Disease Dynamics Assignment Submission Report

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INTRODUCTION

Disease control is a very complex problem for health officers, this is why mathematical models are used to predict and understand diseases. The transmission of Ebola virus is better described by a SEIR model. This is because it takes a certain time for an infected individual to become infectious. During that period of time, such individuals are in the exposed/latent compartment.

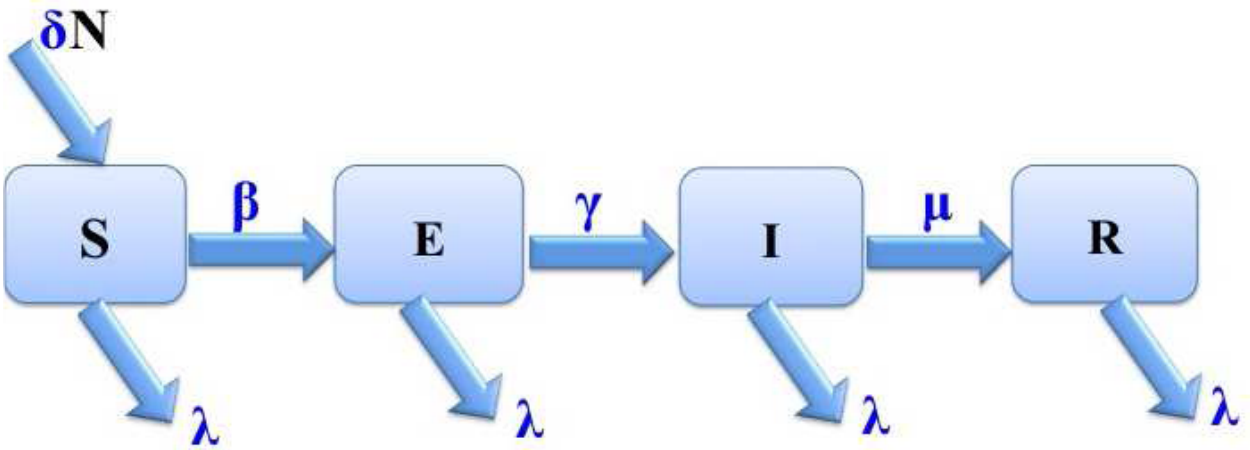
Discrete SEIR time models to Ebola epidemics are available but in our work, we are demonstrating continuous time model, which is more common with respect to Ebola modeling. It also turns out that in available Ebola studies with SEIR models, the population is assumed to be constant. This assumption is far from being true in West African countries. For example, in Liberia, the birth rate is approximately four times the death rate. Motivated by this fact, we aim is to stimulate the 2014 outbreak of Ebola virus in Liberia through an appropriate SEIR model with vital dynamics, which takes into account the demographic effects on the population.

MODEL ASSUMPTIONS

The practical use of models is based on the fact that they can be kept realistic depending on the assumptions given. Here, we state the the assumptions for the adopted model

-Constant birth rate -Natural death rate -Recovered sub-populations remain immune once they recover from the disease -Since we are fitting the uncontrolled model, it is important to use the data for the spread of Ebola prior to major effective intervention. Therefore, our fitting only uses data before the peak of the infectious period

COMPARTMENTAL DIAGRAM



The description of the transmission of Ebola virus by the SEIR model is based on the subdivision of the population into four compartments(also known as states): • Susceptible compartment S(t), which denotes individuals who are susceptible to catch the virus, and so might become infectious if exposed. • Exposed compartment E(t), which denotes the individuals who are infected but the symptoms of the virus are not yet visible. • Infectious compartment I(t), which denotes infectious individuals who are suffering the symptoms of Ebola and are able to spread the virus through contact with the susceptible class of individuals. • Recovered compartment R(t), which denotes individuals who have immunity to the infection and, consequently, do not affect the transmission dynamics, in any way, when in contact with other individuals.

Other parameters used in the model include:
β - transmission rate γ - infectious rate μ - recovery rate σ - birth rate Λ - death rate

SYSTEM OF DIFFERENTIAL EQUATIONS FOR THE MODEL

The typical SEIR model is expanded by including demographic effects on the population(birth and death rate)

Figure shows the relationship between the variables of system of equations which describes the SEIR model with vital dynamics, that is, birth and death rate.

$$\begin{cases} \frac{dS(t)}{dt} = \delta N - \beta S(t) I(t) - \lambda S(t), \\ \frac{dE(t)}{dt} = \beta S(t) I(t) - \gamma E(t) - \lambda E(t), \\ \frac{dI(t)}{dt} = \gamma E(t) - \mu I(t) - \lambda I(t), \\ \frac{dR(t)}{dt} = \mu I(t) - \lambda R(t). \end{cases}$$

ANALYSIS OF THE EQUILIBRIA

Let's find the equilibria points of the system of equations above that describes the model by by setting the right-hand side to zero.

