Susceptible-Infectious-Recovered modelling

A well-known mathematical model to describe the dynamics of an infectious disease in a population is the so called susceptible-infectious-recovered (SIR) compartment model (Kermack and McKendrick 1927). This model assumes that each individual in the population population belongs to one of three states:

- *S*usceptible: the individual has not yet had the disease, but is not immune to the disease and thus can become infectious when having an infectious contact with an infected individual
- *I*nfectious: a person currently affected by the disease and able to transmit the disease to others
- *R*ecovered: an infectious person who is not affected anymore by the disease and not able to transmit the disease anymore. No re-infection can occur, i.e. recovered individuals are immune to the disease once they had it.

It is assumed that at time zero everyone is susceptible except for m individuals, which are infectious at time zero. Once infected an individual becomes infectious and then recovers. Mathematically, we shall by $S(t)$, $I(t)$ and $R(t)$ denote the number of susceptible, infectious and recovered in the population at time t. Furthermore, it is assumed that the population consists of a constant number of N individuals and at all times $S(t)+I(t)+R(t)=N$. In other words the population is closed and does not vary over time.

The dynamics in the number of susceptibles, infectious and recovered are now described using the following deterministic ordinary differential equation (ODE) system:

$$
\begin{eqnarray*}
\frac{dS(t)}{dt} &=& -\beta S(t) I(t), \\
\frac{dI(t)}{dt} &=& \beta S(t) I(t) – \gamma I(t), \\
\frac{dR(t)}{dt} &=& \gamma I(t).
\end{eqnarray*}
$$

What does this mean? It denotes the movement of individuals between the three categories, in particular the movement from $S\rightarrow I$ and $I \rightarrow R$. The most important term in the equation system is $\beta S(t) I(t)$ and can be motivated as follows: Consider one specific infectious individual at time t, this individual meets a specific other person in the population at the rate of β contacts per time unit (say day). It is assumed that this rate is the same no matter which other person we talk about (aka. homogeneous mixing in the population). Of course this is a very strong simplification, because it ignores, e.g., the distance between two individuals and that you tend to mix with more with peers. But in a large population, the average is a good description. Hence, the number of contacts with susceptible individuals per time unit is $\beta S(t)$. Now summing these contacts over all infectious individuals at time t leads to $\sum_{j=1}^{I(t)}\beta S(t) = \beta I(t) S(t)$. Note that this is a non-linear term consisting of both $I(t)$ and $S(t)$.

In the above process description,for the ease of exposition, it is assumed that once an infectious individual meets a susceptible person, then the disease is always transmitted from the infected to the susceptible person. Hence, the transmission probability does not depend on, e.g., how long the infectious individual has already been infectious. An equivalent way of formulating this statement is to say that each individual has contacts at rate α for meeting a specific other person, and a proportion p of these contacts results in an infection. Then $\beta = \alpha p$ is the rate at which infectious contacts occur.

The second component of the model is the term $\gamma I(t)$. Again considering one infectious individual it is assumed that the rate at which $I\rightarrow R$ transition occurs happens at the constant rate γ. This means that individuals are on average $1/\gamma$ days infectious before they recover from the disease. In other words: The smaller γ is the longer people are infectious and, hence, the longer they can transmit the disease to others. Note: Recovering from an epidemic modelling point of view does not distinguish between individuals which recover by becoming healthy or by dying – what is important is that they do not contribute to the spread of the disease anymore.

One important quantity, which can be derived from the above ODE equation system is the so called **basic reproduction number**, aka. R_0 and is defined as (Diekmann, Heesterbeek, and Britton 2013)

the expected number of secondary cases per primary case in a completely susceptible population. It is computed as** $R_0 = N \frac{\beta}{\gamma}$.

This means that if we consider the dynamics of a disease in generation time, i.e. in a time scale where one time unit is the time period between infection in the primary case and infection in the secondary case, then R_0 denotes the growth factor in the size of the population at the beginning of the outbreak. What is special about the beginning of the outbreak? Well, more or less all contacts an infectious individual has, will be with susceptible individuals. However, once a large part of the population has already been infected, then R_0 does not necessarily describe the expected number of cases per primary anymore. For the COVID-19 outbreak, since it is assumed that little immunity exists against the disease, all individuals will be susceptible and, hence, almost all contacts an infectious individual has, will be with susceptible persons. However, at a later stage in the epidemic, due to the depletion of susceptibles, the number of secondary cases since the population

