Next generation matrix method

MATH 8xyz – Lecture 08

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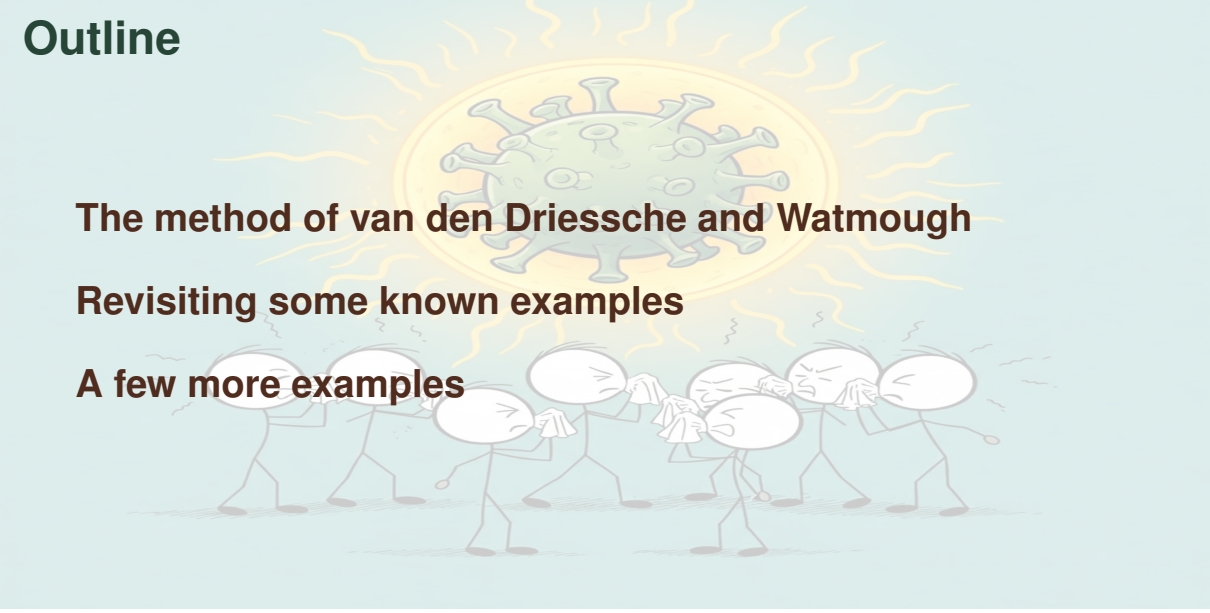
The University of Manitoba campuses are located on original lands of Anishinaabeg, Ininew, Anisininew, Dakota and Dene peoples, and on the National Homeland of the Red River Métis. We respect the Treaties that were made on these territories, we acknowledge the harms and mistakes of the past, and we dedicate ourselves to move forward in partnership with Indigenous communities in a spirit of Reconciliation and collaboration.

