Einführung in die Mathematische Epidemiologie: Introduction to Mathematical Epidemiology: The Basic Reproductive Number

Nakul Chitnis
Universität Basel
Mathematisches Institut
Swiss Tropical and Public Health Institute

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1 Introduction

As seen before, the basic reproductive number, R_0, is defined as the expected number of new infections from one infected individual in a fully susceptible population through the entire duration of the infectious period. For simple homogenous models, we can define R_0 as,

$$R_0 = \left(\begin{array}{c} \text{Number of} \\ \text{contacts} \\ \text{per unit time} \end{array} \right) \left(\begin{array}{c} \text{Probability of} \\ \text{transmission} \\ \text{per contact} \end{array} \right) \left(\begin{array}{c} \text{Duration of} \\ \text{infection} \end{array} \right). \tag{1}$$

R_0 forms a threshold quantity for most models of infectious diseases since for $R_0 < 1$, the disease-free equilibrium point is locally asymptotically stable while for $R_0 > 1$, the disease-free equilibrium point is unstable. In many models, there is a transcritical bifurcation at $R_0 = 1$ and a locally asymptotically stable endemic equilibrium appears in the positive orthant for $R_0 > 1$.

2 Estimating R_0

Remember that for the endemic SIR model,

$$\frac{dS}{dt} = \Lambda - r\beta S\frac{I}{N} - \mu S, \tag{2a}$$
$$\frac{dI}{dt} = r\beta S\frac{I}{N} - (\gamma + \mu)I, \tag{2b}$$
$$\frac{dR}{dt} = \gamma I - \mu R, \tag{2c}$$

with state variables in Table 1 and parameters in Table 2. The endemic equilibrium point is given by,

$$S^*_{ee} = \frac{N^*}{R_0}, \tag{3a}$$
$$I^*_{ee} = \frac{\mu N^*}{r\beta}\left(R_0 - 1\right), \tag{3b}$$
$$R^*_{ee} = \frac{\gamma N^*}{r\beta}\left(R_0 - 1\right), \tag{3c}$$

with,

$$R_0 = \frac{r\beta}{\gamma + \mu}. \tag{4}$$

We assume that the initial conditions are such that the total population size is at equilibrium,

$$S + I + R = N = N^* = \frac{\Lambda}{\mu}. \tag{5}$$

Table 1: Description of state variables of compartmental models of infectious disease dynamics.

S:	Susceptible humans
I:	Infectious humans
R:	Recovered humans

Table 2: Description of parameter values in compartmental models of infectious disease dynamics.

r:	Number of contacts per unit time
β:	Probability of disease transmission per contact
γ:	Per-capita recovery rate
Λ:	Constant recruitment rate
μ:	Per-capita removal rate

The endemic SIR model assumes an exponential waiting time for death and infection. With a death rate of μ, the average life span is $1/\mu$. We label this as,

$$L = \frac{1}{\mu}. \tag{6}$$

From (2a), the rate at which susceptible individuals get infected is $r\beta I/N$ and at the endemic equilibrium point, this rate is, $r\beta I_{ee}/N^*$. Therefore, the average age of first infection at equilibrium is,

$$\begin{aligned} A &= \frac{1}{r\beta I^*_{ee}/N^*}, \\ &= \frac{1}{\mu}\frac{1}{R_0 - 1}, \\ &= \frac{L}{1 - R_0}. \end{aligned} \tag{7}$$

Rearranging this equation provides,

$$R_0 = 1 + \frac{L}{A}. \tag{8}$$

While this equation is exactly true for the homogenous SIR model, it is an approximation for models incorporating heterogeneity and can be used to estimate R_0 from available data on age of first infection and expected life span. Diseases with a high R_0 tend to have a low age of first infection. Note that this approximation is not valid when immunity is temporary or non-existent.

