Models incorporating a spatial component

Potchefstroom – Course 02

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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

Outline

Spatio-temporal spread of diseases

Metapopulation models

Spatial propagation on a “road”

A diffusion-type spatial spread model

Spatio-temporal spread of diseases

Metapopulation models

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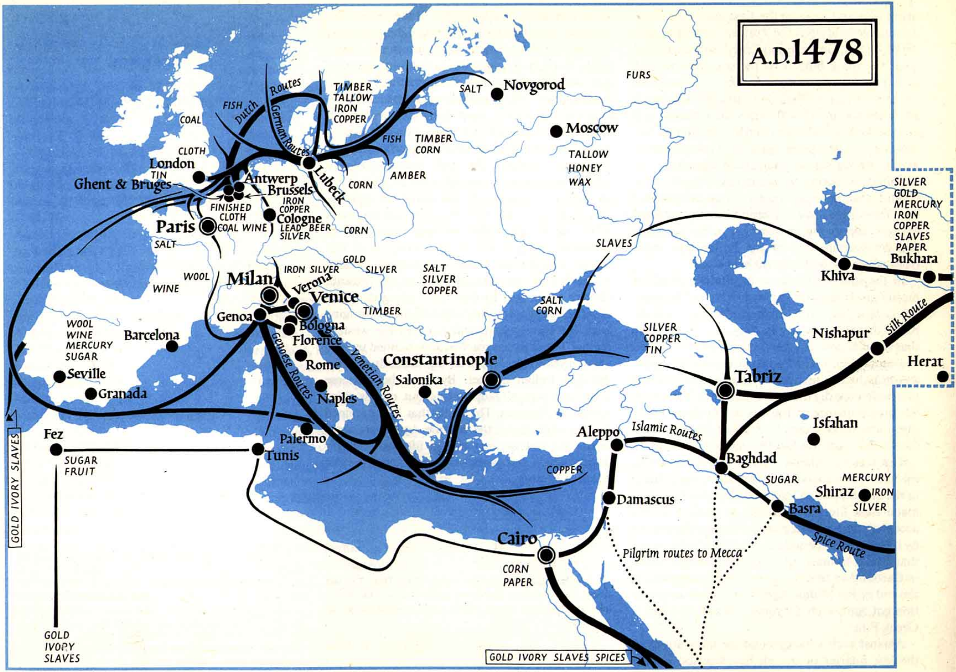
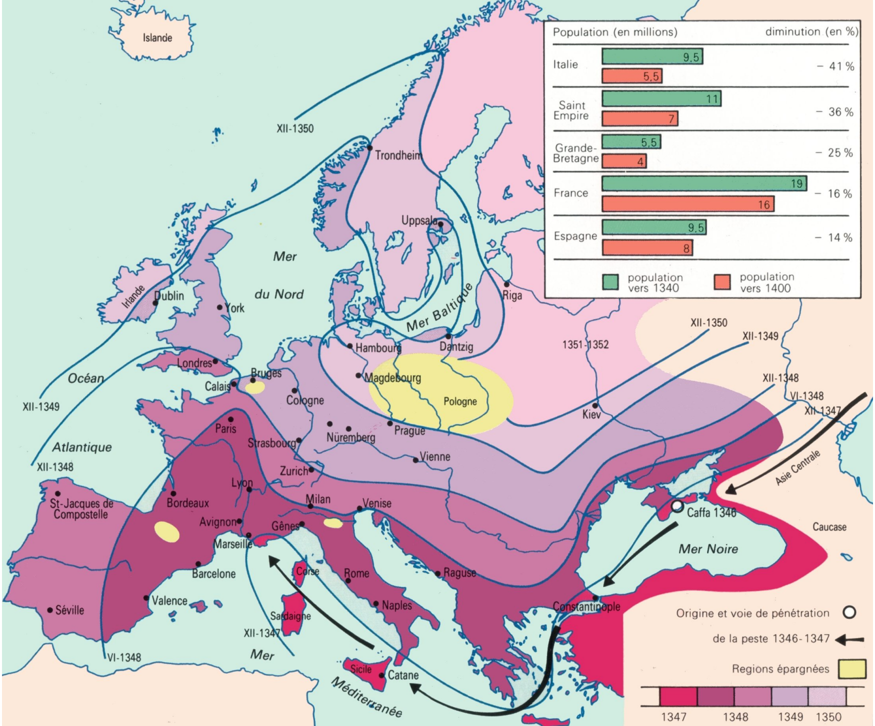
Pathogen spread has evolved with mobility

Pathogens use trade routes

In ancient times, trade routes were “simple”


A.D.1478
FURS
SALT
Novgorod
Moscow
TALLOW
HONEY
WAX
TIMBER
TALLOW
IRON
COPPER
FISH
Dutch
Routes
German Routes
COAL
CLOTH
London
TIN
Ghent & Bruges
Antwerp
Brussels
Lubeck
FISH
TIMBER
CORN
AMBER
CORN
IRON
COPPER
FINISHED
CLOTH
COAL WINE
Cologne
LEAD BEER
SILVER
CORN
Paris
SALT
WOOL
WINE
Milan
IRON SILVER
GOLD
SILVER
SALT
SILVER
COPPER
Verona
Venice
TIMBER
Genoa
Bologna
Florence
Rome
Naples
Genoese Routes
Venetian Routes
WOOL
WINE
MERCURY
SUGAR
Barcelona
Seville
Granada
Fez
SUGAR
FRUIT
Tunis
Palermo
GOLD IVORY SLAVES
GOLD
IVORY
SLAVES
SLAVES
SALT
CORN
Constantinople
Salonika
SILVER
COPPER
TIN
Tabriz
Khiva
Bukhara
SILVER
GOLD
MERCURY
IRON
COPPER
SLAVES
PAPER
Nishapur
Silk Route
Herat
Isfahan
Aleppo
Islamic Routes
Baghdad
SUGAR
MERCURY
Shiraz
IRON
SILVER
Basra
Spice Route
COPPER
Damascus
Pilgrim routes to Mecca
Cairo
CORN
PAPER
GOLD IVORY SLAVES SPICES