Assuming $R(0)$ and letting $I(0)=m$ we obtain $S(0) = N-m$. We can use this initial configuration together with a numerical solver for ODEs as implemented, e.g., in the `lsoda` function of the R package `deSolve` (Soetaert, Petzoldt, and Setzer 2010). For this, we need to implement a function, which describes the derivative of the ODE system:

```
######################################################################
# Function to compute the derivative of the ODE system
#
#  t - time
#  y - current state vector of the ODE at time t
#  parms - Parameter vector used by the ODE system
#
# Returns:
#  list with one component being a vector of length two containing
#  dS(t)/dt and dI(t)/dt
######################################################################

sir <- function(t, y, parms) {
  beta <- parms[1]
  gamma <- parms[2]
  S <- y[1]
  I <- y[2]
  return(list(c(S = -beta * S * I, I = beta * S * I - gamma * I)))
}

# Population size
N <- 1e6
# Rate at which person stays in the infectious compartment (disease specific and
tracing specific)
gamma <- 1/5
# Infectious contact rate - beta = R0/N*gamma and when R0 \approx 2.25 then
2.25/N*gamma
beta <- 4.5e-07
# R0 for the beta and gamma values
R0 <- beta*N/gamma
```

Assuming a hypothetical population of $N = 1,000,000$ and a contact rate of $\beta = 0.0000004$ means that the contact rate with a given individual is 0.0000004 contacts per day. The choice of $\gamma = 0.2$ corresponds to an average length of the infective period of 5 days. Furthermore, assuming Altogether, this leads to an R_0 of 2.25, which roughly corresponds to the R_0 of SARS-CoV-2.

We can now solve the ODE system using the above parameters and an initial number of infectious of, say, 10:

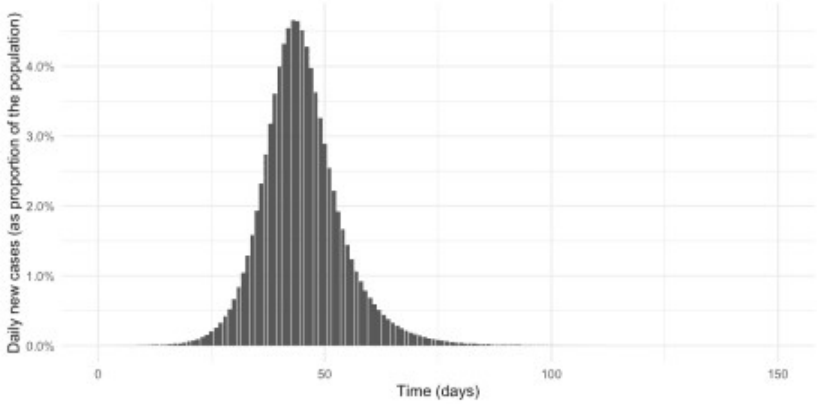
```
# Load package to numerically solve ODEs
suppressPackageStartupMessages(library(deSolve))

# Grid where to evaluate
max_time <- 150
times <- seq(0, max_time, by=0.01)

# Solve ODE system using Runge-Kutta numerical method.
ode_solution <- rk4(y = c(N - 10, 10), times = times, func = sir, parms =
c(beta, gamma)) %>%
    as.data.frame() %>%
    setNames(c("t", "S", "I")) %>%
    mutate(beta = beta, gama = gamma, R0 = N * beta / gamma, s = S / N, i = I /
N, type = "without_intervention")
```

Here we have introduced \(s(t) = S(t)/N\) and \(i(t) = I(t)/N\) as, respectively, the proportion of susceptible and infectious individuals in the population. Note that \(I(t)\) is the number of currently infectious persons. Since a person is usually infectious for more than one day this curve is not equivalent to the number of **new** infections per day. If interest is in this value, which would typically be what is reported by health authorities, this can be computed as \[
C(t) = \int_{t-1}^t \beta S(u) I(u) du.
\] or due to the SIR structure where re-infections are not possible simply as \(S(t-1) – S(t)\).

The epidemic curve of new infections per day is shown below:



Another important quantity of the model is an estimate for how many individuals are ultimately infected by the disease, i.e. \(1-s(\infty)\) in a population where initially everyone is susceptible to the disease. This can be either calculated numerically from the above numerical solution as:

```
(1 - tail(ode_solution, n=1) %>% pull(s))
```

```
## [1] 0.8534244
```

or by numerically solving the following recursive equation (Diekmann, Heesterbeek, and Britton 2013, 15): \[
s(\infty) = \exp(-R_0 (1-s(\infty)))
\] This can be solved in R using:

```
# Function to compute the final size.
s_inf <- function(R0) {

  f_target <- function(x) { x - exp(-R0*(1-x)) }

  result <- uniroot(f_target, lower=1e-12, upper=1-1e-12)$root

  return(result)
}
```

```
# Final proportion of infected.
1 - s_inf(R0)
```

```
## [1] 0.8534382
```

We can use the above equation to verify that the larger \(R_0\), the larger is the final size of the outbreak:

```
R0_grid <- c(1.25, 1.5, 1.75,2, 2.25, 2.5, 3)
map_dbl( R0_grid, ~ 1-s_inf(.x)) %>% setNames(R0_grid) %>%
scales::percent(accuracy=1)
```

```
##  1.25   1.5  1.75     2  2.25   2.5     3
## "37%" "58%" "71%" "80%" "85%" "89%" "94%"
```

However, despite a value of \(R_0>1\), not the entire population will be infected, because of the depletion of susceptibles. Hence, the exponential growth rate interpretation of \(R_0\) is only valid at the beginning of an outbreak.

