

# Metapopulation models

## Use in ecology and epidemiology

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## A brief history of metapopulations

### The general context

A metapopulation of sources and sinks with explicit movement

Diseases in metapopulations

Computational considerations

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Metapopulations à la Levins

Metapopulations with explicit movement

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# Spatial aspects in ecology/population biology/epidemiology

Species have a spatial range

How to capture this spatial range from a conservation or control point of view?

Invasions/colonizations

Disease spread

# What are metapopulations?

Metapopulations are *populations of populations*.

Two types of metapopulation models:

- ▶ *patch occupancy models.* Describe whether a location is *occupied* by a species or not. Depends on the occupancy of neighboring or connected locations. Dynamics describes the number of occupied locations
- ▶ Models with *explicit movement*. Movement between locations is described explicitly. In each location, a set of differential equations describes the dynamics of the populations present

Focus here is on models with explicit movement, although we briefly discuss the others

# What is a location?

A *location* is a unit (typically geographical) within which the population is considered homogeneous

- ▶ city
- ▶ region
- ▶ country
- ▶ but also, location where a given species lives (for example, forest, swamp, etc.)

Locations may or may not overlap

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## A model of Richard Levins (1969)

R. Levins. Some Demographic and Genetic Consequences of Environmental Heterogeneity for Biological Control. Bulletin of the Entomological Society of America **15**(3): 237-240 (1969)

Cited 4,400+ times, numerous higher order “offspring”

Quickly evolved to include prey-predators or competition systems

## The Levins model

Rate of change of # of local populations  $P$ :

$$P' = \beta P \left(1 - \frac{P}{T}\right) - \mu P \quad (1)$$

$\beta$  immigration rate between *locations*,  $T$  total number of locations  
and  $\mu$  extinction rate of local populations

Ecologists & mathematicians think of patches differently. For mathematicians, typically, one place in space. To be clear, in the remainder of these slides, I will speak of *locations*

# Metapopulations with implicit movement

Same philosophy as the Levins model

- ▶ There is a set  $\mathcal{P}$  of locations called *locations*
- ▶ Each location  $p \in \mathcal{P}$  has an internal dynamics  $x_p = f_p(x_p)$ , where  $x_p \in \mathbb{R}_+^{n_p}$  and  $f_p : \mathbb{R}^{n_p} \rightarrow \mathbb{R}^{n_p}$
- ▶ No flow of individuals between locations
- ▶ The influence of location  $q \neq p$  on  $p$  is described through a function  $g_{qp}(x_p, x_q)$ , where  $x_q \in \mathbb{R}^{n_q}$  and  $g_p : \mathbb{R}^{n_p} \times \mathbb{R}^{n_q} \rightarrow \mathbb{R}^{n_p}$

So the population in location  $p \in \mathcal{P}$  has dynamics

$$x'_p = f_p(x_p) + \sum_{\substack{q \in \mathcal{P} \\ q \neq p}} g_{qp}(x_p, x_q) \quad (2)$$

(I will show a few examples later)

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## Levins-type vs Explicit movement

Levins model and its offspring: movement is implicit

$$P' = \beta P \left(1 - \frac{P}{T}\right) - \mu P$$

$\beta$  immigration rate between locations incorporates geography

Sometimes we have explicit movement information or want to incorporate known spatial information  $\implies$  models with explicit movement

Levin (1974)

## Metapopulations with explicit movement

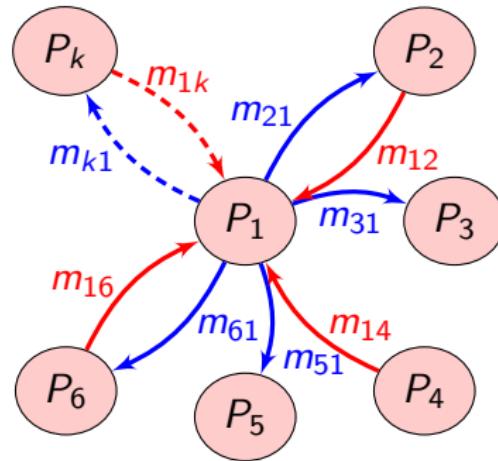
Split continuous space into  $N$  discrete geographical locations (*patches*)

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

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

## Eulerian vs Lagrangian metapopulations

You may encounter this terminology, here is what that means..

- ▶ Eulerian metapopulation models are Levins-type
- ▶ Lagrangian metapopulation models have explicit movement of individuals

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The movement matrix

Behaviour of the mobility component

Behaviour of the mobility component with demography

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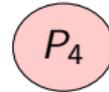
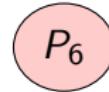
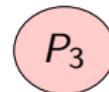
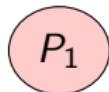
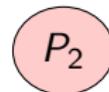
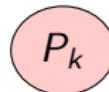
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# title

Make some random graph



## 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  $\mathcal{G}^c = (\mathcal{P}_c, \mathcal{A}_c)$

## Direct access

Define the binary relation  $R^c$  by

$R^c(X, Y)$  (*compartment c has direct access to location Y from location X*) if, for compartment  $c \in \mathcal{C}$ , there exists an arc  $A \in \mathcal{A}$  between  $X$  and  $Y$

### Definition 1 (Direct access)

We write  $R(X, Y)$ , and say that location  $X$  has **direct access** to location  $Y$  or that location  $Y$  can be accessed directly from location  $X$ , if there exists  $c \in \mathcal{C}$  such that  $R^c(X, Y)$

### Definition 2 (Full direct access)

We write  $\overline{R}(X, Y)$  and say that location  $X$  has **full direct access** to location  $Y$  if  $R^c(X, Y)$  for all  $c \in \mathcal{C}$

## Notations

For a given location  $X$ , define

$$\mathcal{P}_{X \rightarrow}^c = \{Y \in \mathcal{P} : R^c(X, Y)\}$$

and

$$\mathcal{P}_{X \rightarrow} = \{Y \in \mathcal{P} : \exists c \in \mathcal{C} \text{ such that } R^c(X, Y)\},$$

the sets of locations that can be directly accessed from location  $X$ ,  
and

$$\mathcal{P}_{\rightarrow X}^c = \{Y \in \mathcal{P} : R^c(Y, X)\}$$

and

$$\mathcal{P}_{\rightarrow X} = \{Y \in \mathcal{P} : \exists c \in \mathcal{C} \text{ such that } R^c(Y, X)\},$$

sets of locations that have direct access to location  $X$

## 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

## Indirect access

### Definition 3 (Indirect access for a compartment)

A compartment  $c \in \mathcal{C}$  has **indirect access** to location  $Y$  from location  $X$  if, for compartment  $c \in \mathcal{C}$ , there exists a path from  $X$  to  $Y$  in  $\mathcal{G}_c$  but compartment  $c$  does not have direct access from  $X$  to  $Y$

In other words, there exists  $X_1, \dots, X_n \in \mathcal{P}$  such that

$R^c(X, X_1)R^c(X_1, X_2) \dots R^c(X_n, Y)$ , but  $R^c(X, Y)$  does not hold

### Definition 4 (General indirect access)

Location  $X$  has **general indirect access** to location  $Y$  if there exists  $X_1, \dots, X_n \in \mathcal{P}$  and  $c_1, \dots, c_{n+1} \in \mathcal{C}$  such that

$$R^{c_1}(X, X_1)R^{c_2}(X_1, X_2) \dots R^{c_{n+1}}(X_n, Y)$$

while  $X$  does not have direct access to  $Y$

(Indices used only to indicate the order in which the relations hold)

Indirect access for compartment  $c \in \mathcal{C}$  can be evaluated using the connection matrix  $\mathcal{N}_c$

Indeed, entries of  $\mathcal{N}_c^2$  give the paths of length exactly 2 in  $\mathcal{G}_c$  for compartment  $c$ , and by induction, entries of  $\mathcal{N}_c^k$  give the paths of length exactly  $k$  in  $\mathcal{G}$

General indirect access can be evaluated similarly by using the matrix

$$\mathcal{N} = \sum_{c \in \mathcal{C}} \mathcal{N}_c$$

## Access

Access = combination of direct and indirect access.

