SISMID Exersice 1 – Solution

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Exercise 1.1 (Final Outbreak Size)

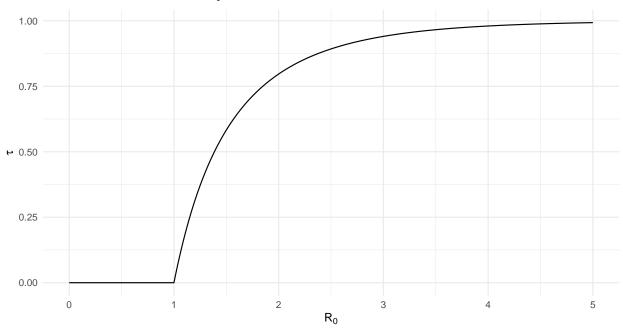
(a) Solve the final size equation. Create a function of R_0 solving for τ numerically.

```
# Function of R_0 solving for tau numerically
# R_0 - reproduction number
# tau - final size
# Return: tau
tau <- function(R_0) {
 final_eq <- function(tau) {</pre>
   ############################
   # give the expression here
   ##########################
   1 - tau - exp(-R_0 * tau)
 }
 Note: This final size equation is always a solution tau = 0.
 When R_0 <=1, it gives only one solution tau = 0;
 if R_0 > 1, then there are two solutions.
 result1 <- uniroot(final_eq, lower = 0, upper = 1)$root
 result2 <- uniroot(final_eq, lower = 1e-12, upper = 1, extendInt = "yes")$root
 # fill in here (minimum or maximum of result1 and 2 or others?)
 result <- max(result1, result2)</pre>
 return(result)
```

Compute and plot τ against $R_0 \in [0, 5]$:

```
RO_{vec} \leftarrow seq(from = 0, to = 5, length.out = 10000)
# Create a vector of the corresponding values of tau
tau_vec <- as.vector(10000)</pre>
for (i in 1:10000) {
 RO <- RO vec[i]
 # fill in here (use the previous function tau(...))
 tau vec[i] \leftarrow tau(R \ 0 = R0)
 }
# Create a plot of tau against RO
ggplot(mapping = aes(x = RO_vec, y = tau_vec)) +
 geom_line() +
 xlab(expression("R"[0])) +
 ylab(expression(tau)) +
 ggtitle(expression("Final size as a function of R"[0])) +
 theme_minimal()
```

Final size as a function of R₀



(b) Now suppose there is a fraction r of initially immune, then the final fraction infected among the initially susceptible. Create a function of R_0 and r solving for τ numerically

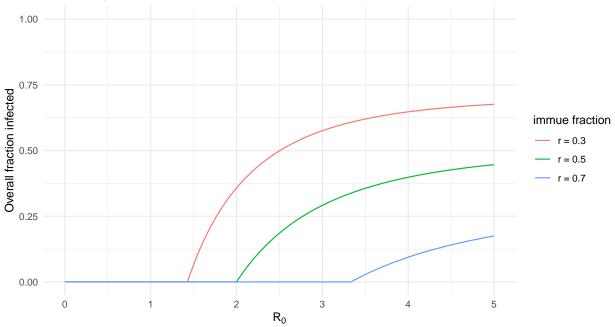
```
tau_overall <- function(R_0, r) {</pre>
 final eq <- function(tau) {</pre>
   #############################
      YOUR CODE HERE
   ##########################
   # give the equation
   1 - \tan - \exp(-R_0 * (1 - r) * \tan)
 }
 Note: This final size equation only gives the fraction infected among
 those who are initially susceptible.
 result1 <- uniroot(final_eq, lower = 0, upper = 1)$root
 result2 <- uniroot(final_eq, lower = 1e-12, upper = 1, extendInt = "yes")$root
 # fill in here (minimum or maximum or others?)
 result <- max(result1, result2)</pre>
 Note: this result is the final size among initially susceptibles.
 then what is the overall fraction infected?
 # fill in here (here we want the OVERALL fraction infected!)
 return(result * (1 - r))
}
```