Population (en millions)
diminution (en %)
Italie
9,5
5,5
– 41 %
Saint Empire
11
7
– 36 %
Grande-Bretagne
5,5
4
– 25 %
France
19
16
– 16 %
Espagne
9,5
8
– 14 %
🟩 population vers 1340
🟥 population vers 1400
Islande
XII-1350
Trondheim
Uppsala
Mer
du Nord
Mer Baltique
Riga
Irlande
Dublin
York
Hambourg
Dantzig
1351-1352
XII-1350
XII-1349
Londres
Océan
Atlantique
XII-1349
Calais
Bruges
Magdebourg
Pologne
XII-1348
VI-1348
XII-1347
Cologne
Kiev
Paris
Strasbourg
Nüremberg
Prague
Vienne
XII-1348
Zurich
Lyon
Asie Centrale
St-Jacques de Compostelle
Bordeaux
Milan
Venise
Caffa 1346
Caucase
Avignon
Gênes
Marseille
Mer Noire
Corse
Rome
Raguse
Barcelone
Valence
Séville
Sardaigne
Naples
Constantinople
XII-1347
VI-1348
Mer
Méditerranée
Sicile
Catane
Origine et voie de pénétration de la peste 1346-1347
Regions épargnées
1347
1348
1349
1350


Plague
An Dom 1637
Burials 315
Libera nos Domine

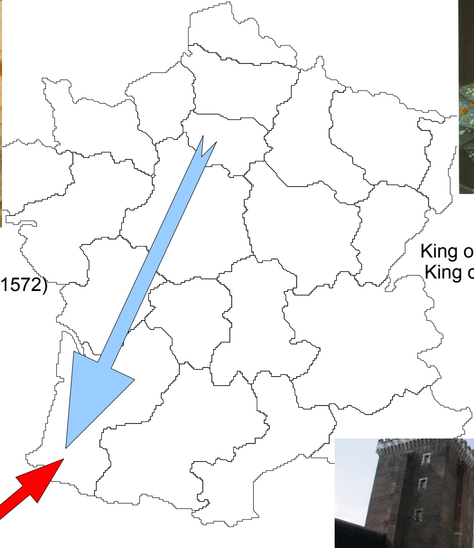

Plague
Anº. Dom. 1637.
Burials. 315.
Libera nos Domine

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

Liverpool to Winnipeg

PROVINCE OF MANITOBA.

MANITOBA offers the most easily accessible and the most promising and productive Lands of any Colonial Province in the world. Situated in a pure, healthy climate, under a free form of government, and within close proximity by direct rail communication to the great centres of the Continent, which afford ready markets for Live Stock, Grain, and other products.

THE LAND IS PRAIRIE

NOT BUSH LAND,

—IN—

MANITOBA

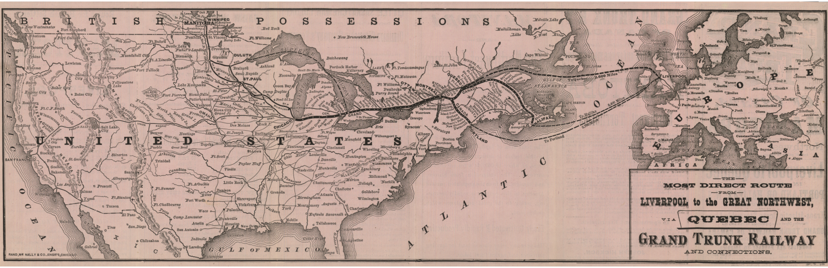
AND THE NORTHWEST TERRITORIES.

Total area of Lands fit for cultivation is estimated at 375,184,000 acres, of which 10,660,369 acres are already surveyed.

THE DOMINION HOMESTEAD LAW

Is one of the most liberal character. Every actual settler is entitled to enter one quarter section of 160 acres as a Homestead, for which a patent is given on proof of three years' residence and cultivation.

He may at the same time enter by PRE-EMPTION any adjacent quarter section, the patent for which will issue to him on payment of $1.00 per acre, and when he has completed his Homestead duties he may enter a quarter section for forest tree cultivation and obtain a patent for it at the expiration of six years, on proof of having planted eight acres of trees for four years subsequent to year of entry. The ordinary Dominion Lands are open for sale at the rate of One Dollar per acre, payable in Cash, Scrip, or Military Bounty Warrants.



—THE—

MOST DIRECT ROUTE

—FROM—

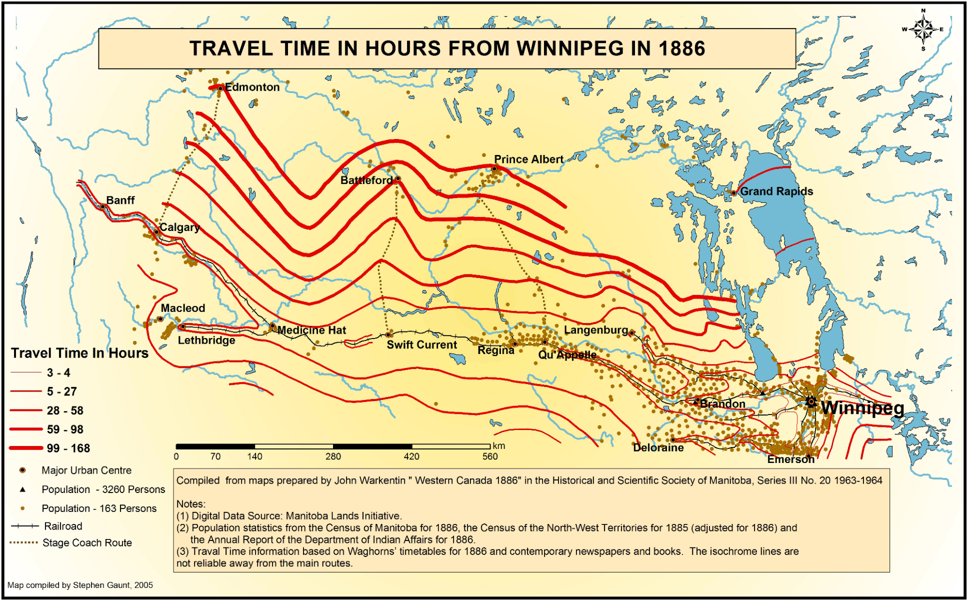
LIVERPOOL to the GREAT NORTHWEST,

VIA **QUEBEC** AND THE

GRAND TRUNK RAILWAY

AND CONNECTIONS.

