Computation of the basic reproduction number

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These notes are meant as a handout for the lectures and are not complete lecture notes. You should also read the chapter on $R_0$ in the Springer lecture notes.

1 The basic reproduction number

1.1 Definition

1.1.1 The basic reproduction number

$R_0$, is the expected number of secondary infections produced by an index case in a completely susceptible population[1, 2].

Computations of $R_0$ typically involve products of infection rates and durations of infection.

$$R_0 = \text{(Rate of secondary infection)} \times \text{(duration of infection)}$$

There are three aspects of this number to explore:

1. the distribution of the infectious period;
2. structure of the host population
   - age
   - behaviour
   - treatment
   - multiple species (vector host)
   - heterogeneities in space.
3. dynamics of the disease-free population.

1.2 Age of infection

1.2.1 Age of infection models

The simplest approach to modelling the infectious period is as follows:

- Let $S_t$ be the number of susceptible individuals at time $t$.
- Let $I_{t\tau}$ be the number of infectious individuals at time $t$ who have been infectious since time $t - \tau$. We say these individuals have disease-age $\tau$.
- Let $\beta_{t\tau}$ be the rate of infectivity for an infectious individual of disease-age $\tau$. The rate new infections appear at time $t$ is assumed to be

$$\text{incidence} = S_t \sum_{\tau=0}^{\infty} \beta_{t\tau} I_{t\tau},$$

since this rate must be proportional to both the number of infectious individuals and the number of remaining susceptibles. This assumes that all infections are independent and that the population is homogeneously mixing.
Let \( B_{\tau} \) be the probability of an individual surviving to a disease-age of at least \( \tau \).

The basic reproduction number follows from summing up the number of secondary infections produced by a cohort of initially infected individuals, that is, we assume that \( I_{t\tau} = I_0 B_{\tau} \) for some constant \( I_0 \). Since all individuals in the cohort we are following have the same disease-age at any time \( t \), the rate secondary infections arise from contacts with these individuals is simply \( S_t \beta_t I_0 B_{\tau} \). Now suppose that the population is large enough that we can ignore the small change in \( S_t \) during the infectious period of the \( I_0 \) index cases. Summing the secondary infections over the infectious period, with \( I_0 = 1 \), gives the basic reproduction number.

\[
R_o = S_0 \sum_{\tau=0}^{\infty} \beta_{\tau} B_{\tau}.
\]

This sum gives the mean infectivity, or the expected number of secondary infections for a single infectious individual in a disease-free population.

If time is continuous, we write the basic reproduction number as

\[
R_o = S_0 \int_0^{\infty} \beta(\tau) B(\tau) d\tau.
\]

### 1.3 Compartmental ODE models

#### 1.3.1 Compartmental ODE models

- Suppose the infection is divided into \( n \) disease stages, or compartments.
- Let \( x(t) \) be the vector of populations in each stage.
- Assume the total population is large, and that the total number of infected individuals is small, so that we may assume the number of susceptible hosts is roughly constant.

\[
x'(t) = Fx(t) - Vx(t),
\]

- The \((i, j)\) entry of the transition matrix \( V \) is the rate individuals in stage \( j \) progress to stage \( i \).
- The \((i, j)\) entry of the infection matrix \( F \) is the number of new infections at stage \( j \) caused by contacts with diseased individuals in stage \( i \).

#### 1.3.2 The transition matrix \( V \)

- Progression through the disease states is modelled by the differential equations

\[
x'(t) = -Vx(t).
\]

- Integrating \( x \) gives the expected times individuals spend in each compartment

\[
\int_0^{\infty} x(t) \, dt = V^{-1}x(0).
\]

- The \((i, j)\) entry of \( V^{-1} \) is the expected time spent in compartment \( i \) by an individual initially in compartment \( j \) over the course of its infection.
Note that $x(0)$ is an initial cohort of infected individuals, or index cases. If $x(0)$ is normalized so that each entry is a fraction, then $x_i(t)$ is the fraction of the initial cohort in compartment $i$ after a time $t$, or the probability a given member of the cohort is in compartment $i$ at time $t$. Thus integrating $x(t)$ gives expected times, conditional on the initial distribution $x(0)$.