Compute and plot τ against $R_0 \in [0, 5]$ for r = 0.3, 0.5, 0.7.

```
# Plot the overall final size of R_O in [0,5]
# in three cases: r = 0.3, 0.5, 0.7
# Create a vector of 10000 RO values between 0.00001 and 5
RO_{vec} \leftarrow seq(from = 0, to = 5, length.out = 10000)
df_tau_r <- data.frame(RO = RO_vec)</pre>
# Create a vector of the corresponding values of tau for r = 0.3
tau_vec <- as.vector(10000)</pre>
r < -0.3
for (i in 1:10000) {
 RO <- RO vec[i]
 tau_vec[i] \leftarrow tau_overall(R_0 = R0, r = r)
df_tau_r <- cbind(df_tau_r, overall_infected.3 = tau_vec)</pre>
# Create a vector of the corresponding values of tau for r = 0.5
tau_vec <- as.vector(10000)</pre>
r < -0.5
```

```
for (i in 1:10000) {
  R0 <- R0_vec[i]</pre>
  tau_vec[i] \leftarrow tau_overall(R_0 = R0, r = r)
df_tau_r <- cbind(df_tau_r, overall_infected.5 = tau_vec)</pre>
###########################
# YOUR CODE HERE
#############################
# As in the codes for r = 0.3 and 0.5, create a vector of the corresponding
# values of tau for r = 0.7, and consider it as the column in the data frame
\# "df_tau_r" , with name "overall_infected.7".
# Create a vector of the corresponding values of tau for r = 0.7
tau_vec <- as.vector(10000)</pre>
r < -0.7
for (i in 1:10000) {
 R0 <- R0_vec[i]</pre>
 tau_vec[i] \leftarrow tau_overall(R_0 = R0, r = r)
df_tau_r <- cbind(df_tau_r, overall_infected.7 = tau_vec)</pre>
# Create a plot of tau against RO in three cases
ggplot(df_tau_r) +
  geom_line(aes(x = R0, y = overall_infected.3, color = "r = 0.3")) +
  geom_line(aes(x = R0, y = overall_infected.5, color = "r = 0.5")) +
  geom\_line(aes(x = R0, y = overall\_infected.7, color = "r = 0.7")) +
  scale_color_discrete(name = "immue fraction") +
  labs(title = " Assuming there is a fraction r of initially immune") +
  ylab("Overall fraction infected") +
  xlab(expression("R"[0])) +
  ylim(0, 1) + theme_minimal()
```

Assuming there is a fraction r of initially immune



Exercise 1.2 (Determinstic and stochastic SIR Model)

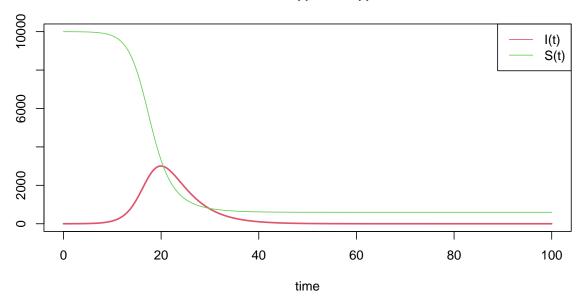
(a) Consider a continuous-time deterministic SIR model with parameter values. Create a function to compute the derivative of the ODE system for SIR Model.

```
# Function to compute the derivative of the ODE system for SIR Model:
\# S(t): number of susceptible
# I(t): number of infectives
\# dS(t) / dt = -beta / N * S(t) * I(t)
\# dI(t) / dt = beta / N * S(t) * I(t) - gamma * I(t)
\# t - time
# y - current state vector of the ODE at time t
# parms - Parameter vector used by the ODE system
# Returns:
# list containing dS(t)/dt and dI(t)/dt
# Parameter values
gamma <- 0.25
beta <- 0.75
# We assume a closed population of size
times \leftarrow seq(0, 100, length = 1000)
deter_sir <- function(t, y, parms) {</pre>
 beta <- parms[1]</pre>
 gamma <- parms[2]</pre>
```

