The Basic Reproduction Number

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Overview

- Derive a basic reproduction number, $\mathcal{R}_0$, for compartmental ODE models.
- Focus on the compartmental variations of the Kermack–McKendrick model.
- End with a teaser on type reproduction numbers and target reproduction numbers

Further Reading

- van den Driessche and Watmough (2002), "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission", http://www.sciencedirect.com/science/article/pii/S0025564402001086
- Diekmann, Heesterbeek and Roberts (2010), "The construction of next-generation matrices for compartmental epidemic models", J. Roy. Soc. Int., https://royalsocietypublishing.org/doi/10.1098/rsif.2009.0386
- Lewis, Shuai and van den Driessche (2019), "A general theory for target reproduction numbers with applications to ecology and epidemiology", J. Math. Biol., http://link.springer.com/10.1007/s00285-019-01345-4
- van den Driessche (2017), "Reproduction numbers of infectious disease models", Infectious Disease Modelling, https://www.sciencedirect.com/science/article/pii/S2468042717300209

The General Kermack–McKendrick Epidemic Model

$$S'(t) = -x(t)$$

$$x(t) = S(t) \int_0^\infty x(t-a)\beta(a)P(a)\,da$$

$S(t)$	number of susceptible individuals remaining at time t
$x(t)$	incidence of new infections at time t
$\beta(a)$	effective force-of-infection of an individual of infection-age a
$P(a)$	probability of surviving to infection-age a

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The total number of infected people at time t is given by the integral

$$I(t) = \int_0^\infty x(t-a)P(a)\,da.$$

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- Models of this type are often called evolution equations: the equations specify how to determine all future state from the current state.
- A solution of the model is a pair of functions, (x, S), satisfying the two equations.
- To pick out a specific solution we must specify initial data:

$$S(0) = S_0$$
$$x(t) = x_0(t), \qquad t < 0$$

Overview of main results for the deterministic model

There are two main theorems arising from this model.

Theorem (A threshold condition)

The incidence $x(t)$ will be initially increasing only if $R_0 > 1$, where the basic reproduction number, R_0, is defined as

$$R_0 = S_0 \int_0^\infty \beta(a)P(a)\,da$$

Theorem (The final size relation)

The final size of the epidemic,

$$z = 1 - \lim_{t\to\infty} S(t)/S_0$$

is a root of the simple transcendental equation

$$\log(1-z) + R_0 z = 0$$

The Basic Reproduction Number

$$R_0 = \int_0^\infty S_0 \beta(a) P(a)\, da$$

- R_0 is the expected number of secondary infections arising from the index case.
- If $R_0 > 1$, then an index case causes an epidemic.
- If $R_0 < 1$, then no epidemic occurs.

Dietz(1993), Stat. Methods Med. Res. 2:23

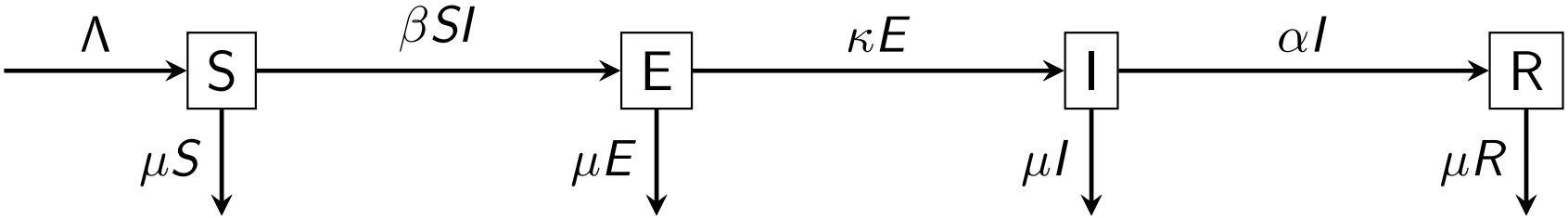
Compartmental ODE models

- Suppose the infected population is divided into n stages .
- Let $x(t)$ be the vector of populations in each stage.
- 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 rate new infections in stage j are caused by contact with an infected individual in stage i.

