MA4M1 Epidemiology By Example Assessed Worksheet 2

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February 9, 2022

Question 1

Q1(a)

R_0 is the average number of infections from 1 infectious person in a completely susceptible population. Hence R_0 = Number of Susceptible $\times$ contact rate $\times$ average time spent infectious. As assumed entire population is susceptible, number of susceptibles is N so:

$$\begin{aligned} R_0 &= N \times \frac{\beta}{N} \times \frac{1}{(1-p_D)\gamma + p_D\gamma} \\ &= \frac{\beta}{\gamma} \\ &= 15 \end{aligned}$$

Effective reproduction number is average number of secondary infections from an infected individual at time t, if conditions remained at time t. Therefore $R_e(t)$ =number of new infections per infected$\times$ average infection length. This gives in general:

$$\begin{aligned} R_e(t) &= \frac{\beta S(t)}{N} \times \frac{1}{(1-p_D)\gamma + p_D\gamma)} \\ &= \frac{\beta S(t)}{N\gamma} \end{aligned}$$

In our situation, 90% of the population are immune. Therefore $S(0) = 0.1N$, and $R_e(0) = 0.1 \times R_0 = 1.5$.

Q1(b)

In figure 1 we show the evolution of infections for an SEIRD model, an SEIR model where infected can either recover to R or die and move to D. We use parameters $\beta = 5$, $\gamma = 1/3$, $\sigma = 1/10$ all in days^{-1}. The population is 100,000 and assumed that 90% are immune, none are dead and 1 is infections at $t = 0$, with a probability of in infectious person dying of $p_D = 0.01$. After the epidemic ends, we record the final element in the "death" class to see total deaths causes were 58. As we had no deaths at $t = 0$ this is the total number of deaths caused by the disease.

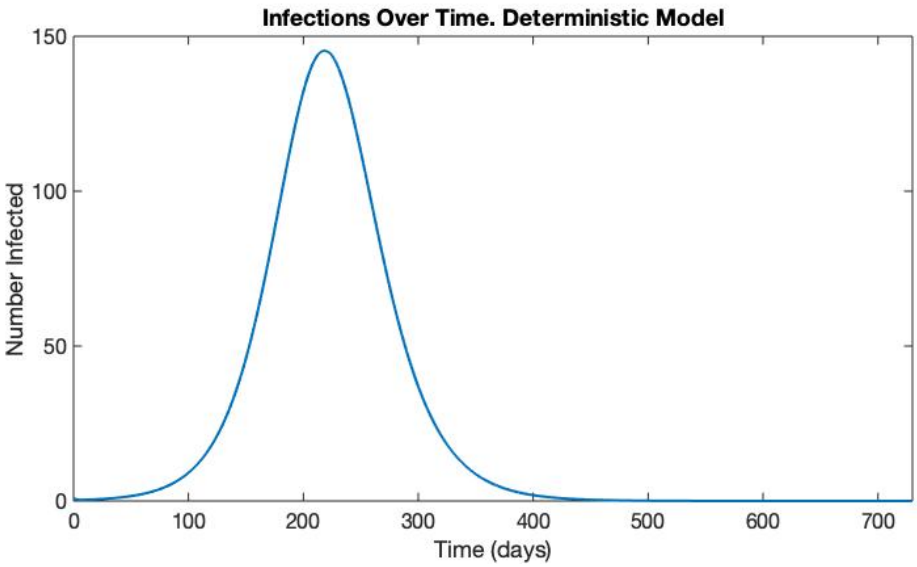

Figure 1: Deterministic model of infection dynamics.

Question 2

Q2a

The events table for the SEIRD model is

Event	Rate	Change In Model State
Exposure	$\frac{\beta SI}{N}$	$S \mapsto S-1 \quad E \mapsto E+1.$
Infection	σE	$E \mapsto E-1 \quad I \mapsto I+1$
Recovery	$(1-p_D)\gamma I$	$I \mapsto I-1 \quad R \mapsto R+1$
Death	$p_D \gamma I$	$I \mapsto I-1 \quad D \mapsto D+1$

Q2b-c

In figure 2 we plot the deterministic model of the SEIRD model with given initial conditions and parameters, with a Stochastic model implemented via the Gillespie algorithm.

