Mathematics 4MB3/6MB3 Mathematical Biology

http://www.math.mcmaster.ca/earn/4MB3

2019 ASSIGNMENT 4

Group Name: The Plague Doctors

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This assignment is **due in class** on **Wednesday March 13 2019 at 10:30am**.

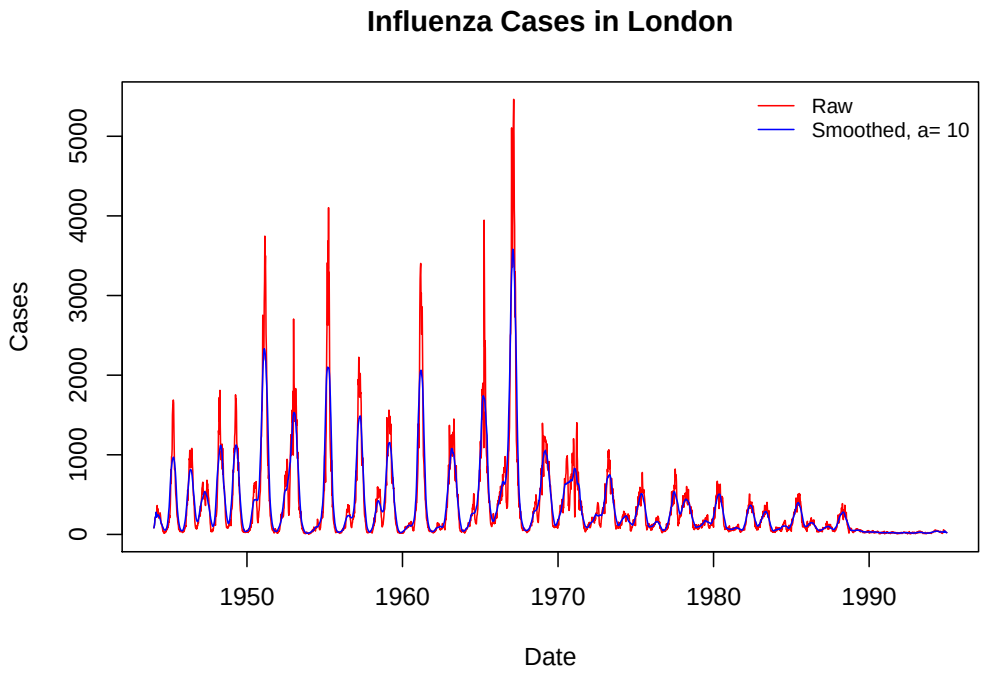
1. (a) You should have received the following data files by e-mail:

`meas_uk_lon_1944-94_wk.csv`
`meas_uk_lpl_1944-94_wk.csv`

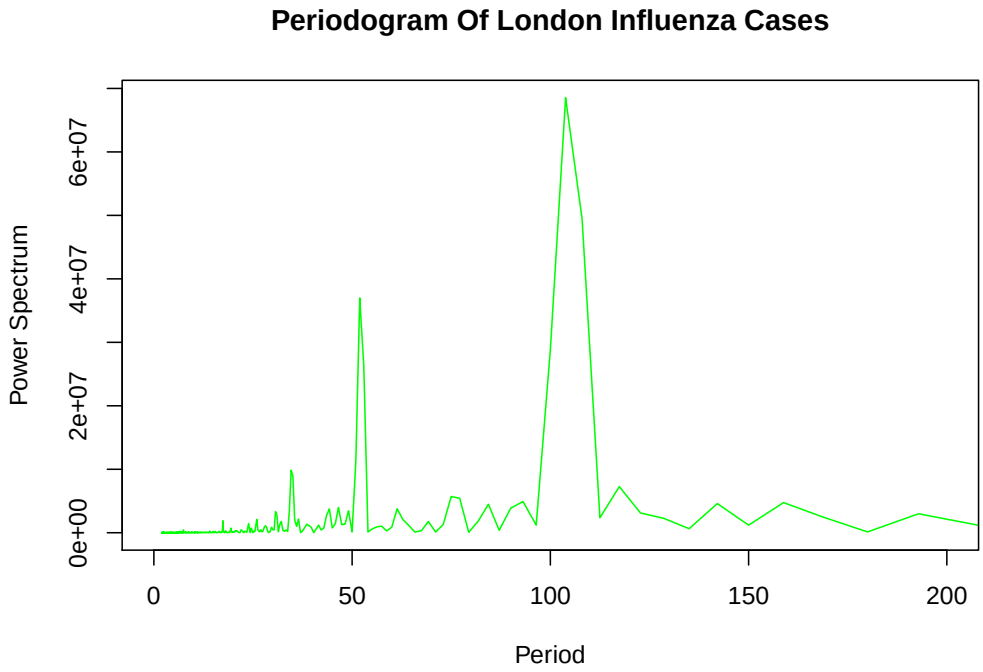
These plain text comma-separated-value files list weekly cases of measles (in London and Liverpool, England, from 1944 to 1994). Depending on which research direction you select, you might receive other files in the same `ymdc` (year,month,day,count) format, where the count column might contain cases or deaths, for example. Write the following R functions:

