A Qualitative Analysis of Methodologies for Effective Viral Control

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1 Introduction

In the past few recent years, the Coronavirus pandemic has clearly demonstrated the need for a preparedness strategy to combat novel viruses. In particular, the varying early stage responses demonstrated by varying world governments, and the drastically different infection and death counts amongst these nations [1], has emphasized the need for having a plan ready prior to the outbreak of a virus. In this light, we explore a mathematical analysis of a model virus, one that could be more devastating given the current demonstrated lack of pandemic preparedness in the United States - a Zombie Apocalypse.

In contrast to past pandemics we have experienced, a zombie apocalypse scenario presents several different factors that should be considered in generating a mathematical modeling of the underlying epidemiology. Principally, a zombie virus would be characterized by a more aggressive virus spread and the need to simultaneously work on curing the virus as well as eliminating parts of the infected population to control the spread.

To take a more analytical look into this model, we seek to modify existing epidemiological models to better fit the notable characteristics of the proposed scenario, and hopefully to draw conclusions regarding ways to optimally respond to such a potential virus down the road.

2 Basis for the Approach

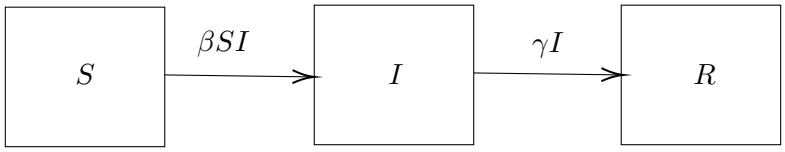
A methodology for modeling disease spread, proposed over a century ago by Kermack and McKendrick [2], is the Susceptible-Infected-Recovered (SIR) model, which assumes a compartmentalization of a constant, fixed size populace into the aforementioned three categories. The SIR model does not take into account spatial dispersion of the population and additionally assumes a disease transmission rate, denoted as

$$R_{trans} = bI \cdot \frac{S}{N} = \beta SI, \beta = \frac{b}{N}$$

where $b \in \mathbb{R}^+$ represents the rate of transmission, I represents the number of infected individuals, S the number of susceptible individuals, and N the total fixed-sized population. Note that N is equivalent to $S(t) + I(t) + R(t)$ for any t by neglecting birth and death rates. Further, assume a recovery rate denoted as

$$R_{recov} = \gamma I$$

in which $\frac{1}{\gamma}, \gamma \in \mathbb{R}^+$ is the mean residence time of the pathogen within an individual. Thus, the compartmentalized model can be visualized with the following transitions between populations as



Then, the model can be mathematically structured as the following nonlinear system.

$$\begin{cases} \frac{dS}{dt} = -\beta SI \\ \frac{dI}{dt} = (\beta S - \gamma)I \\ \frac{dR}{dt} = \gamma I \end{cases} \tag{1}$$

This model assumes that all infected individuals will fully recover from and thus be immune to the disease, which is an assumption that cannot be fully applied to future viruses regarding which we have no current data on [3]. This is especially true regarding our proposed scenario, in which an assumption of progression from infection to naturally recovered and immunized state cannot be made.

Additionally, the SIR model does not account for deaths in the population due to the severity of an infection, which once again requires the tweaking of the current model to better fit our framework.

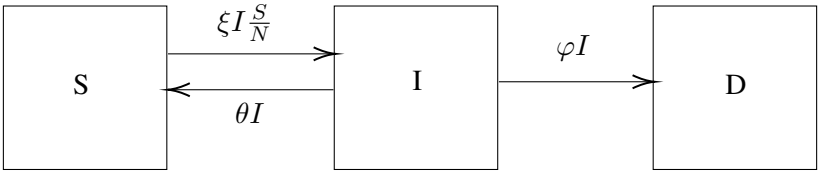
3 A Framework For Mortality Inclusion

We make two principal changes to better fit the principles of a SIR model to our scenario.

First, we redirect the flow of infected individuals recovering back into the susceptible compartment. This helps to handle the issue of the SIR model not considering the possibility of reinfection which we assume to be prevalent not only in our model scenario but also true in the case of real world viruses such as evidenced by the ongoing Coronavirus pandemic.

Additionally, we introduce a compartment which represents the proportion of the population which has died, either naturally due to severity of infection or government initiatives to curtail the spread of the infection.

The resulting "SID" model is then



We now have the following parameters in our model: θ which represents the recovery rate of infected individuals, ξ represents the infection rate of susceptible individuals, and φ represents the death rate of individuals carrying the infection. Note that $\{\theta, \xi, \varphi\} \in \mathbb{R}^+$ and the recovered compartment previously denoted "R" has been replaced with a death compartment denoted "D". Mathematically, we obtain the following nonlinear system.

$$\begin{cases} \frac{dS}{dt} = \theta I - \xi I\frac{S}{N} \\ \frac{dI}{dt} = \xi I\frac{S}{N} - \theta I - \varphi I \\ \frac{dD}{dt} = \varphi I \end{cases} \tag{2}$$

3.1 Assumptions

Population. In this model, we start of with a set population of size N. We assume individuals transition between compartments depending on the status of their health, and no individual leaves or enters the compartment model. In other words, factors such as birth and non-disease related deaths are not considered.