Solve the SIR differential equation system with initial conditions: S(0) = N - 1, I(0) = 1:

Plot the curves of I(t) and S(t) over time:

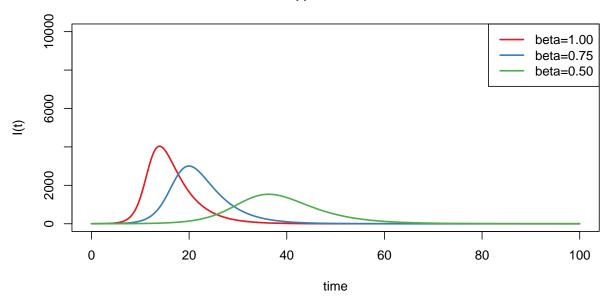
Plot of I(t) and S(t)



(b) Now fix $\gamma = 0.25$, but choose different values of $\beta = 1, 0.75$ and 0.25. In each case, solve the SIR differential equation system with initial condition (S(0) = N - 1, I(0) = 1). Plot the curves of I(t) and compare them.

```
# set a vector of different values of beta
beta.grid \leftarrow c(1, 0.75, 0.5)
# summarize the I(t) for each case of beta
I <- sapply(</pre>
 beta.grid,
 function(beta) {
   # YOUR CODE HERE, fill in the blank space
   # again, using lsoda(...) function solve the ODE, compute the I(t)
   lsoda(y = c(10000 - 1, 1), times = times, func = deter sir,
         parms = c(beta, gamma, N = 10000))[, 3]
# plot the three curves of I(t)
pal <- brewer.pal(length(beta.grid), "Set1")</pre>
matplot(times, I, type = "l", lwd = 2, lty = 1, col = pal,
       xlab = "time", ylab = "I(t)", ylim = c(0, 10000))
legend(x = "topright", paste("beta=", sprintf("%.2f", beta.grid), sep = ""),
      lty = 1, lwd = 2, col = pal)
title("Plot of I(t) for different beta")
```

Plot of I(t) for different beta



(c) Now the rate β depends on time when different measures take place. Create a function to compute the derivative of the ODE system for the SIR Model with beta(t).

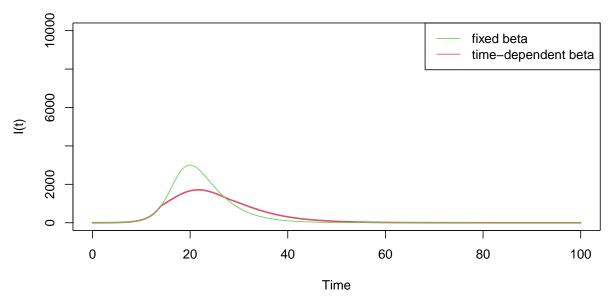
```
sir_change <- function(t, y, parms) {</pre>
 beta0 <- parms[1]
 beta1 <- parms[2]</pre>
 beta2 <- parms[3]</pre>
 t1 <- parms[4]
 t2 <- parms[5]
 gamma <- parms[6]</pre>
 S \leftarrow y[1]
 I \leftarrow y[2]
 # YOUR CODE HERE, fill in the blank space
 # create a time-dependent rate \beta(t) as function of t
 beta <- function(t) {</pre>
   ifelse(t <= t1, beta0, ifelse(t > t2, beta2,
   ))
 }
 return(list(c(
   S = -beta(t) / N * S * I, # list containing dS(t)/dt
   I = beta(t) / N * S * I - gamma * I
 ))) # and dI(t)/dt
```

```
# set the paramter values
beta0 <- 0.75
beta1 <- 0.65 * 0.75
beta2 <- 0.75 * 0.75
t1 <- 14
t2 <- 28
gamma <- 0.25
N <- 10000
time <- seq(0, 100, length = 1000)</pre>
```

Solve the changed SIR differential equation system with initial conditions: S(0) = N - 1, I(0) = 1.