(i)
```
## [1] "First 5 rows of the dataframe"
##   year month day cases       date
## 1 1944     1   7    82 1944-01-07
## 2 1944     1  14    98 1944-01-14
## 3 1944     1  21   118 1944-01-21
## 4 1944     1  28   153 1944-01-28
## 5 1944     2   4   206 1944-02-04
## 6 1944     2  11   217 1944-02-11
```

(ii)
```
## [1] "smoothing with moving average, a = 10"
```



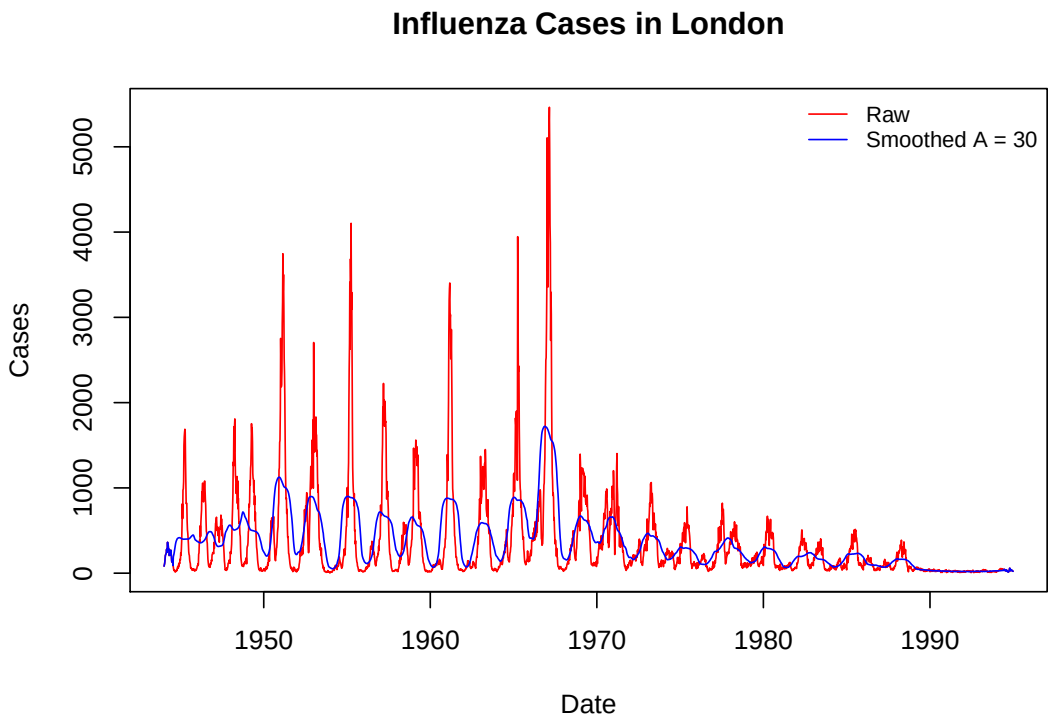
(iii)
```
## [1] "Using pgram estimation method"
```