Infection. In the model, we have a compartment for infected individuals. We assume that infected individuals are infectious to other susceptible individuals, and are the only source of transmission. We assume an infected individual will infect a certain number of people ξ per unit time.

Recovery. Recovery in this model is transitioning from being infected to susceptible again. Recovering from the infection does not grant the individual immunity. The likeliness of recovery and death does not vary across different individuals.

Death. Death is when an infected individual dies either due to the mortality rate innate to the virus or due to external factors controlled in response to the virus. Once an individual reaches this compartment, they remain there without exception and no longer influence the flow of individuals between the compartments.

3.2 Model Simplification

In this model, we assume that the total population N is constant. The population N is defined as follows.

$$N = S + I + D$$

It is also important to note that the total population N does not depend on time t. This is shown as follows.

$$\begin{aligned}
N &= S + I + D \\
\frac{dN}{dt} &= \frac{d}{dt}(S + I + D) \\
\frac{dN}{dt} &= \frac{dS}{dt} + \frac{dI}{dt} + \frac{dD}{dt} \\
\frac{dN}{dt} &= (\theta I - \xi I\frac{S}{N}) + (\xi I\frac{S}{N} - \theta I - \varphi I) + (\varphi I) \\
\frac{dN}{dt} &= 0
\end{aligned}$$

Hence the population is constant, and we can recover the dead population from the other two variable populations via the equation

$$\begin{cases} N = S + I + D \\ D(t) = N - S(t) - I(t) \end{cases}$$

Therefore, our reduced model is

$$\begin{cases} \frac{dS}{dt} = \theta I - \xi I\frac{S}{N} \\ \frac{dI}{dt} = \xi I\frac{S}{N} - \theta I - \varphi I \end{cases} \tag{3}$$

With three parameters θ, ξ, and φ.

3.3 Nondimensionalization

To normalize time, define $\tau := \theta t$, and further, convert S and I to functions $(u, v)(\tau)$ of a closed population with size N. We arrive at the following results:

$$\begin{cases} u(\tau) = u(\theta t) = \frac{S(t)}{N} \\ v(\tau) = v(\theta t) = \frac{I(t)}{N} \end{cases}$$

which is equivalently,

$$\begin{cases} S(t) = Nu(\tau) \\ I(t) = Nv(\tau) \end{cases}$$

Then, deriving ordinary differential equations for $(u, v)(\tau)$, starting with $u(\tau)$:

$$\begin{aligned}
LHS &= \frac{dS(t)}{dt} = \frac{d}{dt}(Nu(\theta t)) = \theta N\frac{du}{d\tau}(\tau) \\
RHS &= \theta I - \xi I\frac{S}{N} \\
&= \theta N v(\tau) - \xi N v(\tau)u(\tau)
\end{aligned}$$

Setting LHS equal to RHS and simplifying, we arrive at:

$$\frac{du}{dt} = v(\tau) - \frac{\xi}{\theta}u(\tau)v(\tau)$$

Similarly, for $v(\tau)$:

$$
\begin{aligned}
LHS &= \frac{dI(t)}{dt} = \frac{d}{dt} Nv(\theta t) = \theta N \frac{dv}{dt}(\tau) \\
RHS &= \xi I \frac{S}{N} - \theta I - \varphi I \\
&= \xi N v(\tau) \frac{Nu(\tau)}{N} - \theta N v(\tau) - \varphi N v(\tau) \\
&= \xi N u(\tau) v(\tau) - \theta N v(\tau) - \varphi N v(\tau) \\
&= N(\xi u(\tau) v(\tau) - \theta v(\tau) - \varphi v(\tau)) \\
\frac{dv}{dt} &= \frac{\xi}{\theta} u(\tau) v(\tau) - v(\tau) - \frac{\varphi}{\theta} v(\tau)
\end{aligned}
$$

Define $R_o \coloneqq \frac{\xi}{\theta}$, the "basic reproduction number" for a given disease. We now have the following system of equations:

$$
\begin{cases}
\frac{du}{dt} = v - R_o uv \\
\frac{dv}{dt} = R_o uv - v - \frac{\varphi}{\theta} v
\end{cases} \tag{4}
$$

For each of the above equations, the existence and uniqueness theorem applies; for $\frac{du}{dt}$ and $\frac{dv}{dt}$, the right-hand side is continuously differentiable in all u, v. Thus there must exist unique solutions.

4 Behavior and Analysis of Viral Spread with SID Model

From the algebraic system (4), we can derive and analyze the behavior of a viral infection according to the SID model. To analyze the behavior and critical points of the system, we begin by finding the equilibria and subsequently evaluating the Jacobian at those equilibria.

