COVID-19 Epidemiology

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Computational Modeling of Biological Systems

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Introduction

The paper I chose to look at is *A mathematical model for COVID-19 pandemic - SIIR model: Effects of asymptomatic individuals*. COVID-19 is unique in that the traditional modeling methods of SIR (susceptible-infected-recovered) and SEIR (susceptible-exposed-infected-recovered) do not adequately cover all characteristics of the disease. These unique features are as follows: the existence of individuals who are infectious before showing symptoms of the disease during its incubation period, the existence of individuals who are infectious and asymptomatic after the incubation period, and a finite period of immunity of recovered individuals. With these features being considered, a modified version of the SIR model was developed to model the COVID-19 disease. This SIIR model accounts for the fact that COVID-19 has two infectious states.

This model starts with the S population, where individuals in S are susceptible to the disease. They then transition into the I populations, where I_1 is the first step where individuals are presymptomatic and susceptible. I_1 individuals are able to move to either I_2 - the asymptomatic and infectious population, or the R_1 population - the symptomatic, but quarantined and not infectious population. I_2 individuals then move into the R_2 population - recovered with antibodies and not infectious, whereas individuals in R_1 either move into R_2 or R_3 - fatalities of COVID-19. The cycle is able to start again when the finite immunity time of the R_2 population leads them back into the initial S population.

Modeling Approach

This model is illustrated in Figure 1, where the rates of movement from one population to the next correspond to the equations or variables near each arrow. First, all reactions are

normalized with respect to N, the overall population, where $N = S + I_1 + I_2 + R_1 + R_2 + R_3$, and the differential equations used are defined in Figure 2. The first reaction rate, from S to I_2, is defined as $\beta(I_1(t) + I_2(t))$. β is the probability that susceptible individuals are infected by contact with infectious individuals, and was determined to have a value of 0.2. $b1$ and $b2$ are related in that an individual in I_1 must transition into either R_1 or I_2, after incubation time $t1$, leading to the equation $b1 + b2 = 1/t1$, where $b1 = 0.3/t1$, $b2 = 1/t1 - b1$. The c reaction rates all follow a similar conservation, where $c1 = c2 + c3 = 1/t2$, where $t2$ is the time of infection. This is then used to find that $c1 = 1/t2$, $c2 = 0.8/t2$, and $c3 = 1/t2 - c1$. $d1$ is the rate at which immune individuals lose their immunity and become susceptible again, and although there is no data given to calculate this rate, it is tested in the report with values of 0.001 and 0.003. All parameters and initial values, including $N = 1$, $t1 = 5$, $t2 = 17$, $\beta = 0.2$ and all reaction rate constants were determined using data from the WHO and the Ministry of Health, Labor, and Welfare in Japan. In this model, it is also assumed that prior health conditions do not have major effects on data relating to COVID-19.

Findings

This model was used in a way that allows for discussion in 5 main areas, listed as follows: numerical solutions, basic reproduction number and effective reproduction number, condition for herd immunity, cumulative fatalities, and comparison between SIIR and SIR models for COVID-19.

The numerical solutions section explains system behavior and generally discusses how changing parameters, specifically t_1 and t_2, change model behavior. In the scope of this model, t_1

determines how quickly populations move from the incubation phase to the infectious phase, as well as controlling how much of the population reaches the incubation phase in a given amount of time. t_2 directly determines how infected populations decline from their peak values, whether that be faster or slower over a given time period.

The reproduction number section first discusses the basic reproduction number of the SIIR model. The basic reproduction number is a condition in the SIR model that needs to be met for infection to spread and it must have a value greater than 1. The SIIR model is different from the SIR model because it allows for a basic reproduction number less than 1, which is entirely due to the presence of asymptomatic individuals. The effective reproduction number depends on the basic reproduction number in this model, and in this case it was determined that the effective reproduction number must depend on t_1 and t_2.

The condition for herd immunity is found to be that the effective reproduction number must fall below 1. In the case that there is an infinite time that antibodies are effective, the herd immunity threshold increases in comparison to the SIR model. This is due to the fact that the SIIR model accounts for asymptomatic individuals. In the case that there is a finite time for antibody effectiveness, the infection model will have peaks multiple times around periods of the antibody duration.

Cumulative fatalities in this model have one important finding, which is that cumulative fatalities are proportional to 1 - the susceptible population density, which is the same as the cumulative density of the infected population. The cumulative fatality function has a maximum value when viewed as a function of b_1. This b_1 function is then found to depend on t_1, t_2, and the basic reproduction number.

Most information is summarized in the comparison between SIIR and SIR models of COVID-19. The most important observations from this comparison are that the two models have very different reproduction numbers, herd immunity thresholds, and antibody durations. The SIR model has much simpler values for these characteristics, and also only has one infection peak. The SIIR model has much more complex values which account for an incubation period as well as an infection period, and has possible models with single or multiple infection peaks.

