Modelling the Dengue Epidemic in Singapore

Academic Year 2019/2020, Semester II

Abstract

Our paper aims to model the spread of dengue in Singapore using a system of differential equations. It uses a modified SIR (SusceptibleInfected-Removed) model, which accounts for the vaccination of individuals with the approved drug, Dengvaxia. Based on our assumptions, our model predicts that population will decrease over time. To determine the best fit for our model, particle swarm optimization was implemented to estimate suitable parameters, followed by numerical simulation. The stability of critical points of the model are then analysed and the critical point (0,0,0) was determined to be asymptotically stable, which supports our model.

Contents

1 Introduction

1.1 Background

Dengue fever is a disease caused by the dengue virus, which can cause symptoms such as high fever, joint pain, headache and skin rash [1]. It is caused by five different serotypes of dengue, which are named DENV-1 to DENV-5 [2], and is spread by several species of Aedes mosquitoes. People who recover from one strain of dengue mostly become immune to that specific strain of dengue, but have increased risk of getting severe dengue fever if infected with other strains. In most cases, patients can recover within a week without any complications [3]. A vaccine for dengue fever, known as Dengvaxia, has been licensed in December 2015 and approved for use in around 20 countries, including Singapore.

1.2 Literature Review

Differential equations have been widely used in the studies of natural sciences, physical sciences, biopharmaceuticals and predictions among many other uses. To have a comprehensive understanding of the spread of

epidemics, researchers use various mathematical modelling techniques, such as gravity models.

Gravity models have a long history of use in describing and forecasting the movements of people as well as goods and services, making them a natural basis for disease transmission rates over distance. In agent-based microsimulations, gravity models can be directly used to represent movement of individuals and hence diseases. An accurate representation of disease transmission between spatially-distinct regions is an essential part of modelling epidemic behaviour on a national or international scale. Gravity models, which describe movement fluxes between regions in terms of their populations and distance from each other, have a history of successful use in the geography and economics and are increasingly used in epidemiology. In particular, we compare the behaviour of a simple flu-like epidemic model on synthetic networks generated by fitted gravity models and on the original network present in the data, using time to first infection [4]. Gravity models offer a simple model of disease transmission strength between meta-populations. Xia et al. model the dynamics of pre-vaccination measles as city meta populations connected by a gravity-based movement of infectious individuals [5]. The model succeeds in capturing most of the spatiotemporal properties of epidemics, including case rates, periodicity and fade-out behaviour. A similarly structured model was applied to seasonal influenza data in the US by Viboud et al [6]. In this case, it was found that fitting the underlying gravity model to commuting data successfully captured the observed synchrony in epidemics as a function of distance, population size and transmission. Gravity models are now increasingly used in both metapopulation- and individual-based epidemic micro-simulations.

However, the most common modelling technique is the SIR (SusceptibleInfected-Removed) model [7]. The SIR model, also known as the KermackMcKendrick deterministic model, has been widely used to model the spread of diseases such as dengue, HIV and even the recent Covid-19 [8]. The model was created by Kermack and McKendrick in 1927, and is used to model the number of infections as time passes [9]. Researchers have employed the use of the SIR model to model several past epidemics. For instance, the SIR model was used to model the spread of dengue alongside

with the perturbation iteration model [7], which proved to be very effective in improving the accuracy of the SIR model. The SIR model was also used to model the spread of Covid-19 in China with other methods [8]. The SIR model had the benefits of 'improved accounting for real variables and increases the opportunity for quantifying uncertainties', which made it more reliable compared to other prediction models. However, the standard SIR model is insufficient to model real life epidemics as there are other important factors that affect the number of infections, such as the use of vaccinations.

1.3 Objective

This research is motivated by the recent surge in dengue cases in Singapore in 2020 [10]. In this paper, we are concerned with modelling the spread of DENV-2 dengue in Singapore over 1 year using a modified SIR model, which accounts for the vaccine, Dengvaxia. The new immune class M consists of people who have become immune to dengue, which include the recovered and vaccinated people. We will be focusing only on the human population and not the mosquito population for simpler analysis. Our objective is to provide an improved model that can analyze and predict the periods of time where there would be a large outbreak of dengue fever.