To find the equilibria, set $\frac{du}{dt}$ and $\frac{dv}{dt}$ equal to zero as follows:

$$
\begin{aligned}
\frac{du}{dt} &= v - R_0 uv = 0 \\
\frac{dv}{dt} &= R_0 uv - v - \frac{\varphi}{\theta} v = 0
\end{aligned}
$$

Factoring to find roots of the system:

$$
\begin{aligned}
f = \frac{du}{dt} &= v(1 - R_0 u) = 0 \\
g = \frac{dv}{dt} &= v(R_0 u - 1 - \frac{\varphi}{\theta}) = 0
\end{aligned}
$$

We find that the only valid rest state which satisfies equilibrium condition is then $(u_*, 0)$. Then, to analyze the behavior of the system in equilibrium, evaluate the Jacobian at that equilibrium. The Jacobian of the system is:

$$
J_{sys} = \begin{pmatrix}
\frac{\partial f}{\partial u} = -R_0 v & \frac{\partial f}{\partial v} = 1 - R_0 u \\
\frac{\partial g}{\partial u} = R_0 v & \frac{\partial g}{\partial v} = R_0 u - 1 - \frac{\varphi}{\theta}
\end{pmatrix}
$$

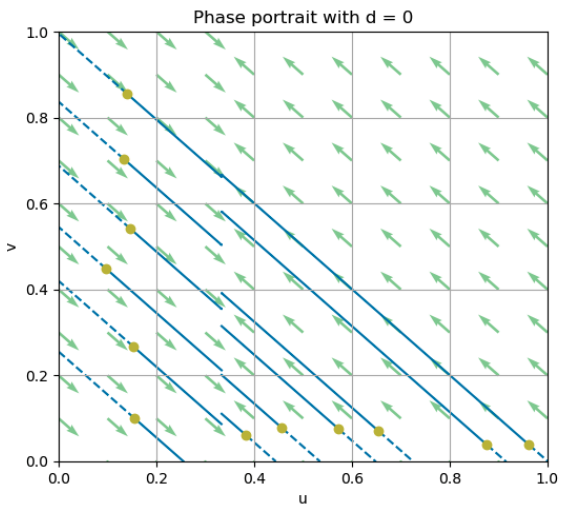
Evaluating the Jacobian at the rest state $(u_*, 0)$ results in:

$$
J_{sys}\big|_{(u_*,0)} = \begin{pmatrix}
0 & 1 - R_0 u_* \\
0 & R_0 u_* - 1 - \frac{\varphi}{\theta}
\end{pmatrix}
$$

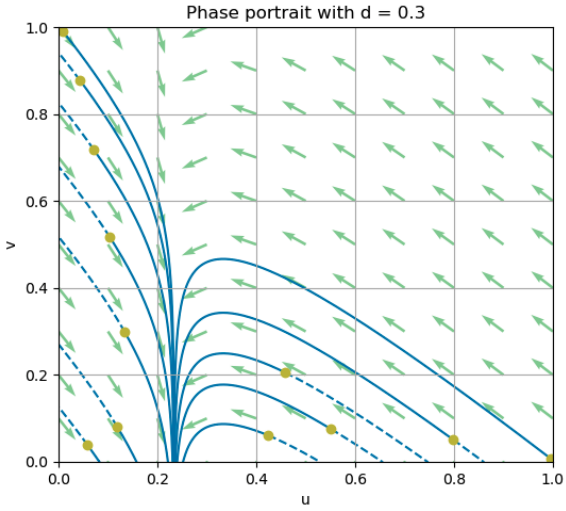
From this, we can extrapolate the stability and general behavior of the model at the equilibrium point. Specifically, we find the eigenvalues of the evaluated Jacobian to be $\lambda_1 = 0, \lambda_2 = R_0 u_* - 1 - \frac{\varphi}{\theta}$. In the $\lambda_1 = 0$ case, the system is neutral. However, in the λ_2 case, we find that:

$$\lambda_2 = R_0 u_* - 1 - \frac{\varphi}{\theta} \begin{cases} > 0 \text{ for } u_* > \frac{1+\varphi/\theta}{R_0} & \text{(unstable)} \\ < 0 \text{ for } u_* < \frac{1+\varphi/\theta}{R_0} & \text{(stable)} \end{cases} \tag{5}$$

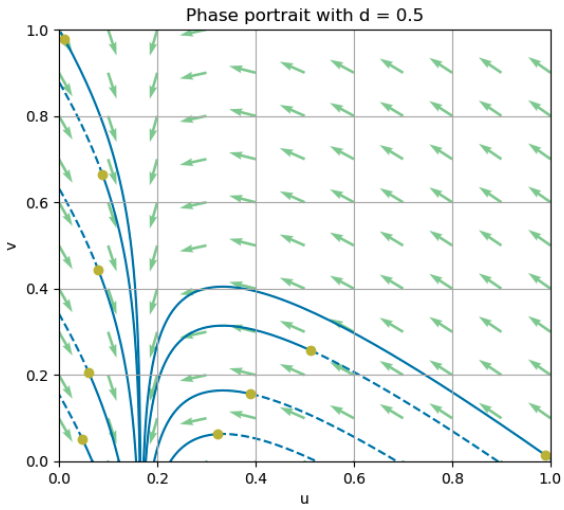
We can graph representative solution of the system to observe the dynamics of a population with different death rates (denoted d in the diagrams) and a fixed $\xi = 3$ which was arbitrarily chosen for the sake of visualization.



