Next-generation matrix method for calculating R_0

- Emphasis on *how* to calculate R_0
- Introduces some matrix language
- Develops a recipe
- Two worked examples
- Demo maxima (no slides)

Analogy with population ecology

$$n_{t+1} = \lambda n_t; \quad n_t = \lambda^t n_0$$

Population grows if $\lambda > 1$

For age structure:

$$n_{t+1} = L n_t; \quad n_t = L^t n_0$$

where L is a Leslie matrix

This population grows if dominant eigenvalue of L (also usually termed λ and more on this later) > 1

So we can work out if homogeneous or heterogeneous populations will grow each generation

Sometimes calculating R_0 is quite straightforward

This example is homogeneous because there is only ever one class involved in being created by, and creating infection

$$\begin{aligned}\dot{S} &= -\beta S I \\ \dot{I} &= \beta S I - \gamma I \\ \dot{R} &= \gamma I\end{aligned}$$

Infection increases in population if $\dot{I} > 0$

$$\beta S I > \gamma I; \quad \beta S > \gamma$$

At initial invasion, whole population susceptible

$$\beta N > \gamma; \quad \beta N/\gamma > 1$$

Infection grows in completely susceptible population if

$$R_0 \equiv \beta N/\gamma > 1$$

Structured compartment models: heterogeneous populations

With basic SIR - we only concern ourselves with “I” class

But we are often interested in

- Sex structure
- Species structure (incl. host & vector)
- Age structure
- Behavior structure (e.g. high risk group)
- etc...

Solution: Identify all compartments for which either

- An infection event increases this class
- Loss from this class means loss of current or future infector

Matrices

As we have to deal with more than one class, matrix notation helps keep us organized. E.g.

$$\begin{bmatrix} \dot{S} \\ \dot{E} \\ \dot{I} \\ \dot{R} \end{bmatrix} = \begin{bmatrix} \text{lots} \\ \text{of} \\ \text{rules} \\ \cdots \end{bmatrix} \begin{bmatrix} S \\ E \\ I \\ R \end{bmatrix}$$

It also turns out that matrix algebra is convenient for calculating R_0 - so first some basics ...

Matrix multiplication (2x2)

$$\begin{bmatrix} a & b \\ c & d \end{bmatrix} \begin{bmatrix} w & x \\ y & z \end{bmatrix} = \begin{bmatrix} (aw + by) & (ax + bz) \\ (cw + dy) & (cx + dz) \end{bmatrix}$$

Inverting a matrix (2x2)

If you take any number (e.g. 3.14) and multiply by 1 then nothing changes

Also, if a number is multiplied by its inverse you get 1 (e.g. $2 \times 1/2$)

Similarly if you multiply a matrix by the identity matrix then nothing changes

$$\begin{bmatrix} a & b \\ c & d \end{bmatrix} \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

Also, if a matrix is multiplied by its inverse then you recover the identity matrix

$$\begin{bmatrix} a & b \\ c & d \end{bmatrix} \begin{bmatrix} ? & ? \\ ? & ? \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

Inverting a matrix (2x2)

$$M = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

$$M^{-1} = \frac{1}{|M|} \begin{bmatrix} d & -b \\ -c & a \end{bmatrix}$$

$$|M| = ad - bc$$

$$M^{-1} = \begin{bmatrix} \frac{d}{ad-bc} & \frac{-b}{ad-bc} \\ \frac{-c}{ad-bc} & \frac{a}{ad-bc} \end{bmatrix}$$

$$M \times M^{-1} = \begin{bmatrix} a & b \\ c & d \end{bmatrix} \begin{bmatrix} \frac{d}{ad-bc} & \frac{-b}{ad-bc} \\ \frac{-c}{ad-bc} & \frac{a}{ad-bc} \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

Eigenvalues (2x2)

$$M = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

$$M - \lambda I = \begin{bmatrix} a - \lambda & b \\ c & d - \lambda \end{bmatrix}$$

$$|M - \lambda I| = \begin{vmatrix} a - \lambda & b \\ c & d - \lambda \end{vmatrix}$$

$$|M - \lambda I| = 0 \implies (a - \lambda)(d - \lambda) - bc = 0$$

$$\lambda^2 - (a + d)\lambda + (ad - bc) = 0$$

Eigenvalues (2x2)

$$M = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

$$\lambda^2 - (a + d)\lambda + (ad - bc) = 0$$

$$\lambda^2 - T\lambda + D = 0$$

$$\lambda = \frac{T}{2} \pm \sqrt{\left(\frac{T}{2}\right)^2 - D}$$

Next generation matrix: recipe

1. Identify classes for which
   - An infection event increases this class (gain terms)
   - Loss from this class means loss of current or future infector (loss terms)
2. Calculate the full disease-free equilibrium
3. List the gain and loss terms for each class
4. Create a matrix (F) of gain terms of each class differentiated w.r.t. each class and evaluated at the disease-free equilibrium
5. Create a matrix (V) of loss terms of each class differentiated w.r.t. each class and evaluated at the disease-free equilibrium
6. Invert matrix V to get V^{-1}
7. Evaluate matrix $G = FV^{-1}$
8. R_0 is the dominant eigenvalue of G