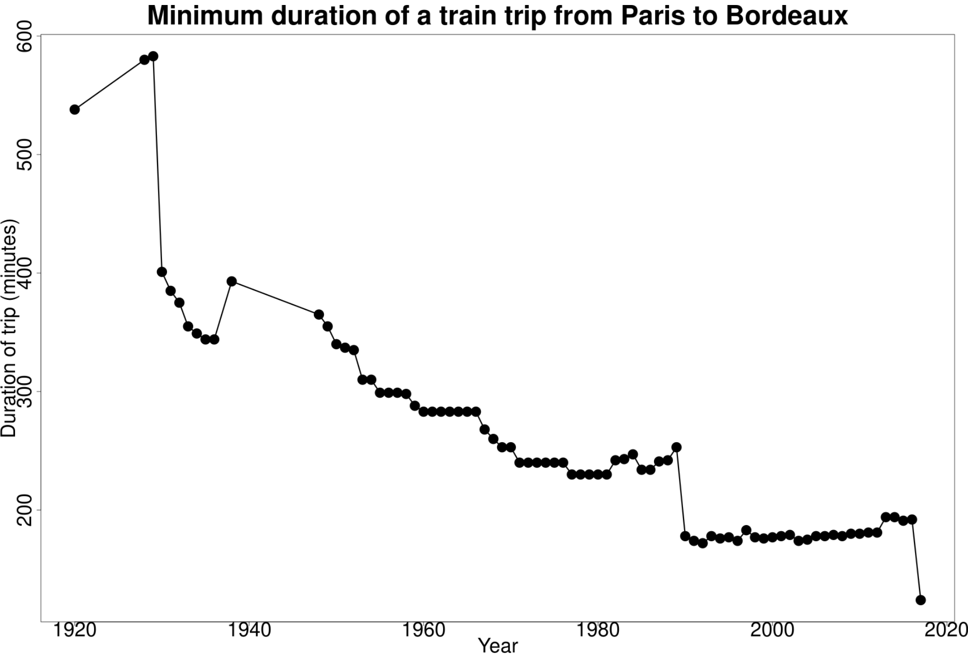
TRAVEL TIME IN HOURS FROM WINNIPEG IN 1886

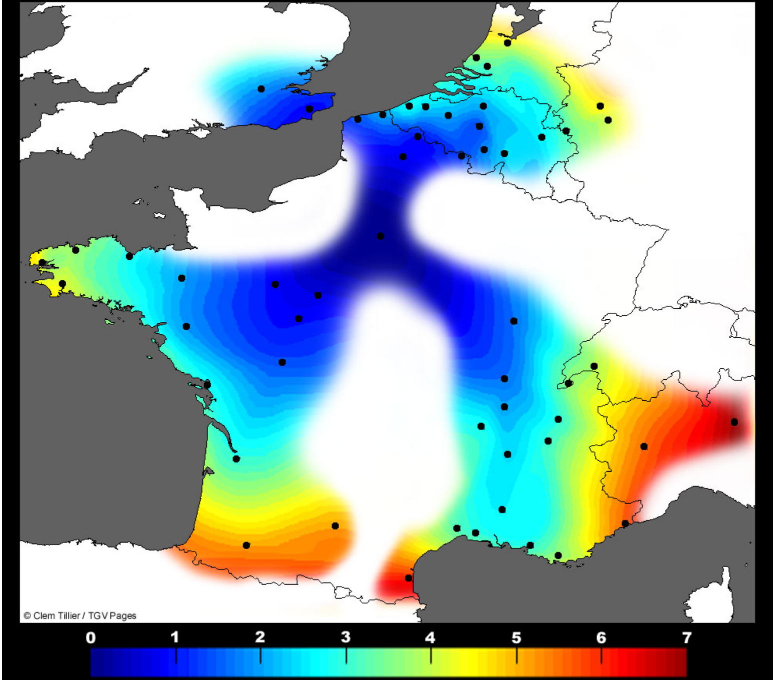


Compiled from maps prepared by John Warkentin " Western Canada 1886" in the Historical and Scientific Society of Manitoba, Series III No. 20 1963-1964

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) Traval Time information based on Waghorns' timetables for 1886 and contemporary newspapers and books. The isochrome lines are not reliable away from the main routes.