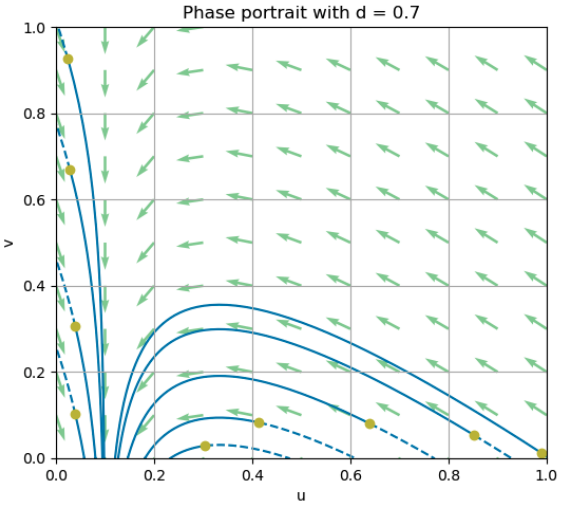
(a) System with death rate = 0



(b) System with death rate = 0.3



(c) System with death rate = 0.5



(d) System with death rate = 0.7

Figure 1: Phase portraits with representative solutions of the system at varying death rates and $\xi = 3$

From the resulting phase diagrams in Figure 1, we observe that for different death rates that are characteristic of various diseases, the particular solutions that describe the fraction of susceptible versus infected people are also different.

For each of the phase portraits, the equilibrium points are along the x-axis described by points of the form $(u_*, 0)$. Additionally, for all systems there exists a point u where the solutions behave asymptotically. This point is when $u = \frac{1+\frac{\varphi}{\theta}}{R_0}$. At this point $\lambda_1 = 0$ and $\lambda_2 = 0$, which describes a neutral

equilibrium point. This means that the fraction of the population that is susceptible does not change, and the infected population diminishes. This indicates that as we move towards $t \to \infty$, the population only consists of susceptible and dead individuals.

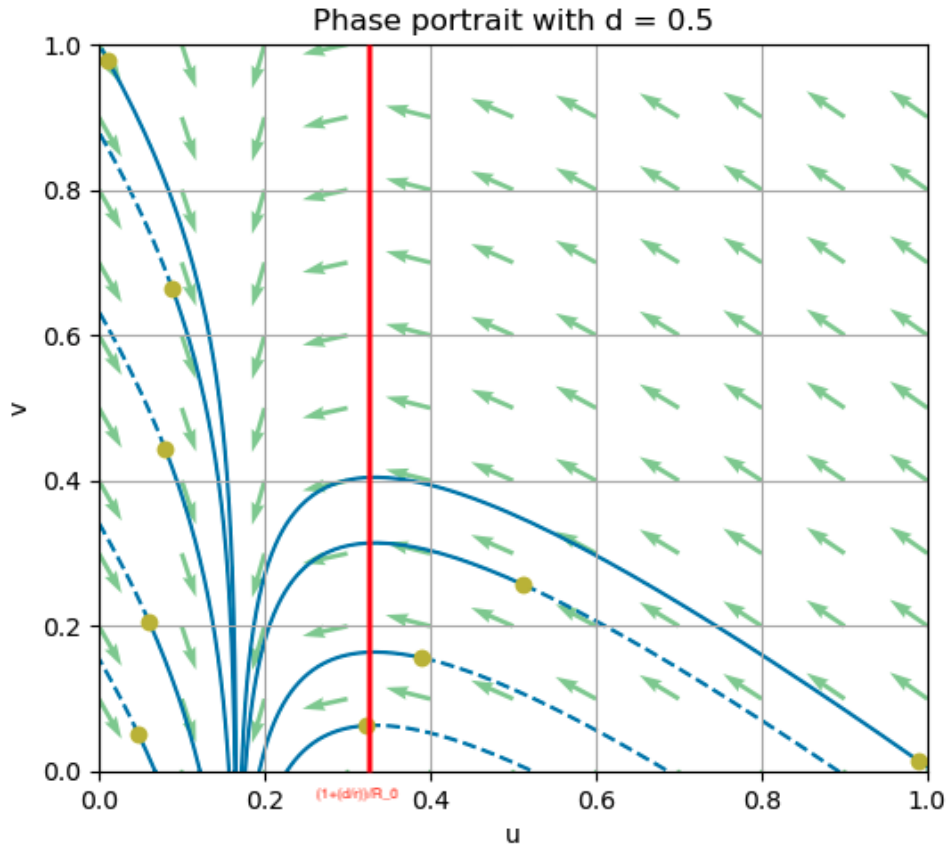


Figure 2: Phase portrait of system with death rate = 0.5

Consider Figure 2, the phase portrait of a system with $\varphi = 0.5$. The red line represents the value where $u_* = \frac{1+\frac{\varphi}{\theta}}{R_0}$. When $u_* > \frac{1+\frac{\varphi}{\theta}}{R_0}$, $\lambda_2 > 0$ and the population fraction of infected individuals increases, indicating an outbreak. Figure 2 shows that, if we start on the right of $u_* = \frac{1+\frac{\varphi}{\theta}}{R_0}$, v increases, suggesting an increase in the population fraction of infected individuals.