2 Data Collection

The population in Singapore will be categorised into the susceptible, infected and immune groups but we will only be considering the infected and susceptible cases. Infected cases in 2019 [11] are shown in Figure 1. With regards to the susceptible data, it was calculated by removing the number of infected and death cases from the total population in 2019 [12]. The cumulative infected cases and susceptible cases in 2019 are plotted, as shown in Figure 2 and Figure 3 respectively.

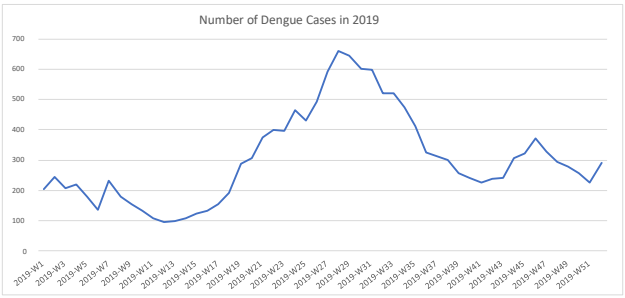

Figure 1: Number of Dengue Cases in 2019

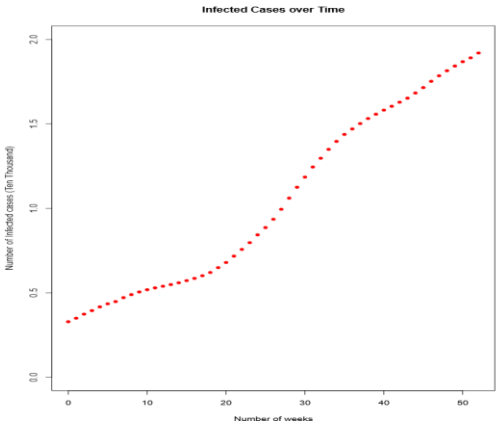

Figure 2: Data for Infected

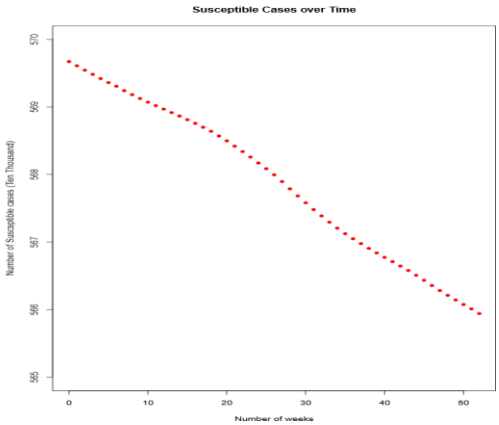

Figure 3: Data for Susceptible

3 Modelling

3.1 Modified SIR model

Our model consists of 3 different groups as mentioned before:

- Susceptible (S): Individuals who are susceptible to dengue
- Infected (I): Individuals who are infected with dengue
- Immune (M): Individuals who are immune to dengue (i.e. recovered and vaccinated)

Some of the key assumptions taken into consideration for our model are as follows:

1) There are no live births
2) There is no movement of people in and out of Singapore
3) Every individual has an equal chance of getting infected
4) Vaccinated individuals will become immune to dengue
5) Patients who recover from dengue are considered immune and will not re-enter susceptible group

With this, we have the following model:

$$\frac{dS}{dt} = -\beta S - pS - \sigma IS, \qquad S(0) = 569. \tag{1}$$

67

$$\frac{dI}{dt} = \sigma IS - \beta I - \mu I, \qquad I(0) = 0. \tag{2}$$

$$\frac{dM}{dt} = pS + \mu I - \beta M, \qquad M \tag{3}$$

3285

(0) = 0

3.2 Parameters of Model

The parameters of the model are β, σ, μ and p, satisfying $0 < \beta,\sigma,\mu,p < 1$. They represent the following:

β - Death Rate, σ - Infection Rate, μ - Recovery Rate, p - Vaccination Rate In Equation (1), the rate of change in susceptible is defined by subtracting the number of susceptible deaths (βS), the number of vaccinated (pS) and the number of infected (σIS). In Equation (2), the rate of change in infected is defined by the number of infected (σIS), subtracted by the number of infected deaths (βI) and the number of recovered (μI). In Equation (3), the rate of change in immune refers to the sum of number of vaccinated (pS) and number of recovered (μI), subtracted by the number of immune deaths (βM). It can be observed that

$$\frac{dS}{dt} + \frac{dI}{dt} + \frac{dM}{dt} = -\beta S - \beta I - \beta M < 0,$$

resulting in a decrease in population over time due to the number of deaths in each group.