1.3.3 The basic reproduction number as an eigenvalue

- If $x(t)$ is the distribution of the initial cohort at time $t$, and $F$ is a matrix of infection rates, then the expected number of secondary infections is

$$\int_0^\infty Fx(t) \, dx = FV^{-1}x(0) = Kx(0).$$

- The $(i,j)$ entry of the next generation matrix $K = FV^{-1}$ is the expected number of secondary infections produced in compartment $i$ by an index case initially in compartment $j$.

- $K$ has a positive real eigenvalue $R_0$, which is at least as large in modulus as all other eigenvalues of $K$. This eigenvalue is the logical candidate for the basic reproduction number.

Due to the nature of $V$ and $F$, the next generation matrix $K$ will always be a nonnegative matrix, and the theory of such matrices guarantees the existence of a positive eigenvalue whose modulus is at least as large as all other eigenvalues. Mathematically and ecologically, it makes sense to use this eigenvalue as the basic reproduction number[4].

2 Examples

2.1 SEIR-like models

As a simple first example, suppose all new infections arise in the first stage, so that the only nonzero entries in the matrix $F$ are in the first row. In this case, the only nonzero entries of $K$ will also be in the first row, and the only nonzero eigenvalue of $K$ is its $(1,1)$ entry. This entry is the scaler product of the first row of $F$ with the first column of $V^{-1}$ and is the sum of the products of the rates of infection and sojourn times for each compartment.

2.1.1 The SEIR model

$$S' = -\beta SI$$
$$E' = \beta SI - \kappa L$$
$$I' = \kappa E - \alpha I$$
$$R' = f \alpha I$$

Here $\kappa$ is the rate of progression from the latent stage $E$ to the infectious stage $I$, $\alpha$ is the rate of progression from the infectious stage to the removed stage $R$, $\mu$ is the mortality rate from natural causes and $\delta$ is the additional rate of disease-induced mortality. In the initial stages
of the epidemic, we can assume $S$ is near the disease-free value $S_0$ and approximate the middle two equations for $E$ and $I$ with the linear system

$$
\begin{pmatrix}
E' \\
I'
\end{pmatrix} =
\begin{pmatrix}
0 & \beta S_0 \\
0 & 0
\end{pmatrix}
\begin{pmatrix}
E \\
I
\end{pmatrix} -
\begin{pmatrix}
(k + \mu) & 0 \\
-\kappa & (\alpha + \mu + \delta)
\end{pmatrix}
\begin{pmatrix}
E \\
I
\end{pmatrix}

$$

In this linearization, we have separated the dynamics into two parts. The first matrix is a matrix of infection rates, and the second matrix is a matrix of transition rates.

### 2.1.2 $K$ and $R_0$ for the SEIR model

For the simple SEIR model, it is straightforward to compute $V^{-1}$. Doing so we find

$$
V^{-1} =
\begin{pmatrix}
1 & 0 \\
\kappa & 0 \\
0 & \kappa \\
(\kappa + \mu)(\alpha + \mu + \delta) & 1
\end{pmatrix},
$$

and

$$
K =
\begin{pmatrix}
\beta S_0 \kappa & \beta S_0 \\
(\kappa + \mu)(\alpha + \mu + \delta) & \alpha + \mu + \delta
\end{pmatrix}.
$$

This matrix has a single nonzero eigenvalue:

$$
R_0 = \frac{\beta S_0 \kappa}{(\kappa + \mu)(\alpha + \mu + \delta)}.
$$

### 2.1.3 The SLIAR model

The SLIAR model for influenza consists of five compartments: susceptible (S), latent (L), infectious (I), asymptomatic (A) and removed (R). Only the middle three of these are considered disease states, so $x = (L, I, A)$. Infection and progression through the disease states is summarized in the following diagram.