Example: SEIR

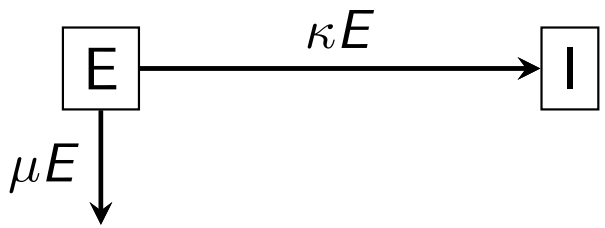


$$F = \begin{pmatrix} 0 & \beta S_0 \\ 0 & 0 \end{pmatrix} \qquad V^{-1} = \begin{pmatrix} \frac{1}{\kappa+\mu} & 0 \\ \frac{\kappa}{(\kappa+\mu)(\alpha+\mu)} & \frac{1}{\alpha+\mu} \end{pmatrix}$$

$$V = \begin{pmatrix} (\kappa+\mu) & 0 \\ -\kappa & (\alpha+\mu) \end{pmatrix} \qquad FV^{-1} = \begin{pmatrix} \frac{\kappa\beta S_0}{(\kappa+\mu)(\alpha+\mu)} & \frac{\beta S_0}{\alpha+\mu} \\ 0 & 0 \end{pmatrix}$$

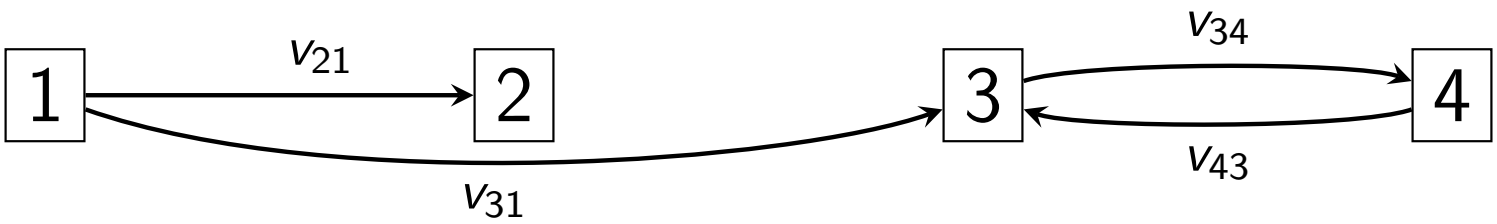
$$\mathcal{R}_0 = \frac{\kappa\beta S_0}{(\kappa+\mu)(\alpha+\mu)}$$

A brief digression



- Progression and death, the two routes out of E, are assumed to be independent 'risks'.
- We add the two rates to get the total rate-of-exit $(\kappa + \mu)$.
- $\dfrac{1}{\kappa + \mu}$ is the average time spent in compartment E.
- $\dfrac{\kappa}{\kappa + \mu}$ is the fraction of individuals that end up in I.

Progression through the disease compartments



$$V = \begin{pmatrix} v_{21} + v_{31} + \alpha_1 & 0 & 0 & 0 \\ -v_{21} & \alpha_2 & 0 & 0 \\ -v_{31} & 0 & v_{34} + \alpha_3 & -v_{43} \\ 0 & 0 & -v_{34} & v_{43} + \alpha_4 \end{pmatrix}$$

The transition matrix V

- Progression through the disease states is modelled by

$$x'(t) = -Vx(t).$$

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

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$$x'(t) = -Vx(t).$$

- 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.

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

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

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- 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 $\mathcal{R}_0$ 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.

