

Models incorporating a spatial component

Arba Minch – Course 03

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Diseases have been known to be mobile for a while

The plague of Athens of 430 BCE

It first began, it is said, in the parts of Ethiopia above Egypt, and thence descended into Egypt and Libya and into most of the [Persian] King's country. Suddenly falling upon Athens, it first attacked the population in Piraeus [...] and afterwards appeared in the upper city, when the deaths became much more frequent.

Thucydides (c. 460 BCE - c. 395 BCE)
History of the Peloponnesian War



Spatio-temporal spread of diseases

Metapopulation models

Computational considerations

Spatio-temporal spread of diseases

Metapopulation models

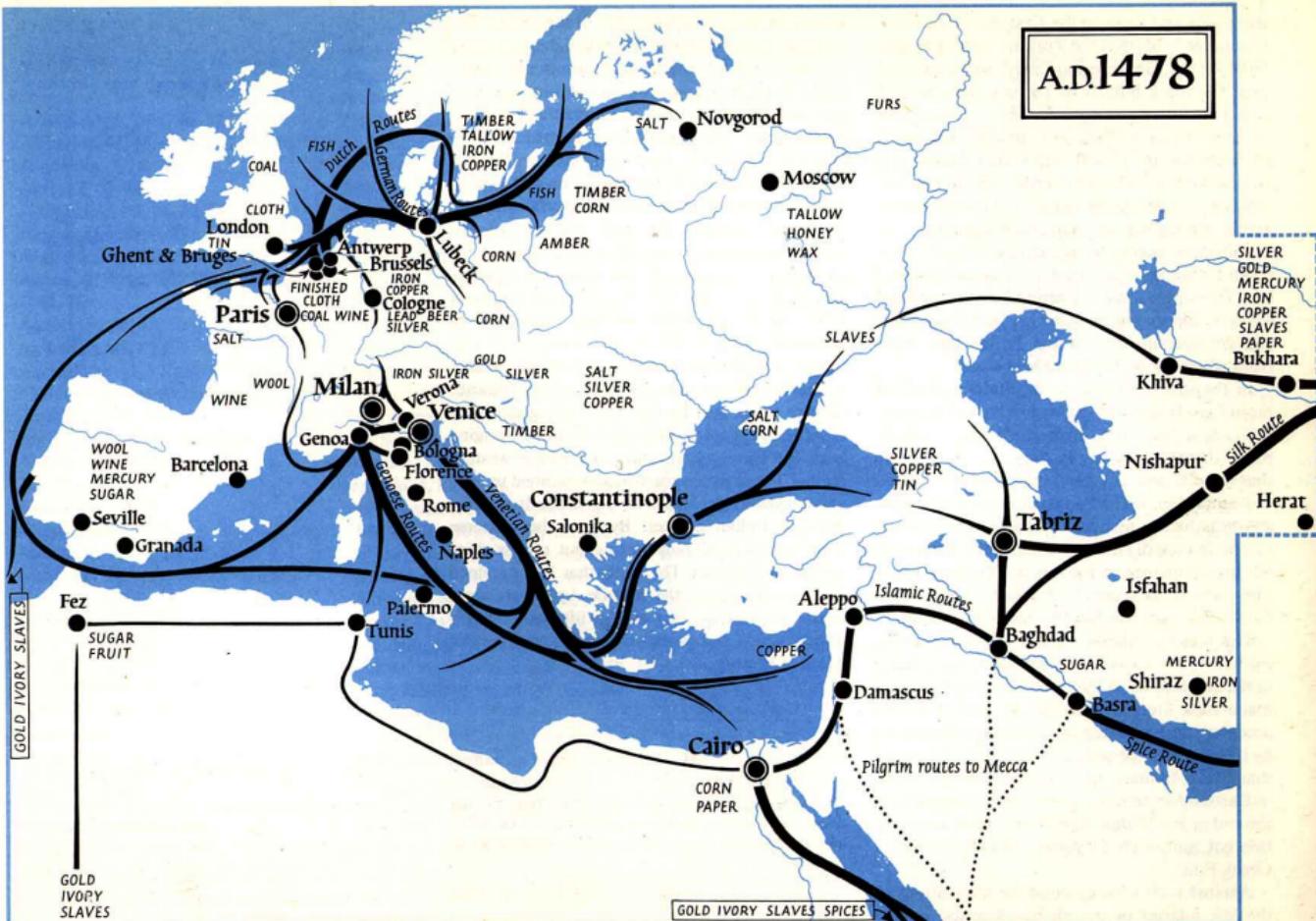
Computational considerations

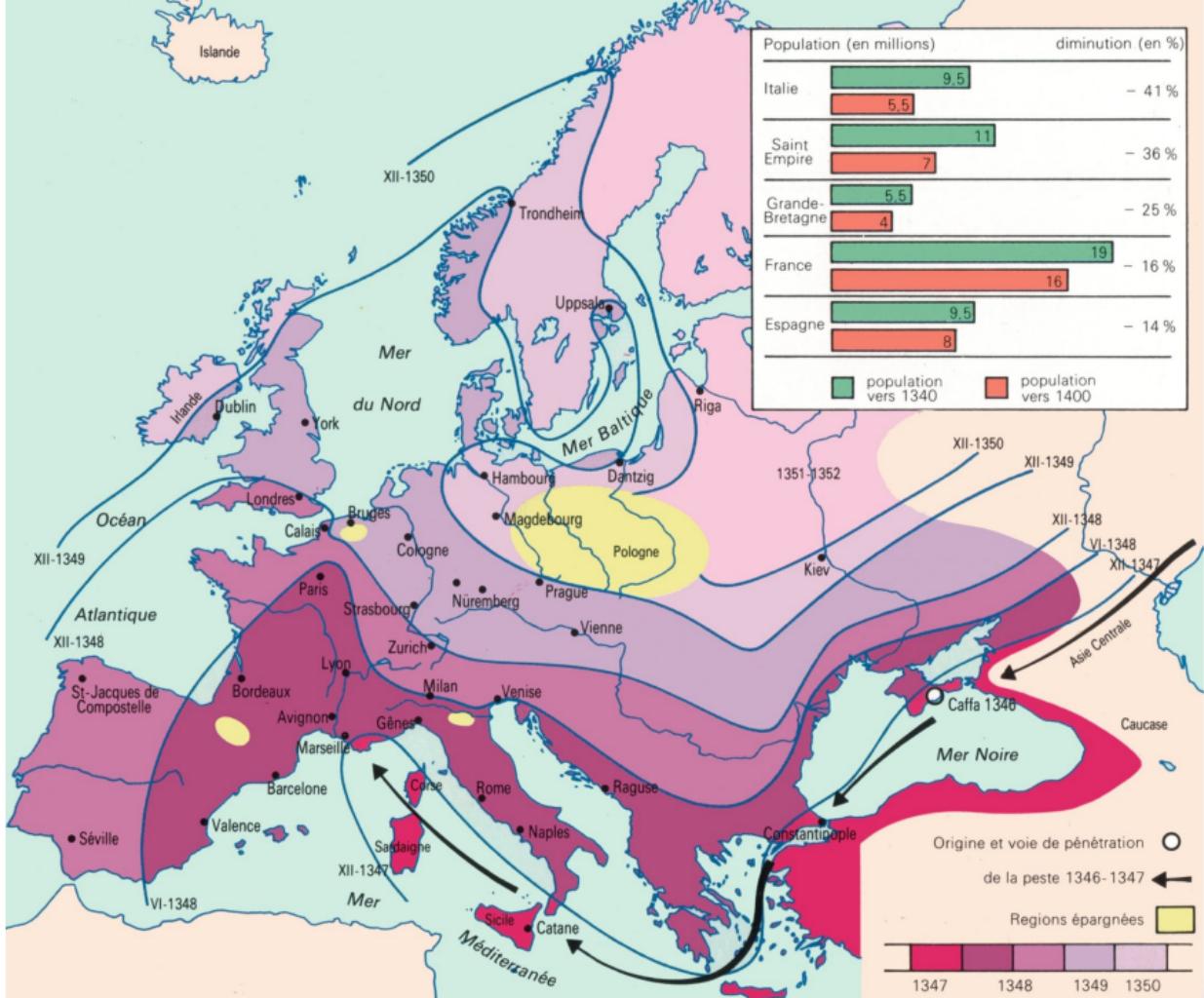
Pathogen spread has evolved with mobility

Pathogens use trade routes

In ancient times, trade routes were “simple”

A.D.1478







Plague
An Dom 1637
Burials 315
Hera nos Domine

Pathogen spread has evolved with mobility

Pathogens use trade routes

With the acceleration and globalization of mobility, things are changing



Jeanne d'Albret
(1528-1572)
Queen of Navarre (1555-1572)



Henri IV
(1553-1610)
King of Navarre (1572-1610)
King of France (1589-1610)



Cosy turtle shell crib in Pau
(then capital of Béarn & Navarre)



ONLY 15 DAYS
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PROVINCE OF MANITOBA

MANITOBA offers the most easily accessible
lands in the world, the most promising and productive
lands in the world, lands which have been selected
as a pure, healthy climate, under a
form of government, and within easy
reach by rail, road, and water, to the
great centre of the Continent, which afford
the products.

THE LAND IS PRAIRIE
NOT BUSH LAND,
—
MANITOBA
AND THE NORTHWEST TERRITORIES.

Total area of Land fit for cultivation is estimated
at 21,000,000 acres, about 10,000,000
acres are already surveyed.

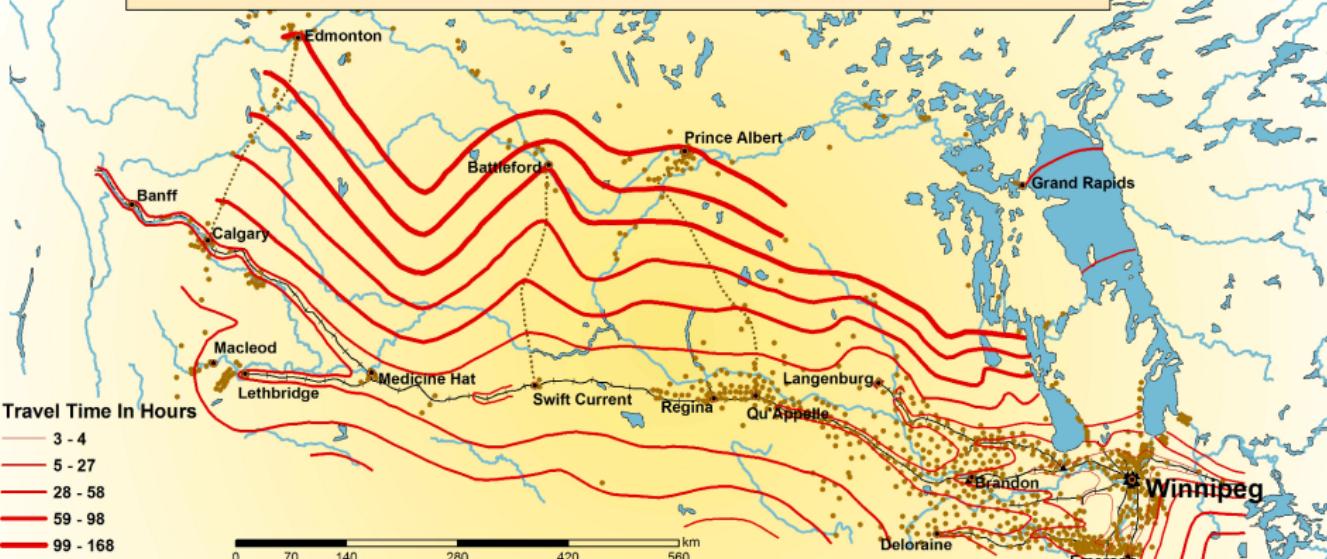
THE DOMINION HOMESTEAD LAW

In one of the best legal systems. Every grant holder is entitled
to a tract of land of 160 acres, or a part of it, if he wishes.
The land is free from all taxes for three years, and if he retains
it for five years, he may add another 160 acres to his original
grant. He may also add 160 acres to his original grant, if he
wishes, at any time during the five years, and if he retains it
for five years, he may add another 160 acres to his original
grant. He may also add 160 acres to his original grant, if he
wishes, at any time during the five years, and if he retains it
for five years, he may add another 160 acres to his original
grant.