Model Implementation

This report provided two main models, one with a d1 value of 0.001 and another with a d1 value of 0.003. Figure 3 has a time frame of 200 days in the initial report and d1 = 0.001, so that is what I used to plot it, whereas Figure 4 has a time frame of 500 days and d1 = 0.003 in the initial report.

The system in Figure 3 appears to remain relatively stable until around 25 days, where there is a noticeable decline in the S population where it continues to decline sharply until around 85 days. After that, it reaches its minimum density of around 0.1 around 100 days and then begins to grow. At 25 days, there is also a jump in the population densities of the I1 and I2 groups, which correspond to the incubation phase and asymptomatic infected populations. The I1 population peaks at around 0.17 population density around day 55, while the I2 population peaks around 0.21 around day 70, after which they both slowly decline back towards 0. The R1 and R2 groups increase next chronologically, with both experiencing their first jumps around the 37 day mark. R1 peaks much sooner and lower, at around 0.1 density around the 70 day mark. However, R2 continues to grow for a substantial time and peaks around 0.82 at around 125 days. After these peaks, they both begin to regress. R3 is interesting in that it begins to grow and reaches its

peak at the same times as R2, although it remains constant after it hits its peak. This all corresponds to the infection reaching its peak around day 100, with all subsequent populations following this trend in relation to how quickly their population is converted into another according to the rate constants.

Figure 4 is a visualization of the model with d1 = 0.003 over a time span of 500 days. In the first 200 days, the S and R2 populations follow similar trends to those in Figure 3, although they have steeper slopes after their initial peaks. Following day 200, they begin to oscillate between peaks and valleys, with those points of interest appearing around the 350 and 450 day marks. Each subsequent point appears to have a less drastic slope than the previous point, suggesting that they may approach a steady state at some point. R3 has corresponding periods of growth at the peaks of R2 only, signifying that more deaths are expected when more people are infected. R1 follows similar trends as in Figure 3, although it has one additional, smaller peak near the second peak of R2. The same can be said for I1 and I2. This all makes sense as this parameter set appears to model a situation where there are multiple peaks of infection, meaning populations which had reached steady concentrations would begin to exhibit growth again, although in smaller amounts.

New Findings

For my model extension, I decided to focus on the Delta variant of the COVID-19 virus. Compared to the data used in the initial report, the Delta variant has a shorter incubation period of $t_1 = 4$ days according to Pathak. The $\boldsymbol{\beta}$ value is the probability that an individual with the virus will transfer it to someone else, and it is stated by Liu and Rochlov that the Delta variant is nearly twice as infective as the original strain. So I chose to make $\boldsymbol{\beta}$ value of the Delta variant 0.4

to demonstrate this near double increase in infectivity. The best estimate I was able to find for the infectious period was around 10 days, according to ABC News, so that is what I am using for t_2. I decided to model based on the same d1 values as used in the original report, with d1 = 0.001 in Figure 5 and d1 = 0.003 in Figure 6. Other than those parameters, everything else was kept the same as the overall behavior of the virus does not differ greatly from the original strain. Given that the Delta variant was a much faster acting variant, I was also able to shorten the time span of the model to only 100 days to capture most of the behavior of the populations.

Figures 5 and 6 are very similar in their behavior, the only noticeable difference is the slightly more rapid slope of the S and R2 populations when d1 = 0.003. Other than that, they are similar to the original COVID-19 model with d1 = 0.001, except for the fact that the model behavior occurs nearly twice as fast. Almost every population exhibits mirrored behavior to the aforementioned model, with the only difference being with the I1 populations. With the Delta variant parameters the I1 population begins to exhibit growth slightly sooner than the I2 population, whereas the I1 and I2 populations grow at the same time in the original COVID model. The Delta variant also allows for the I1 population to reach a higher population density than in the original model, with a density of about 0.27 compared to about 0.17.

Intuitively, this behavior makes sense given that the Delta variant was determined to be nearly twice as infective as the original COVID variant. The increase in the amount of infected individuals follows what I expect from a more infective virus, although I did not expect for nearly everything else to exhibit similar behavior, albeit at nearly twice the speed. This may be due to the fact that the parameters that were kept the same were mostly unaffected by the changes required by the Delta variant.