Plot the curves of I(t) for fixed beta and time-dependent beta.

Plot of I(t) in SIR model with fixed and time-dependent



(d) Here we turn our focus to stochastic SIR model in continuous time. Always assume that there are fraction c = 10% of initial infectives.

Simulate simple SIR model using the Gillespie-Algorithm.

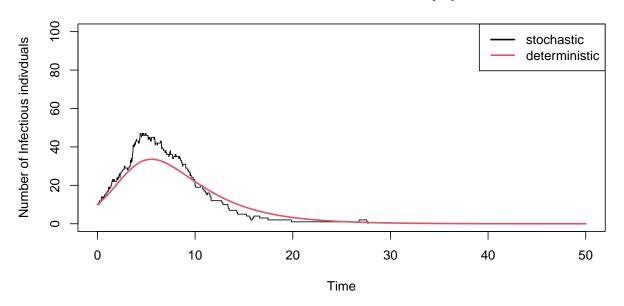
```
# Params:
 [0,T] - time horizon
# beta - infection rate
 gamma - recovery rate
# n - initial number of susceptibles.
# m - initial number of infectives
stoch_SIR <- function(T, beta, gamma, n, m, N) {</pre>
 # Initialize (x= number of S, y=number of I, t=event time)
 x <- n
 y <- m
 z \leftarrow 1
 t <- 0
 N \leftarrow n + m
 # Possible events: Infection(S->I) and Removal(I->R)
 eventLevels <- c("S->I", "I->R")
 # Initialize result
 df_SIR <- data.frame(t = t, x = x, y = y, totalinfected = z, event = NA)
 # Loop until time T or the epidemic stops(there is no infectives)
 while (t < T & (y > 0)) {
   # YOUR CODE HERE, fill in the blank space
```

```
# Draw the waiting type for each possible event
  wait \leftarrow rexp(2, c(
   "S->I" = beta / N * x * y, # here insert the rate for "S->I"
    "I->R" = gamma * y # the rate for "I->R"
  ))
  From those two rates, we draw two exponential
  random numbers for each possible event
  # Determine which event occurs first
  # i.e. the event with the smaller or bigger random number?
  # which.min(wait) or which.max(wait)?
  i <- which.min(wait)</pre>
  # Record Event Time
  t <- t + wait[i]
  \# Update the number of S and I according to the event type
  # if an infection occurs,
  if (eventLevels[i] == "S->I") {
    x \leftarrow x - 1 # the number of S will decrease by 1.
    # what happen to y, z?
    y < -y + 1
    z < -z + 1
  # if an recovery occurs,
  if (eventLevels[i] == "I->R") {
    # what happen to x, y, z?
    y <- y - 1
  }
  # Store result
  df_SIR <- rbind(df_SIR, c(t, x, y, z, i))</pre>
# Re-code event type and return
df_SIR$event <- factor(eventLevels[df_SIR$event], levels = eventLevels)</pre>
return(df_SIR)
```

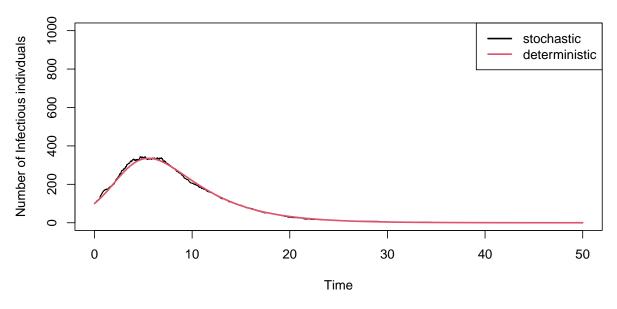
Plot I(t) for one simulated stochastic epidemic and deterministic limit for different size of population N = 100, 1000 and 10000.

```
gamma <- 0.25
Tmax <- 50 \# time limit
c <- 0.1 # initial infectious fraction
compare_DS <- function(N) {</pre>
  # do one simulated stochastic epidemic
 traj <- stoch_SIR(T = Tmax, beta = beta, gamma = gamma,</pre>
                    n = N * (1 - c), m = N * c, N = N)
  # plot the stochastic curve of I
 plot(traj$t, traj$y,
   type = "s", ylim = c(0, N), xlab = "Time",
   ylab = "Number of Infectious indivduals", xlim = c(0, Tmax), col = 1
  # Solve the deterministic ODE
  solution <- lsoda(</pre>
   y = c(N * (1 - c), N * c),
   times = seq(0, Tmax, length = 1000),
   func = deter_sir,
   parms = c(beta, gamma, N = N)
 # add the deterministic curve of I
 lines(solution[, "time"], solution[, 3], col = 2, lwd = 2)
## Compare deterministic and stochastic for different N
set.seed(123)
compare_DS(N = 100)
legend(x = "topright", c("stochastic", "deterministic"),
       col = c(1, 2), lty = 1, lwd = 2)
title("Stochastic vs. Deterministic when size of population = 100")
```

