Computation of $\mathcal{R}_0$ for Models of Infectious Disease

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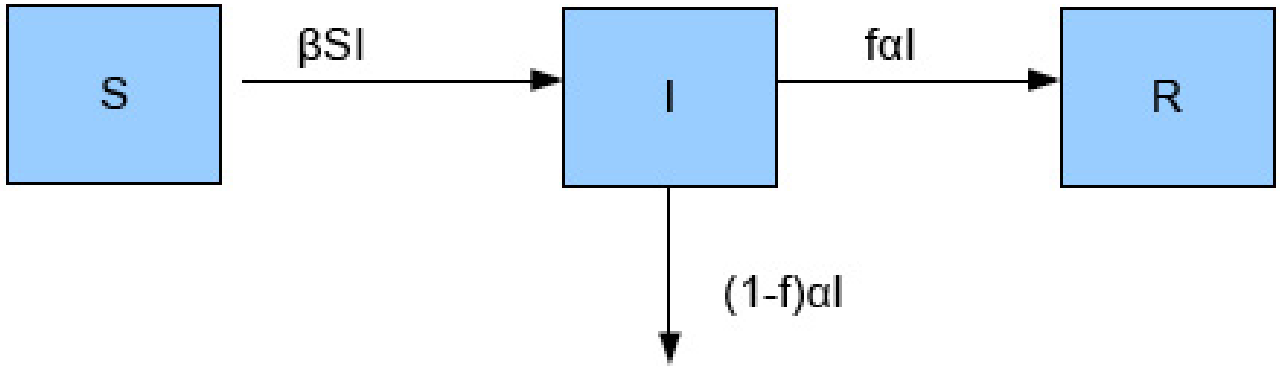
SIR Compartmental Epidemic Model



Simple model for influenza

S, I, R : number susceptible, infectious, recovered at time t
β: transmission coefficient between I and S, mass action βSI
$\frac{1}{\alpha}$: mean infectious time f: fraction of I recovering

$$\frac{dI}{dt} = \beta SI - \alpha I$$

Disease free equilibrium (DFE): $S = S_0, \quad I = 0, \quad R = 0$

$$\frac{dI}{dt} = \beta SI - \alpha I$$

DFE is locally asymptotically stable (LAS) if $\mathcal{R}_0 = \dfrac{\beta S_0}{\alpha} < 1$
unstable if $\mathcal{R}_0 > 1$

$\mathcal{R}_0$ is the *basic reproduction number*
= (transmission coefficient)(mean infectious time) S_0

$\mathcal{R}_0$: expected number of secondary infections caused by a primary case introduced into a susceptible population

Dynamical behavior:

$\mathcal{R}_0 < 1 \Rightarrow$ number of infectious individuals decreases monotonically to 0

$\mathcal{R}_0 > 1 \Rightarrow$ number first increases (before $\to 0$) : an epidemic

Estimated Mean Values of $\mathcal{R}_0$ from Data

smallpox Indian subcont. (1968-73)	4.5	[Anderson, May 1991]
poliomyelitis Europe (1955-60)	6	[Anderson, May 1991]
measles Ghana (1960-68)	14.5	[Anderson, May 1991]
SARS epidemic (2002-03)	3.5	[Gumel et *al.* 2004]
1918 Spanish flu in Geneva		
spring wave	1.5	[Chowell et *al.* 2006]
fall wave	3.8	[Chowell et *al.* 2006]
H2N2 flu pandemic US (1957)	1.68	[Longini et *al.* 2004]
H1N1 flu Mexico City (2009)	1.7	[Cruz-Pacheco et *al.* 2009]
H1N1 flu South Africa (2009)	1.33	[White et *al.* 2013]
H1N1 flu India (2009)	1.37	[Kadi, Avaradi 2014]
Ebola West Africa (2014)	2.1	[Althaus et *al.* 2014]

SEIR Compartmental Epidemic Model

In many infectious diseases there is an *exposed period* after the transmission of infection from susceptibles but before infected individuals can transmit infection
If this exposed period is relatively long then an exposed compartment E should be included to give an SEIR model with mean exposed period $\frac{1}{\kappa}$, input A, natural death rate $d > 0$

$$\frac{dS}{dt} = A - dS - \beta SI$$
$$\frac{dE}{dt} = \beta SI - (d + \kappa)E$$
$$\frac{dI}{dt} = \kappa E - (d + \alpha)I$$
$$\frac{dR}{dt} = \alpha I - dR$$

with nonnegative initial conditions
DFE $(S_0, E, I, R) = (\frac{A}{d}, 0, 0, 0)$. How to find $\mathcal{R}_0$ for this system?