### Definition 5 (Access for a compartment)

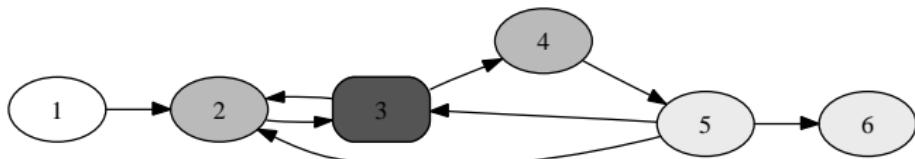
Compartment  $c \in \mathcal{C}$  in location  $X$  has **access** to location  $Y$  if compartment  $c$  has direct or indirect access to location  $Y$  from location  $X$ , and location  $X$  has access to location  $Y$  if it has direct or indirect access to location  $Y$  from location  $X$

### Definition 6 (Connected locations)

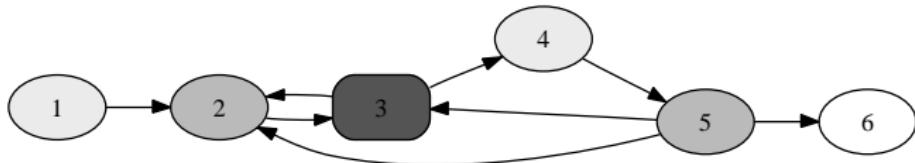
Two locations  $X$  and  $Y$  are **connected** if  $X$  can be accessed from  $Y$  and/or  $Y$  can be accessed from  $X$

For a given location  $X$ , the sets  $\overline{\mathcal{P}}_{X \rightarrow}^c$ ,  $\overline{\mathcal{P}}_{X \rightarrow}$ ,  $\overline{\mathcal{P}}_{\rightarrow X}^c$  and  $\overline{\mathcal{P}}_{\rightarrow X}$  are as before, but for access instead of direct access

## Example of access



Set  $\overline{\mathcal{P}}_{3 \rightarrow}$



Set  $\overline{\mathcal{P}}_{\rightarrow 3}$

Locations directly connected to 3 are darker gray, indirectly connected locations are lighter gray. Locations with no access to 3 or that cannot be accessed from 3 are white

## Symmetric multi-digraph

Definition 7 (Graph symmetric for a compartment)

The multi-digraph  $\mathcal{G}(\mathcal{P}, \mathcal{A})$  is **symmetric** for compartment  $c \in \mathcal{C}$  if for all  $X, Y \in \mathcal{P}$ ,  $R^c(X, Y)$  implies  $R^c(Y, X)$ , that is, if the binary relation  $R^c$  is *symmetric*

Definition 8 (Fully symmetric multi-digraph)

$\mathcal{G}$  is **fully symmetric** if, for all  $X, Y \in \mathcal{P}$ ,  $\overline{R}(X, Y)$  implies  $\overline{R}(Y, X)$

## Movement similar for all compartments

Definition 9 (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  $c \in \mathcal{C}$

## Strongly connected multi-digraph

### Definition 10 (Strongly connected components)

For a given compartment  $s$ , the **strongly connected components** (or **strong components**, for short) are such that, for all locations  $X, Y$  in a strong component, compartment  $s$  in  $X$  has access to  $Y$

### Definition 11 (Strong connectedness for a compartment)

The multi-digraph is strongly connected for compartment  $c$  if all locations belong to the same strong component of  $\mathcal{G}_c$

## Strong connectedness and irreducibility

### Definition 12 (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 13

*Strong connectedness  $\Leftrightarrow$  irreducibility of the connection matrix  $\mathcal{C}_c$*

## Finding an ordering for a reducible matrix

Remember Definition 12: A reducible if  $\exists$  permutation matrix  $P$   
s.t.  $P^TAP$  block upper triangular

In practice,  $P$  can be hard to find, especially when  $A$  becomes large

That's where the link to strong connectedness comes handy:  
Dijkstra's and similar algorithms are extremely fast at identifying  
strong components in digraphs

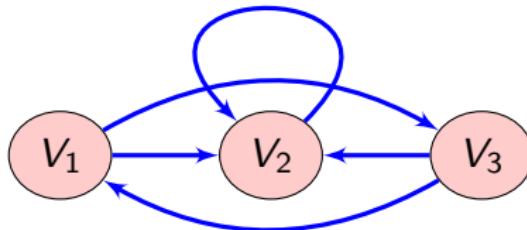
To decide on irreducibility and reduce in case it doesn't hold

- ▶ Run Dijkstra on  $\mathcal{G}(A)$
- ▶ If 1 strong component,  $A$  is irreducible
- ▶ If  $n > 1$  strong components, list first components with  $> 1$  vertex, then those with 1 vertex

## Illustration of the method

Take a simple example (easy to do “by hand” but never mind)

$$A = \begin{pmatrix} 0 & 1 & 1 \\ 0 & 1 & 0 \\ 1 & 1 & 0 \end{pmatrix} \quad (3)$$



Clearly, if we list vertices as  $V_1, V_3, V_2$ , we should be good

$$\begin{pmatrix} 0 & 1 & 1 \\ 1 & 0 & 1 \\ 0 & 0 & 1 \end{pmatrix}$$

## Programmatically

```
# Required for graphs
library(igraph)
# Create the matrix
A = matrix(c(0,1,1,
            0,1,0,
            1,1,0),
           nr = 3, byrow = TRUE)
# Create the associated digraph
G = graph_from_adjacency_matrix(A)
# Find the components of G
comp_G = components(G, mode="strong")
```

We find

```
> comp_G
$membership
[1] 1 2 1
$csize
[1] 2 1
$no
[1] 2
```

Check if the graph is strongly connected (`comp_G$no==1`); otherwise, sort the components by decreasing size. The order in which they are listed in `comp_G$csize` needs to be kept, so use `order` rather than `sort`

```
# Is the graph strongly connected?
if (comp_G$no==1) {
  writeLines("Matrix is irreducible")
} else{
  # Graph has more than 1 strong component, put the matrix
  # in standard form
  idx = order(comp_G$csize, decreasing = TRUE)
  P = c() # Where we store the rows/columns of P
  for (i in idx) {
    P = c(P, which(comp_G$membership == i))
  }
  # The permutation matrix: obtained by applying P to
  # columns of the identity matrix
  P = diag(dim(A)[1])[,P]
  # The reduced matrix
  M = t(P)%*%A%*%P
}
```

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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

$$S'_p = b_p - \beta_p S_p I_p + \gamma_p I_p - d_p S_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (4a)$$

$$I'_p = \beta_p S_p I_p - \gamma_p I_p - d_p I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (4b)$$

(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 (4),  $N_S = (S_1, \dots, S_{|\mathcal{P}|})^T$ ]
- ▶  $N^p = (N_1^p, \dots, N_{|\mathcal{P}|}^p)^T$  composition of the population in location  $p \in \mathcal{P}$   
[E.g., for (4),  $N^p = (S_p, I_p)^T$ ]

## 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  $p \in \mathcal{P}$

$$\frac{d}{dt} N_{cp} = f_{cp}(N^p) + M_{cp}(N_s) \quad (5)$$

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  $c \in \mathcal{C}$

$$\frac{d}{dt} N_c = f^p(N^p) + M_c(N_c) \quad (6)$$

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  $p = 1, \dots, |\mathcal{P}|$

$$\frac{d}{dt} N^p = f^p(N^p) + M^p(N^p) \quad (7)$$

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

$$m_{cpp} = - \sum_{\substack{q \in \mathcal{P} \\ q \neq p}} m_{cqp} \quad (8)$$