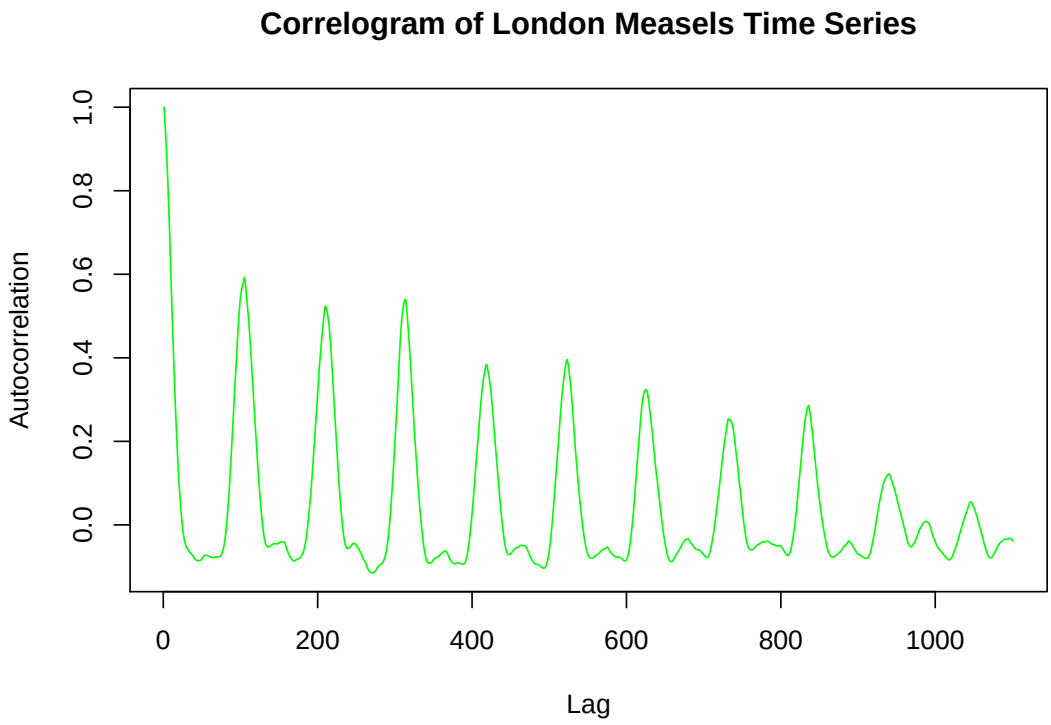
(b) Using your functions, make a multi-panel plot that clearly shows the temporal pattern of the time series and how its frequency structure changes over time. Think carefully about how to make this multi-panel figure as clear as possible for your-

selves and your readers. Describe your figure, explaining what aspects of your figure you feel are puzzling or interesting and may be possible to understand using mechanistic mathematical modelling. (Repeat this for each of the epidemic time series you are given.)

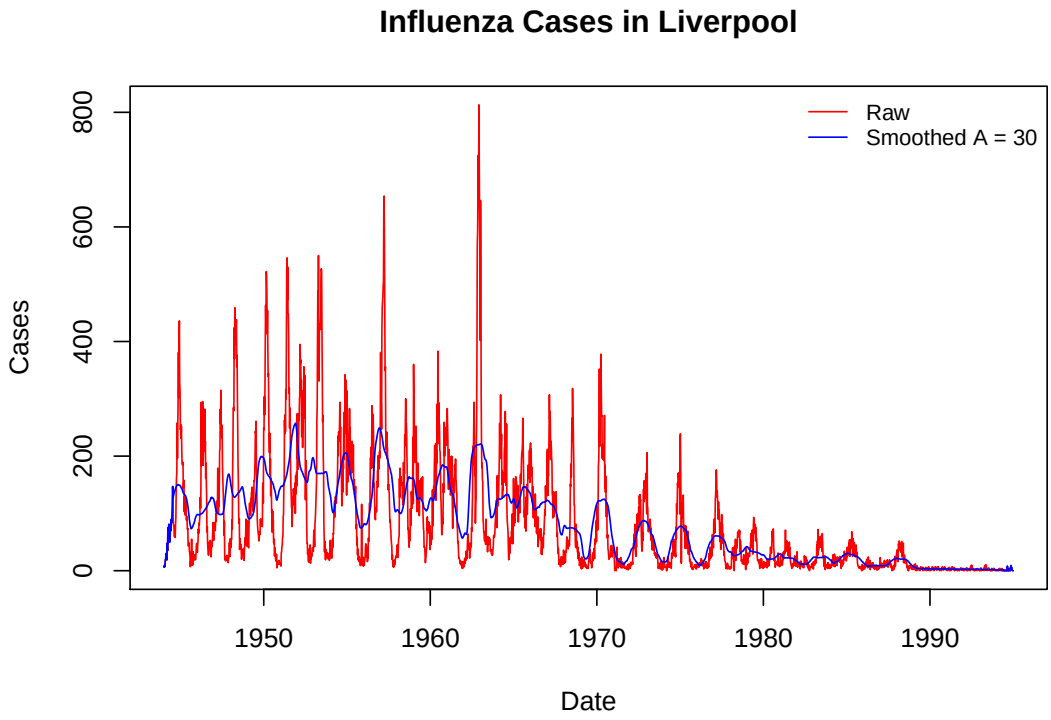
```
## [1] "smoothing with moving average, a = 30"
```