![Diagram](image)

The model consists of the following system of differential equations, together with nonnegative initial conditions:

$$
\begin{align*}
S' &= -\beta S (\epsilon L + I + \delta A) \\
L' &= \beta S (\epsilon L + I + \delta A) - \kappa L \\
I' &= p\kappa L - \alpha I \\
A' &= (1 - p)\kappa L - \eta A \\
R' &= f\alpha I + \eta A
\end{align*}
$$
New infections occur during contacts between susceptible individuals and individuals in any of the infected compartments, L, I or A. The incidence term is a sum of products of $S$ with $L$, $I$ and $A$, with $\epsilon$ and $\delta$ being the relative infectiousness of latent and asymptomatic infections. Technically, the term ‘latent’ only applies if $\epsilon = 0$; otherwise, with $0 < \epsilon < 1$, L represents a first, partially infectious stage, and I a later, fully infectious stage.

The matrix $V$ is given by

$$V = \begin{pmatrix} \kappa & 0 & 0 \\ -p\kappa & \alpha & 0 \\ -(1-p)\kappa & 0 & \eta \end{pmatrix},$$

and

$$F = \begin{pmatrix} \epsilon\beta S_0 & \beta S_0 & \delta\beta S_0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} V^{-1} = \begin{pmatrix} 1/\kappa & 0 & 0 \\ p/\alpha & 1/\alpha & 0 \\ (1-p)/\eta & 0 & 1/\eta \end{pmatrix}.$$

$$R_o = \beta S_0 \left( \frac{\epsilon}{\kappa} + \frac{p}{\alpha} + \frac{\delta(1-p)}{\eta} \right).$$

The reproduction number is a sum of products of the infection rates $\epsilon\beta S_0$, $\beta S_0$ and $\delta\beta S_0$ and the sojourn times $1/\kappa$, $p/\alpha$ and $(1-p)/\eta$. The factors $p$ and $(1-p)$ appear since these are the fractions of infected individuals that progress to the symptomatic and asymptomatics stages, respectively. That is, the expected time an infected individual spends in the I compartment is $p/\alpha$, since a fraction $p$ spend on average $1/\alpha$ times units in compartment I.

### 2.2 Two group models

#### 2.2.1 A simple SI vaccination model

Consider the following SI vaccination model proposed by Gandon et al. [3].

$$S' = (1-p)\Pi - \mu S - (\beta I + \beta_v I_v) S,$$

$$S'_v = p\Pi - \mu S_v - (1-r) (\beta I + \beta_v I_v) S_v,$$

$$I' = (\beta I + \beta_v I_v) S - (\mu + \nu) I,$$

$$I'_v = (1-r) (\beta I + \beta_v I_v) S_v - (\mu + \nu_v) I_v.$$

$$V = \begin{pmatrix} \mu + \nu & 0 \\ \mu + \nu_v & \mu + \nu_v \end{pmatrix},$$

$$F = \begin{pmatrix} \beta S_o \\ (1-r)\beta S_{vo} \end{pmatrix} \begin{pmatrix} \beta_v S_o \\ (1-r)\beta_v S_{vo} \end{pmatrix}.$$

Note that $F$ is a rank one matrix and can be written as the product of the two vectors $\omega = (S_o, (1-r)S_{vo})^T$ and $\beta = (\beta, \beta_v)^T$. This implies the next generation matrix will also be rank one,

$$K = \omega \beta^T V^{-1} = \begin{pmatrix} \frac{\beta S_o}{\mu + \nu} & \frac{\beta_v S_o}{\mu + \nu_v} \\ \frac{(1-r)\beta S_{vo}}{\mu + \nu} & \frac{(1-r)\beta_v S_{vo}}{\mu + \nu_v} \end{pmatrix}.$$
and
\[ R_o = \beta^T V^{-1} \omega = \frac{\beta S_o}{\mu + \nu} + \frac{(1-r)\beta_{v,S} \mu + \nu_v}{\mu + \nu_v}. \]

More generally, suppose \( F \) is rank one. That is, \( F = \omega \beta^T \) for two vectors \( \omega \) and \( \beta \). Then \( R_o = \beta^T V^{-1} \omega \). The interpretation here is that the entries of \( \beta \) are the infection rates for each compartment, and the entries of the (unit) vector \( \omega \) are the distribution of secondary infections among the compartments. The assumption being that the compartment in which the new infection appears is independent of the compartment of the infectious individual that caused the secondary infection. In this case, \( R_o \) is a weighted sum of the infection rates in \( \beta \) with the sojourn times in \( V^{-1} \), and \( \omega \) is the distribution that defines our typical infected individual.