Compartmental ODE models: The NGM and $\mathcal{R}_0$

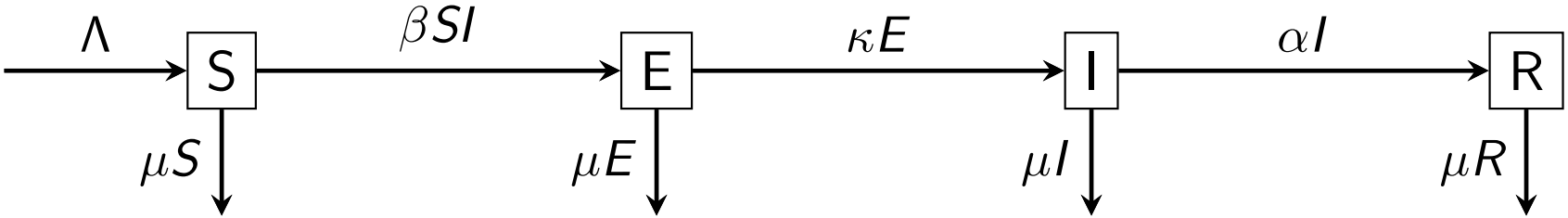
$$x'(t) = (F - V)x(t)$$

- $x = 0$ solution is stable if $s(F - V) < 0$
- $s(A)$ is the spectral abscissa of A
- $\rho(A)$ is the spectral radius of A
- Theorem:

$$s(F - V) < 0 \Leftrightarrow \rho(FV^{-1}) < 1$$

(at least for this F and V)

Back to the SEIR



$$F = \begin{pmatrix} 0 & \beta S_0 \\ 0 & 0 \end{pmatrix} \qquad V^{-1} = \begin{pmatrix} \frac{1}{\kappa+\mu} & 0 \\ \frac{\kappa}{(\kappa+\mu)(\alpha+\mu)} & \frac{1}{\alpha+\mu} \end{pmatrix}$$

$$V = \begin{pmatrix} (\kappa+\mu) & 0 \\ -\kappa & (\alpha+\mu) \end{pmatrix} \qquad FV^{-1} = \begin{pmatrix} \frac{\kappa\beta S_0}{(\kappa+\mu)(\alpha+\mu)} & \frac{\beta S_0}{\alpha+\mu} \\ 0 & 0 \end{pmatrix}$$

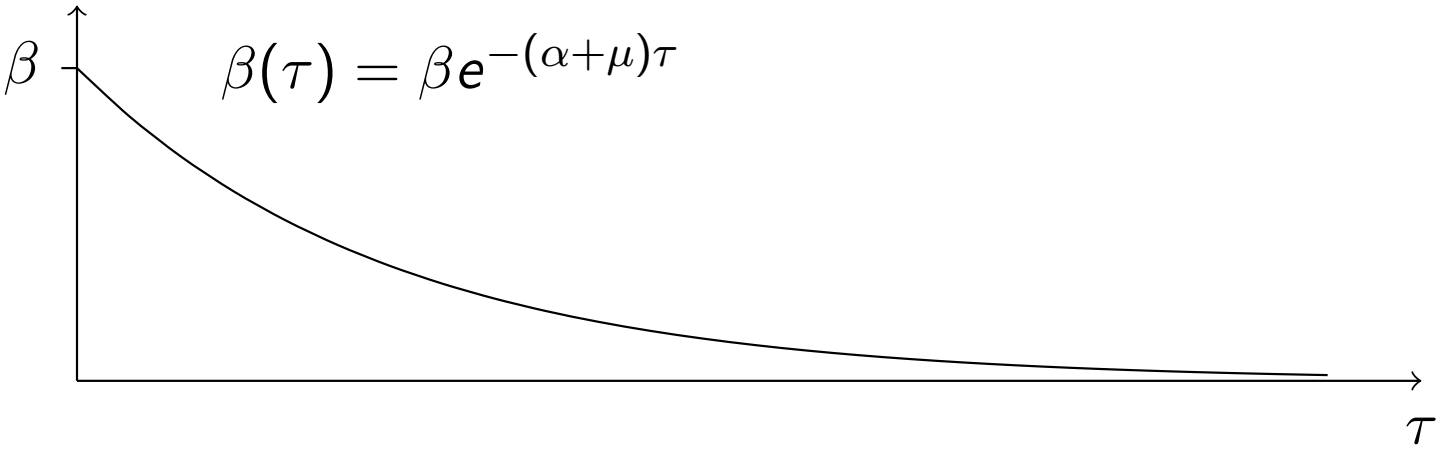
$$\mathcal{R}_0 = \frac{\kappa\beta S_0}{(\kappa+\mu)(\alpha+\mu)}$$