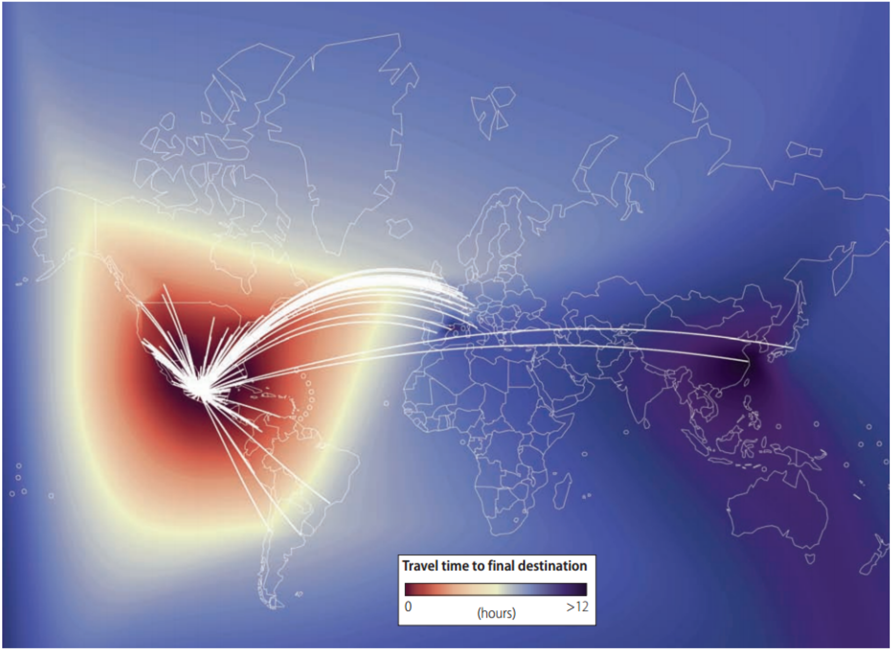
Map compiled by Stephen Gaunt, 2005


Minimum duration of a train trip from Paris to Bordeaux
Duration of trip (minutes)
600
500
400
300
200
Year
1920
1940
1960
1980
2000
2020



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

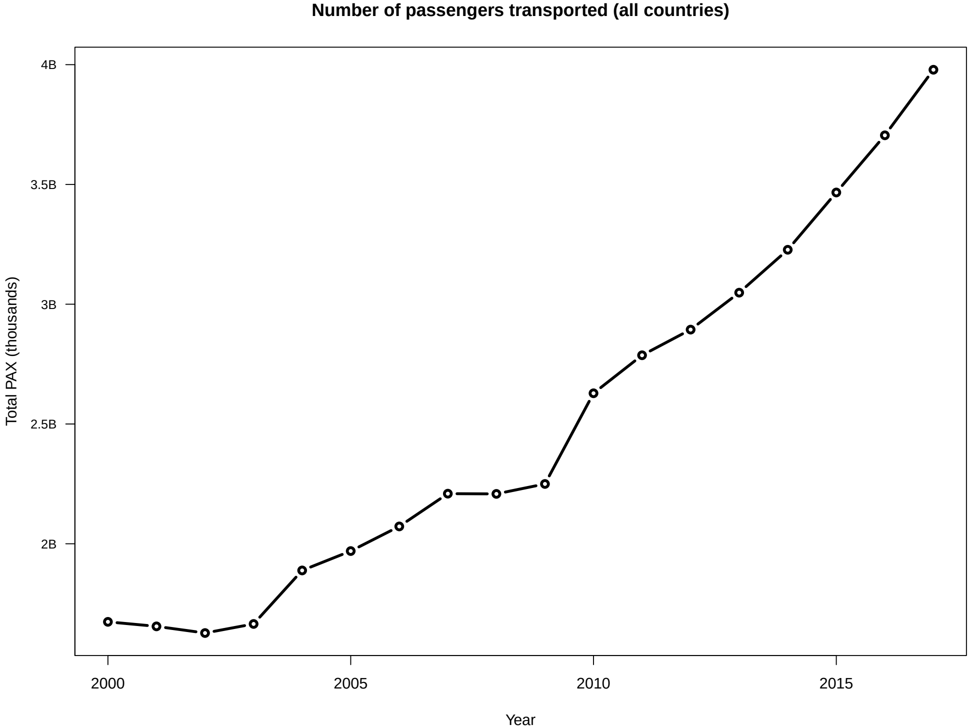
Working definition

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

Takes many different forms

Evolves constantly

Numbers are .. colossal


Number of passengers transported (all countries)
Total PAX (thousands)
4B
3.5B
3B
2.5B
2B
2000
2005
2010
2015
Year

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

Spatio-temporal spread of diseases

Metapopulation models

Spatial propagation on a “road”

A diffusion-type spatial spread model

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)

Metapopulations with explicit movement

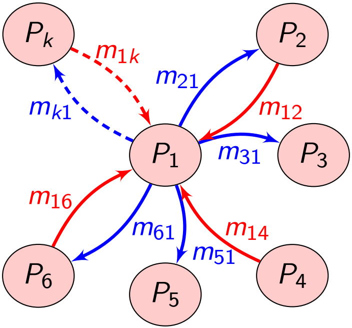
Split continuous space into N discrete geographical locations (*ptatches*)

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 $p = 1, \ldots, N$ to location $q = 1, \ldots, N$

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

$$P_1' = \sum_{j=1}^{N} m_{1j} P_j \text{ assuming } m_{11} = -\sum_{\substack{j=1 \\ j\neq 1}}^{N} m_{j1}$$

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

Srong 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 $i, j = 1, \ldots, n$, 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* $\mathcal{C}_c$

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 $1,\ldots,|\mathcal{P}|$

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

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

$$I_p' = \beta_p S_p I_p - \gamma_p I_p - d_p I_p + \sum_{q\in\mathcal{P}} m_{Ipq} I_q \tag{1b}$$

(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)

- $N_c = \left(N_{c1}, \ldots, N_{c|\mathcal{P}|}\right)^T$ distribution of individuals of compartment $c \in \mathcal{C}$ among the different locations
  [E.g., for (1), $N_S = (S_1, \ldots, S_{|\mathcal{P}|})^T$]

- $N^p = \left(N_1^p, \ldots, N_{|\mathcal{P}|}^p\right)^T$ 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 $p \in \mathcal{P}$

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

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

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

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

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

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

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

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

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

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

Then

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

Vector form of the system

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

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

with

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

Definitions and notation for matrices

- $M \in \mathbb{R}^{n \times n}$ a square matrix with entries denoted m_{ij}
- $M \geq \mathbf{0}$ if $m_{ij} \geq 0$ for all i, j (could be the zero matrix); $M > \mathbf{0}$ if $M \geq \mathbf{0}$ and $\exists i, j$ with $m_{ij} > 0$; $M \gg \mathbf{0}$ if $m_{ij} > 0$ $\forall i, j = 1, \ldots, n$. Same notation for vectors
- $\sigma(M) = \{\lambda \in \mathbf{C}; M\lambda = \lambda \mathbf{v}, \mathbf{v} \neq \mathbf{0}\}$ **spectrum** of M
- $\rho(M) = \max_{\lambda \in \sigma(M)}\{|\lambda|\}$ **spectral radius**
- $s(M) = \max_{\lambda \in \sigma(M)}\{\mathrm{Re}\ (\lambda)\}$ **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

$$\mathcal{M}_c = \begin{pmatrix} -\sum\limits_{k\in\mathcal{P}} m_{ck1} & m_{c12} & \cdots & m_{c1|\mathcal{P}|} \\ \\ m_{c|\mathcal{P}|1} & m_{c|\mathcal{P}|2} & \cdots & -\sum\limits_{k\in\mathcal{P}} m_{ck|\mathcal{P}|} \end{pmatrix} \tag{8}$$