THE MOST DIRECT ROUTE
LIVERPOOL to the GREAT NORTHWEST,
—
QUEBEC AND THE
GRAND TRUNK RAILWAY
AND CONNECTIONS.

TRAVEL TIME IN HOURS FROM WINNIPEG IN 1886

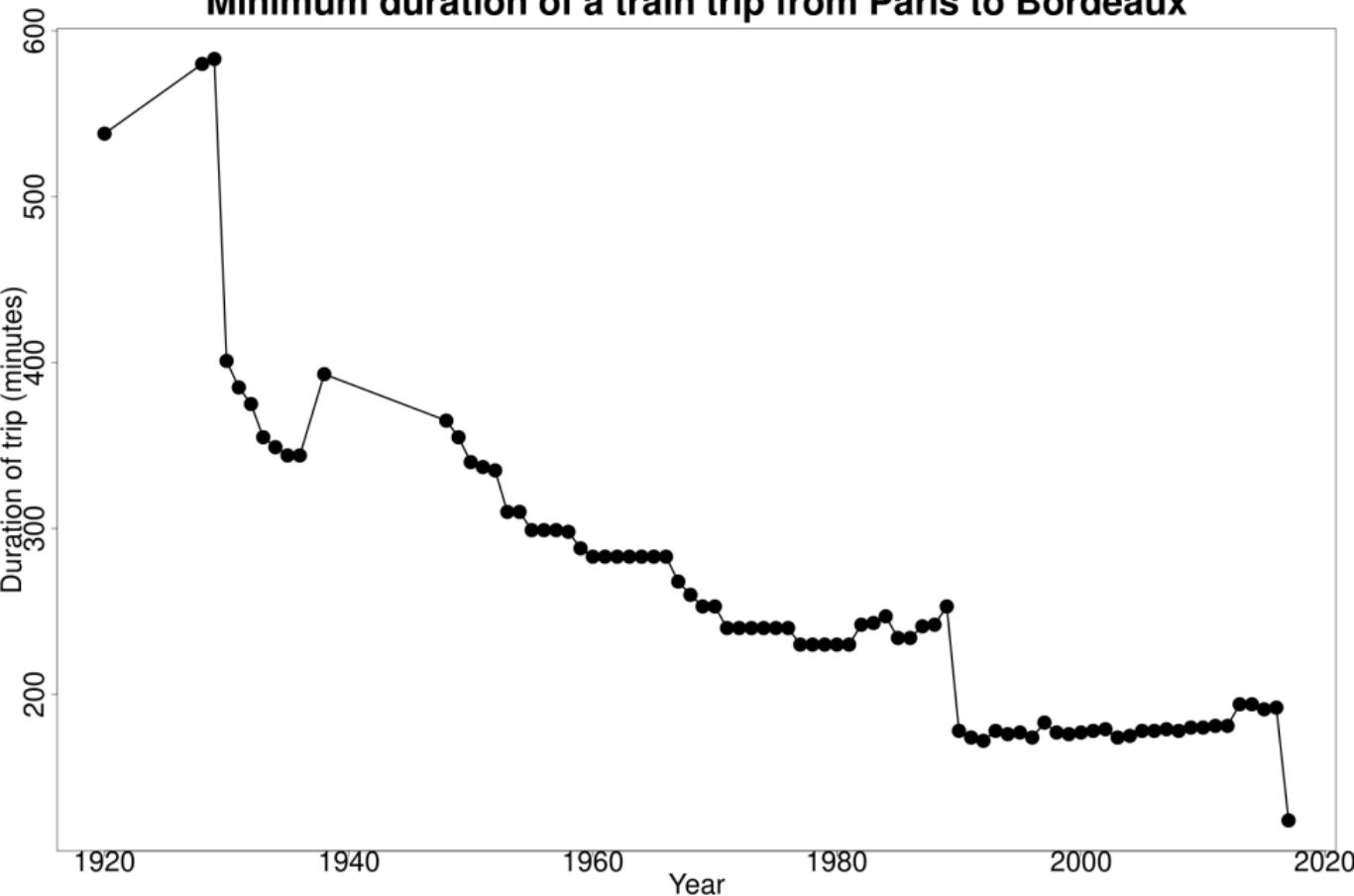


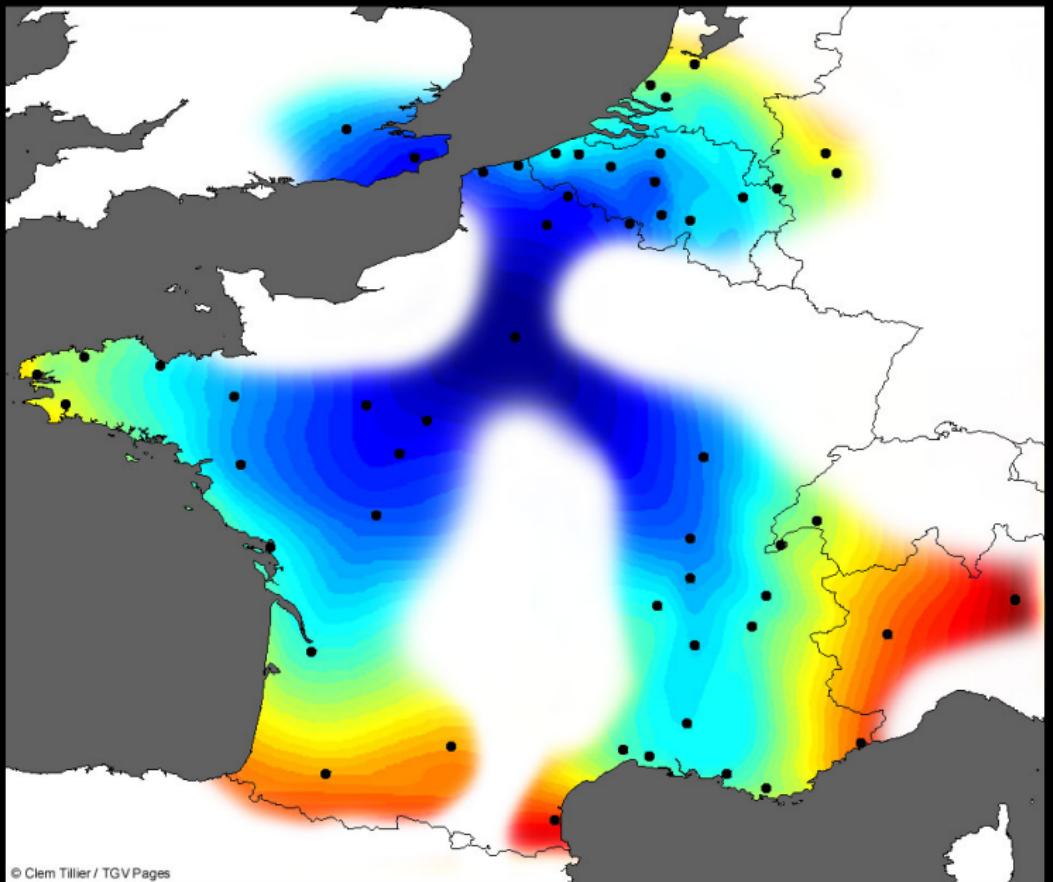
Compiled from maps prepared by John Warkentin "Western Canada 1886" in the Historical and Scientific Society of Manitoba, Series III No. 20 1963-1964

Notes:

- (1) Digital Data Source: Manitoba Lands Initiative.
- (2) Population statistics from the Census of Manitoba for 1886, the Census of the North-West Territories for 1885 (adjusted for 1886) and the Annual Report of the Department of Indian Affairs for 1886.
- (3) Travel Time information based on Waggoner's timetables for 1886 and contemporary newspapers and books. The isochrone lines are not reliable away from the main routes.

Minimum duration of a train trip from Paris to Bordeaux



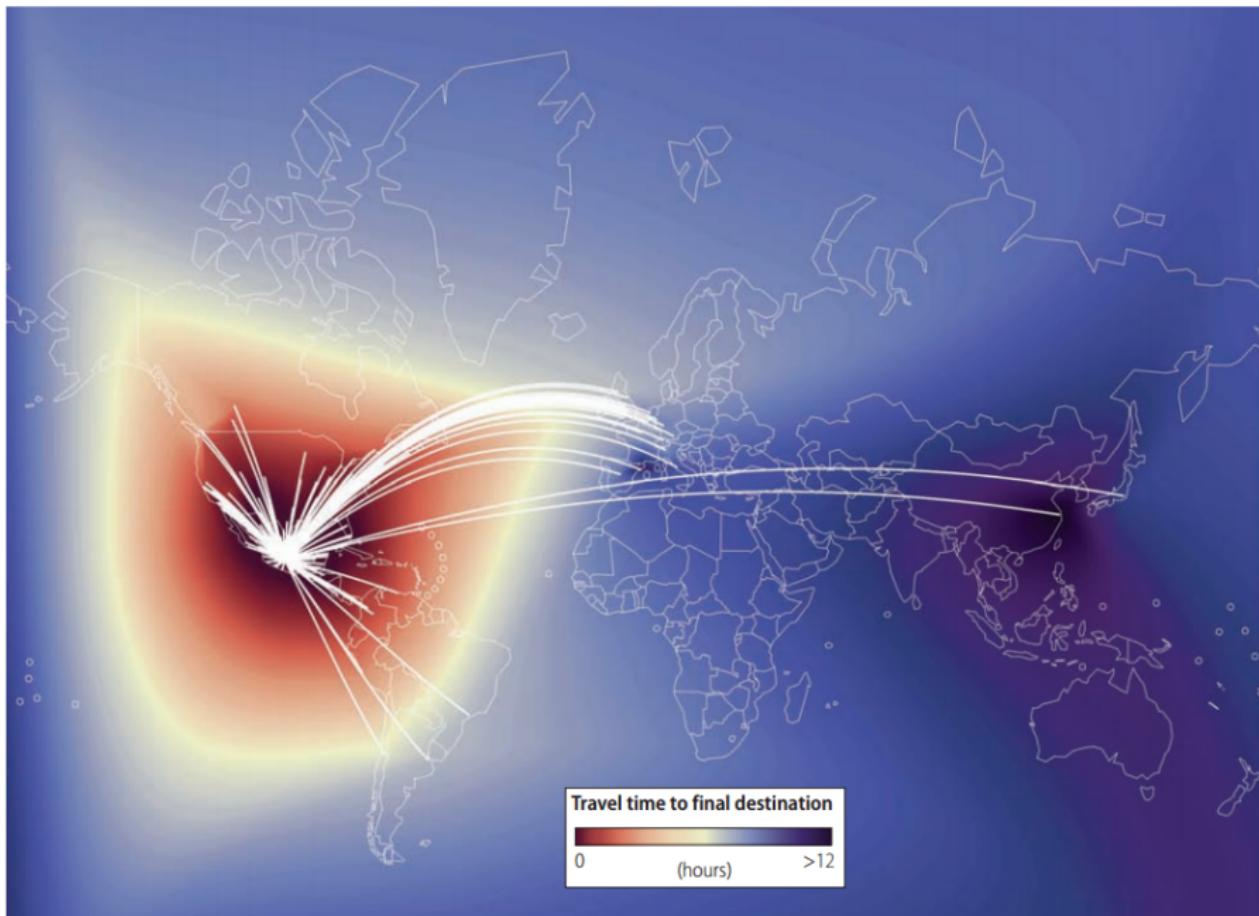


© Clem Tillier / TGV Pages



Travel time from Paris, in hours. Black dots represent selected cities with TGV / Thalys / Eurostar service.

Fig. 2. International flights departing Mexico^a and corresponding travel times, May 2009



^a 82 international cities received flights directly from Mexico in May 2009.

