

6 Mechanistic Modelling of Recurrent Epidemics III; $\mathcal{R}_0$



Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

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Lecture 6

Mechanistic Modelling of Recurrent Epidemics III; $\mathcal{R}_0$
Tuesday 20 October 2026

Announcements

- **Project Description Document** is posted.
 - The project is to be submitted as a paper in the style of a research article for publication. It is not just a big assignment.
 - The project descriptions ask you questions and suggest directions for investigation, but you must construct the final document as a coherent single manuscript, not answers to a bunch of questions.
- **Midterm test:**
 - *Date:* Tuesday 17 November 2026 (tentative)
 - *Time available:* 2:30–5:20 p.m. (test duration: 90 minutes)
 - *Location:* in class, ETB 227
- **Assignment 3** is due Thursday 29 October 2026 at 11:59 p.m.
- **Assignment 4** is due Thursday 12 November 2026 at 11:59 p.m.
 - Make sure you personally can do the question on calculating $\mathcal{R}_0$ on this assignment before the midterm test.

$\mathcal{R}_0$: biological definition

The *basic reproduction number* $\mathcal{R}_0$ is:
the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual

e.g., Anderson and May (1991) "Infectious Diseases of Humans"

$\mathcal{R}_0$: more mathematical definition

The **basic reproduction number** $\mathcal{R}_0$ is:

the number of new infections produced by a typical infective individual in a population at a disease free equilibrium (DFE)

van den Driessche and Watmough (2002) *Mathematical Biosciences* **180**, 29–48

$\mathcal{R}_0$: most mathematical definition

The *basic reproduction number* $\mathcal{R}_0$ is:
the spectral radius of the next generation operator at a disease free equilibrium (DFE)

Diekmann, Heesterbeek & Metz (1990) *J. Math. Biol.* **28**, 365–382

Definitions from matrix analysis

Definition (Spectrum of a matrix)

Let M be an $n \times n$ real (or complex) matrix. The *spectrum of M* is

$$\sigma(M) = \{\lambda : Mv = \lambda v \text{ for some non-zero } v \in \mathbb{C}^n\},$$

i.e., $\sigma(M)$ is the set of eigenvalues of M .

Definition (Spectral radius of a matrix)

Let M be an $n \times n$ real (or complex) matrix. The *spectral radius of M* is

$$\rho(M) = \max\{|\lambda| : \lambda \in \sigma(M)\},$$

i.e., $\rho(M)$ is the maximum modulus of the eigenvalues of M .

Computing $\mathcal{R}_0$

- In very simple models, $\mathcal{R}_0$ is the product of the transmission rate and the mean time in the infectious class. e.g., In the SIR model with vital dynamics,

$$\mathcal{R}_0 = \beta \cdot \frac{1}{\gamma + \mu}.$$

- When there are multiple infected classes, it is more complicated to compute $\mathcal{R}_0$.
- In the SEIR model, we found (based on a biological argument) that

$$\mathcal{R}_0 = \beta \cdot \frac{\sigma}{\sigma + \mu} \cdot \frac{1}{\gamma + \mu}.$$

- Mathematically, the spectral radius of the next generation operator at the DFE is exactly this quantity. With this definition, it is also true that the disease persists if $\mathcal{R}_0 > 1$ and goes extinct if $\mathcal{R}_0 < 1$.

SEIR model (with vital dynamics)

$$\frac{dS}{dt} = \mu N - \frac{\beta SI}{N} - \mu S$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$

- Birth and death rate (μ)
- Transmission rate (β)
- Mean latent period ($1/\sigma$)
- Mean infectious period ($1/\gamma$)

Next generation matrix for the SEIR model

- Consider flows in and out of the infected compartments, and **highlight** flows that correspond to **new infections**:

$$\frac{d}{dt} \begin{pmatrix} E \\ I \end{pmatrix} = \begin{pmatrix} \beta SI - \sigma E - \mu E \\ \sigma E - \gamma I - \mu I \end{pmatrix}$$

- $\mathcal{F}$ = inflow of **new infecteds** to infected compartments $= \begin{pmatrix} \beta SI \\ 0 \end{pmatrix}$
- $\mathcal{V}$ = outflow from infected compartments minus inflow of non-new infecteds $= \begin{pmatrix} \sigma E + \mu E \\ -\sigma E + \gamma I + \mu I \end{pmatrix}$
- Let F = linearization of $\mathcal{F}$ at DFE
- Let V = linearization of $\mathcal{V}$ at DFE
- Then the **next generation matrix** is FV^{-1}
- Analogous to $\beta\gamma^{-1}$ in simple case.

Interpretation of FV^{-1} as next generation matrix

Almost verbatim from p. 33 of van den Driessche and Watmough (2002) *Mathematical Biosciences* **180**, 29–48

- To interpret the entries of FV^{-1} and develop a meaningful definition of $\mathcal{R}_0$, consider the fate of an infected individual introduced into compartment k of a disease free population.
- The (i, j) entry of F is the rate at which infected individuals in compartment j produce new infections in compartment i .
- The (j, k) entry of V^{-1} is the average length of time this individual spends in compartment j during its lifetime, assuming that the population remains near the DFE and barring reinfection.
- Hence, the (i, k) entry of the product FV^{-1} is the expected number of new infections in compartment i produced by the infected individual originally introduced into compartment k .
- Following Diekmann et al. (1990), we call FV^{-1} the next generation matrix for the model and set

$$\mathcal{R}_0 = \rho(FV^{-1}),$$

where $\rho(A)$ denotes the spectral radius of a matrix A .