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 Laplacian matrix, i.e., the adjacency matrix minus the degree matrix

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, Bajeux & 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 $\boldsymbol{v} > \mathbf{0}$. If $\mathcal{M}$ irreducible, $s(\mathcal{M} + D)$ has multiplicity 1 and is associated to $\boldsymbol{v} \gg \mathbf{0}$*
3. *If $\mathrm{diag}(D) \gg \mathbf{0}$, then $D - \mathcal{M}$ invertible M-matrix and $(D - \mathcal{M})^{-1} > \mathbf{0}$*
4. *$\mathcal{M}$ irreducible and $\mathrm{diag}(D) > \mathbf{0} \implies D - \mathcal{M}$ nonsingular irreducible M-matrix and $(D - \mathcal{M})^{-1} \gg \mathbf{0}$*

Behaviour of the mobility component – No demography

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

$$N_c' = \mathcal{M}_c N_c \tag{9}$$

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

$$\lim_{t \to \infty} N_c(t) = N_c^\star \gg 0$$

Note that $N_c^\star$ 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 posssible to obtain, in each location $p \in \mathcal{P}$, an equation for the evolution of the total population that takes the form

$$T_p' = D_p(T_p) + \sum_{c \in \mathcal{C}} \sum_{q \in \mathcal{P}} m_{cpq} N_{cq} \tag{10}$$

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

In what follows, assume

$$D_p(T_p) = b_p - d_p T_p \tag{11}$$

Vector / matrix form of the equation

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

$$\mathbf{T}' = \mathbf{b} - \boldsymbol{d}\boldsymbol{T} + \sum_{c\in\mathcal{C}} \mathcal{M}_c \boldsymbol{N}_c \tag{12}$$

where

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

Movement similar for all compartments

Definition 6 (Movement similar for all compartments)

Movement is **similar for all compartments** if, in the multi-digraph $\mathcal{G}$, existence of a $c \in \mathcal{C}$ such that $R^c(X, Y)$ implies that $R^c(X, Y)$ for all $c \in \mathcal{C}$

The nice case

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

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

(stronger than Definition 6, which only requires zero/nonzero patterns in all $\mathcal{M}_c$, $c \in \mathcal{C}$, to be the same)

Then

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

Equilibria

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

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

Is it?

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

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 $\boldsymbol{d}$ nonsingular). Then $\mathcal{M} - \boldsymbol{d}$ is nonsingular and $\boldsymbol{T}^\star = (\boldsymbol{d} - \mathcal{M})^{-1}\mathbf{b}$ unique

Behaviour of the total population

Equal irreducible movement case

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

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

Indeed, we have

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

Since we now assume that $\boldsymbol{d}$ 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 → $\mathbf{T}^\star \gg 0$ (provided $\mathbf{b} > \mathbf{0}$, of course)

Behaviour of total population

Equal reducible movement case

Theorem 7

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* $\mathbf{v}$ *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

$$\boldsymbol{T}' = \mathbf{b} - \boldsymbol{d}\boldsymbol{T} + \sum_{c\in\mathcal{C}} \mathcal{M}_c \boldsymbol{N}_c$$

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

Let

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

and

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

Cool, no? No!

Then we have

$$\mathbf{b} - \boldsymbol{d}\mathbf{T} + \underline{\mathcal{M}}\mathbf{T} \leq \mathbf{T}' \leq \mathbf{b} - \boldsymbol{d}\mathbf{T} + \overline{\mathcal{M}}\mathbf{T}$$

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

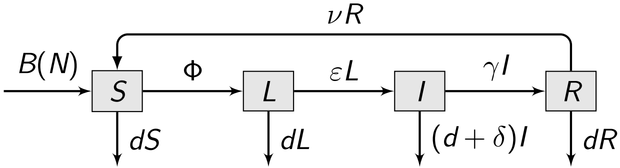
Me, roughly 10 minutes after that previous statement: *Quel con!*

Indeed $\underline{\mathcal{M}}$ and $\overline{\mathcal{M}}$ 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

The toy SLIRS model in patches



$$S' = \mathcal{B}(N) + \nu R - \Phi - dS \tag{14a}$$
$$L' = \Phi - (\varepsilon + d)L \tag{14b}$$
$$I' = \varepsilon L - (\gamma + d + \delta)I \tag{14c}$$
$$R' = \gamma I - (\nu + d)R \tag{14d}$$

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

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

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

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

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

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \qquad q_p \in \{0,1\} \tag{15e}$$

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

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

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

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

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

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

with incidence

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

- 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)

$$
\begin{aligned}
S'_{pq} &= \mathcal{B}_{pq}\left(N_p^r\right) + \nu_{pq}R_{pq} - \Phi_{pq} - d_{pq}S_{pq} + \textstyle\sum_{k\in\mathcal{P}} m_{Spqk}S_{pk} && \text{(17a)}\\
L'_{pq} &= \Phi_{pq} - (\varepsilon_{pq} + d_{pq})L_{pq} + \textstyle\sum_{k\in\mathcal{P}} m_{Lpqk}L_{pk} && \text{(17b)}\\
I'_{pq} &= \varepsilon_{pq}L_{pq} - (\gamma_{pq} + d_{pq})I_{pq} + \textstyle\sum_{k\in\mathcal{P}} m_{Ipqk}I_{pk} && \text{(17c)}\\
R'_{pq} &= \gamma_{pq}I_{pq} - (\nu_{pq} + d_{pq})R_{pq} + \textstyle\sum_{k\in\mathcal{P}} m_{Rpqk}R_{pk} && \text{(17d)}
\end{aligned}
$$

with incidence

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

- Sattenspiel & Dietz. A structured epidemic model incorporating geographic mobility among regions (1995)
- JA & PvdD. A multi-city epidemic model. *Mathematical Population Studies* **10**(3):175-193 (2003)
- JA & PvdD. 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 $\mathcal{B}_p(N_p) = \mathcal{B}_p$