Then

$$N'_s = f_{cp}(N^p) + \sum_{q \in \mathcal{P}} m_{cpq} N_{cq} \quad (9)$$

## Vector form of the system

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

$$N'_c = f(N) + \mathcal{M}_c N_c \quad (10)$$

with

$$\mathcal{M}_c = \begin{pmatrix} -\sum_{k \in \mathcal{P}} m_{ck1} & m_{c12} & \cdots & m_{c1|\mathcal{P}|} \\ m_{c|\mathcal{P}|1} & m_{c|\mathcal{P}|2} & \cdots & -\sum_{k \in \mathcal{P}} m_{ck|\mathcal{P}|} \end{pmatrix} \quad (11)$$

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## Definitions and notation for matrices

- ▶  $M \in \mathbb{R}^{n \times n}$  a square matrix with entries denoted  $m_{ij}$
- ▶  $M \geq \mathbf{0}$  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  $m_{ij} > 0$   
 $\forall i, j = 1, \dots, n$ . Same notation for vectors
- ▶  $\sigma(M) = \{\lambda \in \mathbb{C}; M\lambda = \lambda\mathbf{v}, \mathbf{v} \neq \mathbf{0}\}$  **spectrum** of  $M$
- ▶  $\rho(M) = \max_{\lambda \in \sigma(M)} \{|\lambda|\}$  **spectral radius**
- ▶  $s(M) = \max_{\lambda \in \sigma(M)} \{\operatorname{Re}(\lambda)\}$  **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  $A \geq \mathbf{0}$  and  $s \geq \rho(A)$

# The movement matrix

The matrix

$$\mathcal{M}_c = \begin{pmatrix} -\sum_{k \in \mathcal{P}} m_{ck1} & m_{c12} & \cdots & m_{c1|\mathcal{P}|} \\ m_{c|\mathcal{P}|1} & m_{c|\mathcal{P}|2} & \cdots & -\sum_{k \in \mathcal{P}} m_{ck|\mathcal{P}|} \end{pmatrix} \quad (11)$$

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 14

1.  $0 \in \sigma(\mathcal{M})$  corresponding to left e.v.  $\mathbb{1}^T$  [ $\sigma$  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 14 and Proposition 15 (next page),  
see Arino, Bajeux & Kirkland, BMB 2019

## Proposition 15 ( $D$ 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  $\mathbf{v} > \mathbf{0}$ . If  $\mathcal{M}$  irreducible,  $s(\mathcal{M} + D)$  has multiplicity 1 and is associated to  $\mathbf{v} \gg \mathbf{0}$
3. If  $\text{diag}(D) \gg \mathbf{0}$ , then  $D - \mathcal{M}$  invertible M-matrix and  $(D - \mathcal{M})^{-1} > \mathbf{0}$
4.  $\mathcal{M}$  irreducible and  $\text{diag}(D) > \mathbf{0} \implies D - \mathcal{M}$  nonsingular irreducible M-matrix and  $(D - \mathcal{M})^{-1} \gg \mathbf{0}$

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## Behaviour of the mobility component

Assume no within-location dynamics, just movement. Then (10) takes the form

$$N'_c = \mathcal{M}_c N_c \quad (12)$$

### Theorem 16

For a given compartment  $c \in \mathcal{C}$ , suppose that the movement matrix  $\mathcal{M}_c$  is irreducible. Then for any  $N_c(0) > 0$ , (12) satisfies

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

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

## Proof of Theorem 16

System (12) is overdetermined:

$$\mathbb{1}^T N'_c = \mathbb{1}^T \mathcal{M}_c N_c = (0, \dots, 0)^T N_c = 0$$

so  $\mathbb{1}^T N_c$  is constant. To find the equilibrium value  $N_c^*$ , the system

$$\mathcal{M}_c N_c = 0$$

must be solved, with  $\mathcal{M}_c$  a singular matrix

Consider the augmented system of  $|\mathcal{P}| + 1$  equations in  $|\mathcal{P}|$  unknowns

$$\begin{pmatrix} \mathbb{1}^T \\ \mathcal{M}_c \end{pmatrix} N_c = \begin{pmatrix} \mathbb{1}^T N_c(0) \\ 0 \\ \vdots \\ 0 \end{pmatrix} \quad (13)$$

All column sums of the last  $|\mathcal{P}|$  rows are zero, thus the second equation (for example) can be eliminated

Perform column operations  $c_r \leftarrow c_r - c_1$  for  $r = 2, \dots, |\mathcal{P}|$  on the determinant of the resulting coefficient matrix, reducing it to the  $|\mathcal{P}| - 1$  determinant  $\det(M(1) + T_1)$ , where  $M(1)$  denotes matrix  $\mathcal{M}_c$  with its first row and column deleted, thus

$$M(1) = \begin{pmatrix} -\sum_{q=1}^{|\mathcal{P}|} m_{q2} & m_{23} & \cdots & m_{2|\mathcal{P}|} \\ \vdots & & \ddots & \\ m_{|\mathcal{P}|2} & m_{|\mathcal{P}|3} & \cdots & -\sum_{q=1}^{|\mathcal{P}|} m_{q|\mathcal{P}|} \end{pmatrix}$$

and  $T_1 = m_1 \mathbb{1}_{|\mathcal{P}|-1}^T = [-m_{21}, \dots, -m_{|\mathcal{P}|1}]^T [1, \dots, 1]$ , where  $m_1$  is the vector formed from the first column of  $\mathcal{M}_c$  by omitting the first entry

Since  $m_{pq} \geq 0$ ,  $-M(1)$  is a nonsingular M-matrix (it has the Z-sign pattern and  $\mathbb{1}_{|\mathcal{P}|-1}^T(-M(1)) \geq 0$  and is not the zero vector by the assumption that  $\mathcal{M}_c$  is irreducible)

Thus  $\det(-M(1)) > 0$  and so  $\det M(1)$  has sign  $(-1)^{|\mathcal{P}|+1}$ . Since  $T_1$  has rank 1, it follows from the linearity of the determinant subject to rank 1 perturbations that

$$\det(M(1) + T_1) = \det M(1)(1 + \mathbb{1}_{|\mathcal{P}|-1}^T M(1)^{-1} m_1)$$

As  $-M(1)$  is an M-matrix,  $(-M(1)^{-1}) \geq 0$ , thus  $M(1)^{-1} \leq 0$ . But  $m_1 \leq 0$ , thus  $1 + \mathbb{1}_{|\mathcal{P}|-1}^T M(1)^{-1} m_1$  is positive and so  $\det(M(1) + T_1)$  has the sign of  $\det M(1)$ , namely  $(-1)^{|\mathcal{P}|+1}$

By Cramer's Rule,

$$N_1 = \frac{\det M(1) N^0}{\det(M(1) + T_1)} = \frac{N^0}{1 + \mathbb{1}_{|\mathcal{P}|-1}^T (M(1))^{-1} m_1} > 0$$