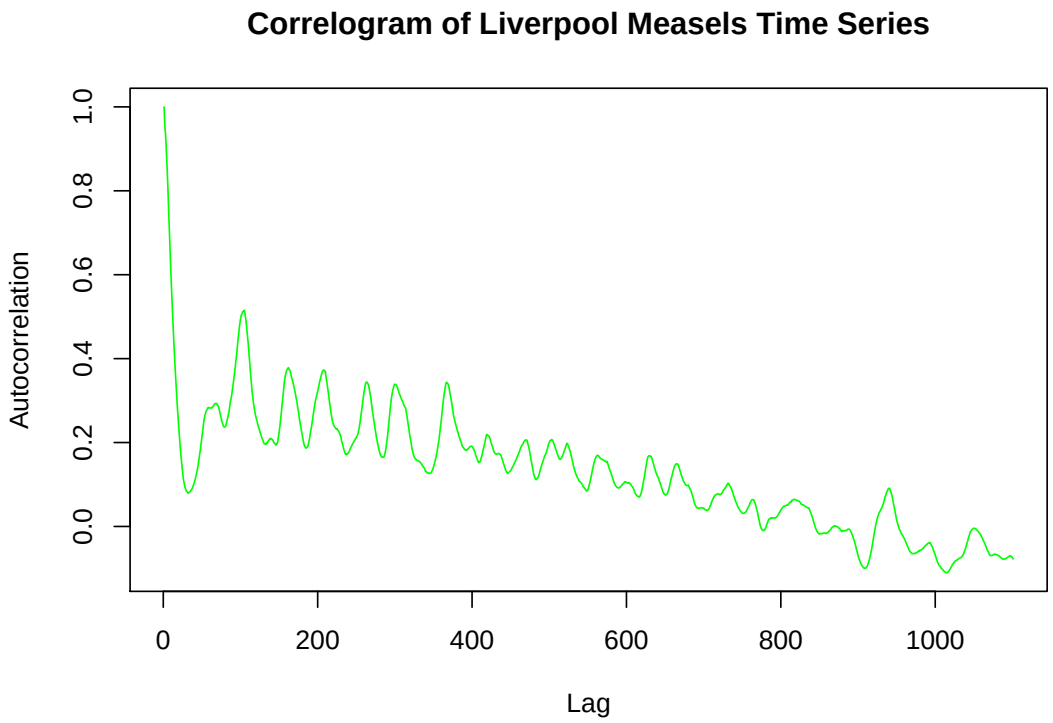

```
## [1] "Using lag k = 1100"
```




```
## [1] "smoothing with moving average, a = 30"
```



```
## [1] "Using lag k = 1100"
```