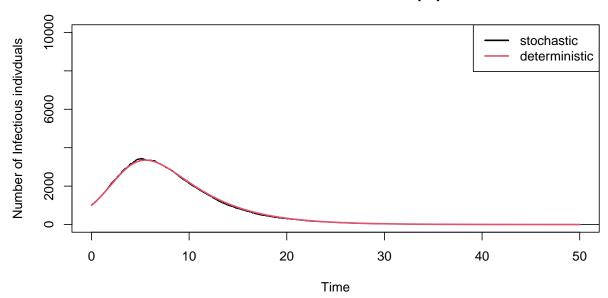
Stochastic vs. Deterministic when size of population = 100



Stochastic vs. Deterministic when size of population = 1000



Stochastic vs. Deterministic when size of population = 10000



(e) Let $\beta = 0.375$ and $\gamma = 0.25$.(implying that $R_0 = 1.5$), do 5000 simulations in three cases when the size of population N = 500, 1000 and 5000 with one initial infective.

Stochastic SIR model create a function final size.

```
# Draw the waiting type for each possible event
  wait \leftarrow \text{rexp}(2, c("S->I" = \text{beta} / N * x * y, "I->R" = \text{gamma * y}))
  # Determine which event occurs first
  i <- which.min(wait)</pre>
  # Record Event Time
  t <- t + wait[i]
  \# Update the number of S and I according to the event type
  if (eventLevels[i] == "S->I") {
    x <- x - 1
    y < -y + 1
   z < -z + 1
  } # if infection
  if (eventLevels[i] == "I->R") {
    y < -y - 1
  } # if recovery
return(z) # return the number of recovered
```

Do 5000 simulations with different size of community N.

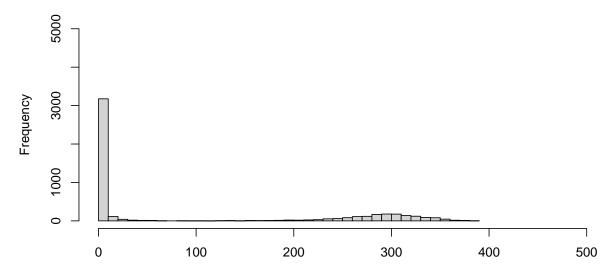
```
# YOUR CODE, fill in the blank space
# set parameter values:
beta <- 0.375
gamma <- 0.25
Tmax <- 500 # time limit [0,500]
IO <- 1
nSim <- 5000 # number of simulations
compare_hist <- function(N) {</pre>
 df_fsize <- data.frame(sim = NA, totalinfected = NA)</pre>
 for (i in 1:nSim) {
   z <- fsize_SIR(T = Tmax, beta = beta, gamma = gamma,
                n = N - IO, m = IO, N = N)
   df_fsize <- rbind(df_fsize, c(i, z))</pre>
 }
 return(df_fsize$totalinfected)
```

Make a histogram of the final size distribution in each case. Give your comments.