In this instance, the stochastic simulation concluded after 408 days. This was found by using the find function in MATLAB to see what the final time entry was in the array of all points of time. A final size of 5479 was computed. I took this to mean total people infected and so found the final entry in the R and D classes, summed them, and subtracted the number of people in the R and D classes in the initial conditions.

Q2d

Figure 3 shows various histograms for epidemic sizes after running 1000 instances of the epidemic. The first gives a global look at all sizes, with the red line showing the final size as predicted by the deterministic ODE model, which fits nicely in the centre of the rightmost data cluster. 100 bins were used. The next two histograms are zoomed in around the two points of interest. The first is zoomed in around where the ODE predicts the final size to be and uses 200 bins in order to reveal further details. The second is

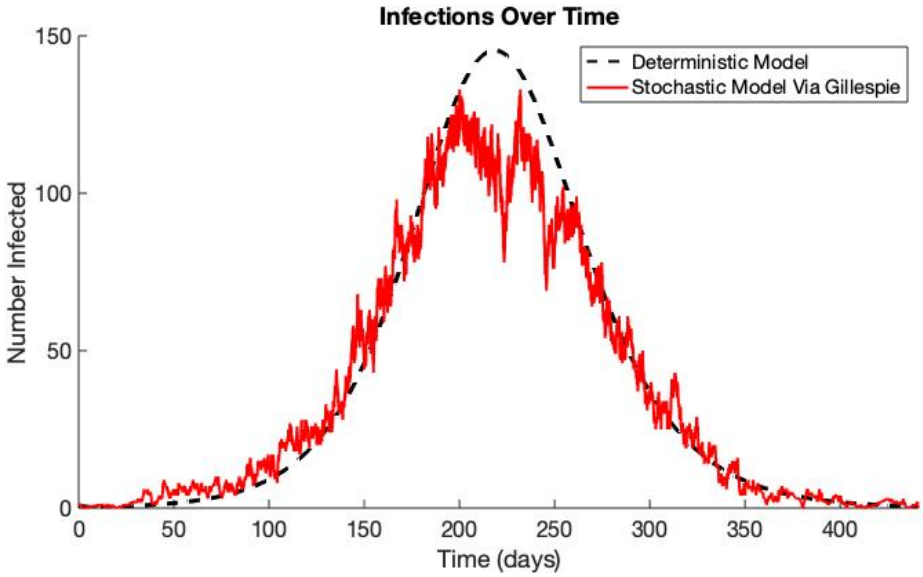

Figure 2: Deterministic and Stochastic model (Gillespie's method) of infection dynamics.

zoomed around sizes 0-50 and shows an exponential distribution of cases, with maximum at 1. Bin size was 700, although this only leads to several bins in the desired range.

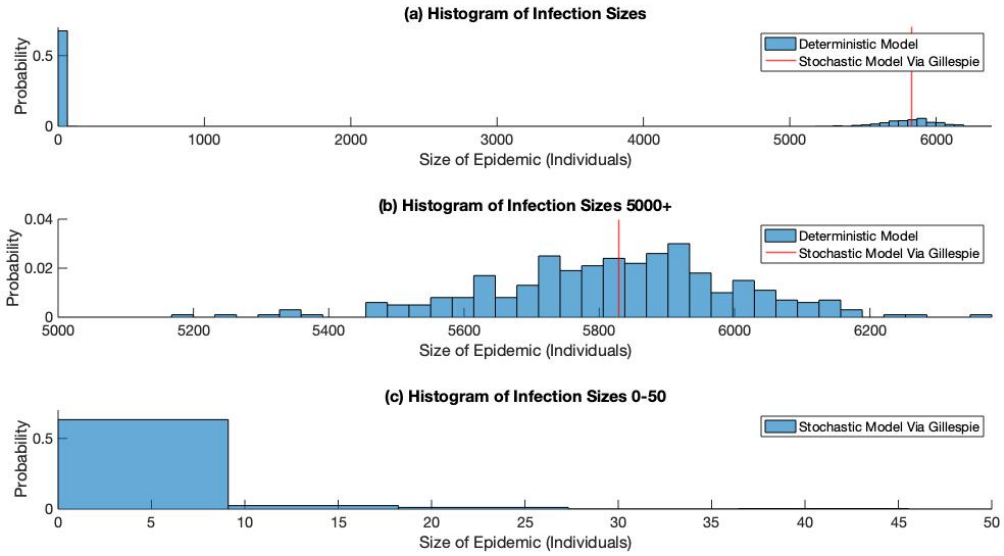

Figure 3: (a) Histogram of final sizes of epidemic. (b) histogram of epidemic size for sizes above 5000. (c) histogram of epidemic size for sizes below 50.