When $u_* < \frac{1+\frac{\varphi}{\theta}}{R_0}$, $\lambda_2 < 0$; thus the population fraction of infected individuals decreases, indicating no outbreak and the disease eventually contains itself. The phase portrait indicates that, if we start on the left of the red line $u_* = \frac{1+\frac{\varphi}{\theta}}{R_0}$, we see that $v \to 0$, indicating that the fraction of infected individuals will eventually decrease to 0.

It is worthy to note that the phase portraits for systems with $\varphi = 0.3$ and $\varphi = 0.7$ portray a similar pattern to that of $\varphi = 0.5$. We can extrapolate and see that for $\varphi > 0$, when $u_* > \frac{1+\frac{\varphi}{\theta}}{R_0}$, the disease will result in an outbreak; when $u_* < \frac{1+\frac{\varphi}{\theta}}{R_0}$, the disease will be contained and there will be no outbreak.

As φ increases, the equilibrium value of u_* increases; this can be easily seen in the calculation for $u_* = \frac{1+\frac{\varphi}{\theta}}{R_0}$, as the numerator $1 + \frac{\varphi}{\theta}$ will increase as well. Thus, as φ increases, there is a higher threshold of the population fraction of susceptible individuals required for an outbreak to occur.

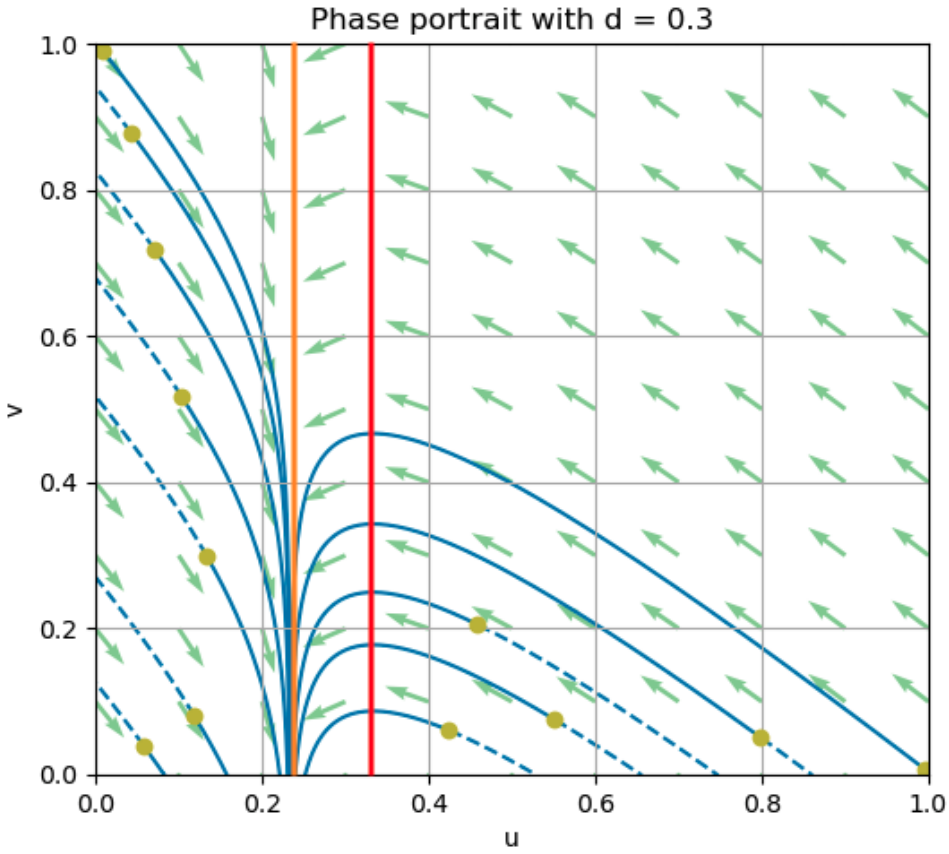


Figure 3: Asymptotic behavior of the system with death rate = 0.3

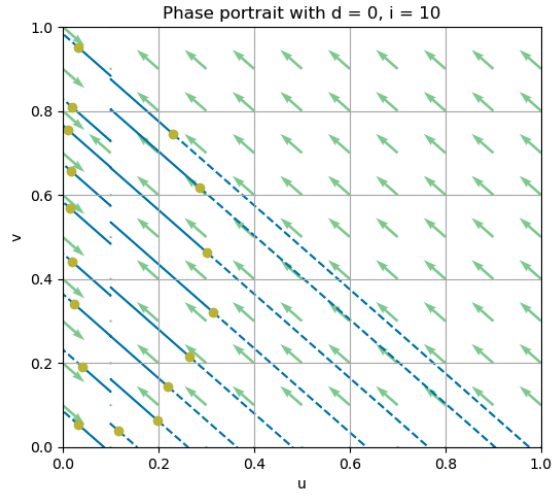
Another interesting feature of the phase diagrams is the asymptotic behavior of the solution. That asymptote is represented by the orange vertical line in Figure 3. The value of u at the orange bar does not change and indicates that there is a balance in the susceptible population. Although the susceptible population fraction does not change, it does not mean there are no new infections, but rather that the effects of recovery and infections on the susceptible fraction match each other, while transitions from infected to death continue to occur.