Similarly by deleting the  $(p+1)^{\text{st}}$  equation in (13),

$$N_p = \frac{\det M(p) N^0}{\det(M(p) + T_p)} = \frac{N^0}{1 + \mathbb{1}_{|\mathcal{P}|-1}^T (M(p))^{-1} m_p} > 0$$

where

$$\begin{aligned} T_p &= m_p \mathbb{1}_{|\mathcal{P}|-1}^T \\ &= [-m_{1,p}, \dots, -m_{p-1,p}, -m_{p+1,p}, \dots, -m_{|\mathcal{P}|,p}]^T \mathbb{1}_{|\mathcal{P}|-1}^T \end{aligned}$$

for  $p = 1, \dots, |\mathcal{P}|$ . Here  $m_p$  is the vector formed from the  $p^{\text{th}}$  column of  $M$  by omitting the  $p^{\text{th}}$  entry. Thus given a value of  $\mathbb{1}^T N_c(0)$ , there is a unique positive solution  $N_p = N_p^*$  for  $p = 1, \dots, |\mathcal{P}|$

Let

$$\bar{d} = \max_i \sum_{k \in \mathcal{P}} m_{cki}$$

Then

$$\mathcal{M}_c + \bar{d}I$$

is nonnegative, and the Perron-Frobenius theorem can be used

Since  $\mathcal{M}_c$  is irreducible, the spectral radius  $\rho(\mathcal{M}_c + \bar{d}I)$  is

- ▶ positive
- ▶ an eigenvalue of multiplicity one
- ▶ the only eigenvalue associated to a nonnegative eigenvector

Thus

$$v^T(\mathcal{M}_c + \bar{d}I) = \rho(\mathcal{M}_c + \bar{d}I)v^T$$

with  $v^T \gg 0$ , and so  $v^T \mathcal{M}_c = (\lambda - \bar{d})v^T$

Since  $\mathbb{1}^T \mathcal{M}_c = 0 \cdot \mathbb{1}^T$ , 0 is the dominant eigenvalue of  $\mathcal{M}_c$  and is of multiplicity one. All other eigenvalues have negative real parts

The zero eigenvalue comes from the overdetermination of the system. Thus the equilibrium is asymptotically stable



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## Reduction to total population per location

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

$$T'_p = D_p(T_p) + \sum_{c \in \mathcal{C}} \sum_{q \in \mathcal{P}} m_{cpq} N_{cq} \quad (14)$$

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

$$D_p(T_p) = b_p - d_p T_p \tag{15}$$

## Vector / matrix form of the equation

Assuming demography is of the form (15), write (14) in vector form

$$\mathbf{T}' = \mathbf{b} - \mathbf{dT} + \sum_{c \in \mathcal{C}} \mathcal{M}_c \mathbf{N}_c \quad (16)$$

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

Then

$$\begin{aligned}\mathbf{T}' &= \mathbf{b} - \mathbf{dT} + \mathcal{M} \sum_{c \in \mathcal{C}} \mathbf{N}_c \\ &= \mathbf{b} - \mathbf{dT} + \mathcal{M} \mathbf{T}\end{aligned}\tag{17}$$

# Equilibria

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

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 15(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

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

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

Indeed, we have

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

Since we now assume that  $\mathbf{d}$  is nonsingular, we have by Theorem 15(1) that  $s(\mathcal{M} - \min_{p \in \mathcal{P}} d_p) = -\min_{p \in \mathcal{P}} d_p < 0$

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

# Behaviour of total population

Equal reducible movement case

## Theorem 17

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

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

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

Let

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

and

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

Cool, no? No!

Then we have

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

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

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## Position of the problem

Assume a metapopulation of locations connected through transport of individuals between them

Some locations are sources, others are sinks:

- ▶ Population tends to persist in sources
- ▶ Population tends to vanish in sinks

*Ceteris paribus*, does there exist a ratio of the number of source to sink locations s.t. the population of the coupled system persists?

Obvious special cases: all sources should be true, all sinks should be false..

## Dynamics in sources and sinks

Return to original Levins framework of just one species and assume that species' range is a heterogeneous environment:

- ▶ *sources*: conditions favourable to species survival
- ▶ *sinks*: conditions not favourable  
( $\simeq$  immigration needed for population to remain present)

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## Gyllenberg and Hanski (1997)

Normalise (1) to have  $P$  fraction of occupied locations:

$$P' = \beta P(h - P) - \mu P$$

where  $h$  is fraction of suitable locations

This exhibits threshold behaviour:

- ▶ if  $h < \mu/\beta$ , then PFE is globally asymptotically stable (GAS)
- ▶ if  $h > \mu/\beta$ , then  $\exists$  unique nontrivial GAS equilibrium  $P^*$

G&H consider numerous variations structured w.r.t. habitat quality

Discretise 1D RD equation, giving, for  $i = 1, \dots, N$ ,

$$P'_i = f(P_i)P_i + m_{i,i+1}(P_{i+1} - P_i) + m_{i,i-1}(P_{i-1} - P_i) \quad (18)$$

with zero Dirichlet boundary condition  $P_0 = P_{N+1} = 0$

For all  $P_i$ ,  $\sup f(P_i) = r > 0$ , so all locations except extremities are sources

Then population goes extinct if

$$r < 2 \left( \underline{m} + \bar{m} \cos \left( \frac{\pi N}{N+1} \right) \right)$$

where  $2\underline{m} = \min_i \{m_{i,i+1} + m_{i,i-1}\}$  and  $\bar{m} = \max_i \{m_{i,i+1}, m_{i,i-1}\}$

Also,  $\exists$  critical location number  $N_c$  such that  $N < N_c$   
 $\implies$  population becomes extinct

# Rael & Taylor (2018)

*A flow network model for animal movement on a landscape with application to invasion*, Theoretical Ecology

$$P'_i = P_i B(P_i) + \sum_{j=1}^N a_{ji} P_j m(P_j, P_i) - P_i \sum_{j=1}^N a_{ij} m(P_i, P_j)$$

where

$$m(P_i, P_j) = \frac{\max\{0, \pi(P_i) - \pi(P_j)\}}{d_{ij}} \quad \pi(P_i) = \frac{P_i}{K_i}$$

$d_{ij}$  distance from  $i$  to  $j$ ,  $K_i$  carrying capacity

$$B(P_i) = \begin{cases} r_i \left(1 - \frac{P_i}{K_i}\right) & \text{sources} \\ -r_i & \text{sinks} \end{cases}$$

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## Model for $N$ locations

W.l.o.g.:  $S \geq 0$  first locations are sources,  $N - S$  remaining are sinks [w.l.o.g. but not that trivial nonetheless]

### Sources:

$$P'_i = r_i P_i \left(1 - \frac{P_i}{K_i}\right) + \sum_{j=1}^N m_{ij} P_j, \quad i = 1, \dots, S \quad (19a)$$

### Sinks:

$$P'_i = -r_i P_i + \sum_{j=1}^N m_{ij} P_j, \quad i = S + 1, \dots, N \quad (19b)$$

$$m_{ii} = -\sum_{\substack{j=1 \\ j \neq i}}^N m_{ji}$$

## Vector form (v1)

$$\mathbf{P} = (P_1, \dots, P_N)^T$$

$$\mathbf{P}' = \mathbf{G}(\mathbf{P})\mathbf{P} + \mathcal{M}\mathbf{P}$$

where

$$\mathbf{G}(\mathbf{P}) = \text{diag} \left( r_1 \left( 1 - \frac{P_1}{K_1} \right), \dots, r_S \left( 1 - \frac{P_S}{K_S} \right), -r_{S+1}, \dots, -r_N \right)$$

$$\mathcal{M} = \begin{pmatrix} - \sum_{\substack{j=1 \\ j \neq 1}}^N m_{j1} & m_{12} & \cdots & m_{1N} \\ m_{21} & - \sum_{\substack{j=1 \\ j \neq 2}}^N m_{j2} & \cdots & m_{2N} \\ & & \ddots & \\ m_{N1} & m_{N2} & \cdots & - \sum_{\substack{j=1 \\ j \neq N}}^N m_{jN} \end{pmatrix}$$