Q2e

Here we account for the fact only 10% of the population are susceptible by using $\beta \mapsto 0.1 \times \beta = 0.5$ days^{-1}. To compute the probability of 0-3 new infections we sum the probabilities of there being exactly 0,1,2 and 3 infections. There is exactly 1 way 0 or 1 new infections can occur. However, there are two and three ways two and three new

infections can occur respectively, with the exact details are included in figure 4. The probability of infection is given by $\frac{\beta}{\beta+\gamma}$ whilst the probability of recovery is $\frac{\gamma}{\beta+\gamma}$. Hence we have:

$$\begin{aligned} P &= \frac{\gamma}{\beta+\gamma} + \frac{\beta}{\beta+\gamma}\left(\frac{\gamma}{\beta+\gamma}\right)^2 + 2\left(\frac{\beta}{\beta+\gamma}\right)^2\left(\frac{\gamma}{\beta+\gamma}\right)^3 + 3\left(\frac{\beta}{\beta+\gamma}\right)^3\left(\frac{\gamma}{\beta+\gamma}\right)^4 \\ &= 0.5587 \end{aligned}$$

From our simulations, we use the sum function with the logical condition of the size of an element in the final size vector being less than 3, which gives the number of runs with a final size less than or equal to 3. Dividing by the number of runs gives an agreeable actual value of 0.56. To compute the probability of extinction, we use branching process to write P_{ext} as:

$$P_{ext} = \frac{\gamma}{\beta+\gamma} + \frac{\beta}{\beta+\gamma}P_{ext}^2$$

From here we solve $P_{ext} = \frac{1}{R_0} = \frac{2}{3}$. When examining the data, we counted all cases that did not get beyond 50 days, where there is a gap between the initial exponential distribution and the later normally distributed histogram. This gave a probability of 0.69 which matches fairly well.

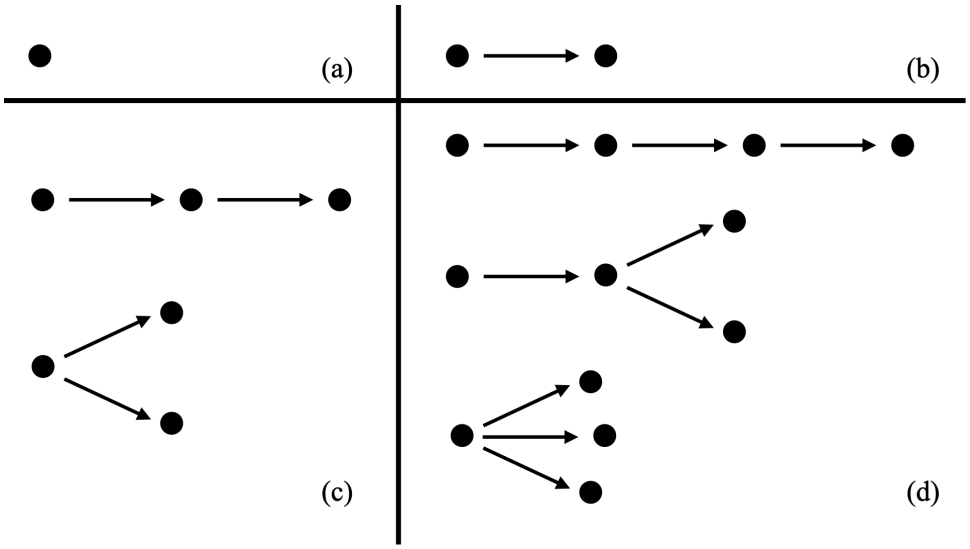

Figure 4: Possible branching processes for (a) zero new infections, (b) one new infection, (c) two new infections, (d) three new infections. We see there are multiple ways such events occur in (c) and (d).