Figures

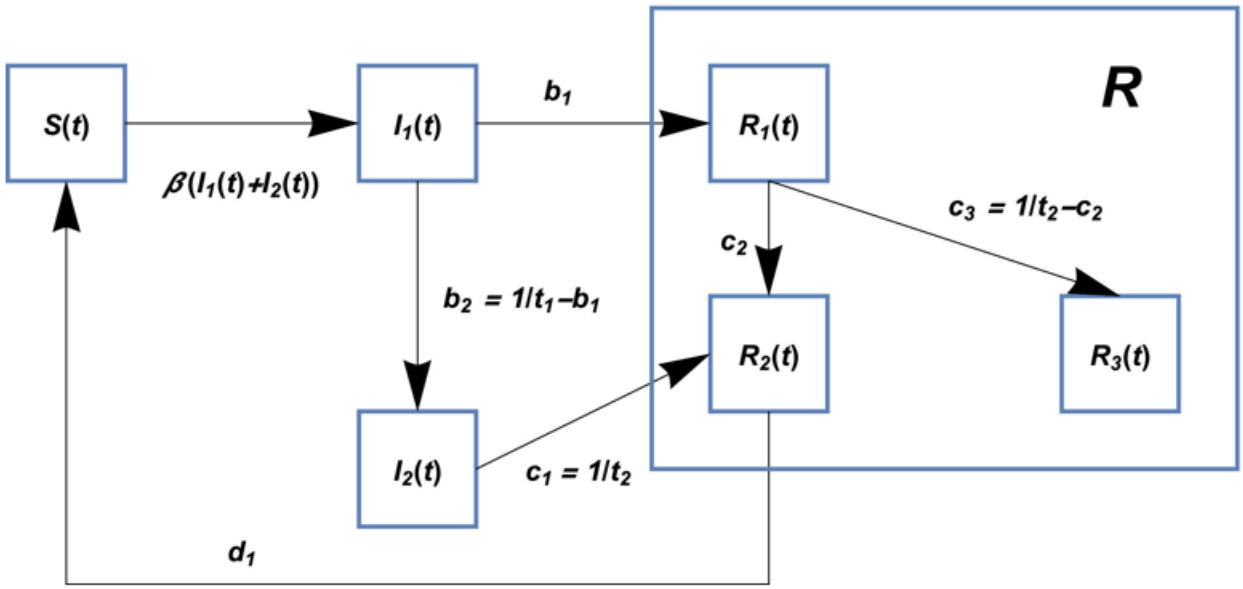

Figure 1: SIIR model for the COVID-19 disease.

$$\frac{dS(t)}{dt} = -\beta S(t)\left(I_1(t) + I_2(t)\right) + d_1 R_2(t),$$

$$\frac{dR_1(t)}{dt} = b_1 I_1(t) - (c_2 + c_3) R_1(t),$$

$$\frac{dI_1(t)}{dt} = \beta S(t)\left(I_1(t) + I_2(t)\right) - (b_1 + b_2) I_1(t),$$

$$\frac{dR_2(t)}{dt} = c_1 I_2(t) + c_2 R_1(t) - d_1 R_2(t),$$

$$\frac{dI_2(t)}{dt} = b_2 I_1(t) - c_1 I_2(t),$$

$$\frac{dR_3(t)}{dt} = c_3 R_1(t),$$

Figure 2: Differential Equations for the COVID-19 Model

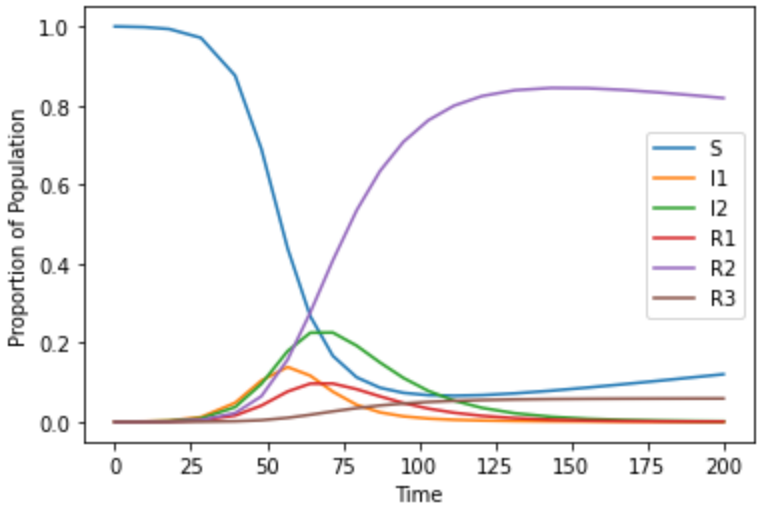

Figure 3: SIIR model implementation, where d1 = 0.001. Time span of 200 days.