## Vector form (v2)

$$\mathbf{P}_s = (P_1, \dots, P_S)^T \text{ (sources)}, \quad \mathbf{P}_t = (P_{S+1}, \dots, P_N)^T \text{ (sinks)}$$

$$\mathbf{P}'_s = \mathbf{G}_s(\mathbf{P}_s)\mathbf{P}_s + \mathcal{M}_s\mathbf{P}_s + \mathcal{M}_{st}\mathbf{P}_t$$

$$\mathbf{P}'_t = -\mathcal{D}_t\mathbf{P}_t + \mathcal{M}_{ts}\mathbf{P}_s + \mathcal{M}_t\mathbf{P}_t$$

where

$$\mathbf{G}_s(\mathbf{P}_s) = \text{diag} \left( r_1 \left( 1 - \frac{P_1}{K_1} \right), \dots, r_S \left( 1 - \frac{P_S}{K_S} \right) \right)$$

$$\mathcal{D}_t = \text{diag}(r_{S+1}, \dots, r_N)$$

$$\begin{pmatrix} \mathcal{M}_s & \mathcal{M}_{st} \\ \mathcal{M}_{ts} & \mathcal{M}_t \end{pmatrix} = \mathcal{M}$$

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## The *population-free equilibrium* (PFE)

We find the PFE  $\mathbf{P}_s = \mathbf{P}_t = \mathbf{0}$

At the PFE,

$$J_{\text{PFE}}^S = \mathcal{M} + (\mathcal{D}_s \oplus -\mathcal{D}_t) \quad (20)$$

where  $\mathcal{D}_s = \mathbf{G}_s(\mathbf{0}) = \text{diag}(r_1, \dots, r_s)$

The matrix

$$\mathcal{D}_s \oplus -\mathcal{D}_t = \text{diag}(r_1, \dots, r_s, -r_{s+1}, \dots, -r_N)$$

has  $S$  diagonal entries  $> 0$  and  $N - S$  diagonal entries  $< 0$

## Mechanism of the existence proof

Start with  $S = 0$  (only sinks)

$\implies \mathcal{D}_s$  vacuous and  $\mathcal{D}_s \oplus -\mathcal{D}_t = \text{diag}(-r_1, \dots, -r_N)$

$\implies s(J_{PFE}^S) < 0$

Finish with  $S = N$  (only sources)

$\implies \mathcal{D}_t$  vacuous and  $\mathcal{D}_s \oplus -\mathcal{D}_t = \text{diag}(r_1, \dots, r_N)$

$\implies s(J_{PFE}^S) > 0$

Eigenvalues of  $J_{PFE}^S$  depend continuously of entries of  $J_{PFE}^S$ , so  $s(J_{PFE}^S)$  changes signs, we are done.. if we are happy with a lot of uncertainty about behaviour of  $s(J_{PFE}^S)$

## Continuous perturbation of the spectrum

For  $S \in \{0, \dots, N - 1\}$

$$J_{\text{PFE}}^{S, \varepsilon} = \mathcal{M} + \text{diag}(r_1, \dots, r_S, \varepsilon, -r_{S+2}, \dots, -r_N)$$

where  $\varepsilon \in [-r_{S+1}, r_{S+1}]$  is in  $(S + 1)^{\text{th}}$  position

For  $S \in [0, N]$

$$J_{\text{PFE}}^S = J_{\text{PFE}}^{\xi, \varepsilon}, \quad \text{with} \quad \xi = \lfloor S \rfloor, \quad \varepsilon = 2(S - \lfloor S \rfloor)r_i - r_i \quad (21)$$

where  $i = \lfloor S \rfloor + 1$  if  $S < N$  and  $i = N$  when  $S = N$

Generally we vary  $\zeta$  continuously in each  $[-r_{S+1}, r_{S+1}]$

$$J_{\text{PFE}}^{S, -r_{S+1}} = J_{\text{PFE}}^S \quad \text{and} \quad J_{\text{PFE}}^{S, r_{S+1}} = J_{\text{PFE}}^{S+1}$$

# Behaviour of the spectral abscissa $s(J_{PFE}^S)$

## Lemma 18

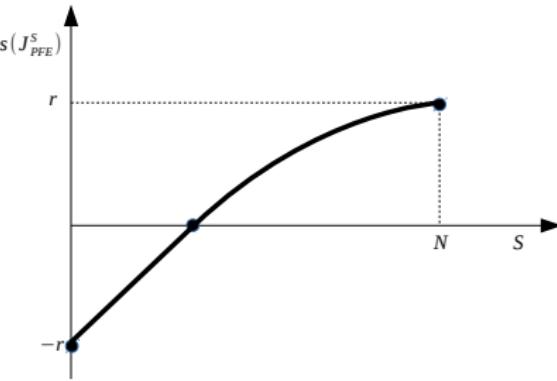
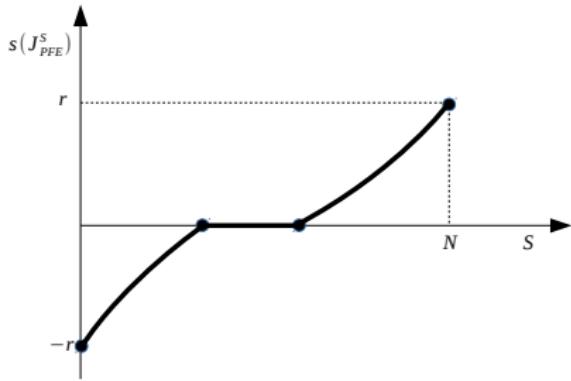
Let  $\underline{r} = \min_{i=1,\dots,N} \{r_i\}$ . Then  $s(J_{PFE}^0) \leq -\underline{r} < 0$  and  $s(J_{PFE}^N) \geq \underline{r} > 0$

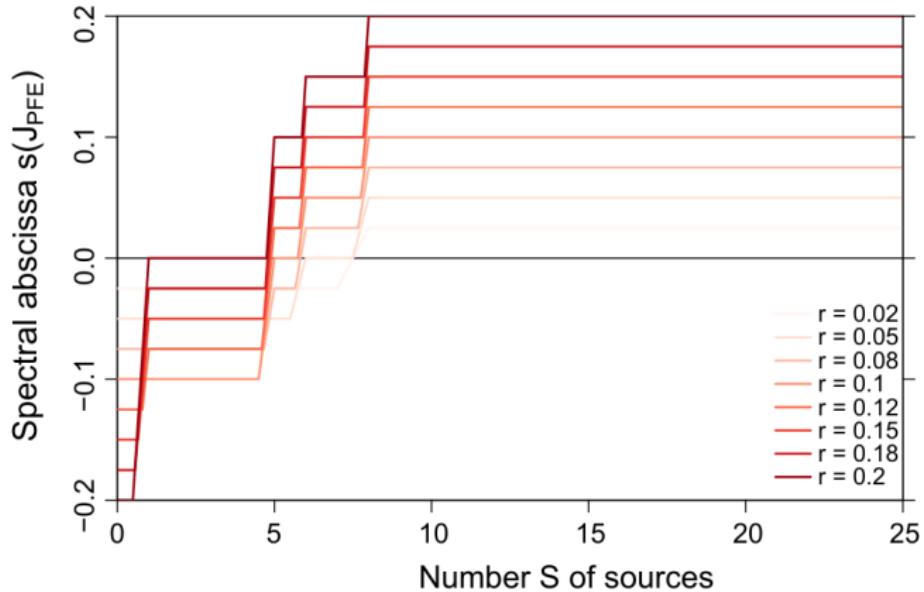
## Proposition 19

$\mathcal{M}$  reducible  $\implies s(J_{PFE}^S)$  nondecreasing for  $S \in [0, N]$