Question 3

Q3a

The new system of ODEs follows the schematics depicted in figure 5:

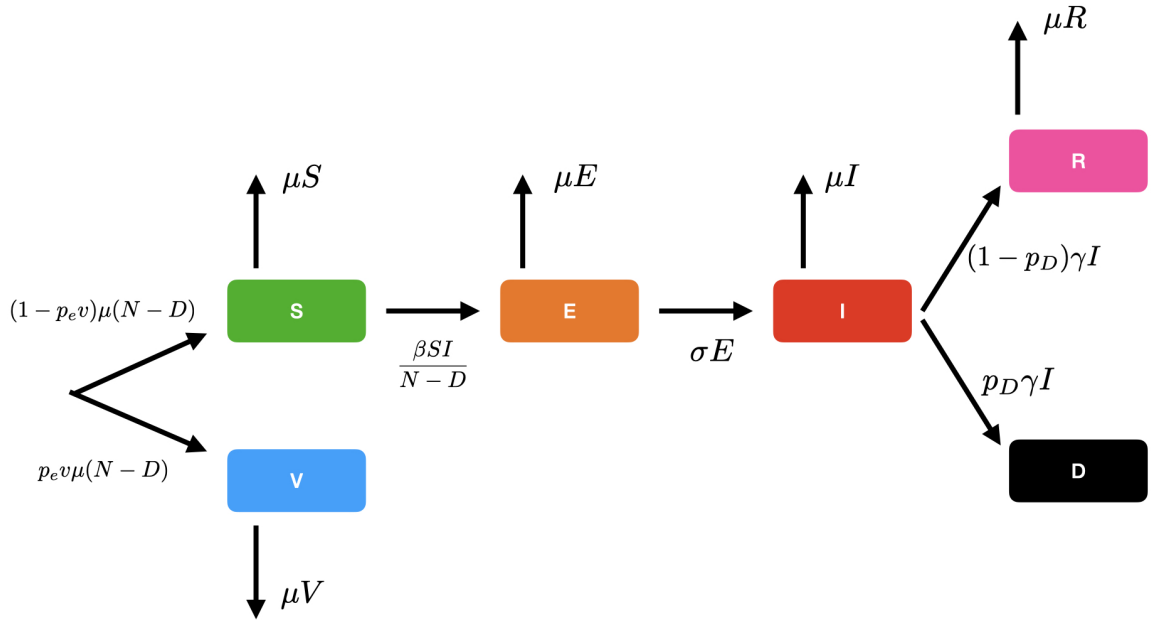

Figure 5: Depiction of ODE model.

$$
\begin{aligned}
\frac{dS}{dt} &= (1-p_e v)\mu(N-D) - \frac{\beta SI}{N-D} - \mu S \\
\frac{dE}{dt} &= \frac{\beta SI}{N-D} - \sigma E - \mu E \\
\frac{dI}{dt} &= \sigma E - \gamma I - \mu I \\
\frac{dR}{dt} &= (1-p_D)\gamma I - \mu R \\
\frac{dD}{dt} &= p_D \gamma I \\
\frac{dV}{dt} &= p_e v\mu(N-D) - \mu V
\end{aligned}
$$

Here we have $S + E + I + R + D + V = N$. We have essentially written the SEIR equation with demography. However, we have not included a term $-\mu D$ for the $\frac{dD}{dt}$ term as this would correspond to people dying twice. Furthermore, we have replaced N in an SEIR model with $N - D$ as interactions are only assumed to occur with living people. This also ensures N is constant. In addition, a new class V for vaccinated is added which has people coming in at rate $p_e v\mu(N - D)$. The $\mu(N - D)$ is the standard birth rate in an SEIR model (modified to account for deaths) and the $p_e v$ factor is the proportion who are chosen to be vaccinated, and then successfully vaccinated. The complimentary $(1 - p_e v)\mu(N - D)$ inflow is then added to the S class.