The implementation here is done in sage

```
#Let's find the equilibria points of the system of equations that describes the model by setting the right-hand side to zero
#First define all states and parameters

y = var('beta, gamma, mu, sigma, Lambda, S, E, I, R, N'); show (y)

#Define system of equations
dS = sigma*N - beta*S*I - Lambda*S
dE = beta*S*I - gamma*E - Lambda*E
dI = gamma*E - mu*I - Lambda*I
dR = mu*I - Lambda*R

#Compute equilibria
soln = solve([dS==0, dE==0, dI==0, dR==0], S, E, I, R)
show(soln)
```

This proves that there is a virus free equilibrium given by

$$\left[S = \frac{N\sigma}{\Lambda}, E = 0, I = 0, R = 0\right]$$

For computing the basic reproduction number R-not, we apply the next generation method. This implementation is in sage

```
#Derive an expression for the basic reproduction number. We apply the next generation method to compute the basic
reproduction number. Since we are only concerned with individuals that spread the infection, we only need to model the
exposed, E, and Infected, I, classes.

#Define f and v; f consists of new infections from susceptible whereas v includes the transfer of infected individuals
from one infecetd class to another  with positive(+) values depicting transfer of individuals out of an infected class and
negative (-) values depicting transfer of individuals into of an infected class

#Values (gamma*E and  Lambda*E) are transfers out of Exposed class, values (mu*I + Lambda*I) are transfers out of Infected
class and value (gamma*E) is transfer into Infected class.
f = matrix(SR, 2, 1, [beta*S*I, 0]) ; show(f)
v = matrix(SR, 2, 1, [gamma*E + Lambda*E , -gamma*E + mu*I + Lambda*I]) ; show(v)

#Compute partial derivatives of f and v since we are to form the next generation matrix form these partial derivatives
F=jacobian(f, (E,I))
F=F(S=sigma*N/Lambda, E=0, I=0, R=0); show(F)

V=jacobian(v, (E,I))
V=V(S=sigma*N/Lambda, E=0, I=0, R=0); show(V)

#Compute inverse of V
V_inv = V.inverse() ; show(V_inv)

#Take the product of the F and V_inv
FV_1 = F*V_inv; show(FV_1)

#The basic reproduction number is given by the dominant eigenvalue of the matrix FV_1
evalues = FV_1.eigenvalues(); show(evalues)

ro = evalues[0]
show(ro)
```

The expression for the basic reproduction number is:

$$R_0 := \frac{\beta\gamma\delta N}{(\mu+\lambda)(\gamma+\lambda)\lambda}$$

SIMULATION OF THE MODEL

Now we present a modeling study of the real outbreak of Ebola virus in Libera in 2014 by using WHO data. Let us start by the analysis of the parameters of the SEIR model with demographic effects and induced death rates. The birth rate = 0.03507 and death rate = 0.0099 of the model are obtained from the specific statistical data of the demography of Liberia.

To estimate the parameters , we adapted the initialization of I with the reported data of WHO by fitting the real data of confirmed cases of infectious in Liberia.

To measure the goodness of fit, we have used a deterministic approach for the estimation of the parameters. Precisely, for fitting procedure we have used a least squares method of the system of differential equations that describes the model. According to the definition of the least squares method, the best-fit curve is the one that provides a minimal squared sum of deviation from real data. In our case, the fitting procedure is associated with the numerical resolution of the system of differential equations that describes the model