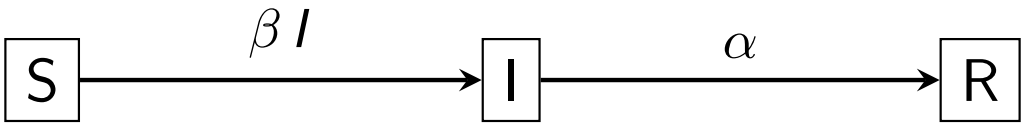
General Compartmental SIR-Epidemic Models

If F is rank one, then the compartmental ODE model is a special case of the general Kermak–McKendrick model above.

- Suppose ω and β are $n \times 1$ and $1 \times n$ matrices, respectively.
- Take $F = \omega\beta S$.
- Then $\beta(a)p(a) = \beta e^{-Va}\omega$

Example 1: The SIR model

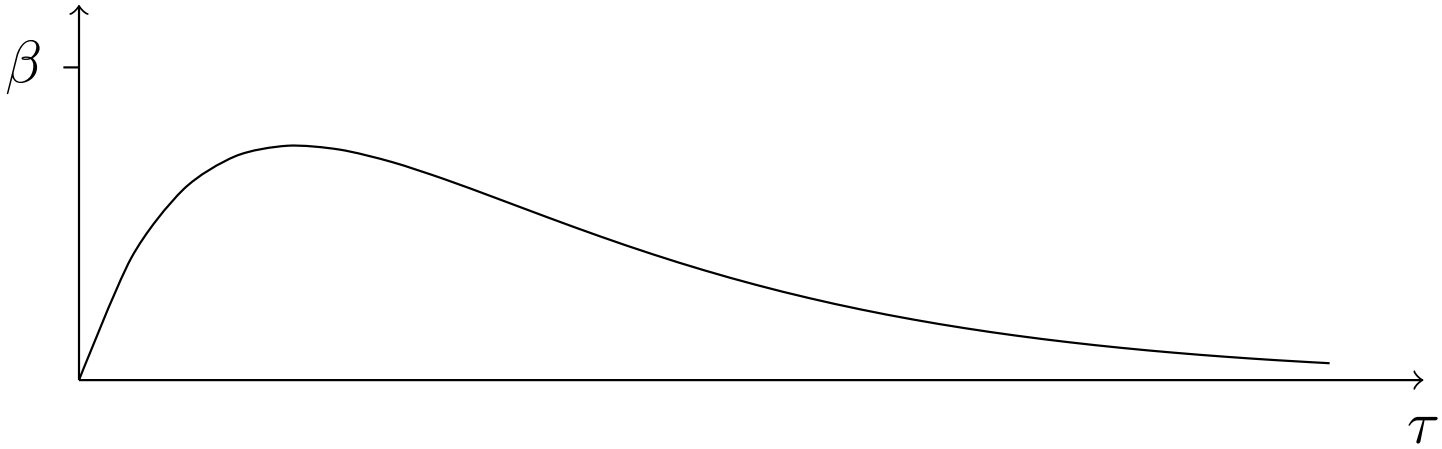


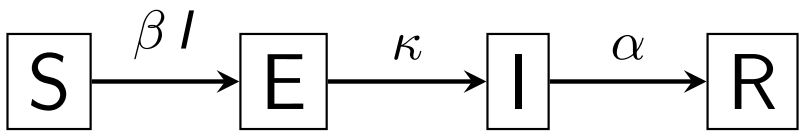


$$S' = -\beta SI$$