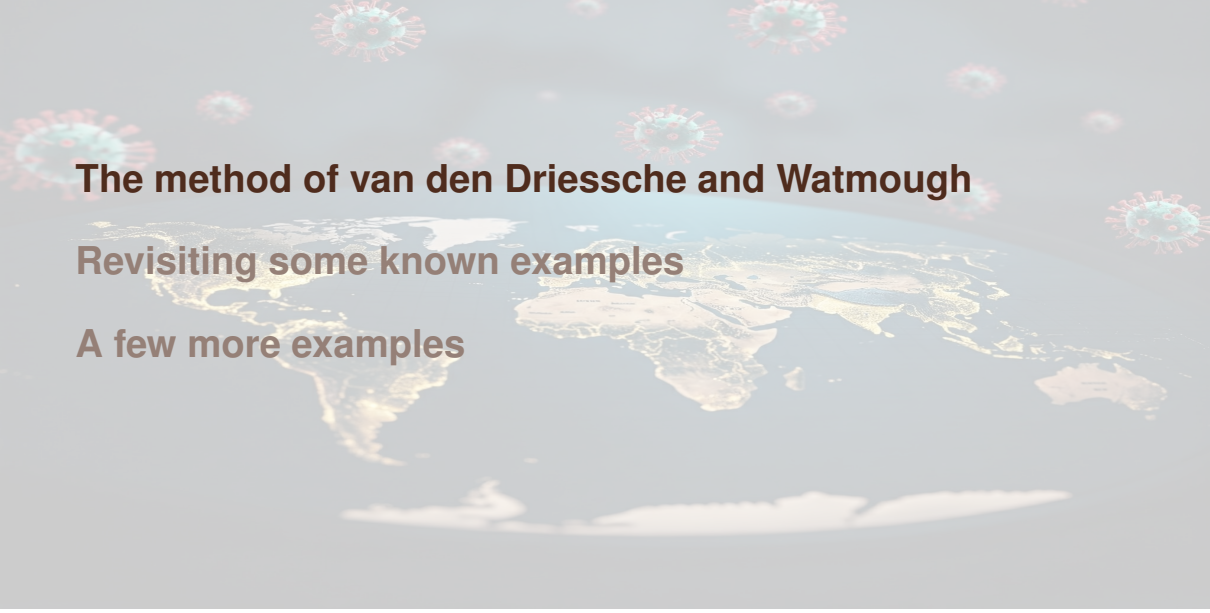
Outline



The method of van den Driessche and Watmough

Revisiting some known examples

A few more examples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Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission

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Dedicated to the memory of John Jacquez

The basic reproduction number $\mathcal{R}_0$

Used frequently in epidemiology (not only math epi)

Definition 1 ($\mathcal{R}_0$)

The basic reproduction number $\mathcal{R}_0$ is the average number of secondary cases generated by the introduction of an infectious individual in a wholly susceptible population

- If $\mathcal{R}_0 < 1$, then on average, each infectious individual infects less than one other person, so the epidemic has chances of dying out
- If $\mathcal{R}_0 > 1$, then on average, each infectious individual infects more than one other person and the disease can become established in the population (or there will be a major epidemic)

The method of van den Driessche and Watmough

The next generation matrix method

Direction of the bifurcation at $\mathcal{R}_0 = 1$

How does this work?

Computation of $\mathcal{R}_0$

Mathematically, $\mathcal{R}_0$ is a bifurcation parameter aggregating some of the model parameters and such that the disease free equilibrium (DFE) loses its local asymptotic stability when $\mathcal{R}_0 = 1$ is crossed from left to right

- As a consequence, $\mathcal{R}_0$ is found by considering the spectrum of the Jacobian matrix of the system evaluated at the DFE
- The matrix quickly becomes hard to deal with (size and absence of “pattern”) and the form obtained is not unique, which is annoying when trying to interpret $\mathcal{R}_0$

Preliminary setup of PvdD & Watmough 2002

$x = (x_1, \ldots, x_n)^T$, $x_i \geq 0$, with the first $m < n$ compartments the infected ones

X_s the set of all disease free states:

$$X_s = \{x \geq 0 | x_i = 0, i = 1, \ldots, m\}$$

Distinguish new infections from all other changes in population

- $F_i(x)$ rate of appearance of new infections in compartment i
- $V_i^+(x)$ rate of transfer of individuals into compartment i by all other means
- $V_i^-(x)$ rate of transfer of individuals out of compartment i

Assume each function continuously differentiable at least twice in each variable

$$x_i' = f_i(x) = F_i(x) - V_i(x), \quad i = 1, \ldots, n$$

where $V_i = V_i^- - V_i^+$

Some assumptions

- **(A1)** If $x \geq 0$, then $F_i, V_i^+, V_i^- \geq 0$ for $i = 1, \ldots, n$

Since each function represents a directed transfer of individuals, all are non-negative

- **(A2)** If $x_i = 0$ then $V_i^- = 0$. In particular, if $x \in X_s$, then $V_i^- = 0$ for $i = 1, \ldots, m$

If a compartment is empty, there can be no transfer of individuals out of the compartment by death, infection, nor any other means

- **(A3)** $F_i = 0$ if $i > m$

The incidence of infection for uninfected compartments is zero

- **A4** If $x \in X_s$ then $F_i(x) = 0$ and $V_i^+(x) = 0$ for $i = 1, \ldots, m$

Assume that if the population is free of disease then the population will remain free of disease; i.e., there is no (density independent) immigration of infectives

One last assumption for the road

Let x_0 be a DFE of the system, i.e., a (locally asymptotically) stable equilibrium solution of the disease free model, i.e., the system restricted to X_s. We need not assume that the model has a unique DFE

Let $Df(x_0)$ be the Jacobian matrix $[\partial f_i/\partial x_j]$. Some derivatives are one sided, since x_0 is on the domain boundary

(A5) If $F(x)$ is set to zero, then all eigenvalues of $Df(x_0)$ have negative real parts

Note: if the method ever fails to work, it is usually with (A5) that lies the problem