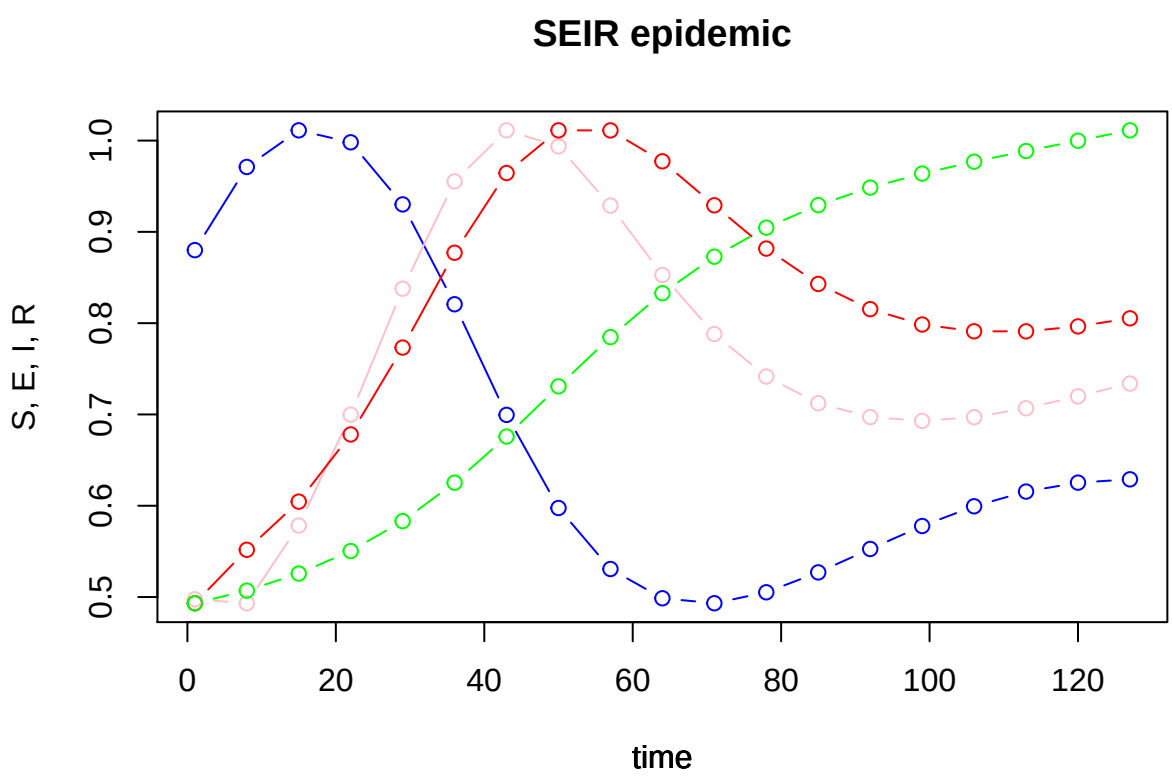
```
## Remove all objects from workspace.
rm(list = ls())

#Load readxl package - to read in excel files
require(readxl)
```

```
## Loading required package: readxl
```

```
#Load deSolve package - contains lsoda and ode functions; these are differential equation solver.
require(deSolve)
```

```
## Loading required package: deSolve
```

```
##Read in ebola data reported by WHO
ebola_data <- read_excel("C:/Users/Administrator/Desktop/who_alldata - June-Oct_2014.xlsx")

## Create an SEIR function
SEIR_model <- function(times, yinit, pars){

  with(as.list(c(yinit,pars)), {
    N = S+E+I+R
    dS <- sigma - beta*S*I  - lambda*S
    dE <- beta*S*I - gamma*E - lambda*I
    dI <- gamma*E - mu*I - lambda*I
    dR <- mu*I - lambda*R
    return(list(c(dS, dE, dI, dR)))})
}


## Initialize values for sub-populations(state values for the differential equations.).
## Proportion in each compartment: Susceptible 0.88, Exposed = 0.07, Infected 0.005, Recovered 0
init <- c(S = 0.88, E = 0.07, I = 0.05, R = 0)

## Set parameters
## beta: transmission parameter; gamma: infectious parameter; mu: recovery parameter; sigma: birth rate
parameters <- c(beta = 0.2, gamma = 0.1887, mu = 0.1, sigma = 0.03507, lambda = 0.0099 )

## Time frame by 7 days; depicting weekly time points as reported in the WHO situation reports
Time <- seq(1, 133, by = 7)

## Simulate the SEIR epidemic.
out = lsoda(init, Time, SEIR_model, parameters)

## Plot dynamics of Susceptibles, Exposed, Infectious and Recovered sub-populations in the same plot.
# susceptible hosts over time
plot (S ~ time, data = out, type='b', col = 'blue', ylab = 'S, E, I, R', main = 'SEIR epidemic')
# remain on same frame
par (new = TRUE)
# exposed hosts over time
plot (E ~ time, data = out, type='b', col = 'pink', ylab = '', axes = FALSE)
# remain on same frame
par (new = TRUE)
# infectious hosts over time
plot (I ~ time, data = out, type='b', col = 'red', ylab = '', axes = FALSE)
# remain on same frame
par (new = TRUE)
# recovered hosts over time
plot (R ~ time, data = out, type='b', col = 'green', ylab = '', axes = FALSE)
```




```
real_data<- ebola_data
real_data$Time <- Time

score<-function(pars){
  output <- ode(y = init, times = Time, func = SEIR_model, parms = parameters)
  output<-as.data.frame(output)
  model_cases <- output$I
  ss<-sum((as.numeric(real_data$Cases) - model_cases)**2)
  return(ss)
}

fit <- optim(score,par=parameters)
newParameters<-fit$par
newParameters
```

```
##    beta   gamma      mu   sigma  lambda
## 0.20000 0.18870 0.10000 0.03507 0.00990
```