$$I' = \beta SI - (\alpha + \mu)I$$
$$R' = \alpha I$$

Example 2: The SEIR model

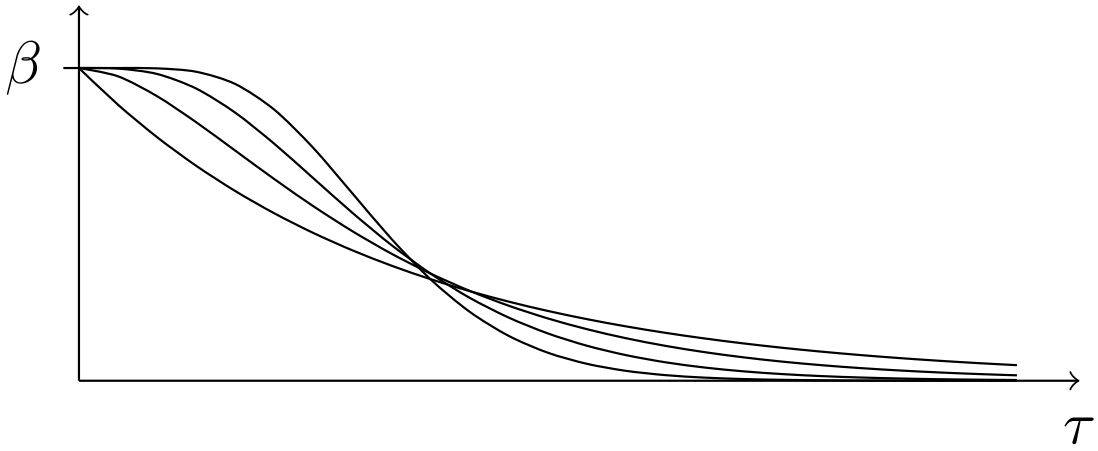
$$\beta(\tau) = \frac{\beta\kappa}{\alpha - \kappa}\left(e^{-\kappa\tau} - e^{-\alpha\tau}\right)$$

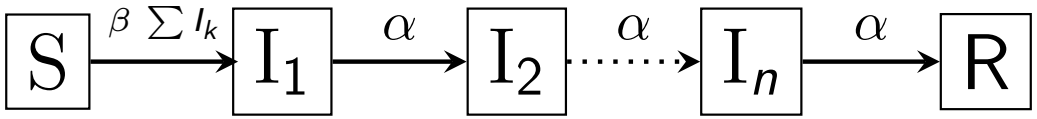




Example 3: The $\mathrm{SI}_n\mathrm{R}$ model

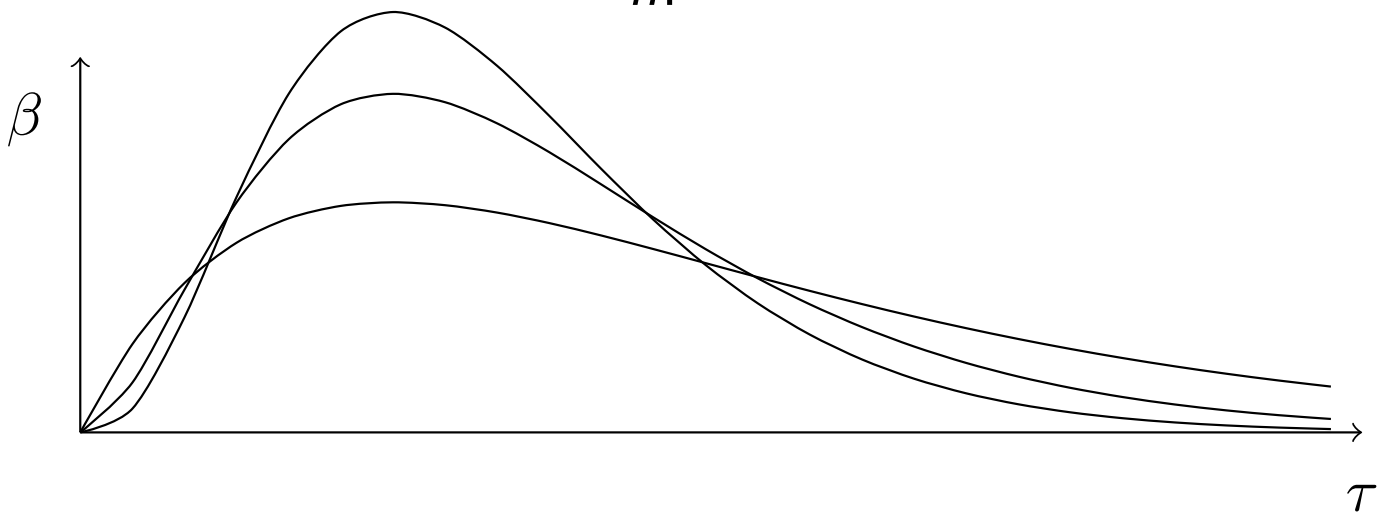
$$\beta(\tau) = \beta\left(1 + \alpha\tau + \cdots + \frac{1}{n!}(\alpha\tau)^n\right)e^{-\alpha\tau}$$