Example 1: An SEIR model

$$\begin{aligned}
\dot{S} &= \lambda - \beta S I - \mu S \\
\dot{E} &= \beta S I - aE - \mu E \\
\dot{I} &= aE - \gamma I - \mu I \\
\dot{R} &= \gamma I - \mu R
\end{aligned}$$

1. We identify classes E and I as being relevant
2. This system has a disease-free equilibrium:

$$x_0 = \{S^* = \lambda/\mu,\ E^* = 0,\ I^* = 0,\ R^* = 0\}$$

Example 1: An SEIR model

$$
\begin{aligned}
\dot{S} &= \lambda - \beta S I - \mu S \\
\dot{E} &= \beta S I - aE - \mu E \\
\dot{I} &= aE - \gamma I - \mu I \\
\dot{R} &= \gamma I - \mu R
\end{aligned}
$$

3. Gains and losses:

$$
\left|
\begin{array}{r|c}
\text{Gains to E:} & \beta S I \\
\text{Gains to I:} & 0 \\
\text{Losses from E:} & (a+\mu)E \\
\text{Losses from I:} & -aE + (\gamma+\mu)I
\end{array}
\right|
$$

The F (gains) and V (losses) matrices

4. $$F = \left[\begin{array}{cc} \frac{\partial}{\partial E}(\beta S I) & \frac{\partial}{\partial E}(0) \\ \frac{\partial}{\partial I}(\beta S I) & \frac{\partial}{\partial I}(0) \end{array} \right]_{x_0}$$

5. $$V = \left[\begin{array}{cc} \frac{\partial}{\partial E}((a+\mu)E) & \frac{\partial}{\partial E}(-aE + (\gamma+\mu)I) \\ \frac{\partial}{\partial I}((a+\mu)E) & \frac{\partial}{\partial I}(-aE + (\gamma+\mu)I) \end{array} \right]_{x_0}$$

The F (gains) and V (losses) matrices

4. $$F = \begin{bmatrix} 0 & 0 \\ \beta\lambda/\mu & 0 \end{bmatrix}$$

5. $$V = \begin{bmatrix} (a+\mu) & -a \\ 0 & (\gamma+\mu) \end{bmatrix}$$

Take inverse of V

6.

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

$$V^{-1} = \begin{bmatrix} \frac{1}{a+\mu} & \frac{a}{(\gamma+\mu)(a+\mu)} \\ 0 & \frac{1}{\gamma+\mu} \end{bmatrix}$$

Calculate $G = FV^{-1}$

7.

$$G = \begin{bmatrix} 0 & 0 \\ \frac{\beta\lambda}{\mu} & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{a+\mu} & \frac{a}{(\gamma+\mu)(a+\mu)} \\ 0 & \frac{1}{\gamma+\mu} \end{bmatrix}$$

$$G = \begin{bmatrix} 0 & 0 \\ \frac{\beta\lambda}{\mu(a+\gamma)} & \frac{\beta\lambda a}{\mu(\gamma+\mu)(a+\mu)} \end{bmatrix}$$

Note: D=0

Eigenvalues of G

8.

$$\lambda_{\max} = \frac{T}{2} + \sqrt{\left(\frac{T}{2}^2\right) - D}$$

Note: when D=0 then $\lambda_{\max} = T$

$$R_0 = \frac{\beta\lambda a}{\mu(a+\mu)(\gamma+\mu)}$$

$$R_0 = \frac{\beta N}{(a+\mu)(\gamma+\mu)}$$

cf $R_0 = \frac{\beta N}{\gamma+\mu}$ in equivalent SIR model

Example 2: Ross-McDonald model

$$\begin{aligned}
\dot{V}_s &= \lambda_v - \frac{b\tau_{hv} V_s H_i}{H_s + H_i + H_r} - \mu_v V_s \\
\dot{V}_i &= \frac{b\tau_{hv} V_s H_i}{H_s + H_i + H_r} - \mu_v V_i \\
\dot{H}_s &= \lambda_h - \frac{b\tau_{vh} H_s V_i}{H_s + H_i + H_r} - \mu_h H_s \\
\dot{H}_i &= \frac{b\tau_{vh} H_s V_i}{H_s + H_i + H_r} - \gamma_h H_i - \mu_h H_i \\
\dot{H}_r &= \gamma H_i - \mu_h H_r
\end{aligned}$$