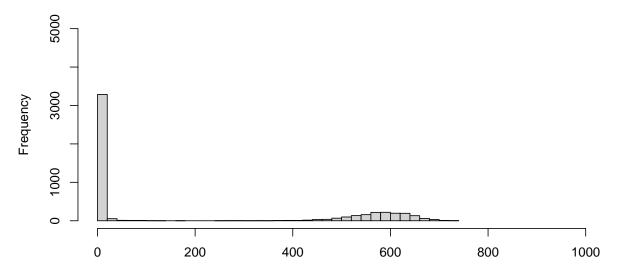
```
N <- 500
hist(compare_hist(N = 500),
  breaks = 50,
  main = "Histogram of final size when N=500",
  xlab = "",
  xlim = c(0, N),</pre>
```

```
ylim = c(0, nSim)
)
```

Histogram of final size when N=500

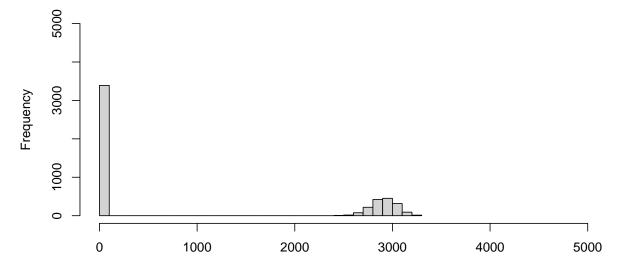


Histogram of final size when N=1000



```
hist(compare_hist(N = 5000),
  breaks = 45, main = "Histogram of final size when N=5000",
  xlab = "", xlim = c(0, 5000), ylim = c(0, 5000)
)
```

Histogram of final size when N=5000

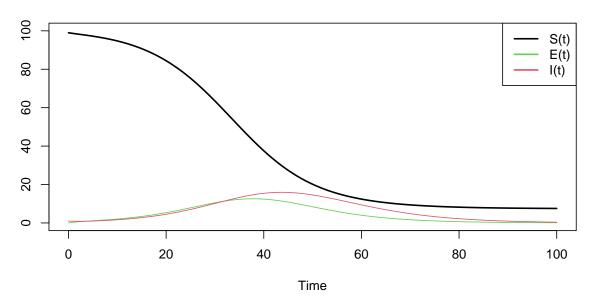


Exercise 1.3 (SEIR Model)

(a)

```
# YOUR CODE HERE, fill in the blank space
# do the same way as for SIR model, but with four states: S E I R
# Function to compute the derivative of the ODE system for SEIR Model
\# t - time
# y - current state vector of the ODE at time t
# parms - Parameter vector used by the ODE system
# Returns:
# list containing dS(t)/dt, dE(t)/dt, and dI(t)/dt
seir <- function(t, y, parms, N) {</pre>
 beta <- parms[1]</pre>
 rho <- parms[2]</pre>
 gamma <- parms[3]</pre>
 N <- parms[4]
 S \leftarrow y[1]
 E \leftarrow y[2]
 I \leftarrow y[3]
 return(list(c(S = -beta / N * S * I, E = beta / N * S * I - rho * E,
             I = \text{rho} * E - \text{gamma} * I)))
}
# Parameter Values:
times <- seq(0, 100, length = 1000)
gamma \leftarrow 1 / 7
beta <- 0.4
rho <- 1 / 5
IO <- 1
N <- 100
# Solve the ODE and plot
sol_seir <- lsoda(</pre>
 y = c(N - 10, 0, 10), # insert the corresponding initial conditions
 times = times,
func = seir,
 parms = c(beta, rho, gamma, N)
plot(times, sol_seir[, 2],
 type = "1", lwd = 2, col = 1, xlab = "Time",
 ylab = "", xlim = c(0, 100), ylim = c(0, N)
```

Plot of S(t), E(t) and I(t)