Scale of modern mobility difficult to apprehend

Working definition

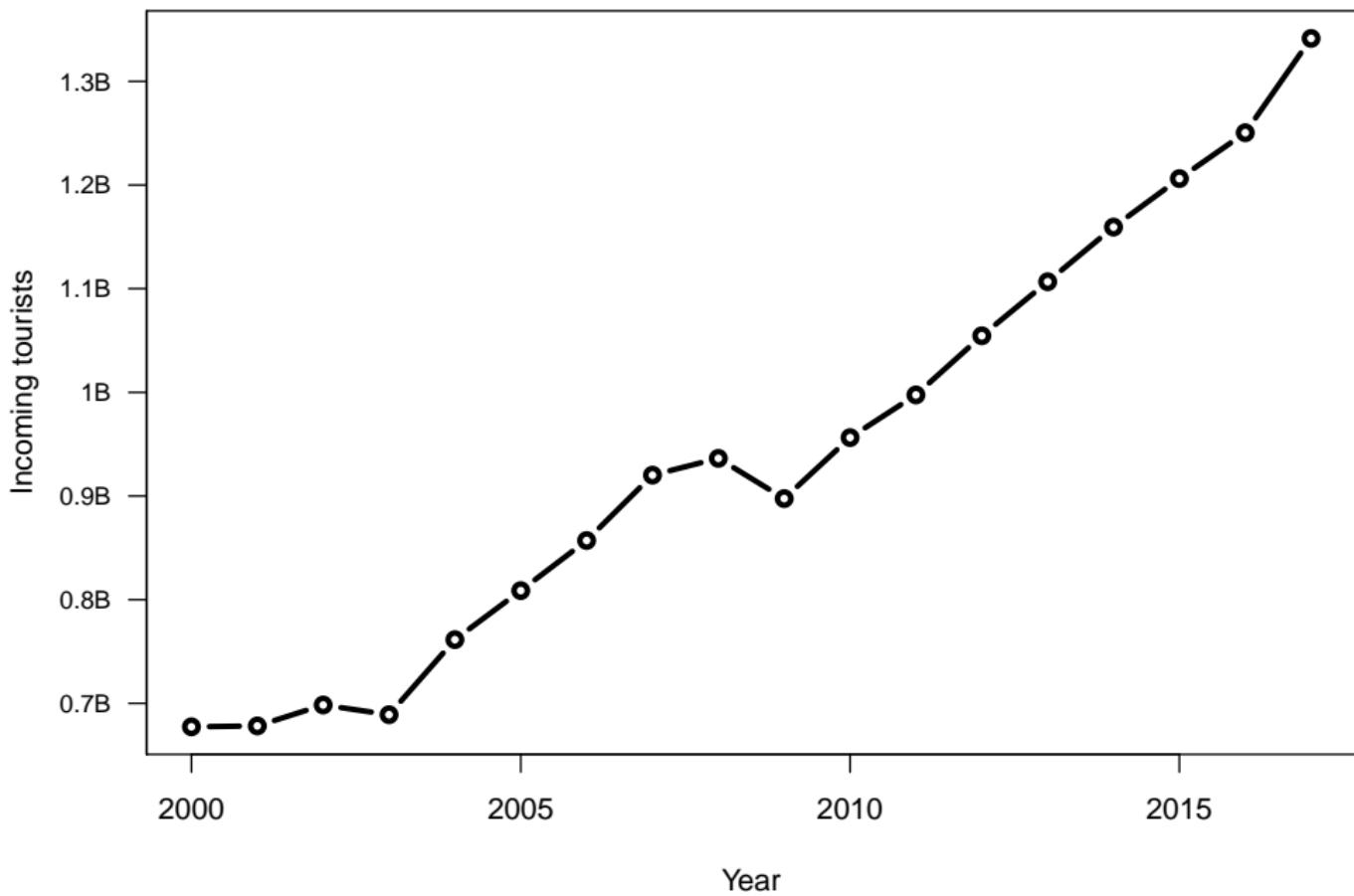
Mobility is the collection of processes through which individuals change their current location

Takes many different forms

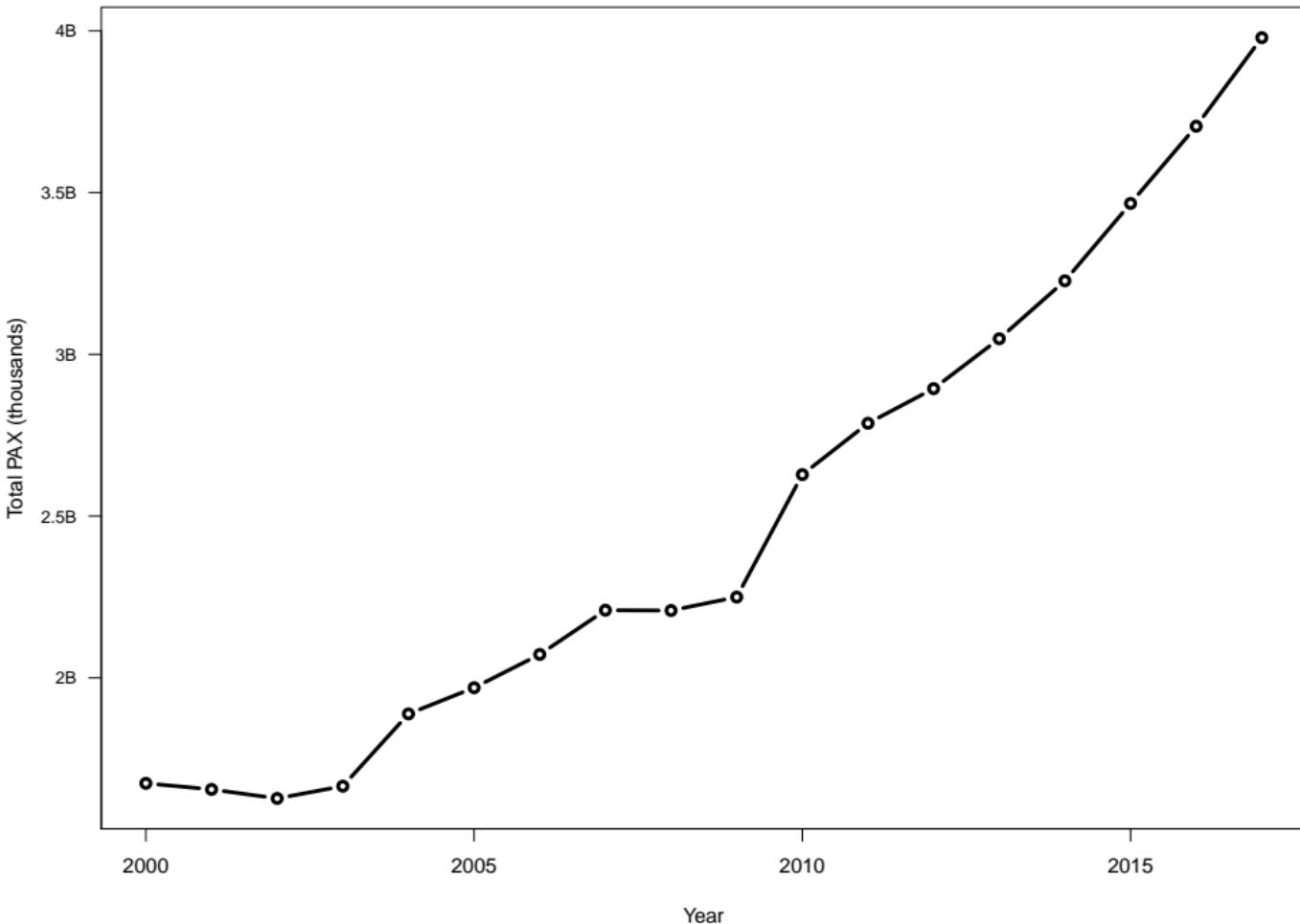
Evolves constantly

Numbers are .. colossal

Number of incoming tourists (all countries)



Number of passengers transported (all countries)



Why mobility is important in the context of health

All migrants/travellers carry with them their “health history”

- ▶ latent and/or active infections (TB, H1N1, polio)
- ▶ immunizations (schedules vary by country)
- ▶ health/nutrition practices (KJv)
- ▶ treatment methods (antivirals)

Pathogens ignore borders and politics

- ▶ e.g., antiviral treatment policies for Canada and USA

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Why use metapopulation models?

Metapopulations with explicit movement

The graph setting

Generic model

The movement matrix

Behaviour of the mobility component

The models considered

Existence of a DFE

Computation of a reproduction number

Global stability of the DFE when $\mathcal{R}_0 < 1$

Metapopulation-specific problems

Why use metapopulations for disease models?

- ▶ Appropriate for the description of spatial spread of some diseases
- ▶ Ease of simulation
- ▶ Aggregation of data by governments is most often done at the jurisdictional level, very easy to reconcile with locations in metapopulations

A few pointers

- ▶ JA & PvdD. Disease spread in metapopulations. *Fields Institute Communications* **48**:1-13 (2006)
- ▶ JA. Diseases in metapopulations. In *Modeling and Dynamics of Infectious Diseases*, World Scientific (2009)
- ▶ JA. Spatio-temporal spread of infectious pathogens of humans. *Infectious Disease Modelling* **2**(2):218-228 (2017)

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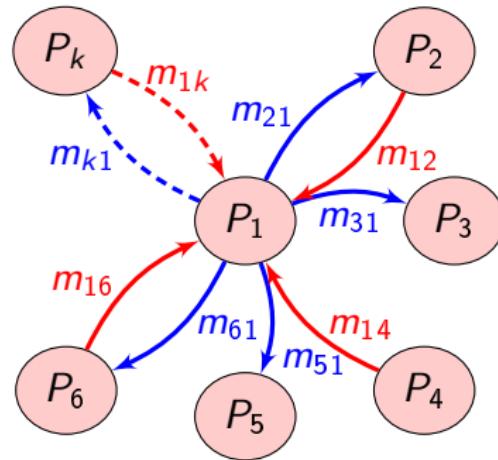
Split continuous space into N discrete geographical locations (*ptatches*)

Each location contains **compartments** (homogeneous groups of individuals). E.g., preys, predators, etc.

Here, we consider a single compartment, the *species of interest*, with no further compartmentalisation

Individuals *may* move between locations; $m_{qp} \geq 0$ rate of movement of individuals from location $p = 1, \dots, N$ to location $q = 1, \dots, N$

Explicit movement (focus on P_1)



$$P'_1 = \sum_{\substack{j=1 \\ j \neq 1}}^N m_{1j} P_j - P_1 \sum_{\substack{j=1 \\ j \neq 1}}^N m_{j1}$$

or

$$P'_1 = \sum_{j=1}^N m_{1j} P_j \text{ assuming } m_{11} = - \sum_{\substack{j=1 \\ j \neq 1}}^N m_{j1}$$

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Graph setting

Suppose

- ▶ $|\mathcal{P}|$ locations, vertices in a (directed) graph \mathcal{G}
- ▶ Each location contains a certain number of compartments belonging to a common set \mathcal{C} of compartments
- ▶ Arcs of \mathcal{G} represent the possibility for a given compartment to move between two locations; any two locations are connected by a maximum of $|\mathcal{C}|$ edges

Graph is a digraph: movement is not always symmetric

$\mathcal{G} = (\mathcal{P}, \mathcal{A})$ is multi-digraph, where

- ▶ \mathcal{P} is the set of vertices (locations)
- ▶ \mathcal{A} is the set of arcs, i.e., an ordered multiset of pairs of elements of \mathcal{P}

Any two vertices $X, Y \in \mathcal{P}$ are connected by at most $|\mathcal{C}|$ arcs from X to Y and at most $|\mathcal{C}|$ arcs from Y to X

Because there are $|\mathcal{C}|$ compartments and movements are compartment-specific, we also define, for all $c \in \mathcal{C}$, \mathcal{P}_c and \mathcal{A}_c as well as the compartment-specific digraphs $\mathcal{G}^c = (\mathcal{P}_c, \mathcal{A}_c)$

Connection matrix

For a given compartment $c \in \mathcal{C}$, a *connection matrix* can be associated to the digraph \mathcal{G}_c

This is the **adjacency matrix** of \mathcal{G}_c , but we emphasize the reason why we use \mathcal{G}_c by using the term *connection*

Choosing an ordering of elements of \mathcal{P} , the (i, j) entry of the $|\mathcal{P}| \times |\mathcal{P}|$ -matrix $\mathcal{N}_c = \mathcal{N}_c(\mathcal{G}_c)$ is one if $R^c(P_i, P_j)$ and zero otherwise, i.e., if P_i has no direct access to P_j

For convenience, the ordering of the locations is generally assumed the same for all compartments

Strong connectedness and irreducibility

Definition 1 (Reducible/irreducible matrix)

A matrix A is **reducible** if there exists a permutation matrix P such that P^TAP is block upper triangular. A matrix that is not reducible is **irreducible**

Matrix $A \in \mathbb{F}^{n \times n}$ is irreducible if for all $i, j = 1, \dots, n$, there exists k such that $a_{ij}^k > 0$, where a_{ij}^k is the (i, j) -entry in A^k

Theorem 2

Strong connectedness \Leftrightarrow irreducibility of the connection matrix C_c

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Dynamics of the system:

- ▶ dynamics in each location resulting from the interactions of the various compartments,
- ▶ operator describing the movements of individuals between the locations.

