+\mu)(\gamma+\delta+\mu)((\nu+\mu)(\rho+\sigma+\mu) - \rho\nu)}$$

After substituting values for each variable we have,

$$R_0 = \frac{0.018 \cdot 7.45x10^{(}-7) \cdot \frac{1}{70} \cdot 163046161 \cdot (0.6 + 0.93 + \frac{1}{70})}{(0.018 + \frac{1}{70}) \cdot (0.6 + 0.125 + \frac{1}{70})((0.94 + \frac{1}{70}) \cdot (0.6 + 0.93 + \frac{1}{70}) - 06 \cdot 0.94)}.$$

Therefore,

$$R_0 \approx 1.44$$

Since R_0 is greater than one, there is a large influx of secondary cases. This is not a positive sign because this means that the number of cases is exponentially increasing.

3 Nullclines and Basic Regions

The nullclines can be observed by setting dE/dt and dI/Dt equal to 0. For this section we bring back in the omitted δ, μ. The I nullcline implies either I, E = 0, which is trivial, or if E = 0, then $\gamma + \delta + \mu$ is equal to 0. We can condition $(\gamma + \delta + \mu)/\alpha$ as relative removal rate / rate of infection. Observe unlike a standard SIR model, we have the added E in SEIR so we observe recovery/infection rates in compartments E and I rather than S and I.

I-Nullcline

Beginning with the I-Nullcline, the E = 0 condition above implies $\gamma + \delta + \mu$ is equal to 0. This would initially imply that for $\gamma = -(\delta + \mu)$. Which makes sense as the number of infected people dying and recovering should be the equal and opposite. This isn't to imply realistically people who die enter the E compartment to match those who recover exiting the apartment. It is simply to observe the absolute values are the same under a fixed E = 0.

If we ignore δ, μ as deaths exiting the system, this would leave γ as the slope on the I-axis. The option to omit is W.O.L.G and entirely depends on valuing rate of recovery or defining the equilibrium of the I-axis. For meaningful analysis, it's best to ignore δ, μ so we can monitor the transition functions between compartments. Note there will be an error term directly correlating to number of deaths exiting the system.

We next observe cases of non-zero E and I. When E is large and I is small we have a large relative removal rate; $\gamma + \delta + \mu/(\alpha)$. Conversely when I is large and E is small we have a low relative removal rate, e.g a large α or a small $\gamma + \delta + \mu$.

$$es\frac{dI}{dt} = \alpha E + \gamma I - \delta I - \mu I \tag{7}$$

$$E = I * (\gamma + \delta + \mu)/(\alpha) \tag{8}$$

Equilibrium points and Nullclines Continued

With dE/dt set to 0 this implies either the trivial solution, E, I = 0, or $\beta SI = \alpha E + \mu E$. An E-Nullcline then implies the rate of susceptible people becoming exposed equals the rate of exposed becoming infected. In other words, the virus may be very virulent. S in this case is generally a function of (t) however for the case in which S is known discretely, we can see the solution is in a line.

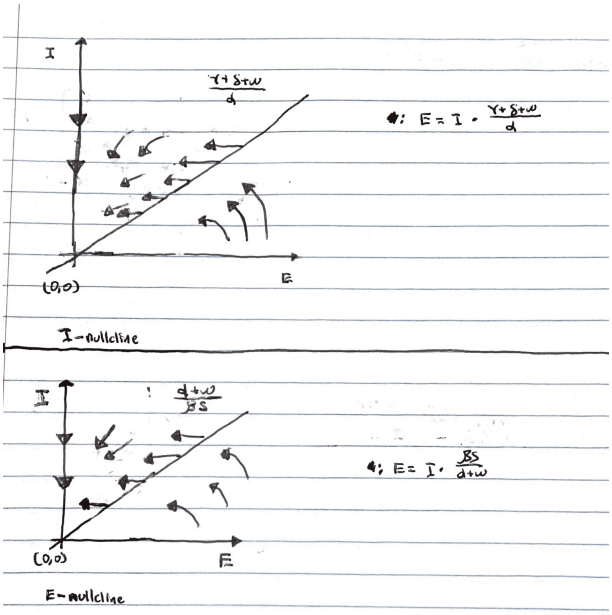

Figure 2: Nullcline Graphs

$$\frac{dE}{dt} = \beta SI - \alpha E - \mu E \tag{9}$$

$$\beta SI = E(\alpha + \mu) \tag{10}$$

Setting $\frac{dI}{dt}$ and $\frac{dE}{dt}$ equal to 0 creates the equality. From (9) we can obtain (10).

$$E = \frac{\gamma I + \delta I + \mu I}{\alpha} \tag{11}$$

$$1 = \frac{(\gamma + \delta + \mu) * (\alpha + \mu)}{\beta S \alpha} \tag{12}$$

Omitting deaths exiting the equation we can reduce (12) into:

$$1 = \frac{\gamma}{\beta S} \tag{13}$$

Equation (13) implies that when there is 0 change between compartments the rate in which susceptible people become exposed to measles is the same rate those exiting the system into recovery. As S increases, so would γ. In this case we have a perfect recovery rate. Lastly the points along the line are equilibrium solutions; equilibrium points.