Stability of the DFE as function of $\mathcal{R}_0$

Theorem 2

Suppose the DFE exists. Let then

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

with matrices F and V obtained as indicated. Assume conditions (A1) through (A5) hold. Then

- *if $\mathcal{R}_0 < 1$, then the DFE is LAS*
- *if $\mathcal{R}_0 > 1$, the DFE is unstable*

Important to stress *local* nature of stability that is deduced from this result. We will see later that even when $\mathcal{R}_0 < 1$, there can be several positive equilibria

The method of van den Driessche and Watmough

- The next generation matrix method
- **Direction of the bifurcation at $\mathcal{R}_0 = 1$**
- How does this work?

Direction of the bifurcation at $\mathcal{R}_0 = 1$

μ bifurcation parameter s.t. $\mathcal{R}_0 < 1$ for $\mu < 0$ and $\mathcal{R}_0 > 1$ for $\mu > 0$ and x_0 DFE for all values of μ and consider the system

$$x' = f(x, \mu) \tag{1}$$

Write

$$D_x f(x_0, 0) = D(\mathcal{F}(x_0) - \mathcal{V}(x_0))|_{\mathcal{R}_0 = 1}$$

as block matrix

$$D\mathcal{F}(x_0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}, \quad D\mathcal{V}(x_0) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix}$$

Write $[\alpha_{\ell k}]$, $\ell = m+1, \ldots, n$, $k = 1, \ldots, m$ the $(\ell - m, k)$ entry of $-J_4^{-1} J_3$ and let v and w be left and right eigenvectors of $D_x f(x_0, 0)$ s.t. $vw = 1$

Let

$$a = \sum_{i,j,k=1}^{m} v_i w_j w_k \left(\frac{1}{2} \frac{\partial^2 f_i}{\partial x_j \partial x_k}(x_0, 0) + \sum_{\ell=m+1}^{n} \alpha_{\ell k} \frac{\partial^2 f_i}{\partial x_j \partial x_\ell}(x_0, 0) \right) \tag{2}$$

$$b = v D_{x_\mu} f(x_0, 0) w = \sum_{i,j=1}^{n} v_i w_j \frac{\partial^2 f_i}{\partial x_j \partial \mu}(x_0, 0) \tag{3}$$

Theorem 3

Consider model (1) *with* $f(x, \mu)$ *satisfying conditions (A1)–(A5) and* μ *as described above*

Assume that the zero eigenvalue of $D_x f(x_0, 0)$ *is simple*

Define a and b by (2) *and* (3)*; assume that* $b \neq 0$*. Then* $\exists \delta > 0$ *s.t.*

- *if* $a < 0$*, then there are LAS endemic equilibria near* x_0 *for* $0 < \mu < \delta$
- *if* $a > 0$*, then there are unstable endemic equilibria near* x_0 *for* $-\delta < \mu < 0$

The method of van den Driessche and Watmough

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- Direction of the bifurcation at $\mathcal{R}_0 = 1$
- **How does this work?**

Two key ingredients to explain

- Where does FV^{-1} come from?

- Why on earth use the spectral radius of FV^{-1}?

The next generation matrix FV^{-1}

The spectral radius

If you know ODE and discrete time systems, the statement in Theorem 2 that the DFE is LAS when the spectral radius of $FV^{-1} < 1$ should be somewhat confusing

LAS in an ODE requires all eigenvalues to have negative real parts (the *spectral abscissa* $s(\cdot)$ is negative), whereas the spectral radius being less than one is typically the condition for local attractivity of a fixed point in a discrete time system

Key ingredient is the equivalence $s(F - V) < 0 \iff \rho(FV^{-1}) < 1$

Let's prove it before explaining its relevance to the disease case

The equivalence

Lemma 4

Let F and V be defined as earlier, $s(\cdot)$ and $\rho(\cdot)$ denote the spectral abscissa and spectral radius of a matrix, respectively. Then

$$s(F - V) < 0 \iff \rho(FV^{-1}) < 1 \tag{4}$$

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Example of the SLIRS model (**??**)

Variation of the infected variables in (**??**) are described by

$$L' = f(S, I, N) - (\varepsilon + d)L$$
$$I' = \varepsilon L - (d + \gamma)I$$

Write

$$\mathcal{I}' = \begin{pmatrix} L \\ I \end{pmatrix}' = \begin{pmatrix} f(S, I, N) \\ 0 \end{pmatrix} - \begin{pmatrix} (\varepsilon + d)L \\ (d + \gamma)I - \varepsilon L \end{pmatrix} =: \mathcal{F} - \mathcal{V} \tag{5}$$