3 Disease Control

Since R_0 defines a threshold condition, control activities aim to change parameter values such that $R_0 < 1$ and the disease-free equilibrium point is locally (or sometimes globally) asymptotically stable. For models

with birth and death (such as the endemic SIR model), this leads to the elimination of disease. For models with fixed population sizes (such as the epidemic SIR model) this prevents the introduction of epidemics.

For the endemic SIR model with,

$$R_0 = \frac{r\beta}{\gamma + \mu}.$$

R_0 can be reduced through a decrease in the contact rate, r through behavior change; a decrease in the probability of disease transmission, β, through medication (for some infectious pathogens) or behavior change (for other pathogens); or through an increase in the recovery rate, γ, through medication[1].

For the epidemic SIR model,

$$\frac{dS}{dt} = -r\beta S\frac{I}{N}, \tag{9a}$$

$$\frac{dI}{dt} = r\beta S\frac{I}{N} - \gamma I, \tag{9b}$$

$$\frac{dR}{dt} = \gamma I, \tag{9c}$$

with $N = S + I + R$, state variables in Table 1 and parameters in Table 2, the basic reproductive number is,

$$R_0 = \frac{r\beta}{\gamma}. \tag{10}$$

R_0 can be reduced with similar strategies as for the endemic SIR model. The replacement number is defined as the expected number of secondary infections that one infected person would produce through the entire duration of the infectious period (where the population need not be fully susceptible),

$$R_e(t) = R_0 s(t), \tag{11}$$

where $s(t) = S(t)/N$. When $R_e < 1$ for $R_0 > 1$, either through an increase in the infectious population or the recovered population (through recovery from infection or vaccination), the disease can no longer sustain itself and will die out or epidemics will not occur. In a fully susceptible population, the proportion of people that we need to effectively vaccinate, r, such that $R_e < 1$, can be calculated from the inequality,

$$R_e = R_0(1 - r) < 1, \tag{12}$$

as,

$$r > 1 - \frac{1}{R_0}. \tag{13}$$

Note that effective vaccination coverage is a product of the efficacy of the vaccine and the proportion of people vaccinated. If this quantity satisfies the inequality (13), then the population has herd immunity and infections cannot propagate because infectious individuals do not encounter enough susceptible individuals to pass on the infection. However, if the efficacy of a vaccine is less than $1 - 1/R_0$, it is not possible to vaccinate enough individuals to provide herd immunity.

4 The Next Generation Operator

We have seen how to define and calculate R_0 for simple homogeneous models. There exist methods to define R_0 for more complicated models that include heterogeneity or seasonality methods. However these methods usually provide only a threshold quantity that describes when the disease-free equilibrium loses stability and does not necessarily satisfy the original definition of the expected number of secondary infections caused by one infected individual in a fully susceptible population through the entire duration of the infectious

[1] Increasing the death rate would also lead to a reduction in R_0 though this is usually not desirable.

period. A lot of these methods derive from the idea of the next generation operator introduced by Diekmann *et al.* (1990) [1]. This method converts a system of ordinary (or partial) differential equations of a model of infectious disease dynamics to an operator that translate from one generation of infectious individuals to the next. The basic reproductive number is defined as the spectral radius (dominant eigenvalue) of this operator. Van den Driessche and Watmough (2002) [2] describe such a method in detail for general deterministic compartmental models. We describe that method here but omit the proofs.

We consider a deterministic model for disease transmission with n compartments (dimensions). We denote the nonnegative orthant of $\mathbb{R}^n$ by $\bar{\mathbb{R}}^n_+$. We let $x(t) \in \bar{\mathbb{R}}^n_+$ where $x_i(t)$ denotes the number of individuals in compartment i at time t. For ease of notation, we order the compartments such that the first m (for $m \leq n$) compartments correspond to the states with infection. Note that the definition of a state with infection needs to be made from an understanding of the system being modeled and not from the infections themselves (and that this definition may not be unique). For the model,

$$\frac{dx_i}{dt} = f_i(x), \tag{14}$$

with nonnegative initial conditions, $x(0) \in \bar{\mathbb{R}}^n_+$, we define X_s as the set of all disease-free states,

$$X_s = \left\{ x \in \bar{\mathbb{R}}^n_+ \middle| \, x_i = 0 \text{ for } 1 \leq i \leq m \right\}. \tag{15}$$