A very simple example to facilitate ingestion

Suppose an SIS model over a set \mathcal{P} of locations. If need be, choose an order on elements of \mathcal{P} and index locations as $1, \dots, |\mathcal{P}|$

Let S_p and I_p be number of susceptible and infectious individuals in location $p \in \mathcal{P}$, respectively

Then, in location $p \in \mathcal{P}$, dynamics governed by

$$S'_p = b_p - \beta_p S_p I_p + \gamma_p I_p - d_p S_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (1a)$$

$$I'_p = \beta_p S_p I_p - \gamma_p I_p - d_p I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (1b)$$

(Don't worry about why this is a metapopulation model this far)

Notation

- ▶ $N_{cp}(t)$ number of individuals of compartment c in location p at time t
(Here and elsewhere: omit dependence on t unless it causes confusion)
- ▶ $N_c = (N_{c1}, \dots, N_{c|\mathcal{P}|})^T$ distribution of individuals of compartment $c \in \mathcal{C}$ among the different locations
[E.g., for (1), $N_S = (S_1, \dots, S_{|\mathcal{P}|})^T$]
- ▶ $N^p = (N_1^p, \dots, N_{|\mathcal{P}|}^p)^T$ composition of the population in location $p \in \mathcal{P}$
[E.g., for (1), $N^p = (S_p, I_p)^T$]

General form of the system

Interaction function f and movement operator M can be time-dependent (not shown)

- ▶ Equation by equation; for all $c \in \mathcal{C}$ and $p \in \mathcal{P}$

$$\frac{d}{dt} N_{cp} = f_{cp}(N^p) + M_{cp}(N_s) \quad (2)$$

with $f_{cp} : \mathbb{R}^{|\mathcal{P}|} \rightarrow \mathbb{R}$ and $M_{cp} : \mathbb{R}^{|\mathcal{C}|} \rightarrow \mathbb{R}$

- ▶ Compartment by compartment; for all $c \in \mathcal{C}$

$$\frac{d}{dt} N_c = f^p(N^p) + M_c(N_c) \quad (3)$$

with $f^p : \mathbb{R}^{|\mathcal{P}|} \rightarrow \mathbb{R}^{|\mathcal{C}|}$ and $M_s^p : \mathbb{R}^{|\mathcal{C}|} \rightarrow \mathbb{R}^{|\mathcal{C}|}$

- ▶ Location by location; for all $p = 1, \dots, |\mathcal{P}|$

$$\frac{d}{dt} N^p = f^p(N^p) + M^p(N^p) \quad (4)$$

with $f^p : \mathbb{R}^{|\mathcal{P}|} \rightarrow \mathbb{R}^{|\mathcal{C}|}$ and $M_s^p : \mathbb{R}^{|\mathcal{C}|} \rightarrow \mathbb{R}^{|\mathcal{C}|}$

Metapopulation models with linear movement

Use a linear autonomous movement operator

Then, for a given compartment $c \in \mathcal{C}$ and in a given location $p \in \mathcal{P}$

$$N'_{cp} = f_{cp}(N^p) + \sum_{\substack{q \in \mathcal{P} \\ q \neq p}} m_{cpq} N_{cq} - \left(\sum_{\substack{q \in \mathcal{P} \\ q \neq p}} m_{cqp} \right) N_{cp}$$

where m_{cpq} rate of movement of individuals in compartment $c \in \mathcal{C}$ from location $q \in \mathcal{P}$ to location $p \in \mathcal{P}$

A more compact notation

To make

$$N'_{cp} = f_{cp}(N^p) + \sum_{\substack{q \in \mathcal{P} \\ q \neq p}} m_{cpq} N_{cq} - \left(\sum_{\substack{q \in \mathcal{P} \\ q \neq p}} m_{cqp} \right) N_{cp}$$

more compact, denote the rate of leaving location p as

$$m_{cpp} = - \sum_{\substack{q \in \mathcal{P} \\ q \neq p}} m_{cqp} \quad (5)$$

Then

$$N'_s = f_{cp}(N^p) + \sum_{q \in \mathcal{P}} m_{cpq} N_{cq} \quad (6)$$

Vector form of the system

For compartment $c \in \mathcal{C}$,

$$N'_c = f(N) + \mathcal{M}_c N_c \quad (7)$$

with

$$\mathcal{M}_c = \begin{pmatrix} -\sum_{k \in \mathcal{P}} m_{ck1} & m_{c12} & \cdots & m_{c1|\mathcal{P}|} \\ m_{c|\mathcal{P}|1} & m_{c|\mathcal{P}|2} & \cdots & -\sum_{k \in \mathcal{P}} m_{ck|\mathcal{P}|} \end{pmatrix} \quad (8)$$

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Definitions and notation for matrices

- ▶ $M \in \mathbb{R}^{n \times n}$ a square matrix with entries denoted m_{ij}
- ▶ $M \geq 0$ if $m_{ij} \geq 0$ for all i, j (could be the zero matrix); $M > 0$ if $M \geq 0$ and $\exists i, j$ with $m_{ij} > 0$; $M \gg 0$ if $m_{ij} > 0 \forall i, j = 1, \dots, n$. Same notation for vectors
- ▶ $\sigma(M) = \{\lambda \in C; M\lambda = \lambda v, v \neq 0\}$ **spectrum** of M
- ▶ $\rho(M) = \max_{\lambda \in \sigma(M)} \{|\lambda|\}$ **spectral radius**
- ▶ $s(M) = \max_{\lambda \in \sigma(M)} \{\operatorname{Re}(\lambda)\}$ **spectral abscissa** (or **stability modulus**)
- ▶ M is an **M-matrix** if it is a **Z-matrix** ($m_{ij} \leq 0$ for $i \neq j$) and $M = s\mathbb{I} - A$, with $A \geq 0$ and $s \geq \rho(A)$

The movement matrix

The matrix

$$\mathcal{M}_c = \begin{pmatrix} -\sum_{k \in \mathcal{P}} m_{ck1} & m_{c12} & \cdots & m_{c1|\mathcal{P}|} \\ m_{c|\mathcal{P}|1} & m_{c|\mathcal{P}|2} & \cdots & -\sum_{k \in \mathcal{P}} m_{ck|\mathcal{P}|} \end{pmatrix} \quad (8)$$

is the **movement matrix**

It plays an extremely important role in the analysis of metapopulation systems, so we'll spend some time discussing its properties

\mathcal{M}_c describes

- ▶ existence of connections
- ▶ when they exist, their “intensity”

Properties of the movement matrix \mathcal{M}

First, remark $-\mathcal{M}_c$ is a Lagrangian matrix (cf. Michael's course)

Lemma 3

1. $0 \in \sigma(\mathcal{M})$ corresponding to left e.v. $\mathbb{1}^T$ [σ spectrum]
2. $-\mathcal{M}$ is a singular M-matrix
3. $0 = s(\mathcal{M}) \in \sigma(\mathcal{M})$ [s spectral abscissa]
4. If \mathcal{M} irreducible, then $s(\mathcal{M})$ has multiplicity 1

For complete proof of Lemma 3 and Proposition 4 (next page), see
Arino, Bajeur & Kirkland, BMB 2019

Proposition 4 (D a diagonal matrix)

1. $s(\mathcal{M} + d\mathbb{I}) = d, \forall d \in \mathbb{R}$
2. $s(\mathcal{M} + D) \in \sigma(\mathcal{M} + D)$ associated to $\nu > 0$. If \mathcal{M} irreducible, $s(\mathcal{M} + D)$ has multiplicity 1 and is associated to $\nu \gg 0$
3. If $\text{diag}(D) \gg 0$, then $D - \mathcal{M}$ invertible M-matrix and $(D - \mathcal{M})^{-1} > 0$
4. \mathcal{M} irreducible and $\text{diag}(D) > 0 \implies D - \mathcal{M}$ nonsingular irreducible M-matrix and $(D - \mathcal{M})^{-1} \gg 0$

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Metapopulation-specific problems

Behaviour of the mobility component – No demography

Assume no within-location dynamics, just movement. Then (7) takes the form

$$N'_c = \mathcal{M}_c N_c \quad (9)$$

Theorem 5

For a given compartment $c \in \mathcal{C}$, suppose that the movement matrix \mathcal{M}_c is irreducible. Then for any $N_c(0) > 0$, (9) satisfies

$$\lim_{t \rightarrow \infty} N_c(t) = N_c^* \gg 0$$

Note that N_c^* depends on $\mathbb{1}^T N_c(0)$

Reduction to total population per location – Demography

Let

$$T_p = \sum_{c \in \mathcal{C}} N_{cp}$$

be the total population in location p

It is often possible to obtain, in each location $p \in \mathcal{P}$, an equation for the evolution of the total population that takes the form

$$T'_p = D_p(T_p) + \sum_{c \in \mathcal{C}} \sum_{q \in \mathcal{P}} m_{cpq} N_{cq} \quad (10)$$

where $D_p(T_p)$ describes the demography in location p

Nature of the demography

Most common types of demographic functions

- ▶ $D_p(T_p) = b_p - d_p T_p$ (asymptotically constant population)
- ▶ $D_p(T_p) = b_p T_p - d_p T_p$
- ▶ $D_p(T_p) = d_p T_p - b_p T_p = 0$ (constant population)
- ▶ $D_p(T_p) = r_p T_p(1 - T_p/K_p)$ (logistic demography)

In what follows, assume

$$D_p(T_p) = b_p - d_p T_p \quad (11)$$

Vector / matrix form of the equation

Assuming demography is of the form (11), write (10) in vector form

$$\mathbf{T}' = \mathbf{b} - \mathbf{dT} + \sum_{c \in \mathcal{C}} \mathcal{M}_c \mathbf{N}_c \quad (12)$$

where

- ▶ $\mathbf{b} = (b_1, \dots, b_{|\mathcal{P}|})^T \in \mathbb{R}^{|\mathcal{P}|}$
- ▶ $\mathbf{T} = (T_1, \dots, T_{|\mathcal{P}|})^T \in \mathbb{R}^{|\mathcal{P}|}$
- ▶ $\mathbf{N} = (N_{c1}, \dots, N_{c|\mathcal{P}|})^T \in \mathbb{R}^{|\mathcal{P}|}$
- ▶ $\mathbf{d} = \text{diag}(d_1, \dots, d_{|\mathcal{P}|}) \in \mathbb{R}^{|\mathcal{P}| \times |\mathcal{P}|}$
- ▶ $\mathcal{M}_c \in \mathbb{R}^{|\mathcal{P}| \times |\mathcal{P}|}$

The nice case

Suppose movement rates **equal for all compartments**, i.e.,

$$\mathcal{M}_c \equiv \mathcal{M}$$

(stronger than Definition ??, which only requires zero/nonzero patterns in all \mathcal{M}_c , $c \in \mathcal{C}$, to be the same)

Then

$$\begin{aligned}\mathbf{T}' &= \mathbf{b} - \mathbf{dT} + \mathcal{M} \sum_{c \in \mathcal{C}} \mathbf{N}_c \\ &= \mathbf{b} - \mathbf{dT} + \mathcal{M} \mathbf{T}\end{aligned}\tag{13}$$

Equilibria

$$\begin{aligned} \mathbf{T}' = 0 &\Leftrightarrow \mathbf{b} - \mathbf{dT} + \mathcal{M}\mathbf{T} = 0 \\ &\Leftrightarrow (\mathbf{d} - \mathcal{M})\mathbf{T} = \mathbf{b} \\ &\Leftrightarrow \mathbf{T}^* = (\mathbf{d} - \mathcal{M})^{-1}\mathbf{b} \end{aligned}$$

given, of course, that $\mathbf{d} - \mathcal{M}$ (or, equivalently, $\mathcal{M} - \mathbf{d}$) is invertible..