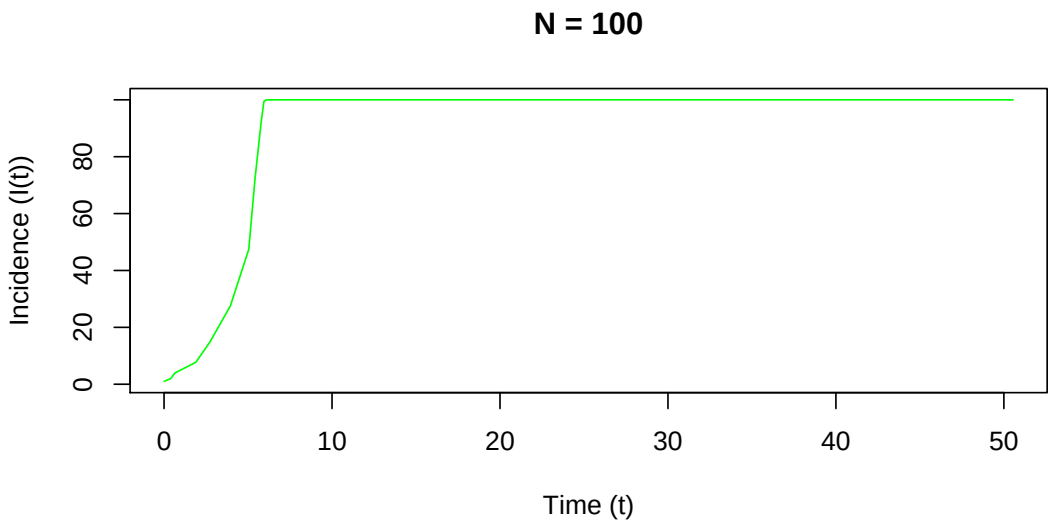


2. Consider the SI model,

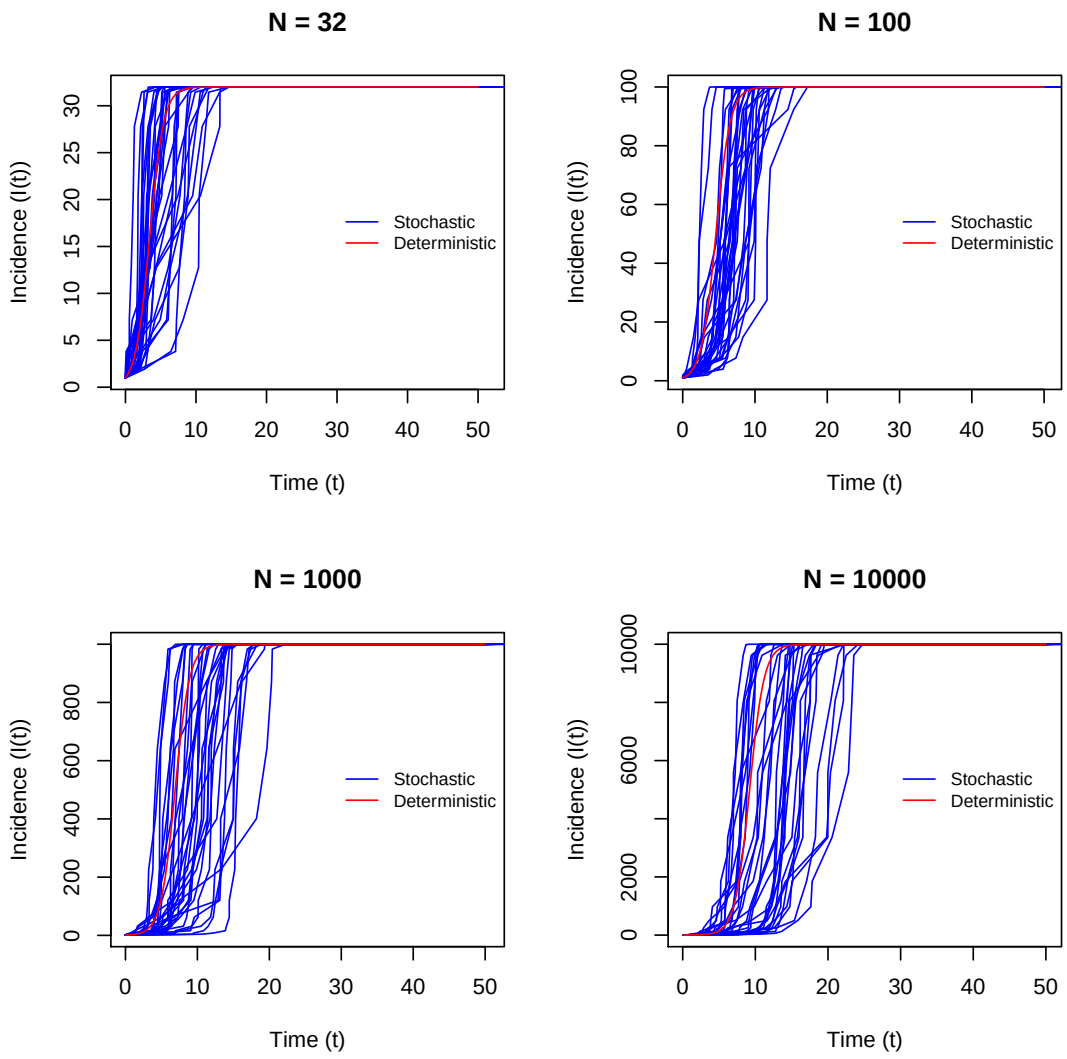
$$\frac{dI}{dt} = \beta(N - I)I\,, \qquad I(0) = I_0, \tag{1}$$