Event	Rate	Change In Model State
New Vaccination	$p_e v\mu(N-D)$	$V \mapsto V+1.$
New Susceptible	$(1-p_e v)\mu(N-D)$	$S \mapsto S+1.$
Exposure	$\frac{\beta SI}{N}$	$S \mapsto S-1 \quad E \mapsto E+1.$
Infection	σE	$E \mapsto E-1 \quad I \mapsto I+1$
Recovery	$(1-p_D)\gamma I$	$I \mapsto I-1 \quad R \mapsto R+1$
Death	$p_D\gamma I$	$I \mapsto I-1 \quad D \mapsto D+1$
Death of Vaccinated	μV	$V \mapsto V-1$
Death of Susceptible	μS	$S \mapsto S-1$
Death of Exposed	μE	$E \mapsto E-1$
Death of Infected	μI	$I \mapsto I-1$
Death of Recovered	μR	$V \mapsto R-1$

Q3b

In figure 6 we see a stochastic simulation of our model where $v = 0$ via tau leaping and a histogram showing the distribution of deaths due to the epidemic drawn from 300 simulations. We see that the infectious dynamics cycle, as expected from an SEIR model with demography. However these cycles have an increasing amplitude, unlike usual SEIR demography models. Furthermore, as these cycles never dip low enough to the line $I = 0$, it seems unlikely that the infection will naturally end within the 20 year time frame considered. In the histogram, we get an approximate normal distribution of the total deaths during the epidemic, whose average agrees with the ODE prediction of $3,104$ deaths.

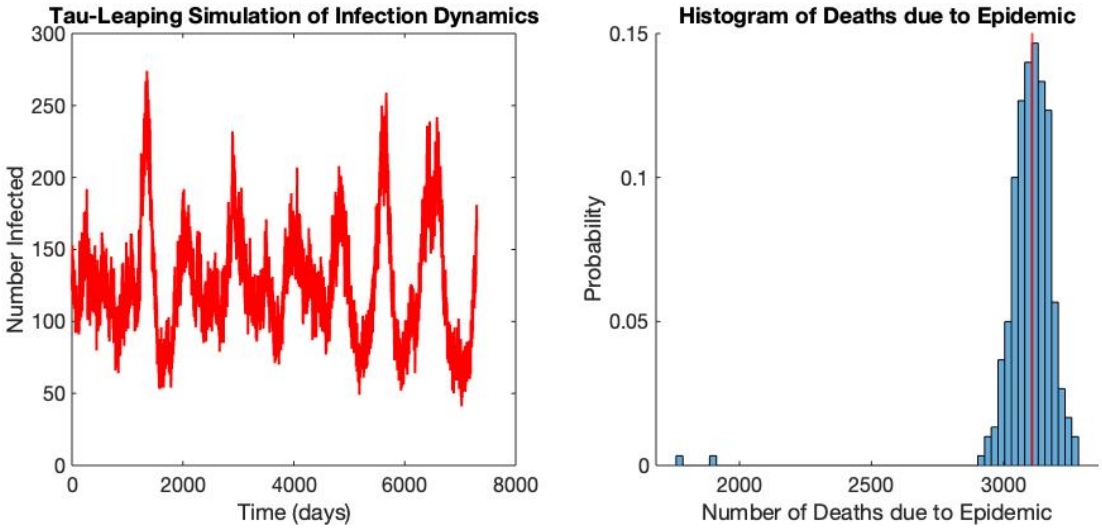

Figure 6: Left: Example tau leaping simulation of system $v = 0$. Right: Histogram of number of deaths due to the epidemic.

Q3c

For this situation, Tau leap is preferable to Gillespie's direct method. Firstly, the population in this model is larger by a factor of 10. This means the simulation may run for

longer so we would prefer to use approximate methods in tau leaping, over the direct stochastic modelling of Gillespie in order to reduce run time. Furthermore, due to the large population size, R_{total} is large and so our time steps in Gillespie can be very small. Using tau leap, we can fix a more desirable time-step of 1 day. Finally, this model has more compartments and more events. this increases the number of calculations required and so the approximating method of Tau leap is proffered the the Direct Gillespie method, in order to save time.