Is it?

Nonsingularity of $\mathcal{M} - \mathbf{d}$

Using the spectrum shift of Theorem 4(1)

$$s\left(\mathcal{M} - \min_{p \in \mathcal{P}} d_p\right) = -\min_{p \in \mathcal{P}} d_p$$

This gives a constraint: for total population to behave well (in general, we want this), we *must assume all death rates are positive*

Assume they are (in other words, assume \mathbf{d} nonsingular). Then $\mathcal{M} - \mathbf{d}$ is nonsingular and $\mathbf{T}^* = (\mathbf{d} - \mathcal{M})^{-1}\mathbf{b}$ unique

Behaviour of the total population

Equal irreducible movement case

$T^* = (\mathbf{d} - \mathcal{M})^{-1}\mathbf{b}$ attracts solutions of

$$T' = \mathbf{b} - \mathbf{dT} + \mathcal{M}T =: f(T)$$

Indeed, we have

$$Df = \mathcal{M} - \mathbf{d}$$

Since we now assume that \mathbf{d} is nonsingular, we have by Theorem 4(1) that $s(\mathcal{M} - \min_{p \in \mathcal{P}} d_p) = -\min_{p \in \mathcal{P}} d_p < 0$

\mathcal{M} irreducible $\rightarrow T^* \gg 0$ (provided $b > 0$, of course)

Behaviour of total population

Equal reducible movement case

Theorem 6

Assume \mathcal{M} reducible. Let a be the number of minimal absorbing sets in the corresponding connection graph $\mathcal{G}(\mathcal{M})$. Then

1. The spectral abscissa $s(\mathcal{M}) = 0$ has multiplicity a
2. Associated to $s(\mathcal{M})$ is a nonnegative eigenvector v s.t.
 - ▶ $v_i > 0$ if i is a vertex in a minimal absorbing set
 - ▶ $v_i = 0$ if i is a transient vertex

From Foster and Jacquez, Multiple zeros for eigenvalues and the multiplicity of traps of a linear compartmental system,
Mathematical Biosciences (1975)

The not-so-nice case

Recall that

$$\mathbf{T}' = \mathbf{b} - \mathbf{dT} + \sum_{c \in C} M_c N_c$$

Suppose movement rates **similar for all compartments**, i.e., the zero/nonzero patterns in all matrices are the same but not the entries

Let

$$\underline{M} = \left[\min_{X \in \{S, L, I, R\}} m_{Xpq} \right]_{pq, p \neq q} \quad \overline{M} = \left[\max_{X \in \{S, L, I, R\}} m_{Xpq} \right]_{pq, p=q}$$

and

$$\overline{\mathcal{M}} = \left[\max_{X \in \{S, L, I, R\}} m_{Xpq} \right]_{pq, p \neq q} \quad \underline{\mathcal{M}} = \left[\min_{X \in \{S, L, I, R\}} m_{Xpq} \right]_{pq, p=q}$$

Cool, no? No!

Then we have

$$b - dT + \underline{M}T \leq T' \leq b - dT + \overline{M}T$$

Me, roughly every 6 months: *Oooh, cooooool, a linear differential inclusion!*

Me, roughly 10 minutes after that previous statement: *Quel con!*

Indeed \underline{M} and \overline{M} are **are not** movement matrices (in particular, their column sums are not all zero)

So no luck there..

However, we can still do stuff, but more on a case-by-case basis

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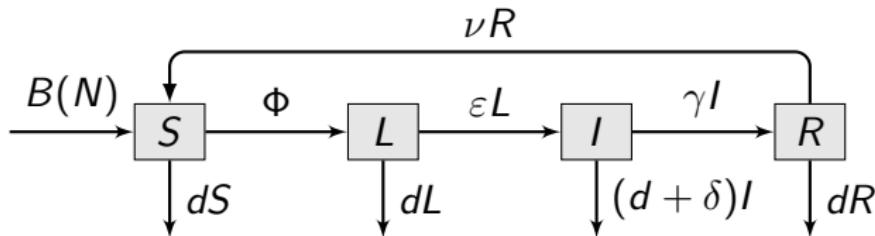
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The toy SLIRS model in patches



$$S' = \mathcal{B}(N) + \nu R - \Phi - dS \quad (14a)$$

$$L' = \Phi - (\varepsilon + d)L \quad (14b)$$

$$I' = \varepsilon L - (\gamma + d + \delta)I \quad (14c)$$

$$R' = \gamma I - (\nu + d)R \quad (14d)$$

Φ force of infection. Depends on S, I , possibly N . In general

$$\Phi = \beta(N)\phi(S, I)$$

Mass action, $\Phi = \beta SI$, proportional incidence, $\Phi = \beta SI/N$

$|\mathcal{P}|$ -SLIRS model

$$S'_p = \mathcal{B}_p(N_p) + \nu_p R_p - \Phi_p - d_p S_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (15a)$$

$$L'_p = \Phi_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q \quad (15b)$$

$$I'_p = \varepsilon_p L_p - (\gamma_p + d_p) I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (15c)$$

$$R'_p = \gamma_p I_p - (\nu_p + d_p) R_p + \sum_{q \in \mathcal{P}} m_{Rpq} R_q \quad (15d)$$

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (15e)$$

$|\mathcal{S}| |\mathcal{P}|$ -SLIRS (multiple species)

$p \in \mathcal{P}$ and $s \in \mathcal{S}$ (a set of species)

$$S'_{sp} = \mathcal{B}_{sp}(N_{sp}) + \nu_{sp}R_{sp} - \Phi_{sp} - d_{sp}S_{sp} + \sum_{q \in \mathcal{P}} m_{Sspq}S_{sq} \quad (16a)$$

$$L'_{sp} = \Phi_{sp} - (\varepsilon_{sp} + d_{sp})L_{sp} + \sum_{q \in \mathcal{P}} m_{Lspq}L_{sq} \quad (16b)$$

$$I'_{sp} = \varepsilon_{sp}L_{sp} - (\gamma_{sp} + d_{sp})I_{sp} + \sum_{q \in \mathcal{P}} m_{Ispq}I_{sq} \quad (16c)$$

$$R_{sp} = \gamma_{sp}I_{sp} - (\nu_{sp} + d_{sp})R_{sp} + \sum_{q \in \mathcal{P}} m_{Rspq}R_{sq} \quad (16d)$$

with incidence

$$\Phi_{sp} = \sum_{k \in \mathcal{S}} \beta_{skp} \frac{S_{sp}I_{kp}}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (16e)$$

- ▶ JA, Davis, Hartley, Jordan, Miller & PvdD. A multi-species epidemic model with spatial dynamics. *Mathematical Medicine and Biology* 22(2):129-142 (2005)
- ▶ JA, Jordan & PvdD. Quarantine in a multi-species epidemic model with spatial dynamics. *Mathematical Biosciences* 206(1):46-60 (2007)

$|\mathcal{P}|^2$ -SLIRS (residents-travellers)

$$S'_{pq} = \mathcal{B}_{pq} (N_p^r) + \nu_{pq} R_{pq} - \Phi_{pq} - d_{pq} S_{pq} + \sum_{k \in \mathcal{P}} m_{Spqk} S_{pk} \quad (17a)$$

$$L'_{pq} = \Phi_{pq} - (\varepsilon_{pq} + d_{pq}) L_{pq} + \sum_{k \in \mathcal{P}} m_{Lpqk} L_{pk} \quad (17b)$$

$$I'_{pq} = \varepsilon_{pq} L_{pq} - (\gamma_{pq} + d_{pq}) I_{pq} + \sum_{k \in \mathcal{P}} m_{Ipqk} I_{pk} \quad (17c)$$

$$R'_{pq} = \gamma_{pq} I_{pq} - (\nu_{pq} + d_{pq}) R_{pq} + \sum_{k \in \mathcal{P}} m_{Rpqk} R_{pk} \quad (17d)$$

with incidence

$$\Phi_{pq} = \sum_{k \in \mathcal{P}} \beta_{pqk} \frac{S_{pq} I_{kq}}{N_p^{q_q}}, \quad q_q = \{0, 1\} \quad (17e)$$

- ▶ Sattenspiel & Dietz. A structured epidemic model incorporating geographic mobility among regions (1995)
- ▶ JA & PvD. A multi-city epidemic model. *Mathematical Population Studies* 10(3):175-193 (2003)
- ▶ JA & PvD. The basic reproduction number in a multi-city compartmental epidemic model. In *Positive Systems* (2003)

Steps for an analysis

Basic steps

1. Well-posedness of the system
2. Existence of disease free equilibria (DFE)
3. Computation of a reproduction number \mathcal{R}_0 , study local asymptotic stability of DFE
4. If DFE unique, prove global asymptotic stability when $\mathcal{R}_0 < 1$

Additional steps

5. Existence of *mixed* equilibria, with some locations at DFE and others with disease
6. Computation of some bounds on \mathcal{R}_0
7. EEP and its LAS & GAS properties

...

Analysis – Toy system

For simplicity, consider $|\mathcal{P}|$ -SLIRS with $\mathcal{B}_p(N_p) = \mathcal{B}_p$

$$S'_p = \mathcal{B}_p - \Phi_p - d_p S_p + \nu_p R_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (18a)$$

$$L'_p = \Phi_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q \quad (18b)$$

$$I'_p = \varepsilon_p L_p - (\gamma_p + d_p) I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (18c)$$

$$R'_p = \gamma_p I_p - (\nu_p + d_p) R_p + \sum_{q \in \mathcal{P}} m_{Rpq} R_q \quad (18d)$$

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (18e)$$

System of $4|\mathcal{P}|$ equations

Don't panic: size is not that bad..

System of $4|\mathcal{P}|$ equations !!!

However, a lot of structure:

- ▶ $|\mathcal{P}|$ copies of individual units, each comprising 4 equations
- ▶ Dynamics of individual units well understood
- ▶ Coupling is linear

⇒ Good case of large-scale system

(matrix analysis is your friend)

Existence and uniqueness

- ▶ Existence and uniqueness of solutions classic, assured by good choice of birth and force of infection functions
- ▶ In the cases treated later, the birth function is either constant or a linear combination of state variables
- ▶ May exist problems at the origin, if the force of infection is not defined there
- ▶ Assumption from now on: existence and uniqueness

Other basic stuff

Skipped until I homogenise notation

Not complicated but sometimes tedious

Easy if it has been proved for the constituting units

Metapopulation models

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Metapopulation-specific problems

Disease free equilibrium

The model is at equilibrium if the time derivatives are zero

Definition 7 (Metapopulation DFE)

In the case of system (18), location $p \in \mathcal{P}$ is at a disease-free equilibrium (DFE) if $L_p = I_p = 0$, and the $|\mathcal{P}|$ -location model is at a **metapopulation DFE** if $L_p = I_p = 0$ for all $p \in \mathcal{P}$

Here, we want to find the DFE for the $|\mathcal{P}|$ -location model. Later, the existence of mixed equilibria, with some locations at the DFE and others at an endemic equilibrium, is considered

(For (16), replace L_p with L_{sp} and I_p with I_{sp} , for (17), replace L_p by L_{pp} and I_p by I_{pp} . To simplify notation, we could write L_\bullet and I_\bullet)

Assume (18) at metapopulation DFE. Then $\Phi_p = 0$ and

$$0 = \mathcal{B}_p - d_p S_p + \nu_p R_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q$$

$$0 = -(\nu_p + d_p) R_p + \sum_{q \in \mathcal{P}} m_{Rpq} R_q$$

Want to solve for S_p, R_p . Here, it is best (crucial in fact) to remember some linear algebra. Write system in vector form:

$$0 = \mathbf{b} - \mathbf{d}\mathbf{S} + \nu\mathbf{R} + \mathcal{M}^S \mathbf{S}$$

$$0 = -(\nu + \mathbf{d}) \mathbf{R} + \mathcal{M}^R \mathbf{R}$$

where $\mathbf{S}, \mathbf{R}, \mathbf{b} \in \mathbb{R}^{|\mathcal{P}|}$, $\mathbf{d}, \nu, \mathcal{M}^S, \mathcal{M}^R$ $|\mathcal{P}| \times |\mathcal{P}|$ -matrices (\mathbf{d}, ν diagonal)

R at DFE

Recall second equation:

$$0 = -(\nu + \mathbf{d})\mathbf{R} + \mathcal{M}^R\mathbf{R} \Leftrightarrow (\mathcal{M}^R - \nu - \mathbf{d})\mathbf{R} = 0$$

So unique solution $\mathbf{R} = 0$ if $\mathcal{M}^R - \nu - \mathbf{d}$ invertible Is it?