where β is the transmission rate, N is the population size and $I(t)$ is the number of infected individuals at time t.

(a)
```
source('gillespie.R')
#simulation vars
beta = 1
N = 100
I0 = 1
tmax = 50
realizations = 30
result <- SI.Gillespie(beta,N,I0,tmax)
plot(result[[1]], result[[2]], col="green", type="l", xlab="Time (t)",
     ylab="Incidence (I(t))", main=paste("N =",N))
```



(b)
```
source('gillespie.R')
#simulation vars
beta = 1
ns = c(32,100,1000,10000)
I0 = 1
tmax = 50
realizations = 30
multipanel(realizations,beta,ns,I0,tmax)
```



3. The natural history of smallpox is shown in Figure 1. The US Centers for Disease Control and Prevention (CDC) has recently discovered that a group of bioterrorists plans to reintroduce smallpox to the United States. The CDC has reason to believe that the terrorists are also bioengineers and have successfully altered the virus so that it causes the early rash stage to be twice as long as it was when the virus was last circulating naturally in the 1970s. Moreover, the existing smallpox vaccine apparently provides no protection against the altered virus. The CDC wants your opinion on how the alterations to the virus will affect $\mathcal{R}_0$ and the expected final size of an epidemic if the planned attack is successful.

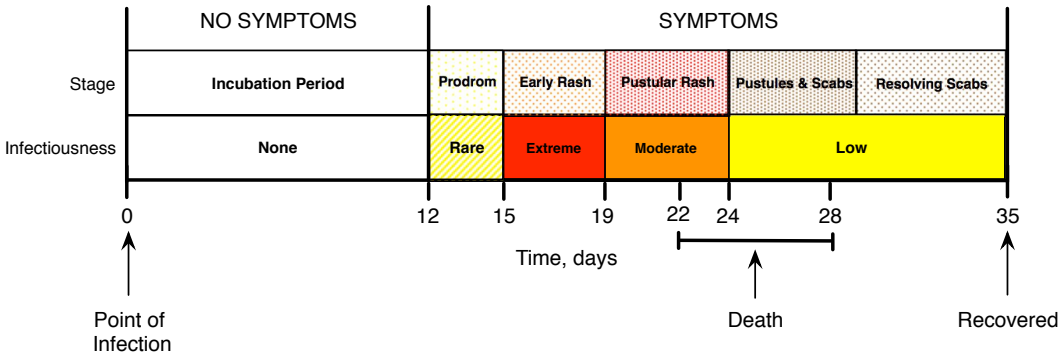


Figure 1: The natural history of smallpox infection. The prodrom stage begins with fever but the patient is very rarely contagious. Early rash is the most contagious stage, when the rash develops and transforms into bumps. During the pustular rash stage bumps become pustules, which then turn into scabs during the pustules and scabs stage and fall off during the resolving scabs stage. The infected person is contagious until the last scab falls off. (*This is Figure 3.4 from page 82 of Olga Krylova's 2011 McMaster University PhD thesis.*)