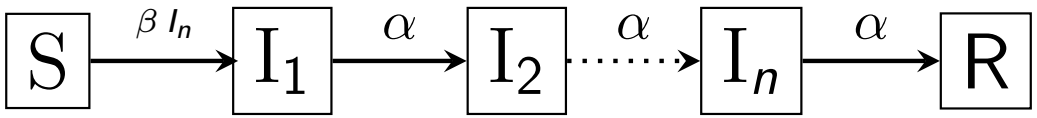




Example 4: The $\mathrm{SI}_n\mathrm{R}$ model

$$\beta(\tau) = \beta \frac{1}{n!} \alpha^{n+1} \tau^n e^{-\alpha\tau}$$





A simple vaccination model

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

$$
\begin{aligned}
S' &= (1-p)\Pi - \mu S - (\beta I + \beta_v I_v)\, S, \\
S_v' &= p\Pi - \mu S_v - (1-r)\,(\beta I + \beta_v I_v)\, S_v, \\
I' &= (\beta I + \beta_v I_v)\, S - (\mu + \alpha) I, \\
I_v' &= (1-r)\,(\beta I + \beta_v I_v)\, S_v - (\mu + \alpha_v) I_v.
\end{aligned}
$$

$$
V = \begin{pmatrix} (\mu+\alpha) & 0 \\ 0 & (\mu+\alpha_v) \end{pmatrix},
$$

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

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

$$K = \omega\beta^T V^{-1} = \begin{pmatrix} \frac{\beta S_o}{\mu+\alpha} & \frac{\beta_v S_o}{\mu+\alpha_v} \\ \frac{(1-r)\beta S_{vo}}{\mu+\alpha} & \frac{(1-r)\beta_v S_{vo}}{\mu+\alpha_v} \end{pmatrix}.$$

and

$$\mathcal{R}_0 = \beta^T V^{-1}\omega = \frac{\beta S_o}{\mu+\alpha} + \frac{(1-r)\beta_v S_{vo}}{\mu+\alpha_v}.$$

Aside: $K\omega = \mathcal{R}_0\omega$

A general vaccination model

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

$$K = \begin{pmatrix} \dfrac{\beta_{uu} S_o}{\mu + \alpha} & \dfrac{\beta_{uv} S_o}{\mu + \alpha_v} \\ \dfrac{\beta_{vu} S_{ov}}{\mu + \alpha} & \dfrac{\beta_{vv} S_{ov}}{\mu + \alpha_v} \end{pmatrix}.$$

Denoting the four entries of K as $\mathcal{R}_{g\,uu}$, $\mathcal{R}_{g\,uv}$, $\mathcal{R}_{g\,vu}$ and $\mathcal{R}_{g\,vv}$, the spectral radius of K is

$$\mathcal{R}_c = \frac{\mathcal{R}_{g\,uu} + \mathcal{R}_{g\,vv}}{2} + \frac{1}{2}\sqrt{(\mathcal{R}_{g\,uu} + \mathcal{R}_{g\,vv})^2 - 4\mathcal{R}_{g\,uu}\mathcal{R}_{g\,vv} + 4\mathcal{R}_{g\,uv}\mathcal{R}_{g\,vu}}.$$