Q3d

In figure 7 the infection dynamics for $v = 0.6$ are plotted along with a histogram of total deaths, derived from 300 simulations. The cycles are still present but after around 3500 days or 10 years infections drop enough to hit $I = 0$ and presumably $E = 0$ also, leading to the epidemic ending. Furthermore the trough of these cycles dips much closer to the $I = 0$ line than before, likely due to increased downward forcing from increased vaccinations. These repeated dips close to $I = 0$ are where the disease is more likely to end and thus in our distribution of deaths we don't have one peak but a series of peaks, presumably each corresponding to a point where the infection cycles tend to be at a minima. That said, one peak does match nicely with the total deaths predicted by the ODE model. To calculate the probability of elimination in 5 years we simply use the sum function in MATLAB to count all runs that end before $5 \times 356 = 1825$ days. I calculated a probability of 0.18 after 300 runs.

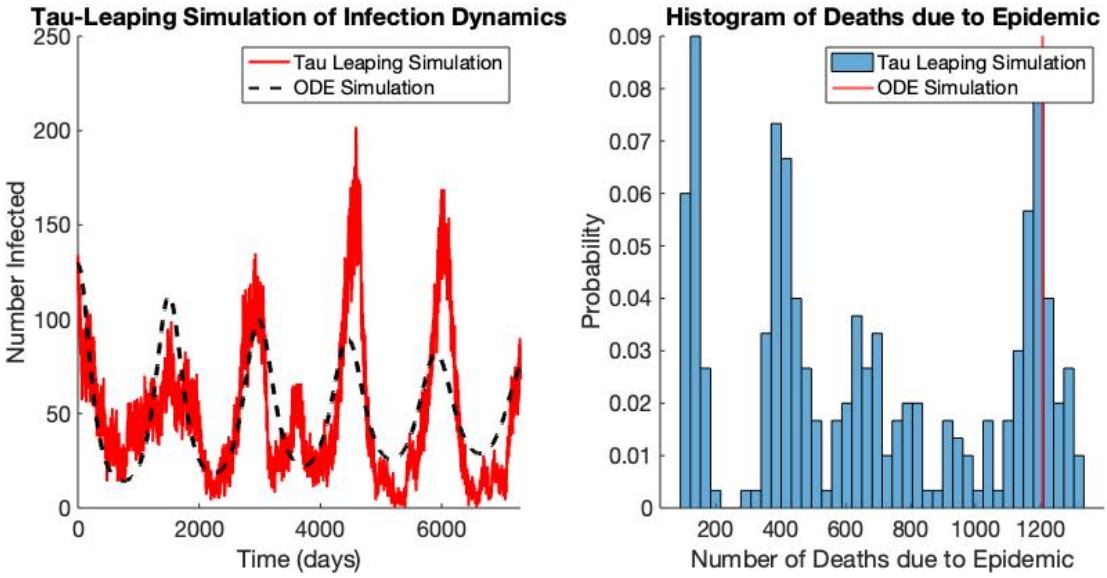

Figure 7: Using Tau-Leaping to model infection dynamics for $v = 0.6$.

To calculate to 1% the value of v such that the disease is eradicated in 5 years with 95% probability, I first did some preliminary investigation with groups of 10 runs. This put v in the 0.7-0.8 range. From here I ran several larger runs checking each case and got that $v = 79\%$.

Q3e

According to WHO, a significant challenge in a vaccination campaign is infrastructure. This is seen in the MSF video, which described a lack of health infrastructure that MSF acted to counteract. Furthermore, due to the size of the regions in the DRP and poor roads, a vaccination campaign may not be feasible due to difficulties transporting people to a vaccination centre or transporting the vaccine to the people. Another challenge is highlighted by WHO's target for 80% vaccination locally, a finding corroborated by our own findings in Q3d of needing 79% of people to be vaccinated for a high chance of disease extinction in 5 years. Due to the infrastructure problems, this target will be challenging to reach. Further damaging to the feasibility of a vaccination campaign is the added effects of not reaching the target. As seen in Q3d, infections can be relatively low, but shoot back up to higher levels when there is little vaccination. This is supported by NSF and WHO, both of which mention how rapidly measles can spread in large unvaccinated populations. Indeed, we saw in Q3d that there is only a 18% chance that the disease will go extinct in 5 years with a vaccination rate of 60%.