We rewrite the model (14) as

$$\frac{dx_i}{dt} = \mathcal{F}_i(x) - \mathcal{V}_i(x), \tag{16}$$

where $\mathcal{F}_i(x)$ is the rate of *new* infections entering compartment i, and

$$\mathcal{V}_i = \mathcal{V}_i^-(x) - \mathcal{V}_i^+(x), \tag{17}$$

where $\mathcal{V}_i^+(x)$ is the rate of transfer *into* compartment i by any other means, and $\mathcal{V}_i^-(x)$ is the rate of transfer *out* of compartment i. We list 5 reasonable assumptions for these functions below.

(A1) If $x \in \bar{\mathbb{R}}^n_+$, then $\mathcal{F}_i(x), \mathcal{V}_i^+(x), \mathcal{V}_i^-(x) > 0$ for $1 \leq i \leq n$.

This implies that no rate of movement can be negative.

(A2) If $x_i = 0$, then $\mathcal{V}_i^-(x) = 0$.

If there are no individuals in a compartment, there can be no movement of individuals out of that compartment[2].

(A3) $\mathcal{F}_i(x) = 0$ for $i > m$.

There can be no infections entering classes that are defined as noninfectious.

(A4) If $x \in X_s$, then $\mathcal{F}_i(x) = 0$ and $\mathcal{V}_i^+(x) = 0$ for $1 \leq i \leq m$.

If there is no infection in the population, there can be no input into the infectious populations. For example, there can be no density-independent, non per-capita immigration of infectious individuals. This ensures that the disease-free subspace is invariant.

(A5) if $\mathcal{F}(x)$ is set to 0, then all eigenvalues of the corresponding $Df|_{x_{dfe}}$ (the Jacobian of (14) evaluated at a disease-free equilibrium point, x_{dfe}) have negative real part. Note that the disease-free equilibrium point is not required to be unique.

This implies that in the absence of new infections, the disease-free equilibrium point is locally asymptotically stable. For example, this excludes an equilibrium point that is unstable due to the dynamics of the total population.

[2] With assumptions **(A1)** and **(A2)**, we can show that the non-negative orthant is forward-invariant.

For a disease-free equilibrium point, x_{dfe}, of (14), where x_{dfe} and $f(x)$ satisfy assumptions **(A1)**–**(A5)**, we define $m \times m$ matrices, F and V,

$$F_{ij} = \left.\frac{\partial \mathcal{F}_i}{\partial x_j}\right|_{x_{dfe}} \quad \text{for } 1 \leq i, j \leq m, \tag{18}$$

$$V_{ij} = \left.\frac{\partial \mathcal{V}_i}{\partial x_j}\right|_{x_{dfe}} \quad \text{for } 1 \leq i, j \leq m. \tag{19}$$

Then, FV^{-1} is the next generation matrix for (14) and the basic reproductive number, R_0 is the spectral radius of FV^{-1},

$$R_0 = \rho\left(FV^{-1}\right). \tag{20}$$

Theorem 4.1 *For a model of an infectious disease, (14), with disease-free equilibrium point, x_{dfe}, that satisfies assumptions **(A1)**–**(A5)**, R_0 defined by (20) forms a threshold condition for x_{dfe}. If $R_0 < 1$, then x_{dfe} is locally asymptotically stable. If $R_0 > 1$, then x_{dfe} is unstable.*

References

[1] O. Diekmann, J. A. P. Heesterbeek, and J. A. J. Metz, *On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations*, Journal of Mathematical Biology, 28 (1990), pp. 365–382.

[2] P. van den Driessche and J. Watmough, *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Mathematical Biosciences, 180 (2002), pp. 29–48.