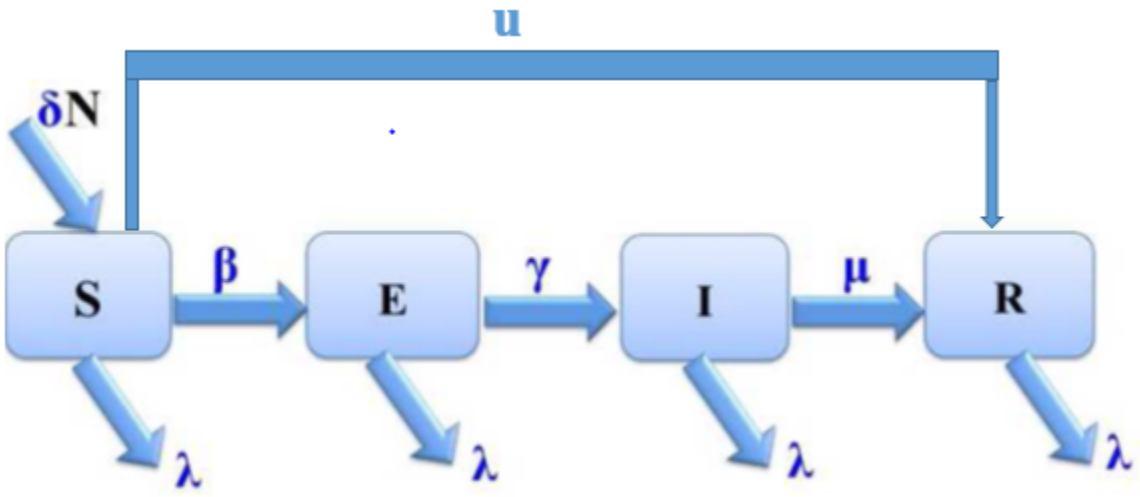
The model parameters that provide a best fit to data are; ##beta gamma mu sigma lambda ##0.20000 0.18870 0.10000 0.03507 0.00990

EXTENSION OF MODEL TO INCLUDE CONTROL MEASURES

Motivated by the fact that there is a vaccine against ebola, we present a strategy for the control of the virus by introducing into the model a control u(t) representing the vaccination rate at time t. Precisely,

the control u(t) is the fraction of susceptible individuals being vaccinated at time t. The SEIR model with vaccination as an intervention is investigated.We assume vaccination to be 100% effective.

Here is the corresponding compartmental diagram of the SEIR model with vaccination as intervention



The mathematical model with control is given by the system of differential equations

$$\begin{cases} \frac{dS(t)}{dt} = \delta N - \beta S(t)I(t) - \lambda S(t) - u(t)S(t), \\ \frac{dE(t)}{dt} = \beta S(t)I(t) - \gamma E(t) - \lambda E(t), \\ \frac{dI(t)}{dt} = \gamma E(t) - \mu I(t) - \lambda I(t), \\ \frac{dR(t)}{dt} = \mu I(t) - \lambda R(t) + u(t)S(t). \end{cases}$$

The goal of the adopted strategy is to reduce the infected individuals and the cost of vaccination on a fixed time interval. Precisely, the optimal control problem consists of minimizing the objective functional J,

$$J(I,u) = \int_0^{t_{end}} \left[I(t) + \frac{\tau}{2} u^2(t) \right] dt \longrightarrow \min$$

Where: u(t) is the control variable, which represents the vaccination rate at time t T denotes the weight on the cost of vaccination tend denote the duration, in days, of the vaccination program

REFERENCES

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