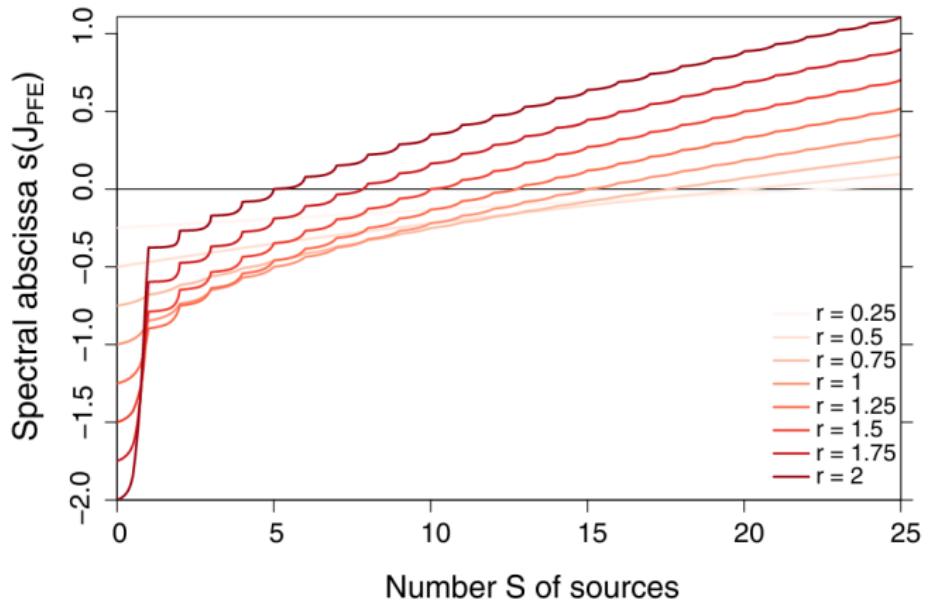
$\mathcal{M}$  irreducible  $\implies s(J_{PFE}^S)$  increasing for  $S \in [0, N]$

- ▶  $\mathcal{M}$  reducible:  $\exists \mathcal{S}_{int} \subset (0, N)$  s.t. PFE LAS if  $S < \min(\mathcal{S}_{int})$  and PFE unstable if  $S > \max(\mathcal{S}_{int})$
- ▶  $\mathcal{M}$  irreducible:  $\exists S^c \in (0, N)$  s.t. PFE LAS if  $S < S^c$  and PFE unstable if  $S > S^c$

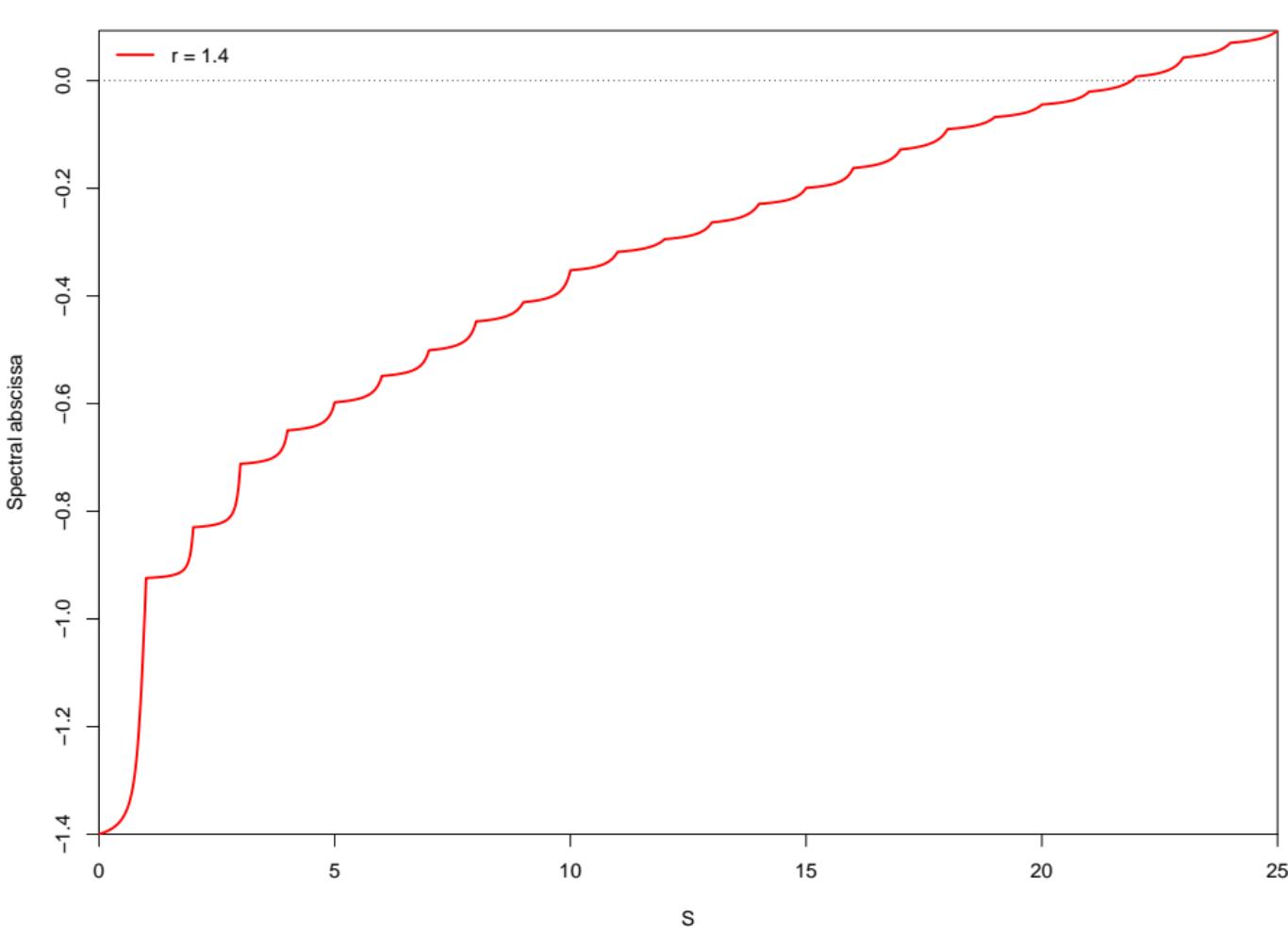




**Fig. 2** Effect of varying  $S$  and  $r$  on the spectral abscissa  $s(J_{\text{PFE}}^S)$ . Here, the total number of patches is  $N = 50$  and  $S$  varies between 0 and  $N/2$ . The underlying graph is an directed Barabasi–Albert graph



**Fig. 1** Situation that prevails when  $N = 50$  with a complete digraph of patches and movement rates taken all equal to 0.05; see text for details. Effect of varying  $S \in [0, N/2]$  on the spectral abscissa  $s(J_{\text{PFE}}^S)$  (Color figure online)



So..

we are done!

.. Are we? The result is only local, can we go further?