In the region between $u = 0$ and the orange line, the susceptible population fraction is increasing. This is explained by the fact that only a very low fraction of the total population is susceptible to infection, which means that the infected population that recovers contributes a greater extent to the flow between the compartments compared to the rate at which new infections occur.

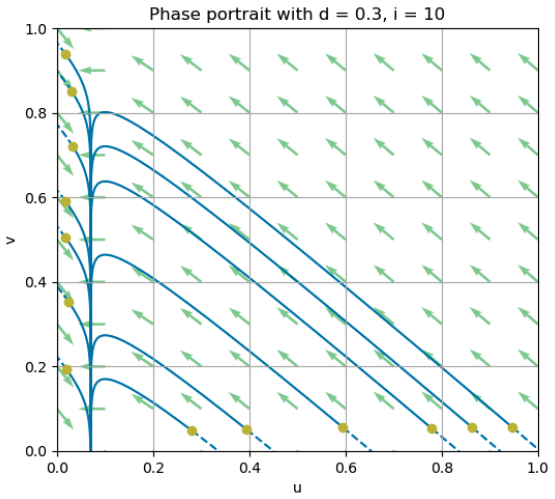
Similarly, in the region between the orange bar and the red bar, the susceptible population decreases. In this region, a large enough fraction of the population is already infected and a sufficient proportion of the population is also susceptible such that new infection cases outpace the rate of recovery.

Finally, looking along the u-axis, we observe that at any equilibrium point, $u_* \neq 0$. This means that under this model, there will remain a fraction of the total population that stays susceptible, uninfected, and alive.

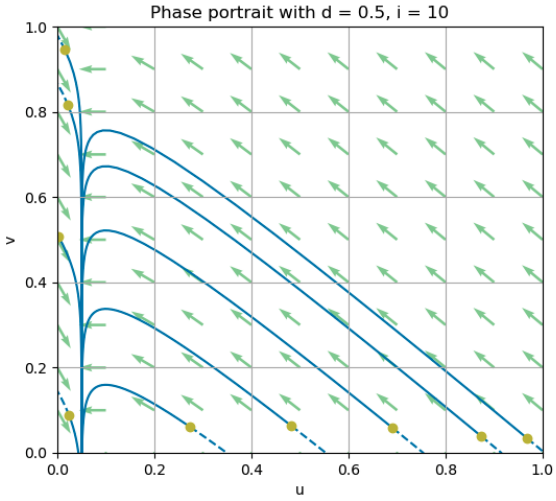
4.1 Increasing Infectiousness



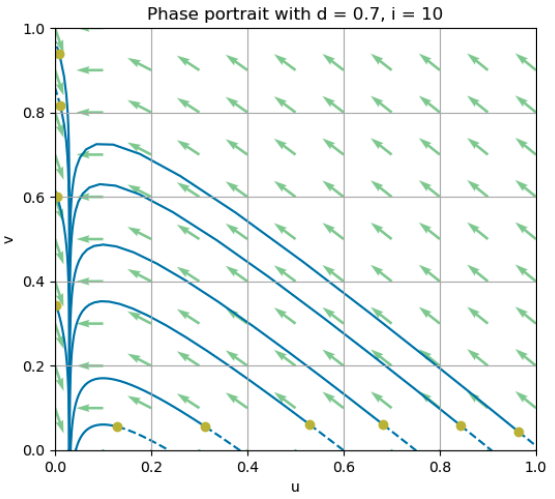
(a) System with death rate = 0



(b) System with death rate = 0.3



(c) System with death rate = 0.5



(d) System with death rate = 0.7

Figure 4: Phase portraits with representative solutions of the system at varying death rates and $\xi = 10$

In the following section, we examine phase portraits of a disease with an infection constant of $\xi = 10$, which means that an infected individual will infect 10 other people per unit time. With a more infectious and aggressive disease, we see that outbreaks happen more aggressively. In other words, in this disease, the fraction of infected population reaches a higher maximum than when $\xi = 3$, and is followed by a sharper decline in infected population fraction. The explanation for this is because so much of the population is infected, a greater portion die off and are no longer eligible to be susceptible.