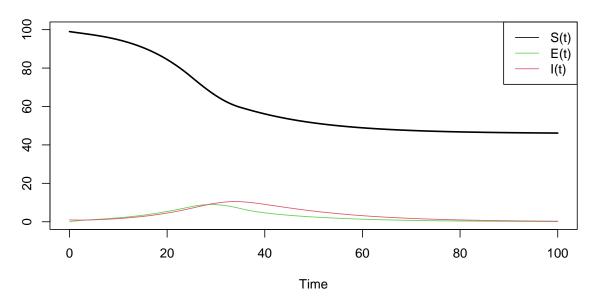
(b) Modify the SEIR model such that $\beta(t)$ becomes a time-dependent function. Create a function to compute the derivative of the ODE system for SEIR Model with changing point.

```
# YOUR CODE HERE, fill in the blank space
#
 t - time
 y - current state vector of the ODE at time t
 parms - Parameter vector used by the ODE system
# Returns:
# list containing dS(t)/dt, dE(t)/dt, and dI(t)/dt
seir_change <- function(t, y, parms, N) {</pre>
 beta0 <- parms[1]
 beta1 <- parms[2]
 t1 <- parms[3]
 w <- parms[4]
 rho <- 1 / 5
 gamma <- parms[5]</pre>
 N <- parms[6]</pre>
```

Take $t_1 = 30, w = 5, \beta_0 = 0.4$ and $\beta_1 = 0.12$, solve the ODE system for the SEIR model with time-varying transmission rate in part (b) numerically using R command 1soda and plot S(t), E(t) and I(t) for $t \in [0, 100]$.

```
# YOUR CODE HERE, fill in the blank space
# set the parameter values: such as
beta0 <- 0.4
beta1 <- 0.12
t1 <- 30
w <- 5
gamma <- 1 / 7
N < -100
IO <- 1
time \leftarrow seq(0, 100, length = 1000)
# solve the ODE system for the changed SEIR model
sol_SEIRchange <- lsoda(</pre>
 y = c(N - I0, 0, I0),
 times = time, func = seir_change,
 parms = c(beta0, beta1, t1, w, gamma, N)
# plot curves of S(t), E(t) and I(t)
plot(times, sol_SEIRchange[, 2],
 type = "1", lwd = 2, col = 1, xlab = "Time",
 ylab = "", xlim = c(0, 100), ylim = c(0, 100)
lines(times, sol_SEIRchange[, 3], col = 3)
lines(times, sol_SEIRchange[, 4], col = 2)
legend(x = "topright", c("S(t)", "E(t)", "I(t)"), col = c(1, 3, 2), lty = 1)
title("Plot of S(t), E(t) and I(t) in SEIR model with time-dependent beta(t)")
```

Plot of S(t), E(t) and I(t) in SEIR model with time-dependent beta(t)



(d) Now for N = 100, 1000 and 10000, do one simulation of the stochastic SEIR epidemic starting from fraction infected 10% with exponentially distributed incubation period with mean 5 days and the above time-changing $\beta(t)$. Overlay it on the plot of the deterministic curve as done in Exercise 2.

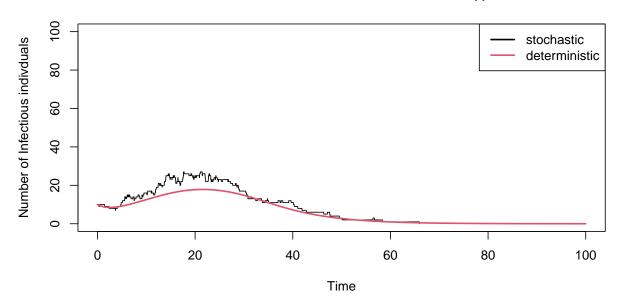
Simulate a stochastic SEIR epidemic model.

```
# YOUR CODE HERE, fill in the blank space
# Params:
  [O,T] - time horizon
 beta - infection rate
  gamma - recovery rate
 rho - rate of (E -> I)
 n - initial number of susceptibles.
 m - initial number of infectives, here m=1
 three events: "S \rightarrow E", "E \rightarrow I", "I \rightarrow R"
stoch_SEIR <- function(T, n, m, parms, N) {</pre>
 beta0 <- parms[1]
 beta1 <- parms[2]
 t1 <- parms[3]
 w <- parms[4]
 gamma <- parms[5]</pre>
 rho <- parms[6]</pre>
```