3.3 Illustration of Model

For simpler visualisation, an illustration of the model can be seen in Figure 4 below.

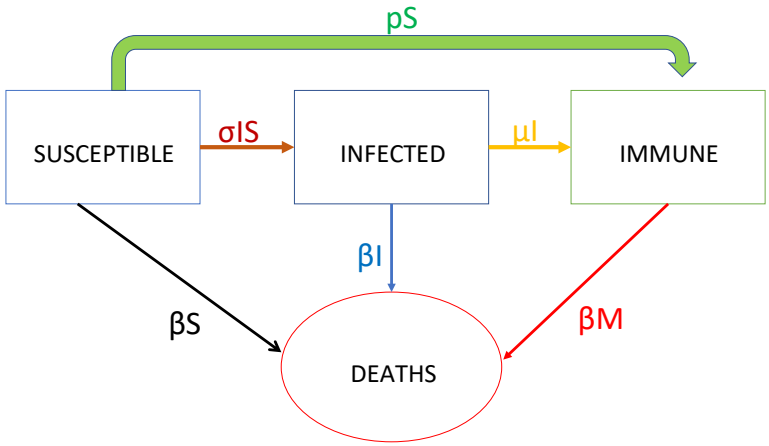

Figure 4: Illustration of modified SIR model

4 Parameter Fitting and Numerical Simulation

4.1 Fitting parameters of the model into data

To fit the parameters of the model into the data, the Particle Swarm Optimization (PSO) algorithm was executed on a chosen error function. The error function that we used is the mean squared error (MSE), which

measures the average squared difference between the estimated values and the actual values. The obtained parameters from PSO are

$\beta = 1.5857 \times 10^{-6}, \sigma = 6.4068 \times 10^{-5}, \mu = 4.5305 \times 10^{-5}, p = 7.3899 \times 10^{-5}$

4.2 Numerical Simulation

With the parameters obtained, we have the following graphs for the Infected Cases (Figure 5) and Susceptible Cases (Figure 6). It can be seen that the model's solution follows closely with the actual data points.

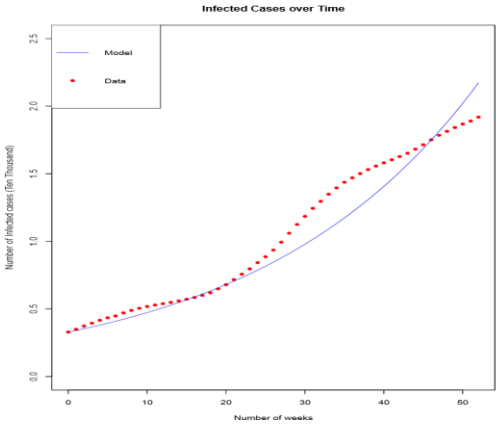

Figure 5: Best Fit for Infected

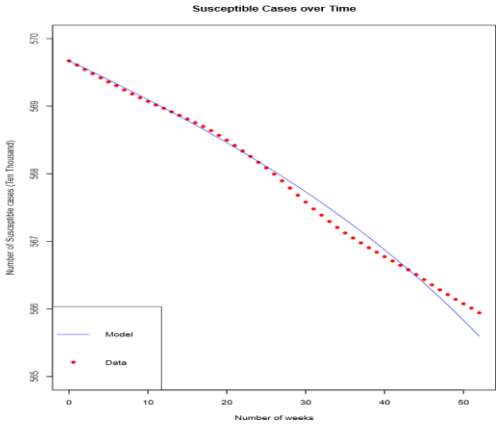

Figure 6: Best Fit for Susceptible

5 Basic Analysis

5.1 Critical Points

In order to find the critical points, we substituted the parameters into the differential equations.

$$\frac{d}{dt}\begin{bmatrix} S \\ I \\ M \end{bmatrix} = \begin{bmatrix} -7.5485 \times 10^{-5}S - 6.4068 \times 10^{-5}IS \\ 6.4068 \times 10^{-5}IS - 4.6891 \times 10^{-5}I \\ 7.3899 \times 10^{-5}S + 4.5305 \times 10^{-5}I - 1.5857 \times 10^{-6}M \end{bmatrix}$$

After equating the differential equation to be 0, we obtain the two critical points in the model; (0,0,0) and (0.63824,–1.1782,–3.9180).