We have been here before!

From spectrum shift, $s(\mathcal{M}^R - \nu - \mathbf{d}) = -\min_{p \in \mathcal{P}}(\nu_p + d_p) < 0$

So, given $L = I = 0$, $\mathbf{R} = 0$ is the unique equilibrium and

$$\lim_{t \rightarrow \infty} \mathbf{R}(t) = 0$$

\implies DFE has $L = I = \mathbf{R} = 0$

S at the DFE

DFE has $L = I = R = 0$ and $b - dS + \mathcal{M}^S S = 0$, i.e.,

$$S = (\mathbf{d} - \mathcal{M}^S)^{-1} b$$

Recall: $-\mathcal{M}^S$ singular M-matrix. From previous reasoning,
 $\mathbf{d} - \mathcal{M}^S$ has **instability modulus** shifted *right* by $\min_{p \in \mathcal{P}} d_p$. So:

- ▶ $\mathbf{d} - \mathcal{M}^S$ invertible
- ▶ $\mathbf{d} - \mathcal{M}^S$ nonsingular M-matrix

Second point $\implies (\mathbf{d} - \mathcal{M}^S)^{-1} > 0 \implies (\mathbf{d} - \mathcal{M}^S)^{-1} b > 0$
(would have $\gg 0$ if \mathcal{M}^S irreducible)

So DFE makes sense with

$$(S, L, I, R) = \left((\mathbf{d} - \mathcal{M}^S)^{-1} b, 0, 0, 0 \right)$$

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Metapopulation-specific problems

- ▶ Linear stability of the disease free equilibrium can be investigated by using the next generation matrix
- ▶ In general, \mathcal{R}_0 depends on the demographic, disease and mobility parameters

Computing the basic reproduction number \mathcal{R}_0

Use next generation method with $\Xi = \{L_1, \dots, L_{|\mathcal{P}|}, I_1, \dots, I_{|\mathcal{P}|}\}$,
 $\Xi' = \mathcal{F} - \mathcal{V}$

$$\mathcal{F} = (\Phi_1, \dots, \Phi_{|\mathcal{P}|}, 0, \dots, 0)^T$$
$$\mathcal{V} = \begin{pmatrix} (\varepsilon_1 + d_1) L_1 - \sum_{q \in \mathcal{P}} m_{L1q} L_q \\ \vdots \\ (\varepsilon_{|\mathcal{P}|} + d_{|\mathcal{P}|}) L_{|\mathcal{P}|} - \sum_{q \in \mathcal{P}} m_{L|\mathcal{P}|q} L_q \\ -\varepsilon_1 L_1 + (\gamma_1 + d_1) I_1 - \sum_{q \in \mathcal{P}} m_{I1q} I_q \\ \vdots \\ -\varepsilon_{|\mathcal{P}|} L_{|\mathcal{P}|} + (\gamma_{|\mathcal{P}|} + d_{|\mathcal{P}|}) I_{|\mathcal{P}|} - \sum_{q \in \mathcal{P}} m_{I|\mathcal{P}|q} I_q \end{pmatrix}$$

Differentiate w.r.t. Ξ :

$$D\mathcal{F} = \begin{pmatrix} \frac{\partial \Phi_1}{\partial L_1} & \dots & \frac{\partial \Phi_1}{\partial L_{|\mathcal{P}|}} & \frac{\partial \Phi_1}{\partial I_1} & \dots & \frac{\partial \Phi_1}{\partial I_{|\mathcal{P}|}} \\ \vdots & & \vdots & \vdots & & \vdots \\ \frac{\partial \Phi_{|\mathcal{P}|}}{\partial L_1} & \dots & \frac{\partial \Phi_{|\mathcal{P}|}}{\partial L_{|\mathcal{P}|}} & \frac{\partial \Phi_{|\mathcal{P}|}}{\partial I_1} & \dots & \frac{\partial \Phi_{|\mathcal{P}|}}{\partial I_{|\mathcal{P}|}} \\ 0 & \dots & 0 & 0 & \dots & 0 \\ \vdots & & \vdots & \vdots & & \vdots \\ 0 & \dots & 0 & 0 & \dots & 0 \end{pmatrix}$$

Note that

$$\frac{\partial \Phi_p}{\partial L_k} = \frac{\partial \Phi_p}{\partial I_k} = 0$$

whenever $k \neq p$, so

$$D\mathcal{F} = \begin{pmatrix} \text{diag} \left(\frac{\partial \Phi_1}{\partial L_1}, \dots, \frac{\partial \Phi_{|\mathcal{P}|}}{\partial L_{|\mathcal{P}|}} \right) & \text{diag} \left(\frac{\partial \Phi_1}{\partial I_1}, \dots, \frac{\partial \Phi_{|\mathcal{P}|}}{\partial I_{|\mathcal{P}|}} \right) \\ 0 & 0 \end{pmatrix}$$

Evaluate $D\mathcal{F}$ at DFE

If $\Phi_p = \beta_p S_p I_p$, then

- ▶ $\frac{\partial \Phi_p}{\partial L_p} = 0$
- ▶ $\frac{\partial \Phi_p}{\partial I_p} = \beta_p S_p$

If $\Phi_p = \beta_p \frac{S_p I_p}{N_p}$, then

- ▶ $\frac{\partial \Phi_p}{\partial L_p} = \beta_p \frac{S_p I_p}{N_p^2} = 0$ at DFE
- ▶ $\frac{\partial \Phi_p}{\partial I_p} = \beta_p \frac{S_p}{N_p}$ at DFE

In both cases, $\partial/\partial L$ block is zero so

$$F = D\mathcal{F}(DFE) = \begin{pmatrix} 0 & \text{diag}\left(\frac{\partial \Phi_1}{\partial I_1}, \dots, \frac{\partial \Phi_{|\mathcal{P}|}}{\partial I_{|\mathcal{P}|}}\right) \\ 0 & 0 \end{pmatrix}$$

Compute $D\mathcal{V}$ and evaluate at DFE

$$V = \begin{pmatrix} \text{diag}_p(\varepsilon_p + d_p) - \mathcal{M}^L & 0 \\ -\text{diag}_p(\varepsilon_p) & \text{diag}_p(\gamma_p + d_p) - \mathcal{M}^I \end{pmatrix}$$

where $\text{diag}_p(z_p) := \text{diag}(z_1, \dots, z_{|\mathcal{P}|})$

Inverse of V easy (2×2 block lower triangular):

$$V^{-1} = \begin{pmatrix} (\text{diag}_p(\varepsilon_p + d_p) - \mathcal{M}^L)^{-1} & 0 \\ \tilde{V}_{21}^{-1} & (\text{diag}_p(\gamma_p + d_p) - \mathcal{M}^I)^{-1} \end{pmatrix}$$

where

$$\tilde{V}_{21}^{-1} = \left(\text{diag}_p(\varepsilon_p + d_p) - \mathcal{M}^L \right)^{-1}$$

$$\text{diag}_p(\varepsilon_p) \left(\text{diag}_p(\gamma_p + d_p) - \mathcal{M}^I \right)^{-1}$$

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

Next generation matrix

$$FV^{-1} = \begin{pmatrix} 0 & F_{12} \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \tilde{V}_{11}^{-1} & 0 \\ \tilde{V}_{21}^{-1} & \tilde{V}_{22}^{-1} \end{pmatrix} = \begin{pmatrix} F_{12}\tilde{V}_{21}^{-1} & F_{12}\tilde{V}_{22}^{-1} \\ 0 & 0 \end{pmatrix}$$

where \tilde{V}_{ij}^{-1} is block ij in V^{-1} . So

$$\mathcal{R}_0 = \rho \left(F_{12} \tilde{V}_{21}^{-1} \right)$$

i.e.,

$$\mathcal{R}_0 = \rho \left(\text{diag} \left(\frac{\partial \Phi_1}{\partial I_1}, \dots, \frac{\partial \Phi_{|\mathcal{P}|}}{\partial I_{|\mathcal{P}|}} \right) \left(\text{diag}_p(\varepsilon_p + d_p) - \mathcal{M}^L \right)^{-1} \right. \\ \left. \text{diag}_p(\varepsilon_p) \left(\text{diag}_p(\gamma_p + d_p) - \mathcal{M}' \right)^{-1} \right)$$

Local asymptotic stability of the DFE

Theorem 8

Define \mathcal{R}_0 for the $|\mathcal{P}|$ -SLIRS as

$$\mathcal{R}_0 = \rho \left(\text{diag} \left(\frac{\partial \Phi_1}{\partial I_1}, \dots, \frac{\partial \Phi_{|\mathcal{P}|}}{\partial I_{|\mathcal{P}|}} \right) \left(\text{diag}_p(\varepsilon_p + d_p) - \mathcal{M}^L \right)^{-1} \right. \\ \left. \text{diag}_p(\varepsilon_p) \left(\text{diag}_p(\gamma_p + d_p) - \mathcal{M}' \right)^{-1} \right)$$

Then the DFE

$$(S, L, I, R) = \left((d - \mathcal{M}^S)^{-1} b, 0, 0, 0 \right)$$

is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$

From PvdD & Watmough, Reproduction numbers and sub-threshold endemic equilibria for

compartmental models of disease transmission, *Bulletin of Mathematical Biology* 180(1-2): 29-48 (2002)

Some remarks about \mathcal{R}_0

The expression for \mathcal{R}_0 in Theorem 8 is exact

However, unless you consider a very small set of locations, you will not get a closed form expression

Indeed, by Theorem 4(3) and more importantly (often \mathcal{M} is irreducible), Theorem 4(4), the two inverses in \mathcal{R}_0 are likely crowded ($\gg 0$ in the irreducible case)

However, numerically, this works easy unless conditioning is bad

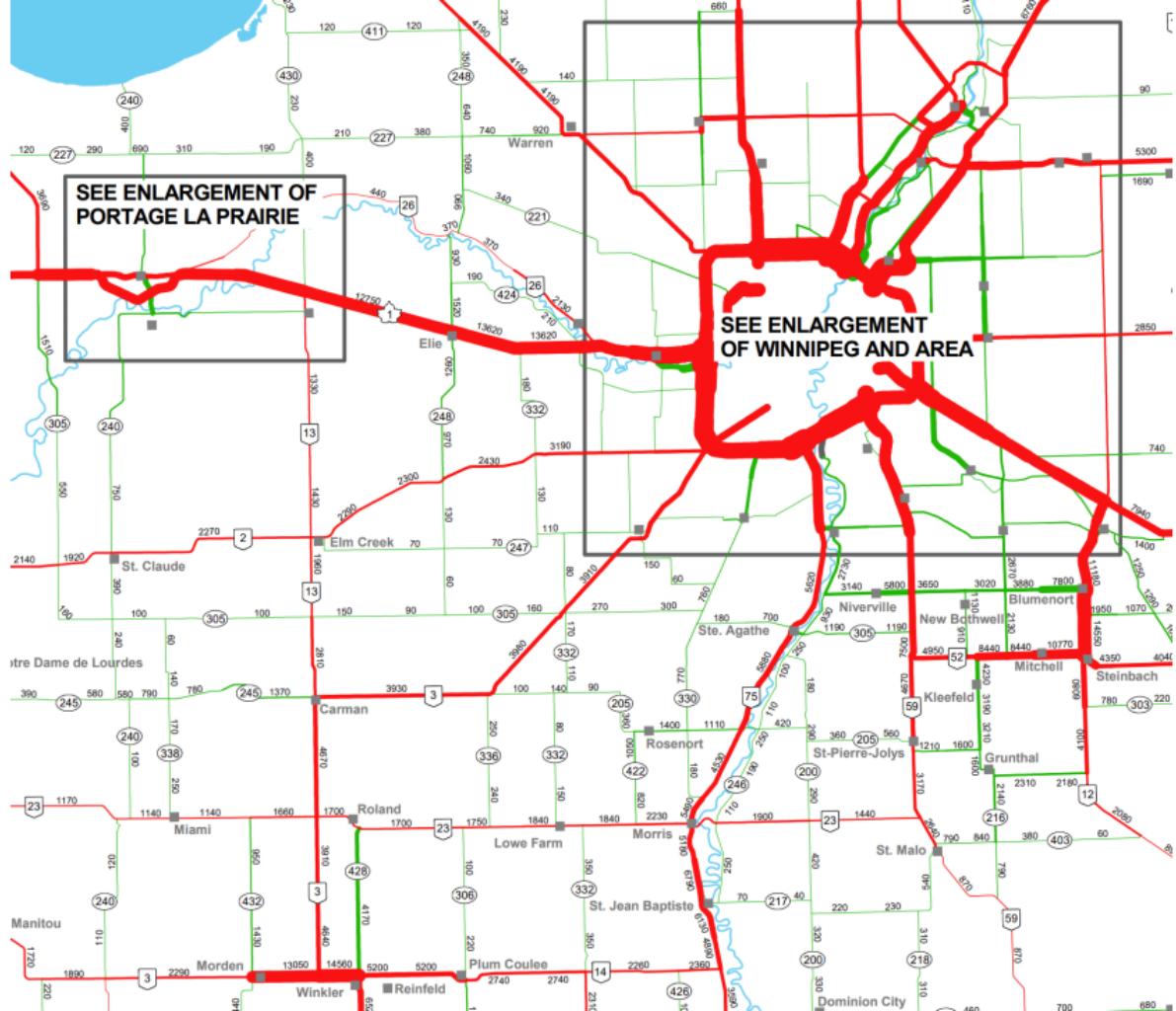
Do not in \mathcal{R}_0 put all your .. interpretation?