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

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

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

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

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \qquad q_p \in \{0, 1\} \tag{18e}$$

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

$\Longrightarrow$ 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 form now on: existence and uniqueness

Other basic stuff

Skipped until I homogeneise notation

Not complicated but sometimes tedious

Easy if it has been proved for the constituting units

Disease free equilibrium

The model is at equilibrium if the time derivatives are zero

Definition 8 (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

$$\begin{aligned} 0 &= \mathcal{B}_p - d_p S_p + \nu_p R_p + \textstyle\sum_{q\in\mathcal{P}} m_{Spq} S_q \\ 0 &= -\left(\nu_p + d_p\right) R_p + \textstyle\sum_{q\in\mathcal{P}} m_{Rpq} R_q \end{aligned}$$

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:

$$\begin{aligned} \mathbf{0} &= \mathbf{b} - \boldsymbol{d}\mathbf{S} + \nu \boldsymbol{R} + \mathcal{M}^S \mathbf{S} \\ \mathbf{0} &= -\left(\nu + \boldsymbol{d}\right) \boldsymbol{R} + \mathcal{M}^R \boldsymbol{R} \end{aligned}$$

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

$\boldsymbol{R}$ at DFE

Recall second equation:

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

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

We have been here before!

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

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

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

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

$\mathbf{S}$ at the DFE

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

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

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

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

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

So DFE makes sense with

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

- 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 $\Xi = \{L_1, \ldots, L_{|\mathcal{P}|}, I_1, \ldots, I_{|\mathcal{P}|}\}$, $\Xi' = \mathcal{F} - \mathcal{V}$

$$\mathcal{F} = \left(\Phi_1, \ldots, \Phi_{|\mathcal{P}|}, 0, \ldots, 0\right)^T$$

$$\mathcal{V} = \begin{pmatrix} \left(\varepsilon_1 + d_1\right) L_1 - \sum_{q \in \mathcal{P}} m_{L1q} L_q \\ \vdots \\ \left(\varepsilon_{|\mathcal{P}|} + d_{|\mathcal{P}|}\right) L_{|\mathcal{P}|} - \sum_{q \in \mathcal{P}} m_{L|\mathcal{P}|q} L_q \\ -\varepsilon_1 L_1 + (\gamma_1 + d_1) I_1 - \sum_{q \in \mathcal{P}} m_{I1q} I_q \\ \vdots \\ -\varepsilon_{|\mathcal{P}|} L_{|\mathcal{P}|} + (\gamma_{|\mathcal{P}|} + d_{|\mathcal{P}|}) I_{|\mathcal{P}|} - \sum_{q \in \mathcal{P}} m_{I|\mathcal{P}|q} I_q \end{pmatrix}$$

Differentiate w.r.t. Ξ:

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

Note that

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

whenever $k \neq p$, so

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

Evaluate $D\mathcal{F}$ at DFE

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

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

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

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

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

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

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

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

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

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

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

where

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

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

Next generation matrix

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

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.,

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

Local asymptotic stability of the DFE

Theorem 9

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

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

Then the DFE

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

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 9 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

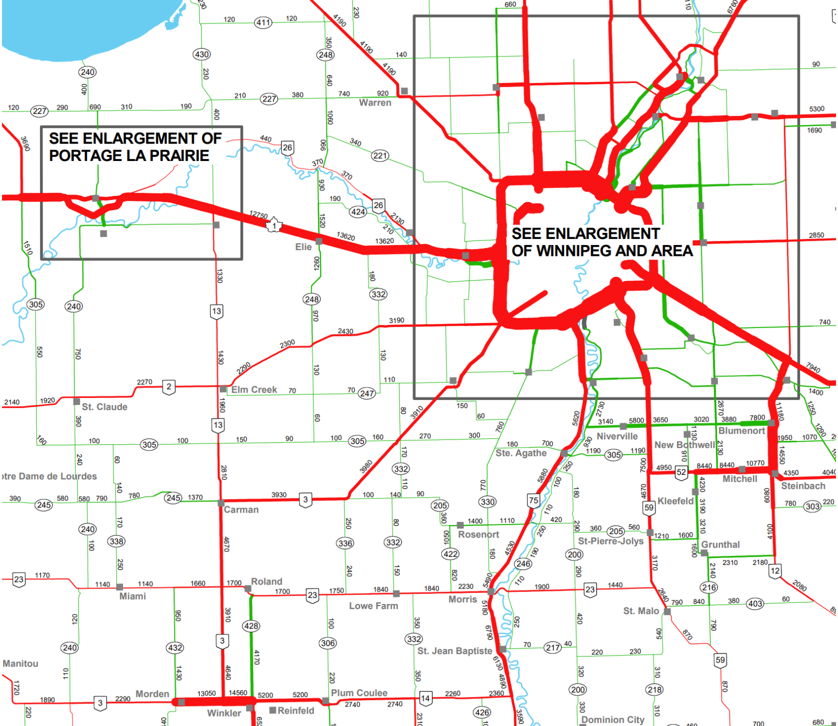
Do not in $\mathcal{R}_0$ put all your .. interpretation?