$\mathcal{R}_0$ via FV^{-1} for the SEIR model

$$\mathcal{F} = \begin{pmatrix} \beta SI \\ 0 \end{pmatrix}$$

$$\mathcal{V} = \begin{pmatrix} \sigma E + \mu E \\ -\sigma E + \gamma I + \mu I \end{pmatrix}$$

$$F = \begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} (\sigma + \mu) & 0 \\ -\sigma & (\gamma + \mu) \end{pmatrix}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{\sigma + \mu} & 0 \\ \frac{\sigma}{(\sigma + \mu)(\gamma + \mu)} & \frac{1}{\gamma + \mu} \end{pmatrix} \implies FV^{-1} = \begin{pmatrix} \frac{\beta\sigma}{(\sigma + \mu)(\gamma + \mu)} & \frac{\beta}{\gamma + \mu} \\ 0 & 0 \end{pmatrix}$$

$$\mathcal{R}_0 = \rho(FV^{-1}) = \frac{\beta\sigma}{(\sigma + \mu)(\gamma + \mu)}$$

- Note wrt [previous slide](#) that the (2, 1) entry of V^{-1} is the average time an individual who enters the E compartment spends in the I compartment: only a proportion $\sigma/(\sigma + \mu)$ of such individuals make it to the I compartment, where the average time spent—by individuals who get there—is $1/(\gamma + \mu)$.

Computing $\mathcal{R}_0$ for other compartmental ODE models

- The method applied in the previous slides to obtain $\mathcal{R}_0$ for the SEIR model works more generally for a very large class of “reasonable” infectious disease ODE models. “Reasonable” means:
 - 1 The vector field can be written $\mathcal{F} - \mathcal{V}$, where $\mathcal{F} \geq 0$ corresponds to new infections and $\mathcal{V}$ can be written $\mathcal{V} = \mathcal{V}^+ - \mathcal{V}^-$, where $\mathcal{V}^+ \geq 0$ corresponds to outflow and $\mathcal{V}^- \geq 0$ corresponds to inflow of infectives that are not new.
 - 2 The biologically relevant part of the state space is forward-invariant. In particular, if a compartment is empty, then there can be no transfer of individuals out of the compartment by death, infection, nor any other means.
 - 3 The DFE is stable in the absence of new infection (if there is more than one DFE, $\mathcal{R}_0$ may depend on which one we focus on).
 - 4 The population size N is constant (or the model is expressed in terms of proportions in each compartment).

Computing $\mathcal{R}_0$ for other compartmental ODE models

Theorem (van den Driessche and Watmough (2002))

If the vector field associated with an ODE infectious disease model satisfies the [conditions specified on the previous slide](#), then

- 1** $\mathcal{R}_0$ can be computed as $\rho(FV^{-1})$;
- 2** if $\mathcal{R}_0 < 1$ then the disease-free equilibrium (DFE) is locally asymptotically stable (LAS), whereas if $\mathcal{R}_0 > 1$ then there is a LAS endemic equilibrium (EE).

$\mathcal{R}_0$ calculation: summary

- The biological method of deriving $\mathcal{R}_0$ is generally more informative in terms of what is going on. But it can be challenging to apply to complex models.
- The formal approach, *i.e.*, $\mathcal{R}_0 = \rho(FV^{-1})$, works in almost any situation you will encounter, even very complicated models with many compartments.
- If possible, it is best to use both methods to find an expression for $\mathcal{R}_0$, and make sure they agree.
- A completely different challenge is to estimate $\mathcal{R}_0$ for a real epidemic from data...

Estimating $\mathcal{R}_0$ based on the SEIR model

- If the SEIR model captures the natural history of some disease

well, how can you estimate $\mathcal{R}_0 = \frac{\beta\sigma}{(\sigma + \mu)(\gamma + \mu)}$?

- Mean latent period $1/\sigma$
- Mean infectious period $1/\gamma$
- Birth rate μ
- Estimate β via initial growth rate r :
 - For the simplest SIR model, $r = \beta - \gamma$ so $\beta = r + \gamma$.
 - More generally, r is the largest positive (or least negative) real part of the eigenvalues of $F - V$.
 - For SEIR model we find:

$$r = \frac{1}{2} \left(\sqrt{4\beta\sigma + (\gamma - \sigma)^2} - (\gamma + \sigma + 2\mu) \right)$$

- Solving this for β we obtain: $\beta = \frac{(r + \sigma + \mu)(r + \gamma + \mu)}{\sigma}$

Estimating $\mathcal{R}_0$ via the renewal equation

Many epidemic models can be expressed with an integro-differential equation known as the *renewal equation*, which relates the *susceptible proportion* $S(t)$ to the *incidence* $\iota(t)$,

$$\begin{aligned}\frac{dS}{dt} &= \mu - \iota(t) - \mu S(t) \\ \iota(t) &= \mathcal{R}_0 S(t) \int_0^\infty \iota(t-s) g(s) ds\end{aligned}$$

where $g(s)$ is the *intrinsic generation interval distribution*.

- *generation interval* = time difference between the moment when a focal individual was infected and the earlier time when the infector was infected

How can we use the renewal equation to obtain a formula that allows us to estimate $\mathcal{R}_0$?

How can we derive the standard SIR model from the renewal equation?