Computing $\mathcal{R}_0$ for Compartmental Models

[Diekmann et *al.* 1990, vdD, Watmough 2002]

$x = (x_1, x_2, \ldots, x_n)^T$ gives number of individuals in each compartment
First $m < n$ compartments contain infected individuals
Assume DFE x_0 exists and is stable in absence of disease
Assume the linearized equations for $x_1, \ldots, x_m$ decouple from the other equations

Consider $\frac{dx_i}{dt} = \mathcal{F}_i(x) - \mathcal{V}_i(x)$ for $i = 1, 2, \ldots, m$

$\mathcal{F}_i(x)$ is rate of appearance of new infections in compartment i
$\mathcal{V}_i(x)$ is rate of other transitions between compartments
Here $\mathcal{F}_i$ and $\mathcal{V}_i \in \mathcal{C}^2$, $\mathcal{F}_i = 0$ if $i > m \ldots$

Define $F = \left[\frac{\partial \mathcal{F}_i(x_0)}{\partial x_j}\right]$, $V = \left[\frac{\partial \mathcal{V}_i(x_0)}{\partial x_j}\right]$ for $1 \leq i, j \leq m$

F is entrywise non-negative ($F \geq 0$)

V is a non-singular M-matrix, $V \in \mathcal{M}$

Let $\psi(0)$ be the number of initially infected individuals

Then $FV^{-1}\psi(0)$ is expected number of new infections

$FV^{-1} \geq 0$ and has (i, j) entry equal to the expected number of new infections in compartment i produced by infected individual introduced in compartment j

FV^{-1} is the *next generation matrix*

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

where ρ denotes the spectral radius

Linear stability of DFE determined by $s(F-V)$
where s is the maximum real part of the eigenvalues

Theorem

If x_0 is a DFE, then x_0 is LAS if $\mathcal{R}_0 = \rho(FV^{-1}) < 1$, but unstable if $\mathcal{R}_0 > 1$, i.e. sign $s(F-V) =$ sign $(\mathcal{R}_0 - 1)$

Proof: Matrix $V-F$ has Z sign-pattern (off-diagonals - or 0)

$$\begin{aligned} s(F-V) < 0 &\Leftrightarrow V - F \in \mathcal{M} \\ &\Leftrightarrow I - FV^{-1} \in \mathcal{M} \\ &\Leftrightarrow \rho(FV^{-1}) < 1 \\ \text{Also } s(F-V) = 0 &\Leftrightarrow \rho(FV^{-1}) = 1 \\ \text{Thus } s(F-V) > 0 &\Leftrightarrow \rho(FV^{-1}) > 1 \end{aligned}$$

Therefore x_0 is LAS if $s(F-V) < 0$, equivalently $\mathcal{R}_0 < 1$, and x_0 is unstable if $s(F-V) > 0$, equivalently $\mathcal{R}_0 > 1$. ■

Computation of $\mathcal{R}_0$ for SEIR Model

$$\frac{dS}{dt} = A - dS - \beta SI$$
$$\frac{dE}{dt} = \beta SI - (d+\kappa)E$$
$$\frac{dI}{dt} = \kappa E - (d+\alpha)I$$
$$\frac{dR}{dt} = \alpha I - dR$$

The infected compartments are E and I
At DFE matrices F and V are

$$F = \begin{bmatrix} 0 & \beta S_0 \\ 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} d+\kappa & 0 \\ -\kappa & d+\alpha \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} \frac{\kappa\beta S_0}{(d+\kappa)(d+\alpha)} & \frac{\beta S_0}{d+\alpha} \\ 0 & 0 \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} \frac{\kappa\beta S_0}{(d+\kappa)(d+\alpha)} & \frac{\beta S_0}{d+\alpha} \\ 0 & 0 \end{bmatrix}$$