Another worthy note is that the end population when $\xi = 10$ is lower than that of $\xi = 3$. This indicates that a more aggressively infectious disease will result in a lower susceptible population once the disease is contained.

Again we see that the susceptible population $u(\infty) > 0$. This shows that at $\xi = 10$, a portion of the total population remains susceptible, uninfected, and alive.

4.2 Model when $\varphi = 0$

An interesting observation to note is that for the case when there is no death rate of a disease, the resulting phase portrait resembles the one of a system where there is no death (i.e. the ordinary SIR

model): $u_* = \frac{1+\frac{0}{\theta}}{R_0} = \frac{1}{R_0}$, which is equivalent to u_* in an SIR model.

5 Strengths and Limitations

5.1 Strengths

Versatility: Through the inclusion of a variable that describes mortality rate, the model can be adjusted as needed to account for both the possibility of recovery as well as death within the population being modeled.

Additionally, the model can be extrapolated to apply to infections that lead to complete or partial immunization by virtue of the fact that the "dead" and "immunized" populations are characteristically equivalent in the model. Since neither of these populations are susceptible nor can spread the virus, they can be thought of as equivalent compartments, and therefore we can draw conclusions about virus spread that lead to immunization once cured using this very same model.

In addition, the model can also be minimally adjusted to model highly lethal outbreaks such as the Ebola outbreak in Zaire that do not present a significant chance of recovery, by removing the backwards flow of people from infected to susceptible. Achieving this simply requires the dialing down of the recovery rate θ to 0, which creates a one-directional flow of cases from susceptible to infected to dead.

The versatility of the model which allows it to be applied to a variety of virus scenarios with minimal adjustments ensures that even as parameters change across the course of an outbreak, the conclusions drawn from the model can be easily changed to be relevant.

5.2 Limitations

Recovery and Mortality Rates: The model's recovery and death rates do not vary across the population; that is, the model assumes that a randomly chosen individual has the same likelihood of recovering or dying from the disease as all other individuals in the population. In reality, the probabilities of recovery or death vary across individuals based on a multitude of factors (e.g. age, prior health concerns, accessibility to health services, etc.) [4], which this model does not account for. As a result, our recovery rate and death rate are likely both different from a realistic set of rates, as individuals recover or pass away at different rates, depending on their own health and the severity of the disease.

Constant Values of Phi and Theta: Our model assumes constant values for the recovery rate, θ, and mortality rate, φ. This means that changes to how effective cures are and mutations in the virus that change the severity of its symptoms cannot be accounted for within the boundaries of our model. This is not a complete limitation, however, since we can simply adjust these two variables throughout the development of a viral outbreak as new estimates regarding the two values are calculated. The only downside to this fixed model, then, is that it is difficult to map out the progression of a virus in hindsight within a single model. However, if we are only looking to use this model in the context of an ongoing pandemic, having fixed values for φ and θ does not present an issue.

Lack of Incubation Period: One downside to this model is that it does not compartmentalize to allow for an incubation period for infection. Many viruses, including the Coronavirus [5], have incubation periods during which symptoms do not develop, but the vector is still able to spread the disease further to other individuals. This compartment would be able to sit between the susceptible and infected compartments, contributing to an increased rate or spread without contributing to the mortality rate. This weakness means that in our interpretation of the mortality rate a virus can have without dying off, we are actually underestimating the maximum upper bound of this rate. This is because in reality, most infections result in a period of spreading without the possibility of immediately dying. Considering this, our final conclusions on the matter of virus mortality limit are conservative approximations, and it is likely that with longer incubation periods, even viruses with higher death rates will successfully live on within the asymptomatic incubation population.

6 Further Development and Research Topics

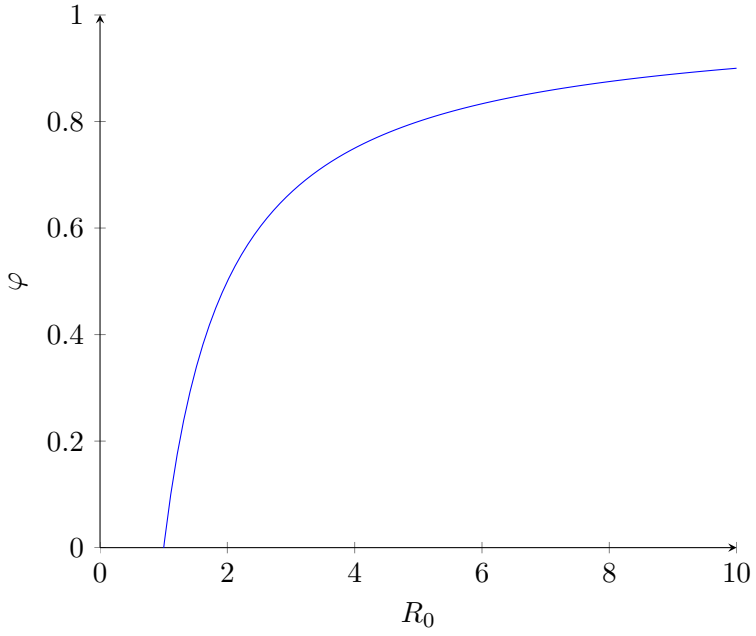
Following topics of research that may be of interest include epidemiological modeling that takes into account a greater variety of factors; for example, ICU constraints, governmental policy, and effect on national and global economies. Additionally, by breaking the SIR compartmentalization model completely and introducing the factor of spatial dispersion and localization, disease spread may be analyzed in further detail or, using statistical graph-based learning, inferred.