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)

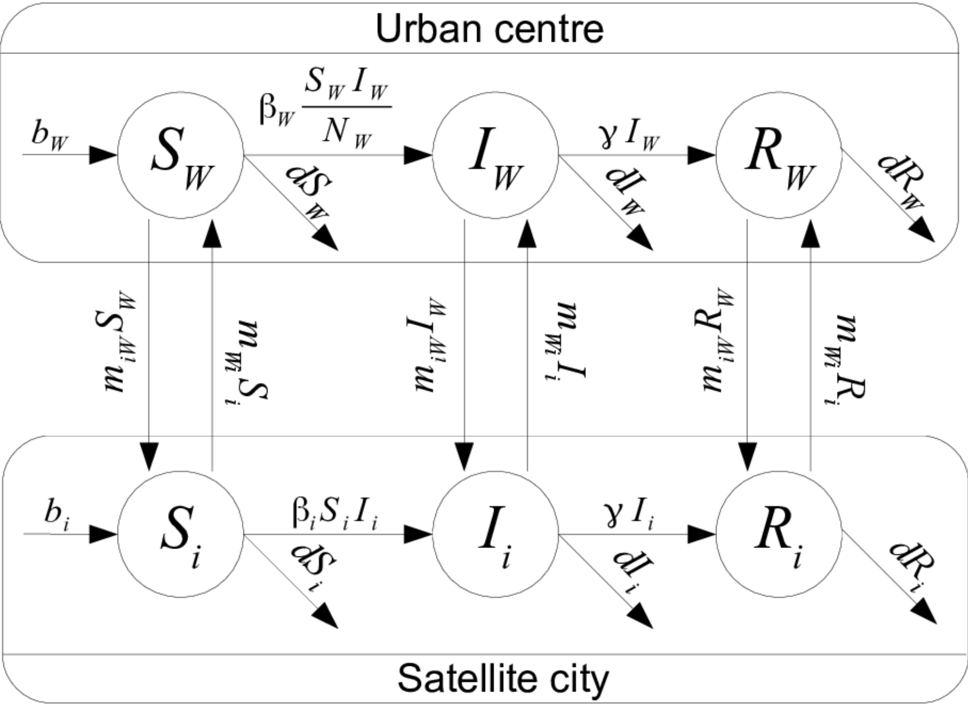


SEE ENLARGEMENT OF PORTAGE LA PRAIRIE

SEE ENLARGEMENT OF WINNIPEG AND AREA

Known and estimated quantities

City	Pop. (2014)	Pop. (now)	Dist.	Avg. trips/
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
b_W
S_W
$\beta_W \frac{S_W I_W}{N_W}$
I_W
γI_W
R_W
dS_W
dI_W
dR_W
$m_{iW} S_W$
$m_{Wi} S_i$
$m_{iW} I_W$
$m_{Wi} I_i$
$m_{iW} R_W$
$m_{Wi} R_i$
b_i
S_i
$\beta_i S_i I_i$
I_i
γI_i
R_i
dS_i
dI_i
dR_i
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.,

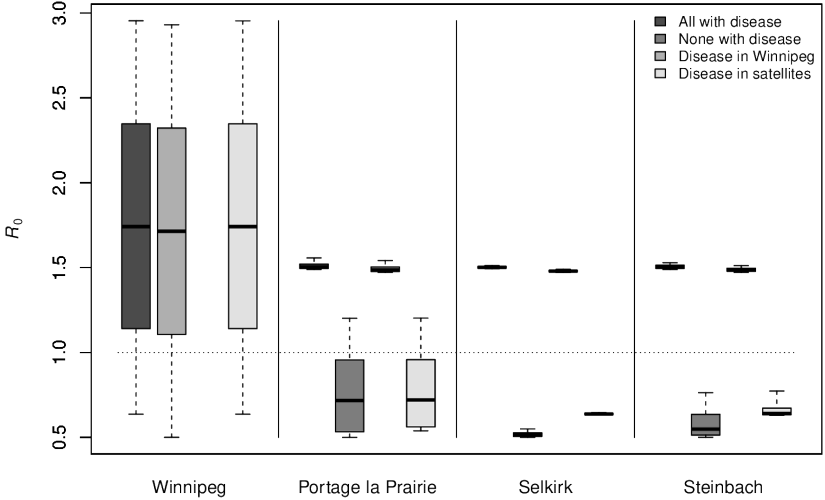
$$m_{yx} = -\ln\left(\frac{N_x(1)}{N_x(0)}\right)$$

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 $\mathcal{R}_0^W < 1$

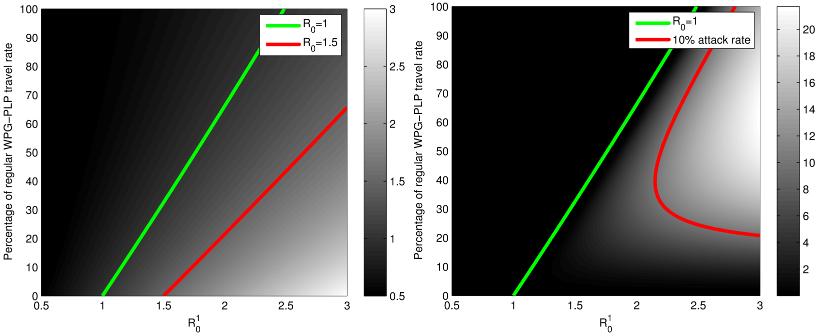
This is due to the movement rate: if $\mathcal{M} = 0$, then

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

since FV^{-1} is then block diagonal

Movement rates to and from PLP are lower → 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
- Computational considerations

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 10

Let $\mathcal{R}_0$ be defined as in Theorem 9 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 10 to show that if $\mathcal{R}_0 < 1$, then the DFE of the $|\mathcal{S}|$ $|\mathcal{P}|$-SLIRS (16) is globally asymptotically stable.

Theorem 11

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*

Metapopulation models

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

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

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

with known properties, what is known of

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

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

- 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 consistuting 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

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

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

with known properties, does

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

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

exhibit some behaviours not observed in the uncoupled system? E.g.: units have $\{\mathcal{R}_0 < 1 \implies$ DFE GAS, $\mathcal{R}_0 > 1 \implies$ 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 12 (Location level EP)

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

Definition 13 (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 14

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 15

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 $c \in \mathcal{C}$

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
- 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)^^I
```

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))
```

```r
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)
  })
}^^I
```

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 $\mathbf{N}^\star = (\boldsymbol{d} - \mathcal{M})^{-1}\mathbf{b}$
Want to maintain $\mathbf{N}(t) = \mathbf{N}^\star$ for all t to ignore convergence to demographic EP. Think in terms of $\mathbf{b}$:

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

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

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

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

Word of warning about that trick, though..