## System (19) is cooperative

Jacobian of (19):

$$J(\mathbf{P}_s, \mathbf{P}_t) = \begin{pmatrix} \mathbf{G}'_s(\mathbf{P}_s)\mathbf{P}_s + \mathbf{G}_s(\mathbf{P}_s) + \mathcal{M}_s & \mathcal{M}_{st} \\ \mathcal{M}_{ts} & -\mathcal{D}_t + \mathcal{M}_t \end{pmatrix} \quad (22)$$

where

$$\mathbf{G}'_s(\mathbf{P}_s) = \text{diag} \left( -\frac{r_1}{K_1}, \dots, -\frac{r_s}{K_s} \right)$$

Thus

$$J(\mathbf{P}_s, \mathbf{P}_t) = \mathcal{M} + ((\mathbf{G}'_s(\mathbf{P}_s)\mathbf{P}_s + \mathbf{G}_s(\mathbf{P}_s)) \oplus -\mathcal{D}_t)$$

with  $\mathbf{G}'_s(\mathbf{P}_s)\mathbf{P}_s + \mathbf{G}_s(\mathbf{P}_s)$  and  $-\mathcal{D}_t$  diagonal

$\implies$  system (19) is cooperative

## A theorem of Hirsch

To move forward, the following result of Hirsch looks quite nice

Theorem 20 (Th. 6.1 in Hirsch (1984) – Bull. AMS 11(1))

Let  $\mathbf{F}$  be a  $C^1$  vector field in  $\mathbb{R}^n$  with flow  $\phi$  preserving  $\mathbb{R}_+^n$  for  $t > 0$  and strongly monotone in  $\mathbb{R}_+^n$ . Suppose that the origin is an equilibrium and all trajectories in  $\mathbb{R}_+^n$  are bounded. Suppose the matrix-valued map  $D\mathbf{F} : \mathbb{R}_+^n \rightarrow \mathbb{R}^{n \times n}$  is strictly antimonotone, i.e.,

$$\mathbf{x} > \mathbf{y} \implies D\mathbf{F}(\mathbf{x}) < D\mathbf{F}(\mathbf{y})$$

Then either all trajectories in  $\mathbb{R}_+^n$  go to the origin, or there exists a unique equilibrium  $\mathbf{P}^* \in \text{Int}\mathbb{R}_+^n$  and all trajectories in  $\mathbb{R}_+^n \setminus \{\mathbf{0}\}$  limit to  $\mathbf{P}^*$

OK, nice, but..

Take

$$\mathbf{P}_1 = (0, \dots, 0, \star, \dots, \star) \text{ and } \mathbf{P}_2 = (0, \dots, 0, \star, \dots, \star)$$

have their first  $S$  entries zero, i.e.,  $\mathbf{P}_1 = (\mathbf{0}_s, \mathbf{P}_t^1)$  and  $\mathbf{P}_2 = (\mathbf{0}_s, \mathbf{P}_t^2)$ ; assume  $\mathbf{P}_1 > \mathbf{P}_2$ , i.e.,  $\mathbf{P}_t^1 > \mathbf{P}_t^2$

Then

$$\begin{aligned} J(\mathbf{0}_s, \mathbf{P}_t^1) &= \mathcal{M} + ((\mathbf{G}'_s(\mathbf{0}_s)\mathbf{0}_s + \mathbf{G}_s(\mathbf{0}_s)) \oplus -\mathcal{D}_t) \\ &= \mathcal{M} + (\mathcal{D}_s \oplus -\mathcal{D}_t) \\ &= J(\mathbf{0}_s, \mathbf{P}_t^2) \end{aligned}$$

i.e.,

$$J_{\mathbf{P}_1}^S = J_{\mathbf{P}_2}^S$$

$\implies$  (19) is not strictly antimonotone

## (non) lasciate ogne speranza, voi ch'intrate

Except for strict antimonotonicity of  $\mathbf{F}$ , all hypotheses of [Hirsch (1984) – Th. 6.1] are satisfied:

- ▶ in the case  $\mathcal{M}$  irreducible, (19) is strongly monotone (by [Hirsch (1984) – Th. 1.7])
- ▶ the origin is an equilibrium
- ▶ all solutions of (19) are bounded in  $\mathbb{R}_+^N$

$\implies$  by other results (e.g., Hirsch *ibid*), there exists  $\mathbf{P}^* \gg \mathbf{0}$

What is the use of strict antimonotonicity in the proof of [Hirsch (1984) – Th. 6.1]? .. To show uniqueness of  $\mathbf{P}^*$

More precisely: let  $\mathbf{z} \in (\mathbf{0}, \mathbf{P}^*)$ , where  $\mathbf{P}^* \gg \mathbf{0}$  is a nontrivial equilibrium

Strict antimonotonicity  $\implies \mathbf{F}(\mathbf{z}) > \mathbf{0}$ , and we can then proceed with the remainder of the proof of [Hirsch (1984) – Th. 6.1]

Let us show that we indeed have  $\mathbf{F}(\mathbf{z}) > \mathbf{0}$  for (19), despite the lack of strict antimonotonicity

As in [Hirsch (1984) – Th. 6.1]: for  $i = 1, \dots, N$ , let

$$\begin{aligned} g_i : [0, 1] &\rightarrow \mathbb{R} \\ s &\mapsto F_i(s\mathbf{P}^*) \end{aligned}$$

Then  $g_i(0) = g_i(1) = 0$  for  $i = 1, \dots, N$  and, for  $i = S + 1, \dots, N$  (sinks),

$$g_i(s) = -r_i s P_i^* + \sum_{j=1}^N m_{ij} s P_j^* = \left( r_i P_i^* + \sum_{j=1}^N m_{ij} P_j^* \right) s = 0$$

However, for  $i = 1, \dots, S$  (sources),

$$g_i(s) = r_i \left( 1 - \frac{s P_i^*}{K_i} \right) s P_i^* + \sum_{j=1}^N m_{ij} s P_j^*$$

Ha!

$$g_i''(s) = -\frac{2r_i P_i^{*2}}{K_i} < 0, \quad i = 1, \dots, S$$

$\implies$  for  $i = 1, \dots, S$ ,  $g_i(s) > 0$  when  $s \in (0, 1)$

$\implies$  when  $S > 0$ ,  $\mathbf{F}(\mathbf{z}) > \mathbf{0}$ ,  $\forall \mathbf{z} \in (\mathbf{0}, \mathbf{P}^*)$

And we can then carry on with the remainder of the proof of  
[Hirsch (1984) – Th. 6.1]

To finish, the case  $S = 0$  is easy:

$$\left( \sum_{i=1}^N P_i \right)' = - \sum_{i=1}^N r_i P_i < 0$$

since at least one of the  $P_i(0) > 0$

$$\implies \left( \sum_{i=1}^N P_i \right) \rightarrow 0 \implies \lim_{t \rightarrow \infty} P_i(t) = 0 \text{ for } i = 1, \dots, N$$

Et hop!  $\square$

## To conclude (mathematically)

### Theorem 21

*There exists a critical interval  $\mathcal{S}_{int} \subset (0, N) \subset \mathbb{R}$  s.t.*

- ▶  $S < \min(\mathcal{S}_{int}) \implies PFE\ LAS$
- ▶  $S > \max(\mathcal{S}_{int}) \implies PFE\ instable$

*Additionally, if the location digraph is strongly connected, then*

- ▶  $\mathcal{S}_{int}$  is reduced to a point  $S^c$
- ▶  $S < S^c \implies PFE\ GAS$
- ▶  $S > S^c \implies \exists! \mathbf{P}^* \gg \mathbf{0} \ GAS \text{ for } \mathbb{R}_+^N \setminus \{\mathbf{0}\}$