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

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). Similarily, 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:

$$
\begin{aligned}
I_h' &= \beta_h S_h I_v - (\mu_h + \gamma) I_h, \\
I_v' &= \beta_v S_v I_h - \mu_v I_v, \\
S_h' &= \Pi_h - \mu_h S_h - \beta_h S_h I_v + \gamma I_h, \\
S_v' &= \Pi_v - \mu_v S_v - \beta_v S_v I_h.
\end{aligned}
$$

Vector-host models

$$I_h' = \beta_h S_{h0} I_v - (\mu_h + \gamma) I_h,$$
$$I_v' = \beta_v S_{v0} I_h - \mu_v I_v,$$

$$F = \begin{pmatrix} 0 & \beta_h S_{h0} \\ \beta_v S_{v0} & 0 \end{pmatrix}, \quad V = \begin{pmatrix} (\mu_h + \gamma) & 0 \\ 0 & \mu_v \end{pmatrix},$$

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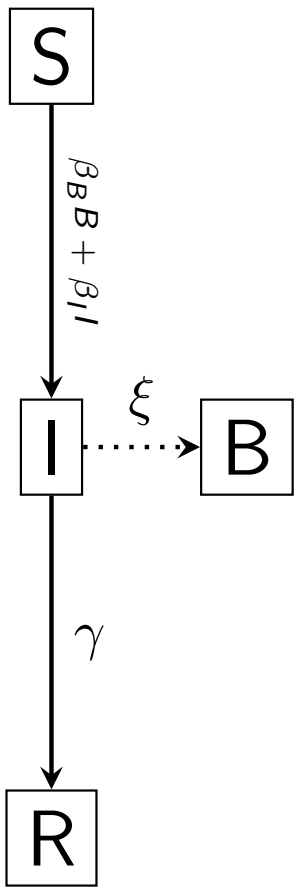
$$K = \begin{pmatrix} 0 & \dfrac{\beta_h S_{h0}}{\mu_v} \\ \dfrac{\beta_v S_{v0}}{\mu_h + \gamma} & 0 \end{pmatrix}.$$

$$\mathcal{R}_0 = \sqrt{\frac{\beta_h \beta_v S_{ho} S_{vo}}{(\mu_h + \gamma)\mu_v}}.$$

Indirect Transmission



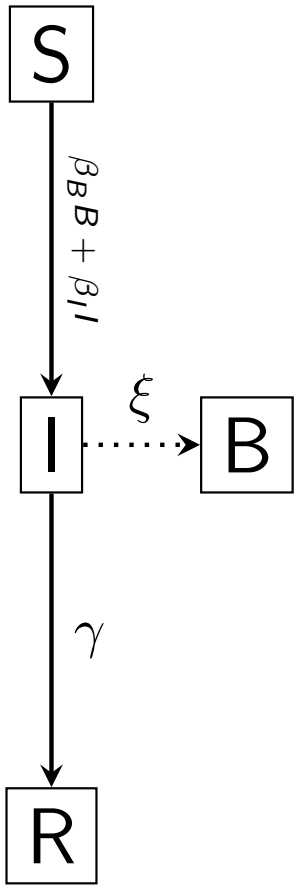
$$
\begin{aligned}
S' &= \Lambda - (\beta_I I + \beta_B B)S - \mu S, \\
I' &= (\beta_I I + \beta_B B)S - (\gamma + \mu)I, \\
R' &= \gamma I - \mu R, \\
B' &= \xi I - \delta B.
\end{aligned}
$$

$$
F = \begin{pmatrix} \beta_I S_0 & \beta_B S_0 \\ \xi & 0 \end{pmatrix} \qquad V = \begin{pmatrix} \gamma + \mu & 0 \\ 0 & \delta \end{pmatrix}
$$

or

$$
\tilde{F} = \begin{pmatrix} \beta_I S_0 & \beta_B S_0 \\ 0 & 0 \end{pmatrix} \qquad \tilde{V} = \begin{pmatrix} \gamma + \mu & 0 \\ -\xi & \delta \end{pmatrix}
$$