An urban centre and satellite cities

Winnipeg as urban centre and 3 smaller satellite cities: Portage la Prairie, Selkirk and Steinbach

- ▶ population density low to very low outside of Winnipeg
- ▶ MB road network well studied by MB Infrastructure Traffic Engineering Branch

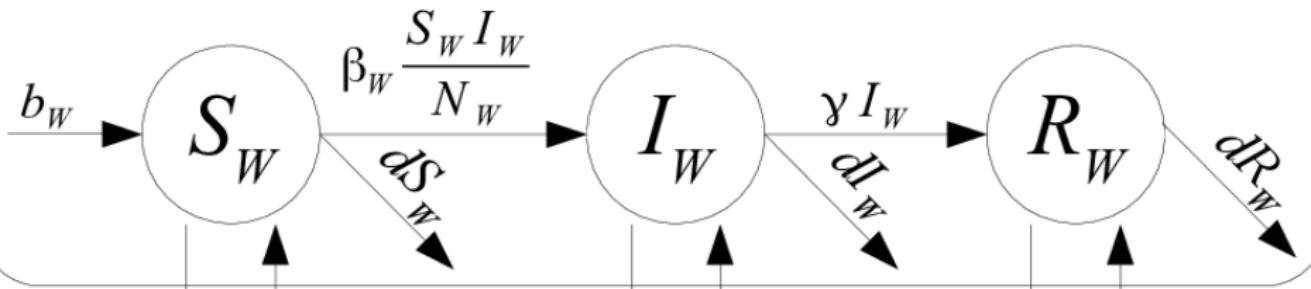
JA & S Portet. Epidemiological implications of mobility between a large urban centre and smaller satellite cities. *Journal of Mathematical Biology* 71(5):1243-1265 (2015)



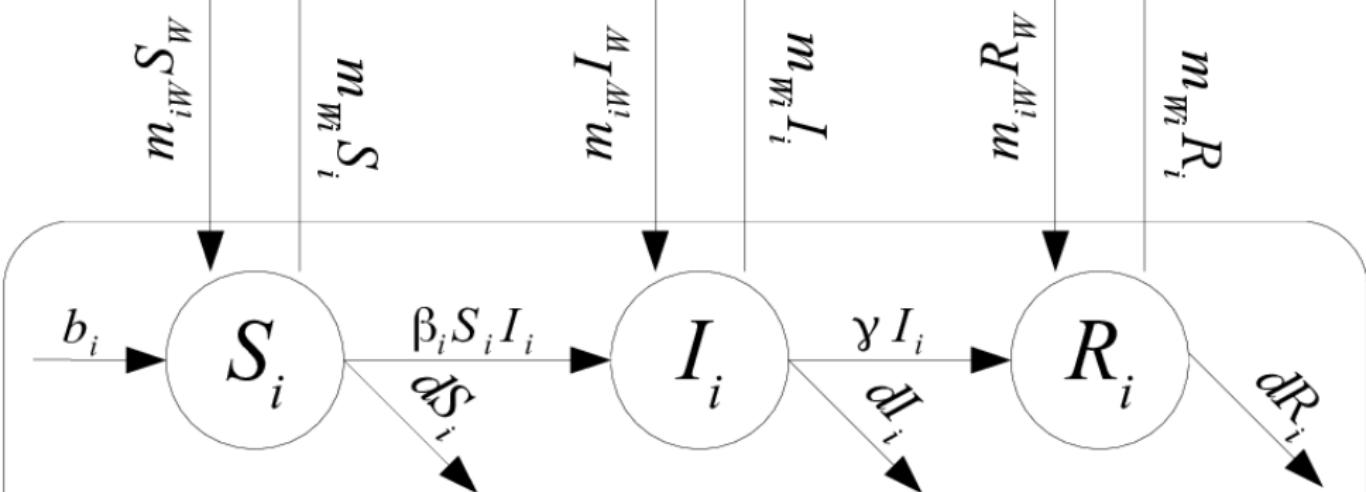
Known and estimated quantities

City	Pop. (2014)	Pop. (now)	Dist.	Avg. trips/capita
Winnipeg (W)	663,617	749,607	-	-
Portage la Prairie (1)	12,996	13,270	88	4,115
Selkirk (2)	9,834	10,504	34	7,983
Steinbach (3)	13,524	17,806	66	7,505

Urban centre



Satellite city



Estimating movement rates

Assume m_{yx} movement rate from city x to city y . *Ceteris paribus*, $N'_x = -m_{yx}N_x$, so $N_x(t) = N_x(0)e^{-m_{yx}t}$. Therefore, after one day, $N_x(1) = N_x(0)e^{-m_{yx}}$, i.e.,

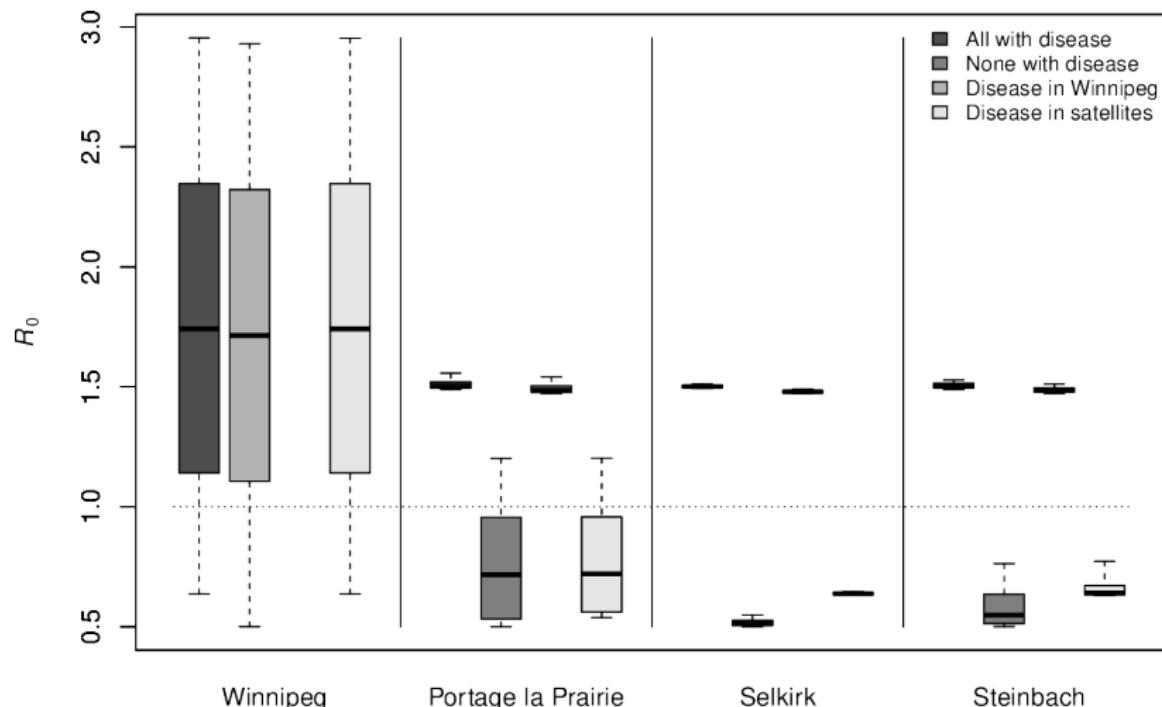
$$m_{yx} = -\ln \left(\frac{N_x(1)}{N_x(0)} \right)$$

Now, $N_x(1) = N_x(0) - T_{yx}$, where T_{yx} number of individuals going from x to y / day. So

$$m_{yx} = -\ln \left(1 - \frac{T_{yx}}{N_x(0)} \right)$$

Computed for all pairs (W, i) and (i, W) of cities

Sensitivity of \mathcal{R}_0 to variations of $\mathcal{R}_0^x \in [0.5, 3]$



with disease: $\mathcal{R}_0^x = 1.5$; without disease: $\mathcal{R}_0^x = 0.5$. Each box and corresponding whiskers are 10,000 simulations

Lower connectivity can drive \mathcal{R}_0

PLP and Steinbach have comparable populations but with parameters used, only PLP can cause the general \mathcal{R}_0 to take values larger than 1 when $\mathcal{R}_0^W < 1$

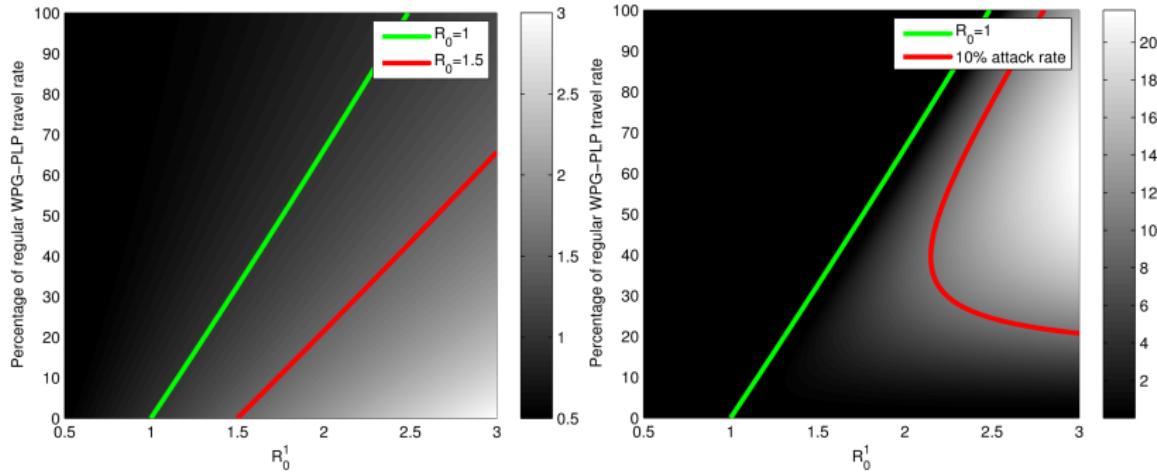
This is due to the movement rate: if $\mathcal{M} = 0$, then

$$\mathcal{R}_0 = \max\{\mathcal{R}_0^W, \mathcal{R}_0^1, \mathcal{R}_0^2, \mathcal{R}_0^3\},$$

since FV^{-1} is then block diagonal

Movement rates to and from PLP are lower \rightarrow situation closer to uncoupled case and \mathcal{R}_0^1 has more impact on the general \mathcal{R}_0

\mathcal{R}_0 does not tell the whole story!