### 2.2.2 A general vaccination model

Now consider the SI vaccination model with a rank two next generation matrix.

\[
K = \begin{pmatrix}
\frac{\beta_{uu} S_o}{\mu + \nu} & \frac{\beta_{uv} S_v}{\mu + \nu_v} \\
\frac{\beta_{vu} S_o}{\mu + \nu} & \frac{\beta_{vv} S_v}{\mu + \nu_v}
\end{pmatrix}.
\]

Denoting the four entries of \( K \) as \( R_{uu} \), \( R_{uv} \), \( R_{vu} \) and \( R_{vv} \), the spectral radius of \( K \) is

\[
R_c = \frac{R_{uu} + R_{vv}}{2} + \frac{1}{2} \sqrt{(R_{uu} + R_{vv})^2 - 4R_{uu}R_{uv} + 4R_{uv}R_{vu}}.
\]

This defies interpretation as anything other than the spectral radius of the next generation matrix.

### 2.2.3 Vector-host models

The simplest vector-host model couples a simple SIS model for the hosts with an SI model for the vectors. Susceptible hosts (\( S_h \)) become infectious hosts (\( I_h \)) at a rate \( \beta_h S_h I_v \) through contact with infected vectors (\( I_v \)). Similarly, susceptible vectors (\( S_v \)) become infectious vectors (\( I_h \)) at a rate \( \beta_v S_v I_h \) by contacts with infected hosts. The model is given by the following equations together with nonnegative initial conditions:

\[
I_h' = \beta_h S_h I_v - (\mu_h + \gamma) I_h, \\
I_v' = \beta_v S_v I_h - \mu_v I_v, \\
S_h' = \Pi_h - \mu_h S_h - \beta_h S_h I_v + \gamma I_h, \\
S_v' = \Pi_v - \mu_v S_v - \beta_v S_v I_h.
\]

To compute the reproduction number, assume that \( S_h \) and \( S_v \) remain constant near their initial values of \( S_{h0} \) and \( S_{v0} \) respectively, and form the matrices \( F \) and \( V \) from the coefficients of \( I_v \) and \( I_h \) in the first two equations.
\[
F = \begin{pmatrix}
0 & \beta_h S_h 0 \\
\beta_v S_v 0 & 0
\end{pmatrix}, \quad
V = \begin{pmatrix}
(\mu_h + \gamma) & 0 \\
0 & \mu_v
\end{pmatrix},
\]
\[
K = \begin{pmatrix}
0 & \beta_h S_h 0 \\
\beta_v S_v 0 & \mu_v \\
\mu_h + \gamma & 0
\end{pmatrix}.
\]
\[
R_o = \sqrt{\frac{\beta_h \beta_v S_h S_v}{(\mu_h + \gamma) \mu_v}}.
\]

The off-diagonal structure of \( K \) comes from the fact that infected hosts produce infected vectors and vice versa. In this case, the reproduction number is the geometric mean of the two entries of \( K \).