4 Phase Diagrams

We computed multiple phase diagrams between different compartments. Here we look at the 2x2 jacobians for [DS,DI], [DE,DI] and [DI,DR]. With [DS,DI] the equilibrium points are a sink since both eigenvalues are negative. We use [DS,DI] as an example as the others are calculated using the same general equation.
[DS,DI] The jacobian is:

$$\begin{bmatrix} -\beta SI - \nu - \mu & -\beta S \\ 0 & -\gamma - \delta - \mu \end{bmatrix} \tag{14}$$

$$\begin{bmatrix} -0.9729 & -0.64319 \\ 0 & -0.7329 \end{bmatrix} \tag{15}$$

The Eigenvalues are λ 1 = -0.9790, λ 2 = -0.7393.
With Eigenvectors: U1: $\begin{bmatrix} 1 \\ 0 \end{bmatrix}$ and U2: $\begin{bmatrix} 2.7699es \\ 1 \end{bmatrix}$
The general formula for this, with α and $\beta = 1$ respectively is listed below. This equation approaches 0 as t approaches infinity. However since the real data lasts for from 2000 to 2016, our t value is at most 16. To see where solution curves intersect we elongate t to 500.

$$\frac{x(t)}{y(t)} = u_1 e^{\lambda_1 t} + u_2 e^{\lambda_2 t} \tag{16}$$

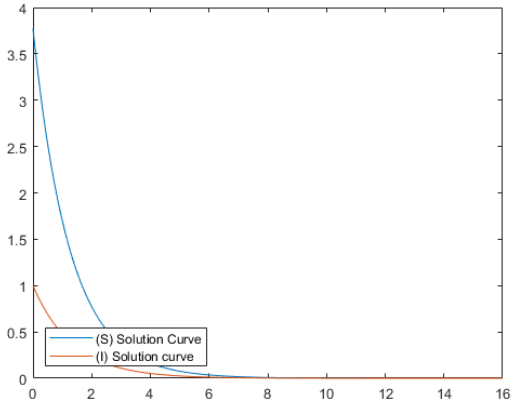

Figure 3: Phase Diagrams (S,I) with T=16

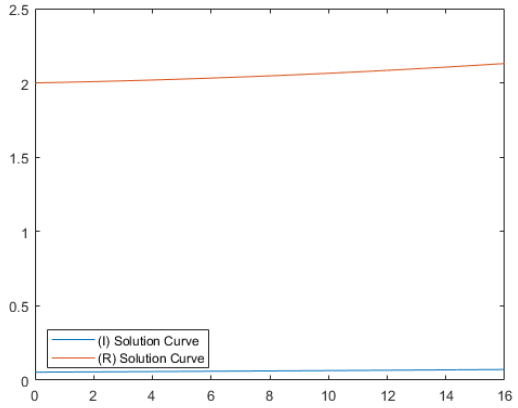

Figure 4: Phase Diagrams (I,R) with T=16

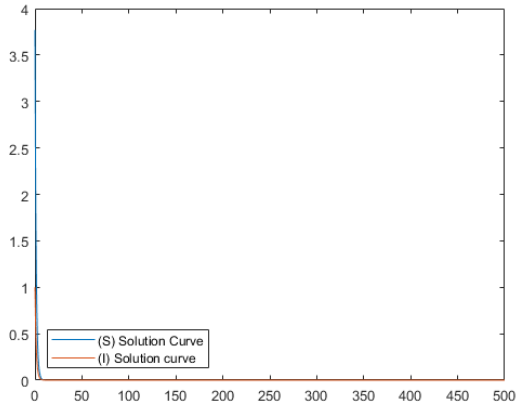

Figure 5: Phase Diagrams (S,I) with T=500

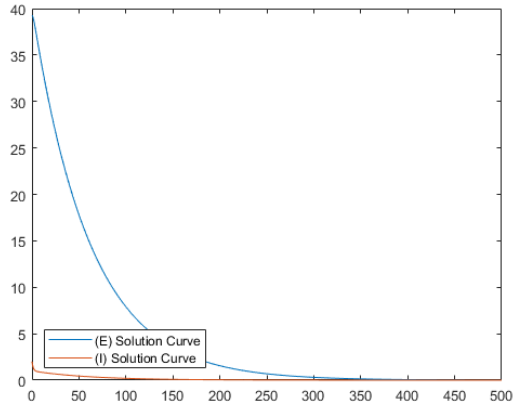

Figure 6: Phase Diagrams (E,I) with T=500

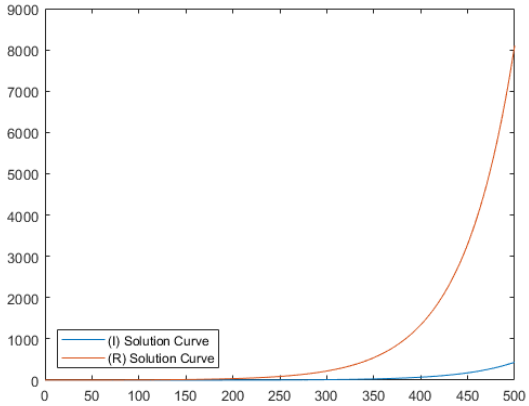

Figure 7: Phase Diagrams (I,R) with T=500

5 Numerical methods

The Runge Kutta method can be implemented to see how a particular stage of the SIR model changes over time. We do this by solving an initial value problem given a function in the form $f(t, y) = \frac{dy}{dt}$, an initial value $y(0) = a$, step size h, and and end point b. In our case, $f(t, y) = \frac{dE}{dt}$ with initial value (0,0) and endpoint 16. This is because our data