FV^{-1} has eigenvalues 0 and $\mathcal{R}_0$ where

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

βS_0 is infection rate of one person in a population of S_0 susceptibles

$\kappa/(d+\kappa)$ is the fraction progressing from E to I
i.e. probability of surviving the E period and progressing to I

$1/(d+\alpha)$ is the mean time in I

The (1,1) entry of FV^{-1} is the expected number of secondary infections produced by an infected person originally in E

If $\mathcal{R}_0 < 1$ then solutions tend to the DFE, the disease dies out

Extension of the SEIR Model

Suppose that individuals in E are mildly infectious at a reduced rate $\epsilon\beta SE$ with $0 < \epsilon < 1$

Show that

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

and interpret the result

A Vector-Host Model

Some disease, e.g., Dengue fever, malaria, West Nile virus, are transmitted through a vector
Simple vector-host model is SIS for the hosts and SI for the vector

Susceptible hosts S_h become infectious hosts I_h at rate $\beta_{vh} S_h I_v$
by bites from infectious vectors I_v

Susceptible vectors S_v become infectious vectors at a rate $\beta_{hv} S_v I_h$
by biting infectious hosts

Let A_h, A_v be recruitment rates, d_h, d_v be removal rates
γ be recovery rate of I_h where I_v are assumed to be infectious for life

$$\frac{dS_h}{dt} = A_h - d_h S_h - \beta_{vh} S_h I_v + \gamma I_h$$
$$\frac{dI_h}{dt} = \beta_{vh} S_h I_v - (d_h + \gamma) I_h$$
$$\frac{dS_v}{dt} = A_v - d_v S_v - \beta_{hv} S_v I_h$$
$$\frac{dI_v}{dt} = \beta_{hv} S_v I_h - d_v I_v$$

Infected compartments are I_h , I_v
DFE is $S_{h0} = A_h/d_h, S_{v0} = A_v/d_v, I_h = I_v = 0$

$$F = \begin{bmatrix} 0 & \beta_{vh} S_{h0} \\ \beta_{hv} S_{v0} & 0 \end{bmatrix}, \; V = \begin{bmatrix} d_h + \gamma & 0 \\ 0 & d_v \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 & \frac{\beta_{vh} S_{h0}}{d_v} \\ \frac{\beta_{hv} S_{v0}}{d_h + \gamma} & 0 \end{bmatrix}$$

The entries of FV^{-1} are interpreted as the number of secondary infections produced by infected vectors and hosts during the course of their infections
Note the cross infection between vectors and hosts

$$\mathcal{R}_0 = \sqrt{\frac{\beta_{vh}\beta_{hv}S_{h0}S_{v0}}{d_v(d_h+\gamma)}}$$

This is a geometric mean of
(vector $\rightarrow$ host) $\frac{\beta_{vh}S_{v0}}{d_v}$ and (host $\rightarrow$ vector) $\frac{\beta_{hv}S_{h0}}{(d_h+\gamma)}$
The square root indicates that it takes two generations for infected hosts to produce new infected hosts

In practise the $\sqrt{\cdot}$ is often omitted giving the same threshold at 1

If $\mathcal{R}_0 < 1$ then solutions tend to the DFE, the disease dies out in host and vector

Disease control

The form of $\mathcal{R}_0$ can be used to help guide policy for disease control by suggesting control measures that reduce it to below 1

$$\mathcal{R}_0 = \sqrt{\frac{\beta_{vh}\beta_{hv}S_{h0}S_{v0}}{d_v(d_h+\gamma)}}$$

with $S_{h0} = A_h/d_h, S_{v0} = A_v/d_v$

Qualitative measures:

reduce S_{v0} by spraying, reduce β_{vh} by bed nets.....

Quantitative measures:

compute *elasticity indices* $\Gamma_p^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial p}$ x $\frac{p}{\mathcal{R}_0}$ measuring the proportional perturbation that changes in parameter p have on $\mathcal{R}_0$

Examples: $\Gamma_{\beta_{vh}}^{\mathcal{R}_0} = 0.5$; $\Gamma_{\gamma}^{\mathcal{R}_0} = \frac{-\gamma}{2(d_h+\gamma)}$

So $\mathcal{R}_0$ is useful!