(a)

$$\begin{aligned}
\frac{dS}{dt} &= \nu - \beta_r I_r S - \beta_e I_e S - \beta_m I_m S - \beta_l I_l S - \mu S \\
\frac{dE}{dt} &= \beta_r I_r S + \beta_e I_e S + \beta_m I_m S + \beta_l I_l S - \sigma_1 E - \mu E \\
\frac{dI_r}{dt} &= \sigma_1 E - \sigma_2 I_r - \mu I_r \\
\frac{dI_e}{dt} &= \sigma_2 I_r - \sigma_3 I_e - \mu I_e \\
\frac{dI_m}{dt} &= \sigma_3 I_e - \sigma_4 I_m - \mu I_m \\
\frac{dI_l}{dt} &= \sigma_4 I_m - \gamma I_l - \mu I_l \\
\frac{dR}{dt} &= \gamma I_l - \mu R
\end{aligned}$$

(b) In this case the susceptible population can come into contact with individuals in 4 different stages of infectiousness. Ergo, each transmission possibility with the infectious individuals in all 4 stages should be calculated similar to the $SEIR$ model, and they can be summed up to return the R_0 value. Putting the 4 equations together we get:

$$\begin{aligned}
R_0 = &\frac{\beta_r \sigma_1}{(\sigma_1+\mu)(\sigma_2+\mu)} + \frac{\beta_e \sigma_1 \sigma_2}{(\sigma_1+\mu)(\sigma_2+\mu)(\sigma_3+\mu)} \\
&+ \frac{\beta_m \sigma_1 \sigma_2 \sigma_3}{(\sigma_1+\mu)(\sigma_2+\mu)(\sigma_3+\mu)(\sigma_4+\mu)} + \frac{\beta_l \sigma_1 \sigma_2 \sigma_3 \sigma_4}{(\sigma_1+\mu)(\sigma_2+\mu)(\sigma_3+\mu)(\sigma_4+\mu)(\mu+\gamma)}
\end{aligned}$$

(c) Assuming that $\mathcal{F}$ = inflow of new infecteds to infected compartments, and $\mathcal{V}$ = outflow from infected compartments minus inflow of non-new infecteds we have:

$$\mathcal{F} = \begin{pmatrix} \beta_r I_r S + \beta_e I_e S + \beta_m I_m S + \beta_l I_l S \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \quad \mathcal{V} = \begin{pmatrix} \sigma_1 E + \mu E \\ -\sigma_1 E + \sigma_2 I_r + \mu I_r \\ -\sigma_2 I_r + \sigma_3 I_e + \mu I_e \\ -\sigma_3 I_e + \sigma_4 I_m + \mu I_m \\ -\sigma_4 I_m + \gamma I_l + \mu I_l \end{pmatrix}$$

Let F = linearization of $\mathcal{F}$ at DFE.
Let V = linearization of $\mathcal{V}$ at DFE. Calculating F and V we have:

$$F = \begin{pmatrix} 0 & \beta_r & \beta_e & \beta_m & \beta_l \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} (\sigma_1 + \mu) & 0 & 0 & 0 & 0 \\ -\sigma_1 & (\sigma_2 + \mu) & 0 & 0 & 0 \\ 0 & -\sigma_2 & (\sigma_3 + \mu) & 0 & 0 \\ 0 & 0 & -\sigma_3 & (\sigma_4 + \mu) & 0 \\ 0 & 0 & 0 & -\sigma_4 & (\gamma + \mu) \end{pmatrix}$$