5.2 Stability

The 3 × 3 Jacobian matrix of the model is

$$\begin{bmatrix} -7.5485 \times 10^{-5} - 6.4068 \times 10^{-5}I & -6.4068 \times 10^{-5}S & 0 \\ 6.4068 \times 10^{-5}I & 6.4068 \times 10^{-5}S - 4.6891 \times 10^{-5} & 0 \\ 7.3899 \times 10^{-5} & 4.5305 \times 10^{-5} & -1.5857 \times 10^{-6} \end{bmatrix}$$

At the critical point (0,0,0), the Jacobian matrix is

$$\begin{bmatrix} -7.5485 \times 10^{-5} & 0 & 0 \\ 0 & -4.6891 \times 10^{-5} & 0 \\ 7.3899 \times 10^{-5} & 4.5305 \times 10^{-5} & -1.5857 \times 10^{-6} \end{bmatrix}$$

By solving the cubic equation formed with the determinant of $(J - I\lambda)$, we can determine that the eigenvalues of (0,0,0) are $\lambda_1 = -1.5857 \times 10^{-6}$, $\lambda_2 = -4.6880 \times 10^{-5}$ and $\lambda_3 = -7.5504 \times 10^{-5}$. Hence, this concludes that the critical point (0,0,0) is an asymptotically stable node, as its eigenvalues are all negative and real. This is expected as for our model, the population decreases over time so *S*, *I* and *M* will approach 0 when *t* approaches infinity.

At the critical point (0.63824,–1.1782,–3.9180), the Jacobian matrix is

$$\begin{bmatrix} -8.2400 \times 10^{-11} & -4.0891 \times 10^{-5} & 0 \\ -7.5485 \times 10^{-5} & -6.0002 \times 10^{-6} & 0 \\ 7.3899 \times 10^{-5} & 4.5305 \times 10^{-5} & -1.5857 \times 10^{-6} \end{bmatrix}$$

By solving the cubic equation formed with the determinant of $(J - I\lambda)$, we can determine that the eigenvalues of (0.63824,−1.1782,−3.9180) are $\lambda_4 = -6.0001 \times 10^{-6}$, $\lambda_5 = -8.2402 \times 10^{-11}$ and $\lambda_6 = -1.5857 \times 10^{-6}$.

Hence, this concludes that the critical point (0.63824,−1.1782,−3.9180) is also an asymptotically stable node, since all eigenvalues are negative and real.

6 Advanced Analysis

6.1 Lyapunov's Second Method

With reference to the textbook by Boyce and DiPrima [13] and [14], we will be applying **Lyapunov's Second Method** to confirm the stability of the critical point (0.63824,−1.1782,−3.9180). We first transform the point to (0,0,0) by letting

$$S = 0.63824 + u, \qquad I = -1.1782 + v, \qquad M = -3.9180 + w$$

After substituting them into equations (1), (2) and (3), we obtain the new system

$$\frac{du}{dt} = -6.4068 \times 10^{-5}uv - 8.2400 \times 10^{-11}u - 4.0888 \times 10^{-5}v - 5.2591 \times 10^{-11}$$
$$\frac{dv}{dt} = 6.4068 \times 10^{-5}uv - 7.5485 \times 10^{-5}u - 5.9702 \times 10^{-6}v + 7.0341 \times 10^{-6}$$
$$\frac{dw}{dt} = 7.3899 \times 10^{-5}u + 4.5305 \times 10^{-5}v - 1.5857 \times 10^{-6}w - 2.8064 \times 10^{-10}$$

Consider the auxiliary function $V(u,v,w) = u^2 + v^2 + w^2$. This function is positive definite as $V(0,0,0) = 0$ and $V(u,v,w) > 0$ when $u,v,w \neq 0$. We compute

$$\begin{aligned}\dot{V}(u,v,w) &= V_u\frac{du}{dt} + V_v\frac{dv}{dt} + V_w\frac{dw}{dt} \\ &= -1.2814\times10^{-4}u^2v + 1.2814\times10^{-4}uv^2 - 1.6480\times10^{-10}u^2 \\ &\quad - 1.1940\times10^{-5}v^2 - 3.1714\times10^{-6}w^2 - 2.3275\times10^{-4}uv \\ &\quad + 1.4780\times10^{-4}uw + 9.0700\times10^{-5}vw - 1.0518\times10^{-10}u \\ &\quad + 1.4068\times10^{-5}v - 5.6128\times10^{-10}w\end{aligned}$$

where $V_u = 2u$, $V_v = 2v$ and $V_w = 2w$. Next, to determine the nature of the critical point at the origin, we construct the **Hessian matrix**,

$$H = \begin{bmatrix} -3.2960\times10^{-10} & -2.3275\times10^{-4} & 1.4780\times10^{-4} \\ 2.3275\times10^{-4} & -2.3880\times10^{-5} & 9.0700\times10^{-5} \\ 1.4780\times10^{-4} & 9.0700\times10^{-5} & -6.3428\times10^{-6} \end{bmatrix}$$