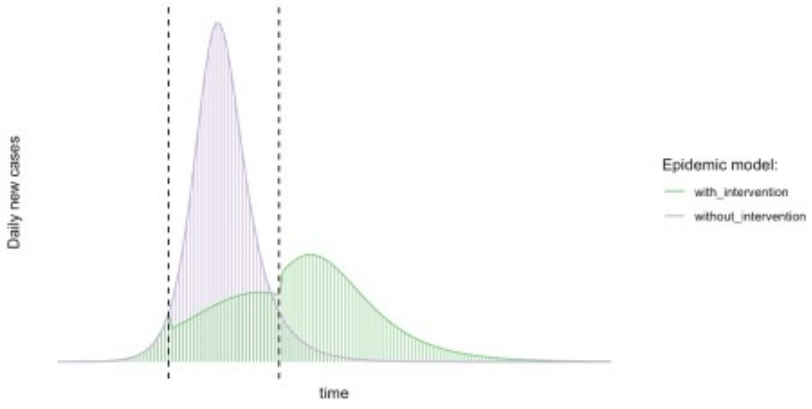
Reducing \(R_0\)

As we could see from the equation defining \(R_0\) in our simple SIR-model, there are two ways to reduce the \(R_0\) of a disease:

1. Reduce the number of contacts persons have with each-other, i.e. make \(\beta\) smaller
2. Reduce the duration for how long people are effectively spreading the disease (e.g. by quarantine), i.e. reduce the average duration \(\gamma\) of how long infectious individuals can infect others.

For simplicity we shall only be interested in the first case and let's purse the following simple strategy, where the measures only depend on time:

\[
\beta(t) =
\left\{
\begin{array}{}
\beta_0 & \text{if } t\leq t_1, \\
\beta_1 & \text{if } t_1 < t\leq t_2, \\
\beta_2 & \text{if } t_2 < t
\end{array}
\right.
\] where \(\beta_0\) is the ordinary \(\beta\) value of the disease. We will use a drastic reduction of the contacts within the interval \([t_1, t_2]\) and thus \(\beta_1 < \beta_0\). After some time, the control measures are reduced slightly, i.e. \(\beta_1 < \beta_2 < \beta_0\). We shall use \(\beta_1 = r_1 \beta_0\) and \(\beta_2 = r_2 \beta_0\) with \(r_1 \leq r_2\). The two epidemic curves can now be plotted as follows:



The final size in the two cases:

```
## # A tibble: 2 x 2
```

```
## # Groups:   type [2]
##   type                final_fraction
##
## 1 without_intervention 85%
## 2 with_intervention    68%
```

Here we used the rather conservative estimate that \(R_0\) can be reduced by 60% to 1.35 for a few weeks, after the reduction is 80% of the original \(R_0\), i.e. 1.8. Things of course become more optimistic, the larger the reduction is. One trap is though to reduce \(R_0\) drastically and then lift the measures too much – in this case the outbreak is delayed, but then almost of the same peak and size, only later.

The simple analysis in this post shows that the final size proportion with interventions is several percentage points smaller than without interventions. The larger the interventions, if done right and timed right, the smaller the final size. In other words: the spread of an infectious disease in a population is a dynamic phenomena. Time matters. The timing of interventions matters. If done correctly, they stretch the outbreak and reduce the final size!

Discussion

The epidemic model based approaches to flatten the curve shows that the effect of reducing the basic reproduction number is not just to stretch out the outbreak, but also to limit the size of the outbreak. This is an aspect which seems to be ignored in some visualizations of the effect.

The simple SIR model used in this post suffers from a number of limitations: It is a deterministic construction averaging over many stochastic phenomena. However, at the large scale of the outbreak we are now talking about, this simplification appears acceptable. Furthermore, it assumes homogeneous mixing between individuals, which is way too simple. Dividing the population into age-groups as well as their geographic locations and modelling the interaction between these groups would be a more realistic reflection of how the population is shaped. Again, for the purpose of the visualization of the flatten-the-curve effect again I think a simple model is OK.…