The next generation matrix is FV^{-1}. Calculating FV^{-1} using a symbolic manipulation software we get:

$$FV^{-1} = \begin{pmatrix} m_1 & m_2 & m_3 & m_4 & m_5 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

where

$$m_1 = \frac{\beta_r\sigma_1}{(\sigma_1+\mu)(\sigma_2+\mu)} + \frac{\beta_e\sigma_1\sigma_2}{(\sigma_1+\mu)(\sigma_2+\mu)(\sigma_3+\mu)} + \frac{\beta_m\sigma_1\sigma_2\sigma_3}{(\sigma_1+\mu)(\sigma_2+\mu)(\sigma_3+\mu)(\sigma_4+\mu)} + \frac{\beta_l\sigma_1\sigma_2\sigma_3\sigma_4}{(\sigma_1+\mu)(\sigma_2+\mu)(\sigma_3+\mu)(\sigma_4+\mu)(\mu+\gamma)}$$

$$m_2 = \frac{\beta_r}{\sigma_2+\mu} + \frac{\beta_e\sigma_2}{(\sigma_2+\mu)(\sigma_3+\mu)} + \frac{\beta_m\sigma_2\sigma_3}{(\sigma_2+\mu)(\sigma_3+\mu)(\sigma_4+\mu)} + \frac{\beta_l\sigma_2\sigma_3\sigma_4}{(\sigma_2+\mu)(\sigma_3+\mu)(\sigma_4+\mu)(\mu+\gamma)}$$

$$m_3 = \frac{\beta_e}{\sigma_3+\mu} + \frac{\beta_m\sigma_3}{(\sigma_3+\mu)(\sigma_4+\mu)} + \frac{\beta_l\sigma_3\sigma_4}{(\sigma_3+\mu)(\sigma_4+\mu)(\mu+\gamma)}$$

$$m_4 = \frac{\beta_m}{\sigma_4+\mu} + \frac{\beta_l\sigma_4}{(\sigma_4+\mu)(\mu+\gamma)}$$

$$m_5 = \frac{\beta_l}{\mu+\gamma}$$

R_0 can be calculated as the spectral radius of the matrix FV^{-1} (or $\rho(FV^{-1})$). Therefore:

$$R_0 = \rho(FV^{-1}) = \frac{\beta_r\sigma_1}{(\sigma_1+\mu)(\sigma_2+\mu)} + \frac{\beta_e\sigma_1\sigma_2}{(\sigma_1+\mu)(\sigma_2+\mu)(\sigma_3+\mu)} + \frac{\beta_m\sigma_1\sigma_2\sigma_3}{(\sigma_1+\mu)(\sigma_2+\mu)(\sigma_3+\mu)(\sigma_4+\mu)} + \frac{\beta_l\sigma_1\sigma_2\sigma_3\sigma_4}{(\sigma_1+\mu)(\sigma_2+\mu)(\sigma_3+\mu)(\sigma_4+\mu)(\mu+\gamma)}$$

(d) The early rash stage of the altered virus is expected to be twice as long as the original strain, meaning that the mean infectious period in the early rash stage ($\frac{1}{\sigma_3}$) has doubled. In other words, σ_3 is divided in half. So the R_0 for the new strain can be written as:

$$R_0 = \frac{\beta_r\sigma_1}{(\sigma_1+\mu)(\sigma_2+\mu)} + \frac{\beta_e\sigma_1\sigma_2}{(\sigma_1+\mu)(\sigma_2+\mu)((\sigma_3/2)+\mu)} + \frac{\beta_m\sigma_1\sigma_2(\sigma_3/2)}{(\sigma_1+\mu)(\sigma_2+\mu)((\sigma_3/2)+\mu)(\sigma_4+\mu)} + \frac{\beta_l\sigma_1\sigma_2(\sigma_3/2)\sigma_4}{(\sigma_1+\mu)(\sigma_2+\mu)((\sigma_3/2)+\mu)(\sigma_4+\mu)(\mu+\gamma)}$$

Since β_e is the highest infectiousness rate (extreme), this change in σ_3 will have the most significant impact on the second fraction of the equation, $\frac{\beta_e\sigma_1\sigma_2}{(\sigma_1+\mu)(\sigma_2+\mu)((\sigma_3/2)+\mu)}$, almost doubling its value.
The changes in the last 2 fractions in R_0 are very minor and can be ignored. Since natural death rate (μ) is much smaller than σ_3, the changes in the numerator almost cancel out the changes in the denominator completely. Thus, R_0 can be expected to increase significantly in the new virus.

(e) tmp

— END OF ASSIGNMENT —

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