starts at the year 2000 and ends in 2016. When, implemented to MatLab, we find that the number of exposed individuals increase exponentially with time. This is highly justified because R_0 is greater than 1. Since $R_0 > 1$, the number of secondary cases increase exponentially. Hence, it is obvious that the number of exposed cases would have a similar rate. The following is a visual of this relationship.

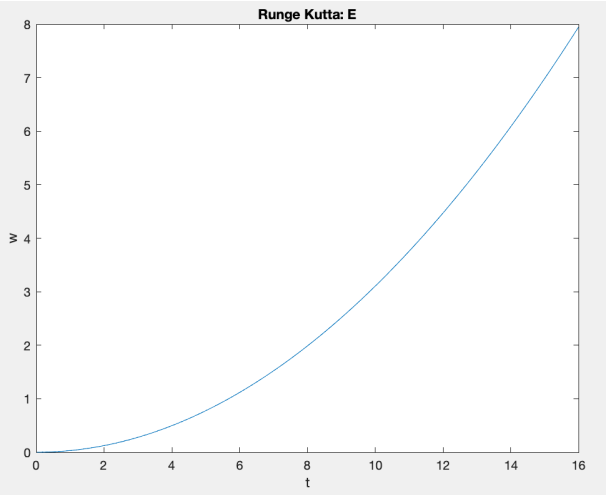

Figure 8: Graph of Runge Kutta for E'

6 Sources

CDC: https://www.cdc.gov/measles/about/history.html
Double Vax Model: https://www.nature.com/articles/s41598-021-95913-8citeas

7 Code

```
a = 0;
b = 16;
N = 1000;
y0 = 0;

S = 1:N;
I = 1:N;
h = (b-a)/N;
t = a;
w = y0;
B = 7.45*10^-7;
alpha = 0.018;
mu = 1/70;


for i = 1:N
    y1 = h .* [B.*S.*I - alpha*y0- mu*y0];
    y2 = (h/2) .*[B.*S.*I - alpha*y1- mu*y1];
    y3 = (h/2) .* [B.*S.*I - alpha*y2- mu*y2];
    y4 = h .*[B.*S.*I - alpha*y3- mu*y3];
    w = w + (1/6)*(y1 + 2*y2 + 2*y3 + y4);
    t(i,:) = a + i*h;
end

plot(t,w)
title('Runge Kutta: E')
xlabel('t')
ylabel('w')
```

Figure 9: Code for Runge Kutta Method of Order 4

```
u1 = [1,0]';
u2 = [2.7699,1]';

v1 = [-0.889711, 1]';
v2 = [40.1627, 1]';

w1 = [0.0538, 1]';
w2 = [0, 1]';

lambda1 = -0.979;
lambda2 = -0.739;
lambda1_1 = -0.755215;
lambda1_2 = -0.01627;
lambda1_1_1 = 0.018;
lambda1_1_2 = -0.0142;
t = linspace(0,10000,10000);

figure(1)
z = u1*exp(lambda1*t) + u2*exp(lambda2*t);
plot(t,z);
legend({'(S) Solution Curve','(I) Solution curve'},'Location','southwest')

figure(2)
z_1 = v1*exp(lambda1_1*t) + v2*exp(lambda1_2*t);
plot(t,z_1);
legend({'(E) Solution Curve','(I) Solution Curve'},'Location','southwest')

figure(3)
z_2 = w1*exp(lambda1_1_1*t) + w2*exp(lambda1_1_2*t);
plot(t,z_2)
legend({'(I) Solution Curve','(R) Solution Curve'},'Location','southwest')
```

Figure 10: Code for Phase Potrait Graphs