Indirect Transmission



$$FV^{-1} = \begin{pmatrix} \frac{\beta_I S_0}{\gamma+\mu} & \frac{\beta_B S_0}{\delta} \\ \frac{\xi}{\gamma+\mu} & 0 \end{pmatrix}$$

or

$$\tilde{F}\tilde{V}^{-1} = \begin{pmatrix} \frac{\beta_I S_0}{\gamma+\mu} + \frac{\beta_B S_0 \xi}{(\gamma+\mu)\delta} & \frac{\beta_I S_0}{\delta} \\ 0 & 0 \end{pmatrix}$$

see Lewis, Shuai and van den Driessche (2019)

Two disease strains

$$
\begin{aligned}
S' &= \Pi - \mu S - \beta_1 S(I_2 + I_{12}) - \beta_1 S(I_1 + I_{21}),\\
I_1' &= \beta_1 S(I_1 + I_{21}) - (\mu + \gamma_1) I_1,\\
I_2' &= \beta_1 S(I_2 + I_{12}) - (\mu + \gamma_2) I_2,\\
S_1' &= \gamma_1 I_1 - \sigma_1 \beta_2 S_1(I_2 + I_{12}) - \mu S_1,\\
S_2' &= \gamma_2 I_2 - \sigma_2 \beta_1 S_2(I_1 + I_{21}) - \mu S_2,\\
I_{21}' &= \sigma_2 \beta_1 S_2(I_1 + I_{21}) - (\mu + \gamma_1) I_{21},\\
I_{12}' &= \sigma_1 \beta_2 S_1(I_2 + I_{12}) - (\mu + \gamma_2) I_{12}.
\end{aligned}
$$

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

$$
\mathcal{R}_i = \frac{\beta_i S_o}{\mu + \gamma_i}, \qquad i = 1, 2.
$$

$$
\mathcal{R}_0 = \max_{i \in \{1,2\}} \mathcal{R}_i.
$$

The small NGM

Defining K from an ode model often results in large blocks of zeros. Diekmann, Heesterbeek, and Roberts have a nice way of shrinking K.

Suppose $F = CR$, and C has fewer columns than F, then it is easy to show that

$$\rho(RV^{-1}C) = \rho(FV^{-1})$$

Basically, every nonzero eigenvalue of $K_s = RV^{-1}C$ is also an eigenvalue of $K_L = FV^{-1}$

The small NGM: example

$$F = \begin{pmatrix} \beta_1 S_o & 0 & \beta_1 S_o & 0 \\ 0 & \beta_2 S_o & 0 & \beta_2 S_o \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} = \begin{pmatrix} 1 & 0 \\ 0 & 1 \\ 0 & 0 \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \beta_1 S_o & 0 & \beta_1 S_o & 0 \\ 0 & \beta_2 S_o & 0 & \beta_2 S_o \end{pmatrix}$$

Define the small NGM, K_S as follows:

$$K_s = RV^{-1}C$$

$$= \begin{pmatrix} \beta_1 S_o & 0 & \beta_1 S_o & 0 \\ 0 & \beta_2 S_o & 0 & \beta_2 S_o \end{pmatrix} \begin{pmatrix} (\mu+\gamma_1)^{-1} & 0 & 0 & 0 \\ 0 & (\mu+\gamma_2)^{-1} & 0 & 0 \\ 0 & 0 & (\mu+\gamma_1)^{-1} & 0 \\ 0 & 0 & 0 & (\mu+\gamma_2)^{-1} \end{pmatrix} \begin{pmatrix} 1 & 0 \\ 0 & 1 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}$$

$$= \begin{pmatrix} \frac{\beta_1 S_o}{\mu+\gamma_1} & 0 \\ 0 & \frac{\beta_2 S_o}{\mu+\gamma_2} \end{pmatrix}$$

Further Reading

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