Ross-McDonald model: steps to R_0

1. We identify V_i and H_i as relevant classes
2. The disease-free equilirium is

$$x_0 = \{V_s^* = \lambda_v/\mu_v,\ V_i^* = 0,\ H_s^* = \lambda_h/\mu_h,\ H_i^* = 0,\ H_r^* = 0\}$$

3. Gains and losses: $\left|\begin{array}{r|c} \text{Gains to } V_i: & \frac{b\tau_{hv} V_s H_i}{H_s+H_i+H_r} \\ \text{Gains to } H_i: & \frac{b\tau_{vh} H_s V_i}{H_s+H_i+H_r} \\ \text{Losses from } V_i: & \mu V_i \\ \text{Losses from } H_i: & \mu H_i - \gamma H_i \end{array}\right|$

The F (gains) and V (losses) matrices

4. $$F = \begin{bmatrix} \frac{\partial}{\partial V_i}\left(\frac{b\tau_{hv} V_s H_i}{H_s+H_i+H_r}\right) & \frac{\partial}{\partial V_i}\left(\frac{b\tau_{vh} H_s V_i}{H_s+H_i+H_r}\right) \\ \frac{\partial}{\partial H_i}\left(\frac{b\tau_{hv} V_s H_i}{H_s+H_i+H_r}\right) & \frac{\partial}{\partial H_i}\left(\frac{b\tau_{vh} H_s V_i}{H_s+H_i+H_r}\right) \end{bmatrix}_{x_0}$$

5. $$V = \begin{bmatrix} \frac{\partial}{\partial V_i}(\mu_v V_i) & \frac{\partial}{\partial V_i}(\mu_h H_i + \gamma H_i) \\ \frac{\partial}{\partial H_i}(\mu_v V_i) & \frac{\partial}{\partial H_i}(\mu_h H_i + \gamma H_i) \end{bmatrix}_{x_0}$$

The F (gains) and V (losses) matrices

4.
$$F = \begin{bmatrix} 0 & b\tau_{vh} \\ \frac{b\tau_{hv}\lambda_v\mu_h}{\mu_v\lambda_h} & 0 \end{bmatrix}$$

5.
$$V = \begin{bmatrix} \mu_v & 0 \\ 0 & \mu_h + \gamma \end{bmatrix}$$

Invert V

6.
$$V = \begin{bmatrix} \mu_v & 0 \\ 0 & \mu_h + \gamma \end{bmatrix}$$

$$V^{-1} = \begin{bmatrix} \frac{1}{\mu_v} & 0 \\ 0 & \frac{1}{\mu_h+\gamma} \end{bmatrix}$$

Calculate $G = FV^{-1}$

7.

$$G = \begin{bmatrix} \mu_v & 0 \\ 0 & \mu_h + \gamma \end{bmatrix} \begin{bmatrix} \frac{1}{\mu_v} & 0 \\ 0 & \frac{1}{\mu_h+\gamma} \end{bmatrix}$$

$$G = \begin{bmatrix} 0 & \frac{b\tau_{vh}}{\mu_h+\gamma} \\ \frac{b\tau_{hv}\lambda_v\mu_h}{{\mu_v}^2\lambda_h} & 0 \end{bmatrix}$$

Eigenvalues of G

8.

$$\lambda_{\max} = \frac{T}{2} + \sqrt{\left(\frac{T}{2}^2\right) - D}$$

Note: when $T=0$ then $\lambda_{\max} = \sqrt{-D}$

$$R_0 = \sqrt{\frac{b^2 \tau_{vh} \tau_{hv} \lambda_v \mu_h}{(\mu_h + \gamma){\mu_v}^2 \lambda_h}}$$

$$R_0 = \sqrt{\frac{b^2 \tau_{vh} \tau_{hv} N_v}{(\mu_h + \gamma)\mu_v N_h}}$$

Further reading

- O. Diekmann and J.A.P. Heesterbeek, 2000. Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis, and Interpretation. Wiley
- J.M. Heffernan, R.J. Smith and L.M. Wahl, 2005. Perspectives on the basic reproductive ratio. Interface
- P. van den Driessche and J. Watmough, 2002. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math. Biosci.
- N.A. Hartemink, S.E. Randolph, S.A. Davis and J.A. Heesterbeek, 2008. The basic reproduction number for complex disease systems: defining R(0) for tick-borne infections. Am. Nat.