Denote

$$f_L^\star := \left.\frac{\partial}{\partial L} f\right|_{(S,I,R)=\boldsymbol{E}_0} \qquad f_I^\star := \left.\frac{\partial}{\partial I} f\right|_{(S,I,R)=\boldsymbol{E}_0}$$

the values of the partials of the incidence function at the DFE $\boldsymbol{E}_0$

Compute the Jacobian matrices of vectors $\mathcal{F}$ and $\mathcal{V}$ at the DFE $\boldsymbol{E}_0$

$$F = \begin{pmatrix} f_L^\star & f_I^\star \\ 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \varepsilon + d & 0 \\ -\varepsilon & d + \gamma \end{pmatrix} \tag{6}$$

Thus

$$V^{-1} = \frac{1}{(d+\varepsilon)(d+\gamma)} \begin{pmatrix} d+\gamma & 0 \\ \varepsilon & d+\varepsilon \end{pmatrix}$$

Also, in the case N is constant, $\partial f/\partial L = 0$ and thus

$$FV^{-1} = \frac{f_I^\star}{(d+\varepsilon)(d+\gamma)} \begin{pmatrix} \varepsilon & d+\varepsilon \\ 0 & 0 \end{pmatrix}$$

As a consequence,

$$\mathcal{R}_0 = \varepsilon \frac{f_I^\star}{(d+\varepsilon)(d+\gamma)}$$

Theorem 5

Let

$$\mathcal{R}_0 = \frac{\varepsilon f_I^\star}{(d+\varepsilon)(d+\gamma)} \tag{7}$$

Then

- *if* $\mathcal{R}_0 < 1$*, the DFE is LAS*
- *if* $\mathcal{R}_0 > 1$*, the DFE is unstable*

It is important here to stress that the result we obtain concerns the **local** asymptotic stability. We see later that even when $\mathcal{R}_0 < 1$, there can be several locally asymptotically stable equilibria

Application

The DFE is

$$(\bar{S}, \bar{L}, \bar{I}, \bar{R}) = (N, 0, 0, 0)$$

- Mass action incidence (frequency-dependent contacts):

$$f_I^\star = \beta \bar{S} \Rightarrow \mathcal{R}_0 = \frac{\epsilon \beta N}{(\epsilon + d)(\gamma + d)}$$

- Standard incidence (proportion-dependent contacts):

$$f_I^\star = \frac{\beta \bar{S}}{N} \Rightarrow \mathcal{R}_0 = \frac{\epsilon \beta}{(\epsilon + d)(\gamma + d)}$$

Links between SLIRS-type models

$$
\begin{aligned}
S' &= b + \nu R - dS - f(S, I, N) \\
L' &= f(S, I, N) - (d + \varepsilon)L \\
I' &= \varepsilon L - (d + \gamma)I \\
R' &= \gamma I - (d + \nu)R
\end{aligned}
$$

SLIR	SLIRS where $\nu = 0$
SLIS	Limit of SLIRS when $\nu \to \infty$
SLI	SLIR where $\gamma = 0$
SIRS	Limit of SLIRS when $\varepsilon \to \infty$
SIR	SIRS where $\nu = 0$
SIS	Limit of SIRS when $\nu \to \infty$
	Limit SLIS when $\varepsilon \to \infty$
SI	SIS where $\nu = 0$

Values of $\mathcal{R}_0$

$(\bar{S}, \bar{I}, \bar{N})$ values of S, I and N at DFE. Denote $\bar{f}_I = \partial f / \partial I(\bar{S}, \bar{I}, \bar{N})$.

SLIRS	$\frac{\varepsilon \bar{f}_I}{(d+\varepsilon)(d+\gamma)}$
SLIR	$\frac{\varepsilon \bar{f}_I}{(d+\varepsilon)(d+\gamma)}$
SLIS	$\frac{\varepsilon \bar{f}_I}{(d+\varepsilon)(d+\gamma)}$
SLI	$\frac{\varepsilon \bar{f}_I}{(d+\varepsilon)(d+\gamma)}$
SIRS	$\frac{\varepsilon \bar{f}_I}{d+\gamma}$
SIR	$\frac{\bar{f}_I}{d+\gamma}$
SIS	$\frac{\bar{f}_I}{d+\gamma}$
SI	$\frac{\bar{f}_I}{d+\gamma}$

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