Plots as functions of \mathcal{R}_0^1 in PLP and the reduction of movement between Winnipeg and PLP. Left: general \mathcal{R}_0 . Right: Attack rate in Winnipeg

Metapopulation models

Why use metapopulation models?

Metapopulations with explicit movement

The graph setting

Generic model

The movement matrix

Behaviour of the mobility component

The models considered

Existence of a DFE

Computation of a reproduction number

Global stability of the DFE when $\mathcal{R}_0 < 1$

Metapopulation-specific problems

The toy $|\mathcal{P}|$ -SLIRS

LAS results for $\mathcal{R}_0 < 1$ can sometimes be strengthened to GAS.
One class of models where this works often is when the population
is either constant or asymptotically constant and incidence is
standard

Theorem 9

Let \mathcal{R}_0 be defined as in Theorem 8 and use proportional incidence
 $\Phi_p = \beta_p S_p I_p / N_p$. If $\mathcal{R}_0 < 1$, then the DFE of system (18) is
globally asymptotically stable

$|\mathcal{S}| |\mathcal{P}|$ -SLIRS with multiple species

In the case in which movement is equal for all compartments and there is no disease death, a comparison theorem argument can be used as in Theorem 9 to show that if $\mathcal{R}_0 < 1$, then the DFE of the $|\mathcal{S}| |\mathcal{P}|$ -SLIRS (16) is globally asymptotically stable.

Theorem 10

For system (16) with $|\mathcal{S}|$ species and $|\mathcal{P}|$ locations, with movement equal for all compartments, define \mathcal{R}_0 appropriately and use proportional incidence. If $\mathcal{R}_0 < 1$, then the DFE is globally asymptotically stable

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Metapopulation-specific problems

Metapopulation-specific problems – Two main types

- ▶ **Inheritance problems** – Which of the properties of the constituting units are inherited by the metapopulation?
- ▶ **Metapopulation-specific behaviours** – Are there dynamic behaviours observed in a metapopulation not observed in the constituting units?

Inherited dynamical properties (a.k.a. I am lazy)

Given

$$s'_{kp} = f_{kp}(S_p, I_p) \quad (19a)$$

$$i'_{\ell p} = g_{\ell p}(S_p, I_p) \quad (19b)$$

with known properties, what is known of

$$s'_{kp} = f_{kp}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{kpq} s_{kq} \quad (20a)$$

$$i'_{\ell p} = g_{\ell p}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{\ell pq} i_{\ell q} \quad (20b)$$

- ▶ Existence and uniqueness ✓
- ▶ Invariance of \mathbb{R}_+^\bullet under the flow ✓
- ▶ Boundedness ✓
- ▶ Location of individual \mathcal{R}_{0i} and general \mathcal{R}_0 ?
- ▶ GAS ?

An inheritance problem – Backward bifurcations

- ▶ Suppose a model that, isolated in a single patch, undergoes so-called backward bifurcations
- ▶ This means the model admits subthreshold endemic equilibria
- ▶ What happens when you couple many such constituting units?

YES, coupling together backward bifurcating units can lead to a system-level backward bifurcation

JA, Ducrot & Zongo. A metapopulation model for malaria with transmission-blocking partial immunity in hosts. *Journal of Mathematical Biology* **64**(3):423-448 (2012)

Metapopulation-induced behaviours ?

“Converse” problem to inheritance problem. Given

$$s'_{kp} = f_{kp}(S_p, I_p) \quad (9a)$$

$$i'_{\ell p} = g_{\ell p}(S_p, I_p) \quad (9b)$$

with known properties, does

$$s'_{kp} = f_{kp}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{kpq} s_{kq} \quad (10a)$$

$$i'_{\ell p} = g_{\ell p}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{\ell pq} i_{\ell q} \quad (10b)$$

exhibit some behaviours not observed in the uncoupled system?

E.g.: units have $\{\mathcal{R}_0 < 1 \implies \text{DFE GAS}, \mathcal{R}_0 > 1 \implies \text{1 GAS EEP}\}$ behaviour, metapopulation has periodic solutions

Mixed equilibria

Can there be situations where some locations are at the DFE and others at an EEP?

This is the problem of **mixed equilibria**

This is a metapopulation-specific problem, not one of inheritance of dynamical properties!

Types of equilibria

Definition 11 (Location level EP)

Location $p \in \mathcal{P}$ at equilibrium is **empty** if $X_p^* = 0$, at the **disease-free equilibrium** if $X_p^* = (s_{k_1 p}^*, \dots, s_{k_u p}^*, 0, \dots, 0)$, where k_1, \dots, k_u are some indices with $1 \leq u \leq |\mathcal{U}|$ and $s_{k_1 p}^*, \dots, s_{k_u p}^*$ are positive, and at an **endemic equilibrium** if $X_p \gg 0$

Definition 12 (Metapopulation level EP)

A **population-free equilibrium** has all locations empty. A **metapopulation disease-free equilibrium** has all locations at the disease-free equilibrium for the same compartments. A **metapopulation endemic equilibrium** has all locations at an endemic equilibrium

Mixed equilibria

Definition 13

A **mixed equilibrium** is an equilibrium such that

- ▶ all locations are at a disease-free equilibrium but the system is not at a metapopulation disease-free equilibrium
- ▶ or, there are at least two locations that have different types of location-level equilibrium (empty, disease-free or endemic)

E.g.,

$$((S_1, I_1, R_1), (S_2, I_2, R_2)) = ((+, 0, 0), (+, +, +))$$

is mixed and so is

$$((S_1, I_1, R_1), (S_2, I_2, R_2)) = ((+, 0, 0), (+, 0, +))$$

Theorem 14

Suppose that movement is similar for all compartments (MSAC) and that the system is at equilibrium

- ▶ If patch $p \in \mathcal{P}$ is empty, then all patches in $\mathcal{A}(p)$ are empty
- ▶ If patch $p \in \mathcal{P}$ is at a disease free equilibrium, then the subsystem consisting of all patches in $\{p, \mathcal{A}(p)\}$ is at a metapopulation disease free equilibrium
- ▶ If patch $p \in \mathcal{P}$ is at an endemic equilibrium, then all patches in $\mathcal{D}(p)$ are also at an endemic equilibrium
- ▶ If \mathcal{G}^c is strongly connected for some compartment $c \in \mathcal{C}$, then there does not exist mixed equilibria

Note that MSAC $\implies \mathcal{A}^c = \mathcal{A}$ and $\mathcal{D}^c = \mathcal{D}$ for all $c \in \mathcal{C}$

Spatio-temporal spread of diseases

Metapopulation models

Computational considerations

- ▶ JA. Spatio-temporal spread of infectious pathogens of humans. *Infectious Disease Modelling* 2(2):218-228 (2017)
- ▶ JA. Mathematical epidemiology in a data-rich world. *Infectious Disease Modelling* 5:161-188 (2020)
- ▶ github repo modelling-with-data

Not very difficult

As for the mathematical analysis: if you do things carefully and think about things a bit, numerics are not hard. Well: not harder than numerics in low-D

Exploit vector structure

Set up parameters

```
pop = c(34.017, 1348.932, 1224.614, 173.593, 93.261) * 1e+06
countries = c("Canada", "China", "India", "Pakistan", "Philippines")
T = matrix(data =
            c(0, 1268, 900, 489, 200,
              1274, 0, 678, 859, 150,
              985, 703, 0, 148, 58,
              515, 893, 144, 0, 9,
              209, 174, 90, 2, 0),
            nrow = 5, ncol = 5, byrow = TRUE)
```

Work out movement matrix

```
p = list()
# Use the approximation explained in Arino & Portet (JMB 2015)
p$M = mat.or.vec(nr = dim(T)[1], nc = dim(T)[2])
for (from in 1:5) {
  for (to in 1:5) {
    p$M[to, from] = -log(1 - T[from, to]/pop[from])
  }
  p$M[from, from] = 0
}
p$M = p$M - diag(colSums(p$M))
```

```
p$P = dim(p$M)[1]
p$eta = rep(0.3, p$P)
p$epsilon = rep((1/1.5), p$P)
p$pi = rep(0.7, p$P)
p$gammaI = rep((1/5), p$P)
p$gammaA = rep((1/3), p$P)
# The desired values for R_0
R_0 = rep(1.5, p$P)
```

Write down indices of the different state variable types

Save index of state variable types in state variables vector (we have to use a vector and thus, for instance, the name "S" needs to be defined)

```
p$idx_S = 1:p$P  
p$idx_L = (p$P+1):(2*p$P)  
p$idx_I = (2*p$P+1):(3*p$P)  
p$idx_A = (3*p$P+1):(4*p$P)  
p$idx_R = (4*p$P+1):(5*p$P)
```

Set up IC and time

```
# Set initial conditions. For example, we start with 2
# infectious individuals in Canada.
L0 = mat.or.vec(p$P, 1)
I0 = mat.or.vec(p$P, 1)
A0 = mat.or.vec(p$P, 1)
R0 = mat.or.vec(p$P, 1)
I0[1] = 2
S0 = pop - (L0 + I0 + A0 + R0)
# Vector of initial conditions to be passed to ODE solver.
IC = c(S = S0, L = L0, I = I0, A = A0, R = R0)
# Time span of the simulation (5 years here)
tspan = seq(from = 0, to = 5 * 365.25, by = 0.1)
```

Set up β to avoid blow up

Let us take $\mathcal{R}_0 = 1.5$ for patches in isolation. Solve \mathcal{R}_0 for β

$$\beta = \frac{\mathcal{R}_0}{S(0)} \left(\frac{1 - \pi_p}{\gamma_{Ip}} + \frac{\pi_p \eta_p}{\gamma_{Ap}} \right)^{-1}$$

```
for (i in 1:p$P) {  
  p$beta[i] =  
    R_0[i] / S0[i] * 1/((1 - p$pi[i])/p$gammaI[i] + p$pi[i] *  
    p$eta[i]/p$gammaA[i])  
}
```

Define the vector field

```
SLIAR_metapop_rhs <- function(t, x, p) {
  with(as.list(p), {
    S = x[idx_S]
    L = x[idx_L]
    I = x[idx_I]
    A = x[idx_A]
    R = x[idx_R]
    N = S + L + I + A + R
    Phi = beta * S * (I + eta * A) / N
    dS = - Phi + MS \%*\% S
    dL = Phi - epsilon * L + p$ML \%*\% L
    dI = (1 - pi) * epsilon * L - gammaI * I + MI \%*\% I
    dA = pi * epsilon * L - gammaA * A + MA \%*\% A
    dR = gammaI * I + gammaA * A + MR \%*\% R
    dx = list(c(dS, dL, dI, dA, dR))
    return(dx)
  })
}
```

And now call the solver

```
# Call the ODE solver
sol <- ode(y = IC,
            times = tspan,
            func = SLIAR_metapop_rhs,
            parms = p,
            method = "ode45")
```

One little trick (case with demography)

Suppose demographic EP is $N^* = (\mathbf{d} - \mathcal{M})^{-1}\mathbf{b}$

Want to maintain $N(t) = N^*$ for all t to ignore convergence to demographic EP. Think in terms of \mathbf{b} :

$$N' = 0 \iff \mathbf{b} - \mathbf{d}N + \mathcal{M}N = 0 \iff \mathbf{b} = (\mathbf{d} - \mathcal{M})N$$

So take $\mathbf{b} = (\mathbf{d} - \mathcal{M})N^*$

Then

$$N' = (\mathbf{d} - \mathcal{M})N^* - \mathbf{d}N + \mathcal{M}N$$

and thus if $N(0) = N^*$, then $N'(0) = 0$ and thus $N' = 0$ for all $t \geq 0$, i.e., $N(t) = N^*$ for all $t \geq 0$

Word of warning about that trick, though..

$$\mathbf{b} = (\mathbf{d} - \mathcal{M})\mathbf{N}^*$$

$\mathbf{d} - \mathcal{M}$ has nonnegative (typically positive) diagonal entries and nonpositive off-diagonal entries

Easy to think of situations where the diagonal will be dominated by the off-diagonal, so \mathbf{b} could have negative entries

⇒ use this for numerics, not for the mathematical analysis