Further, it would be interesting to observe how dynamical systems such as disease transmissions can be scaled for inference by machine learning. In particular, since disease spread is a stochastic process and moreover, does not necessarily follow the assumptions presented by the SIR model, temporal inference models could be used in place in order to take into account the drift and variance in variations of model parameters at different time steps. Thus, recurrent models that extract time-dependent features, e.g. LSTM and other specialized RNN architectures, may be able to infer and model disease spread better than the SIR mathematical model.

As an addendum to the previous remark on temporal dependence in dynamical systems, the usage of partial differential equation systems as opposed to ordinary differential systems would prove to be more capable in extracting insight from. Since partial differential equations are dependent on more than one variable, it allows a system to capture more variance in the results due to interdependent parameters. As an example, it would be beneficial to consider a model where there are multiple categories of infected groups which describe varying severity of infection, all with their own probabilistic distribution on succumbing to death or recovery. However, this would introduce interdependence as the different categories would each affect the susceptible category and thus result in dependence among the infectious groups and a partial differential system. This model would likely be able to capture more "realistic" effects of a viral infection spread and relax the binding assumptions that have to be put in place for analysis relative to an ordinary differential system.

7 Conclusion

The important conclusion that we arrive at in Section 4 is that for a given virus with recovery rate θ and death rate φ, we have that the virus continues to spread without dying out as long as its R_0 characteristic value is greater than $1 + \frac{\varphi}{\theta}$. Combining this with the equation $\varphi + \theta = 1$ gives us the inequality $\varphi < 1 - \frac{1}{R_0}$ for the region in which the virus successfully continues its spread. The curve for this inequality is graphed below.



The region below the curve in the previous graph shows the possible values for φ for given values of R_0 that allow for continued viral spread. Any mortality rates above the curve means that the infected population will die out too quickly, without being able to continue spreading at a sufficient rate, leading to the virus tapering out over time.

To contextualize this in the context of our originally proposed Zombie Apocalypse scenario, it would be possible to contain an outbreak through curtailment of the zombie population post-infection, even without the development of effective cures. Effective zombie population reduction strategies that lead to zombie mortality rates above the given curve will lead to a reduction in the available infected pool over time, eventually concluding the outbreak. This contextualization of the model within the setting of a hypothetical Zombie Apocalypse fits well because the typical portrayal of a zombie infection has a minimal incubation period. This eliminates the core limitation of our model and allows for a rather accurate interpretation of prevention models necessary to stop the outbreak.

Granted, this scenario would likely also be paired with a very high value of R_0 since a zombie virus would spread actively rather than in the passive manner that most viruses are spread, since the virus would have an active carrier seeking to spread the infection as much as possible. Given this, a zombie virus would be able to sustain itself even if it had a very high mortality rate, and would be difficult to manage by curtailing zombie populations. Given this, in a scenario in which a highly aggressive virus such as a zombie virus is the disease being studied, the focus should be on expediting a cure that maximizes the θ rather than seeking to employ combative strategies targeted at maximizing φ.

References

[1] Weinberger, D. M., Chen, J., Cohen, T., Crawford, F. W., Mostashari, F., Olson, D., Pitzer, V. E., Reich, N. G., Russi, M., Simonsen, L., Watkins, A., & Viboud, C. (2020). Estimation of excess deaths associated with the COVID-19 pandemic in the United States, March to May 2020. JAMA Internal Medicine, 180(10), 1336. https://doi.org/10.1001/jamainternmed.2020.3391

[2] Kermack, W.O. & McKendrick, A. G. (1927). A contribution to the mathematical theory of epidemics, Proc. R. Soc. A: Math. Phys. Eng. Sci. 115 (772), 235-240. https://doi.org/10.1098/rspa.1927.0118

[3] Rouse, B. T. & Sehrawat, S. (2010). Immunity and immunopathology to viruses: What decides the outcome? Nature Reviews Immunology, 10(7), 514–526. https://doi.org/10.1038/nri2802

[4] Tencza, C., Stokes, A., & Preston, S. (2014). Factors responsible for mortality variation in the United States: A latent variable analysis. Demographic Research, 21(2), 27-70. https://doi.org.10.4054/DemRes.2014.31.2

[5] Harries, A., & Takarinda, K. C. (2020). The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. Faculty Opinions – Post-Publication Peer Review of the Biomedical Literature. https://doi.org/10.3410/f.737511417.793572133