Since $V_{uu} = -3.2960\times10^{-10} < 0$, $V_{uu}V_{vv} - V_{uv}V_{vu} = 5.4173\times10^{-8} > 0$ and $det(H) = -1.7805\times10^{-13} < 0$, by the **Second Derivative Test** for 3 variables [14], the function has a local maximum at (0,0,0). This means that in the neighbourhood of (0,0,0), the function is negative so the function is negative definite on some domain containing the origin. Applying **Theorem 9.6.1** [13] modified for 3 variables [15], the origin is an asymptotically stable critical point for this modified system, which confirms that (0.63824,−1.1782,−3.9180) is asymptotically stable.

6.2 Basic Reproduction Number, R_0

The basic reproductive number, R_0, is the number of secondary infections that one infected person would produce in a fully susceptible population. It has been used by researchers to model dengue transmission in 2013 and 2014 in Singapore [16]. We compute R_0 [17] and apply the theorem [18] as follows:

$$\begin{aligned}R_0 &= \text{Infection Rate} \times \text{Duration of Infection} \\ &= \frac{\sigma}{p+\mu} = \frac{6.4068\times10^{-5}}{4.5305\times10^{-5} + 7.3899\times10^{-5}} = 0.53747 < 1\end{aligned}$$

Theorem: The disease free equilibrium of the system of equations (1), (2) and (3) is asymptotically stable if $R_0 < 1$

As such, this supports our analysis that the critical point (0,0,0) is asymptotically stable. It should also be noted that our value of R_0 is relatively small as our model has accounted for vaccination, which is a significant control measure that would reduce the spread of dengue.

7 Conclusion

From the results of the analysis of the model, there is an asymptotically stable node at (0,0,0) and (0.63824,−1.1782,−3.9180). The asymptotically stable node (0,0,0) suggests that the population will die out over time, which is expected based on our model. However, at (0.63824,−1.1782,−3.9180), the values of I and M are negative, which is impossible since the number of infected and immune cases cannot be negative. Hence, more should be done to improve the model.

Due to the assumptions we made earlier, it should be noted that our model does not take into account other factors, such as the birth rate of Singapore, age differences in the population or seasonal variations, which could affect the model. Future research could also be conducted on modelling the infected mosquito population to better account for the transmission of dengue from mosquitoes to humans.

References

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Appendices

R Code

```
install.packages("deSolve") install.packages("pso")
1
2
```

```
install.packages("ggplot2")

library(deSolve)
library(pso)
```

```
library(ggplot2)

#################### PLOTTING DATA ######################

#1) Creating the infected cases plot (cumulative)

#First value is 3285 because there were 3285 dengue cases in 2018
#Rest of the values are data collected online
data <- (c(3285,205,245,207,221,179,135,232,181,156,
133,109,96,99,108,125,134,156,192,287,307,
376,400,396,464,430,492,591,661,644,601,597,
521,522,474,412,326,314,299,258,243,226,239,
241,306,321,372,329,295,280,257,226,290)
/10000) #rescale by ten thousand

data_I <- cumsum(data)

#infected cases plot
time <- seq(0, 52, by = 1)
```

```
plot(time, data_I,main = "Infected Cases over Time", xlab = "Number of weeks", ylab
  ="Number of Infected cases (Ten Thousand)", col=2, pch=16,ylim=c(0,2))

#2) Creating the susceptible cases plot