2.2.4 Two disease strains

Consider the following model for a disease with two cocirculating strains.

\[
S' = \Pi - \mu S - \beta_1 S(I_2 + I_{12}) - \beta_1 S(I_1 + I_2),
I'_1 = \beta_1 S(I_1 + I_{12}) - (\mu + \gamma_1)I_1,
I'_2 = \beta_1 S(I_2 + I_{12}) - (\mu + \gamma_2)I_2,
S'_1 = \gamma_1 I_1 - \sigma_1 \beta_2 S_1(I_2 + I_{12}) - \mu S_1,
S'_2 = \gamma_2 I_2 - \sigma_2 \beta_1 S_2(I_1 + I_{21}) - \mu S_2,
I'_{11} = \sigma_1 \beta_2 S_1(I_1 + I_{21}) - (\mu + \gamma_1)I_{21},
I'_{12} = \sigma_1 \beta_2 S_1(I_2 + I_{12}) - (\mu + \gamma_2)I_{12}.
\]

There are four disease compartments: the first two correspond to infection with a single strain, and the second two correspond to infection with both strains, distinguishing the two possible orderings of infection. First, consider the system with \( S, S_1 \) and \( S_2 \) held constant at the values \( S_o, S_{1o} = 0 \) and \( S_{2o} = 0 \) respectively. As before, the matrices \( F \) and \( V \) are formed from the coefficients of \( I_1, I_2, I_{12} \) and \( I_{21} \) in the second, third, sixth and seventh equations.

\[
F = \begin{pmatrix}
\beta_1 S_o & 0 & \beta_1 S_o & 0 \\
0 & \beta_2 S_o & 0 & \beta_2 S_o \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0
\end{pmatrix}, \quad
V = \begin{pmatrix}
\mu + \gamma_1 & 0 & 0 & 0 & 0 \\
0 & \mu + \gamma_2 & 0 & 0 & 0 \\
0 & 0 & \mu + \gamma_1 & 0 & 0 \\
0 & 0 & 0 & \mu + \gamma_2
\end{pmatrix}.
\]

In this case, \( F \), and therefore \( K \) are reducible, and \( K \) has two positive eigenvalues.

\[
R_i = \frac{\beta_i S_o}{\mu + \gamma_i}, \quad i = 1, 2.
\]

These eigenvalues can be interpreted as reproduction numbers for the two strains and the usual practice is to take the basic reproduction number as the larger of the two.
\[ R_o = \max_{i \in \{1, 2\}} R_i. \]

Again, this is the spectral radius of \( K \).

If \( S_{10} \) and \( S_{20} \) are left as arbitrary nonzero constants, then

\[
F = \begin{pmatrix}
\beta_1 S_o & 0 & \beta_1 S_o & 0 \\
0 & \beta_2 S_o & 0 & \beta_2 S_o \\
\sigma_2 \beta_1 S_{20} & 0 & \sigma_2 \beta_1 S_{20} & 0 \\
0 & \sigma_1 \beta_2 S_{10} & 0 & \sigma_1 \beta_2 S_{10}
\end{pmatrix}
\]

\( F \) and \( K \) are again reducible and \( K \) has two positive real eigenvalues that can be interpreted as reproduction numbers.

\[
R_1 = \frac{\beta_1}{\mu + \gamma_1} (S_o + \sigma_2 S_{20}),
\]

\[
R_2 = \frac{\beta_2}{\mu + \gamma_2} (S_o + \sigma_1 S_{10}).
\]

\( R_o \) is defined as the larger of the two.

3 Nonlinear equations

3.1 The disease-free equilibrium: linearization, and local stability

Consider the general model

\[
x' = f(x, y) - v(x, y),
\]

\[
y' = g(x, y),
\]

where

- \( x \) is a vector of populations of the \( n \) disease compartments and
- \( y \) is a vector of populations of the \( m \) non-disease compartments.
- A disease-free equilibrium, \( y_o \), is an asymptotically stable equilibrium of the disease-free model

\[
y' = g(0, y).
\]

- Let \( F \) and \( V \) be the \( n \times n \) matrices with entries

\[
F = \frac{\partial f_i}{\partial x_j}(0, y_o) \quad \text{and} \quad V = \frac{\partial v_i}{\partial x_j}(0, y_o).
\]

- The disease-free equilibrium is a locally asymptotically stable solution of the full model if

\[
R_o = \rho(FV^{-1}) < 1,
\]

and is unstable if \( R_o > 1 \).
References