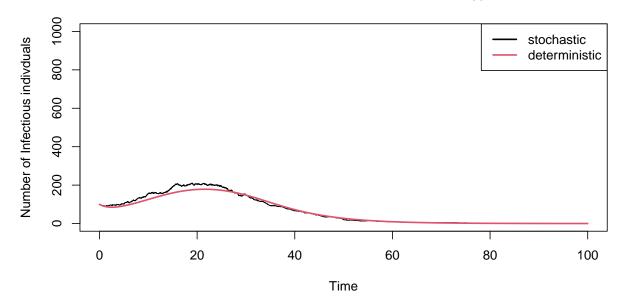
```
N <- parms[7]
  # write the function for beta(t)
  beta <- function(t) {</pre>
    ifelse(t \leq t1 - w, beta0, ifelse(t > t1 + w, beta1,
      beta0 + (beta1 - beta0) / (2 * w) * (t - (t1 - w))
    ))
  # Initialize (x= number of S, y=number of I, z=number of E, t=event time)
  x <- n
 y <- m
 z <- 0
 time \leftarrow 0
  # Possible events:
  eventLevels \leftarrow c("S->E", "E->I", "I->R")
  # Initialize result
  df_SEIR \leftarrow data.frame(time = time, x = x, y = y, z = z, event = NA)
  # Loop until time T or the epidemic stops(there is no infectives)
  while (time < T & (y > 0)) {
    # Draw the waiting type for each possible event
    b <- beta(time)</pre>
    wait <- rexp(3, c("S->E" = b / N * x * y,
                       "E->I" = rho * z, "I->R" = gamma * y))
    # Determine which event occurs first
    i <- which.min(wait)</pre>
    # Record Event Time
   time <- time + wait[i]</pre>
    # Update the number of S, I, E according to the event type
    if (eventLevels[i] == "S->E") {
     x < -x - 1
     z < -z + 1
    }
    if (eventLevels[i] == "E->I") {
     z < -z - 1
      y < -y + 1
    if (eventLevels[i] == "I->R") {
      y <- y - 1
    # Store result
    df_SEIR <- rbind(df_SEIR, c(time, x, y, z, i))</pre>
  # Re-code event type and return
 df_SEIR$event <- factor(eventLevels[df_SEIR$event], levels = eventLevels)</pre>
 return(df_SEIR)
}
```

```
beta0 <- 0.4
beta1 <- 0.12
t1 <- 30
w <- 5
gamma <- 1 / 7
rho <- 1 / 5
c <- 0.1
compare_ds_seir <- function(N) {</pre>
  beta <- function(t) {</pre>
    ifelse(t \leq t1 - w, beta0, ifelse(t > t1 + w, beta1,
      beta0 + (beta1 - beta0) / (2 * w) * (t - (t1 - w))
    ))
  }
  # Do stochastic simulations
  set.seed(123)
  traj \leftarrow stoch_SEIR(T = 100, n = N * (1 - c), m = N * c,
                     parms = c(beta0, beta1, t1, w, gamma, rho, N))
  # plot stochastic I(t)
  plot(traj$time, traj$y,
   type = "s", ylim = c(0, N), xlab = "Time",
    ylab = "Number of Infectious indivduals", xlim = c(0, 100), col = 1
  # Solve the deterministic ODE
  solution <- lsoda(</pre>
   y = c(N * (1 - c), 0, N * c), times = seq(0, 100, length = 1000),
   func = seir_change, parms = c(beta0, beta1, t1, w, gamma, N)
  lines(solution[, "time"], solution[, 4], col = 2, lwd = 2)
  invisible()
}
```

stochastic vs deterministic for SEIR model with beta(t) when N = 100



stochastic vs deterministic for SEIR model with beta(t) when N = 1000



stochastic vs deterministic for SEIR model with beta(t) when N = 10000