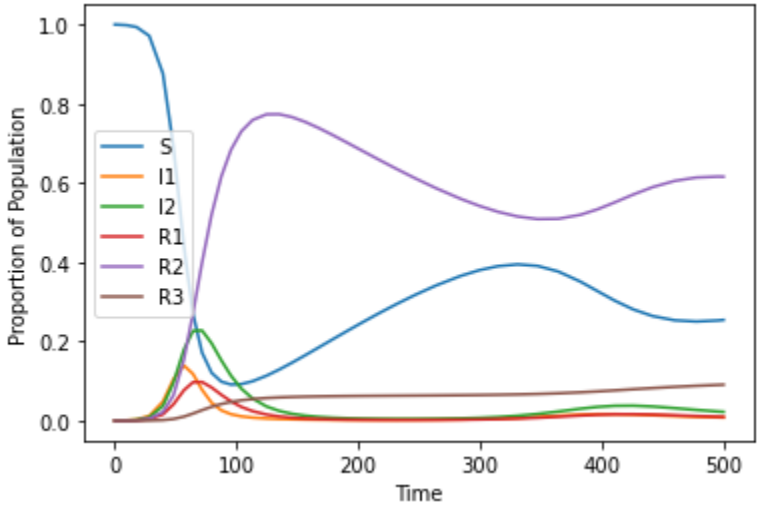

Figure 4: SIIR model implementation, where d1 = 0.003. Time span of 500 days.

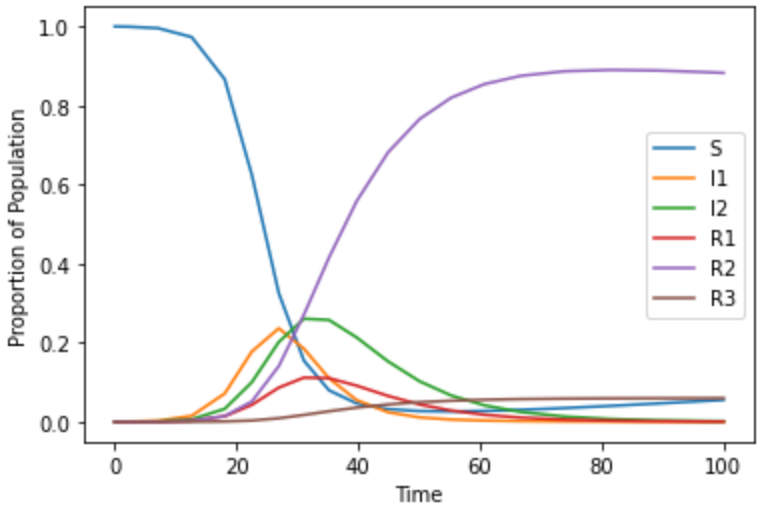

Figure 5: SIIR model of the Delta variant of COVID-19, with d1 = 0.001, over a time span of 100 days.

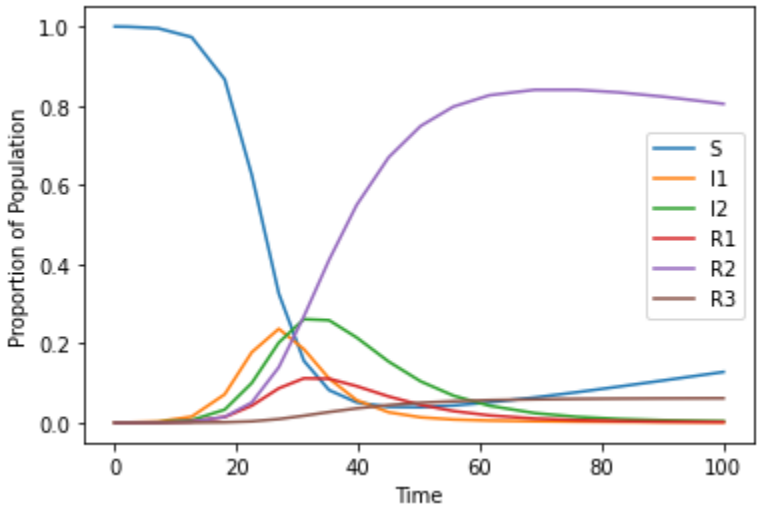

Figure 6: SIIR model of the Delta variant of COVID-19, with d1 = 0.003, over a time span of 100 days.

Citations

ABC News. (2021, October 4). Here's what we know about delta now, after months spent fighting it. ABC News. Retrieved May 5, 2022, from https://www.abc.net.au/news/2021-09-29/covid-delta-variant-what-the-science-says/100497804

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pandemic-SIIR model: Effects of asymptomatic individuals. Journal of general and family medicine. Retrieved May 5, 2022, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7796794/

Notes

I noticed that there were a couple errors in the parameters, specifically with the d1 and c3 parameters. The d1 = 0.03 appears incorrect, as the corresponding plot in Python does not correctly display system behavior as in the report. A value of d1 = 0.003 fixes this issue. Also, the c3 parameter listed in the parameters for Figure 2 is incorrect. It gives incorrect system behavior, and the correct c3 value should be taken from Figure 1.