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

$\boldsymbol{d} - \mathcal{M}$ 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 $\boldsymbol{b}$ could have negative entries

$\implies$ use this for numerics, not for the mathematical analysis

Spatio-temporal spread of diseases

Metapopulation models

Spatial propagation on a “road”

A diffusion-type spatial spread model

PERGAMON

Mathematical and Computer Modelling 29 (1999) 55–69

MATHEMATICAL
AND
COMPUTER
MODELLING

Modelling the Spread of Infections When the Contact Rate Among Individuals is Short Ranged: Propagation of Epidemic Waves

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(Received and accepted July 1998)

Spatial spread of an epidemic on a "road"

- SIS and SIR models
- Consider a road of length L
- $S(x,t)$, $I(x,t)$ and (when relevant) $R(x,t)$ are the densities of individuals in the different compartments at location $x \in [0,L]$ at time t
- For simplicity, denote

$$\frac{\partial}{\partial t} X(x,t) = X_t(x,t)$$

The SIR model on the road

$$S_t(x,t) = -\beta(x,t)S(x,t) - dS(x,t) + dN(x) + \lambda_1 I(x,t) \tag{21a}$$

$$I_t(x,t) = \lambda(x,t)S(x,t) - dI(x,t) - (\gamma_1 + \gamma_2)I(x,t) \tag{21b}$$

$$R_t(x,t) = \gamma_2 I(x,t) - dR(x,t) \tag{21c}$$

where the force of infection is

$$\lambda(x,t) = \frac{1}{N}\int_0^L \beta(x,x')I(x,x')dx' \tag{21d}$$

and the total population along the road is

$$N = \int_0^L N(x')dx' \tag{21e}$$

Take the SIS model as an example ($\gamma_2 = 0, \gamma_1 = \gamma$). Solve (21b) in terms of λ:

$$\begin{aligned} I(x,t) = \exp\left(-\int_0^t \lambda(x,s) - (d+\gamma)tds\right) \\ \times \int_0^t \lambda(x,t')N(x)e^{\int_0^{t'} \lambda(x,s)+(d+\gamma)t'ds}dt' \\ + I(x,0)\exp\left(-\int_0^t \lambda(x,s) - (d+\gamma)tds\right) \end{aligned} \tag{22}$$

Substitute (22) into (21d)

$$\begin{aligned}\lambda(x,t) &= \int_0^L \beta(x,x')n(x') \int_0^t \lambda(x',t') e^{-\int_{t'}^t \lambda(x',s)-(d+\gamma)(t-t')ds} dt'\,dx' \\ &\quad + \int_0^L \beta(x,x') i(x',0) e^{-\int_0^t \lambda(x',s)-(d+\gamma)tds} dx'\end{aligned}$$

where $n(x) = N(x)/N$ and $i(x,t) = I(x,t)/N$. Without demography $(d = 0)$:

$$\begin{aligned}\lambda(x,t) &= \int_0^L \beta(x,x')n(x') \int_0^t \lambda(x',t') e^{-\int_{t'}^t \lambda(x',s)-\gamma(t-t')ds} dt'\,dx' \\ &\quad + \int_0^L \beta(x,x') i(x',0) e^{-\int_0^t \lambda(x',s)-\gamma tds} dx'\end{aligned}$$

Thus the problem is in the form

$$\boldsymbol{B}\lambda(x,t) = \lambda(x,t)$$

In both cases, $\boldsymbol{B}$ is a Hammerstein-type operator in x

- SIR case: $\boldsymbol{B}$ is a nonlinear Volterra operator in t ⇒existence and uniqueness of solutions
- SIS case: $\boldsymbol{B}$ is not a nonlinear Volterra operator in t. However, it resembles one and the authors establish existence and uniqueness of solutions

In both cases, there is a travelling wave front then convergence to a steady state

In the SIS case

$$\lambda(x) = \lim_{t\to\infty} \boldsymbol{B}\lambda(x,t) = \boldsymbol{B}_\infty\lambda(x) = \int_0^L \beta(x,x')n(x')\frac{\lambda(x',\infty)}{\lambda(x',\infty)+\gamma}$$

which does not depend on t

They then discuss conditions s.t. this limit $\neq 0$, by looking for values of z s.t. $\boldsymbol{B}_\infty\lambda(x) = z\lambda(x)$ has a positive solution

Show there exists a threshold $z_{\text{threshold}} = \mathcal{R}_0$ s.t. $\lambda(x) \equiv 0$ if $\mathcal{R}_0 < 1$ and a positive solution if $\mathcal{R}_0 > 1$

Spatio-temporal spread of diseases

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Spatial propagation on a “road”

A diffusion-type spatial spread model

J. theor. Biol. (1992) **156,** 327–348

On the Spatial Spread of Rabies Among Foxes with Immunity

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10 *December* 1991)

Spatial spread of rabies with immunity

$$\frac{\partial S}{\partial t} = (a-b)\left(1-\frac{N}{K}\right)S + a^{\star}R - \beta SI \tag{23a}$$

$$\frac{\partial L}{\partial t} = \beta SI - \sigma L - \left(b + (a-b)\frac{N}{K}\right)L \tag{23b}$$

$$\frac{\partial I}{\partial t} = \sigma L - \alpha I - \gamma I - \left(b + (a-b)\frac{N}{K}\right)I + D_I\frac{\partial^2 I}{\partial x^2} \tag{23c}$$

$$\frac{\partial R}{\partial t} = \gamma I + (a-a^{\star})R + \left(b + (a-b)\frac{N}{K}\right)R \tag{23d}$$

where $N = S + L + I + R$