```

```
#numbers will be in ten thousands, e.g. 570 because population in 2019 is 5.7
    million
#number of deaths in 2019 is 21385, assume constant death rate
#subtract number of deaths and infected from population
data_S <- 570 - (0:52) * 21385 / 52 / 10000 - data_I
data_S

#susceptible cases plot
plot(time, data_S,main = "Susceptible Cases over Time", xlab = "Number of
    weeks",
ylab ="Number of Susceptible cases (Ten Thousand)",
                col=2, pch=16,ylim=c(565,570))


###################### DEFINING ODE ######################
RHS.F <- function(S,I,M,d,i,r,v) {
-d*S-v*S-i*I*S
}

RHS.G <- function(S,I,M,d,i,r,v) {
```

```
47  i*I*S-d*I-r*I
48  }
49
50  RHS.H <- function(S,I,M,d,i,r,v){
51  v*S+r*I-d*M
52  }
53
```

```
RHS <- function(t, state, parameters) {
with(as.list(c(state,parameters)),{
# rate of change
dS <- RHS.F(S,I,M,d,i,r,v)
dI <- RHS.G(S,I,M,d,i,r,v)
dM <- RHS.H(S,I,M,d,i,r,v)
list(c(dS,dI,dM))
})                    # end with(as.list ...
}


################ CREATING ERROR FUNCTION #################

#Error function
error_f <- function(p){
p <- c(d=p[1],i=p[2],r=p[3],v=p[4]) #name the variables
#values of t
time <- seq(0, 52, by = 1)
#initial values, when t=0
 state <- c(S=569.6715, I=0.3285, M=0)
```

```
74  #run numerical simulation
75  out <- ode(y = state, time = time, func = RHS, parms =
        p)
76  #extracting as a data frame
77  out.df <- as.data.frame(out)
```

```
#extract out S and I
S <- out.df[2]
I <- out.df[3]
#change from dataframe to vector
S <- as.vector(t(S))
I <- as.vector(t(I))
model <- c(S,I)
data <- c(data_S,data_I)
error <- 1/106*sum((model-data)**2)
return (error)
}

############ PARAMETER ESTIMATION WITH PSO ##############
set.seed(2020)
pso_outcome <- psoptim(c(NA,NA,NA,NA), error_f,
lower = c(0.0000013, 0.000063,
                                        0.000043, 0.000028),
upper = c(0.0000020, 0.000188,
                                        0.000090, 0.000080),
control = list(maxit=20))
```

```
96
97 cat("d=", pso_outcome$par[1],"\ni =", pso_outcome$par
                                    [2], "\nr =", pso_outcome$par[3],"\nv =", pso_outcome
```

```
    $par[4],"\nerror =", pso_outcome$value)

#Output
#d= 1.585656e-06
#i = 6.406811e-05
#r = 4.530534e-05
#v = 7.389872e-05
#error = 0.01536676


########## SOLVING ODE WITH PARAMETERS FROM PSO ##########

#values of t
time <- seq(0, 52, by = 1)
#initial values, when t=0
state <- c(S=569.6715, I=0.3285, M=0) #0.3285 because number of cases in 2018
    is 3285

parameters <- c(d = pso_outcome$par[1],i = pso_outcome$ par[2],r =
    pso_outcome$par[3],v = pso_outcome$par[4])
out <- ode(y = state, time = time, func = RHS, parms =
    parameters)

#extracting as a data frame
```

```
118 out.df <- as.data.frame(out)
119 out.df
120
121
122
123 ###################### MODEL FITTING ######################
124
```

```
#Plotting of infected cases
plot(time, data_I,main = "Infected Cases over Time", xlab = "Number of weeks",
ylab ="Number of Infected cases (Ten Thousand)",
                col=2, pch=16,ylim=c(0,2.5))
par(new=TRUE)
plot(time, out.df[,3],main = "Infected Cases over Time", xlab = "Number of
    weeks",
ylab ="Number of Infected cases (Ten Thousand)", type='l', col=4, ylim=c(0,2.5))

legend("topleft", c("Model","Data"), lty=c(1,NA),pch=c(
    NA,16),col=c("blue","red"))


#Plotting of susceptible cases
plot(time, data_S,main = "Susceptible Cases over Time", xlab = "Number of
    weeks",
ylab ="Number of Susceptible cases (Ten Thousand)",
                col=2, pch=16,ylim=c(565,570))
 par(new=TRUE)
plot(time, out.df[,2],main = "Susceptible Cases over
    Time",xlab = "Number of weeks",
```

```
        ylab ="Number of Susceptible cases (Ten Thousand)", type='l', col=4,
              ylim=c(565,570))


legend("bottomleft", c("Model","Data"), lty=c(1,NA),pch=
    c(NA,16),col=c("blue","red"))
```