## A brief history of metapopulations

### The general context

#### A metapopulation of sources and sinks with explicit movement

A few older models

The model

Analysis of the model

A special case

### Diseases in metapopulations

### Computational considerations

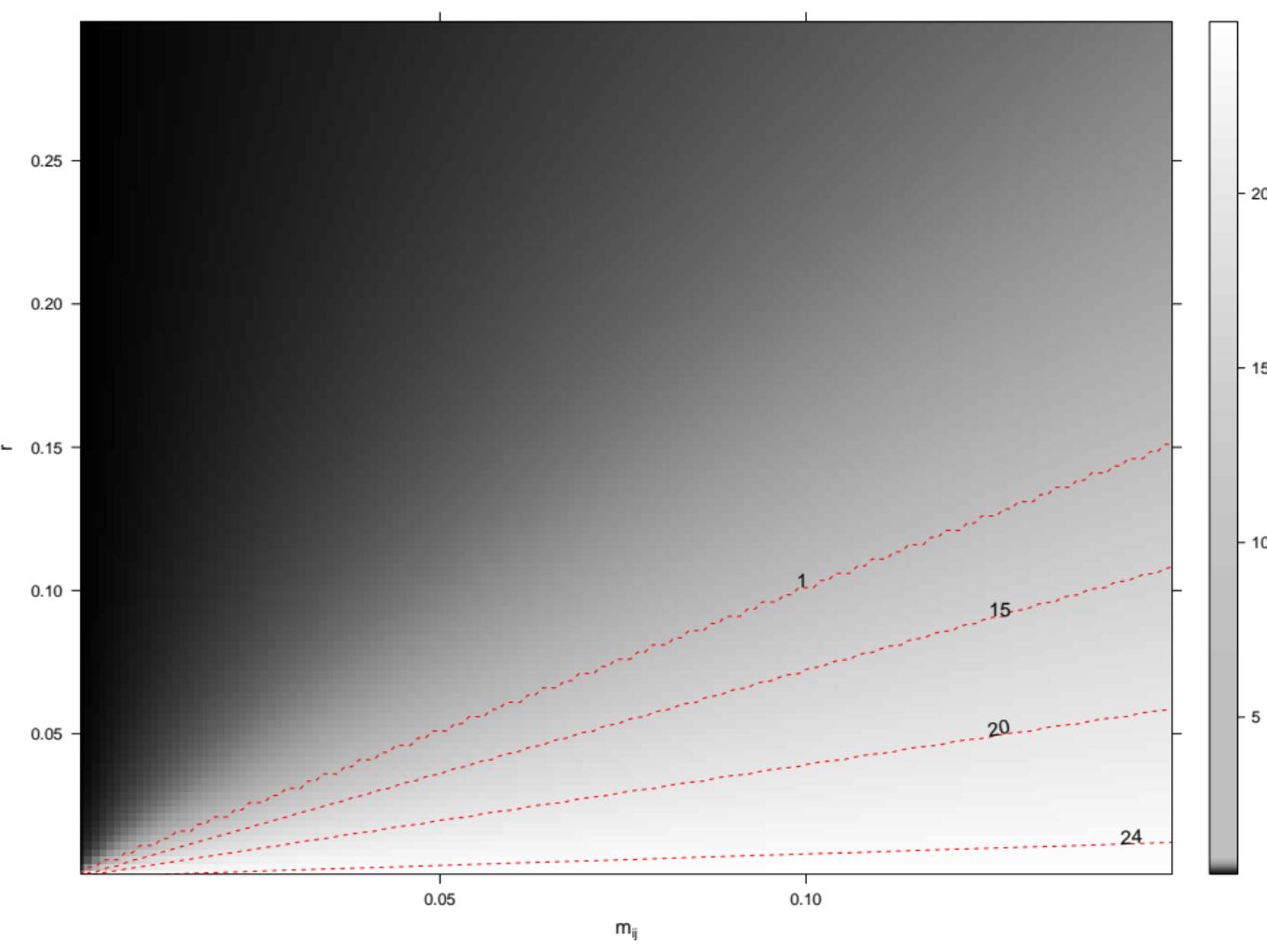
## An interesting special case

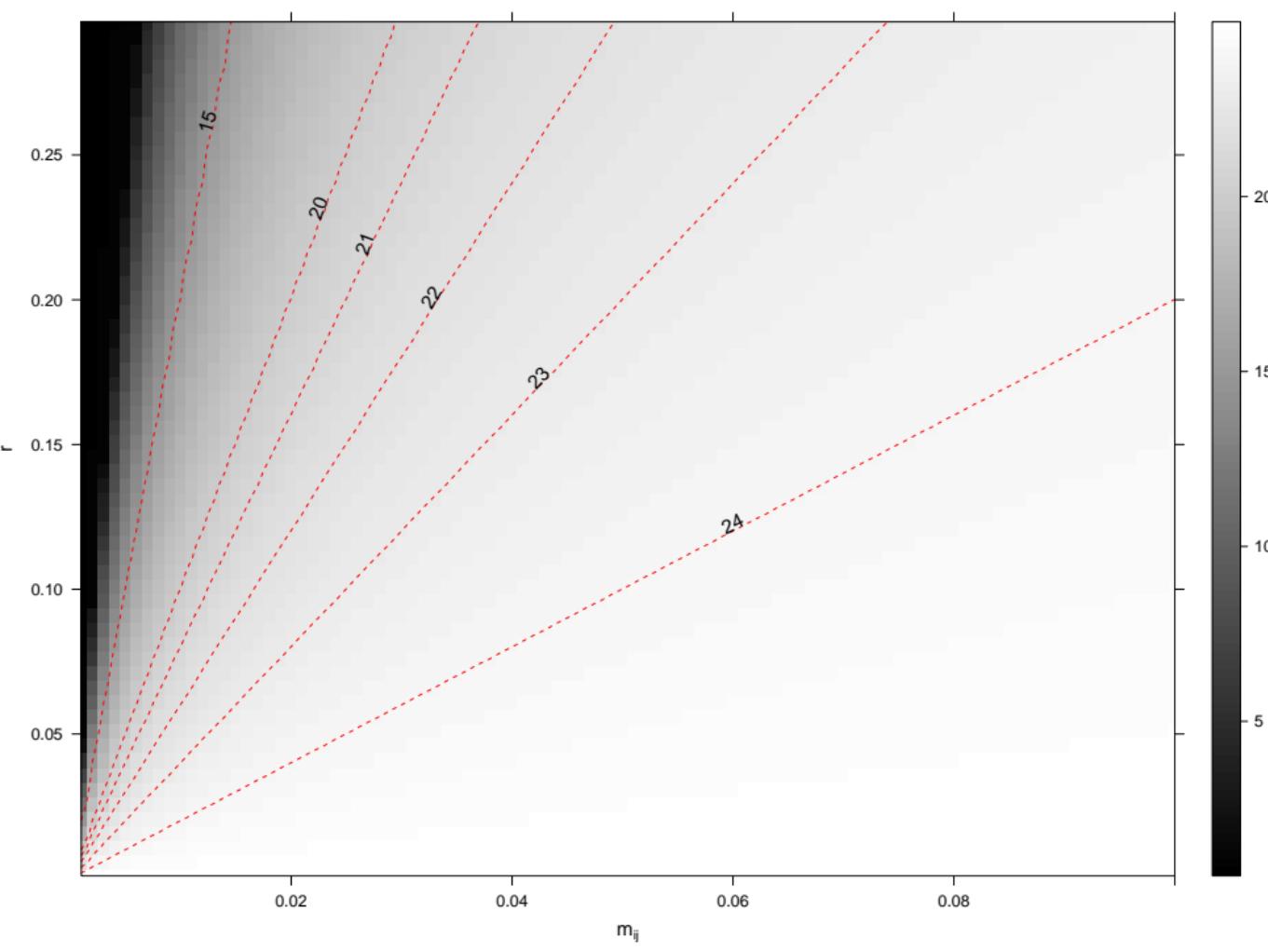
In the 2 figures that follow:

- ▶  $N = 50$
- ▶  $r = r_i, \forall i = 1, \dots, N$
- ▶  $m_{ij} = m, \forall i, j = 1, \dots, N$  s.t.  $m_{ij} > 0$
- ▶ plot is value of  $S^c$  as a function of  $m$  and  $r$

Figure 1: ring of locations

Figure 2: complete digraph





## Case of complete homogeneous movement

### Proposition 22

Suppose that the movement digraph is complete and that  $m_{ij} = m$  for  $i, j = 1, \dots, N, i \neq j$

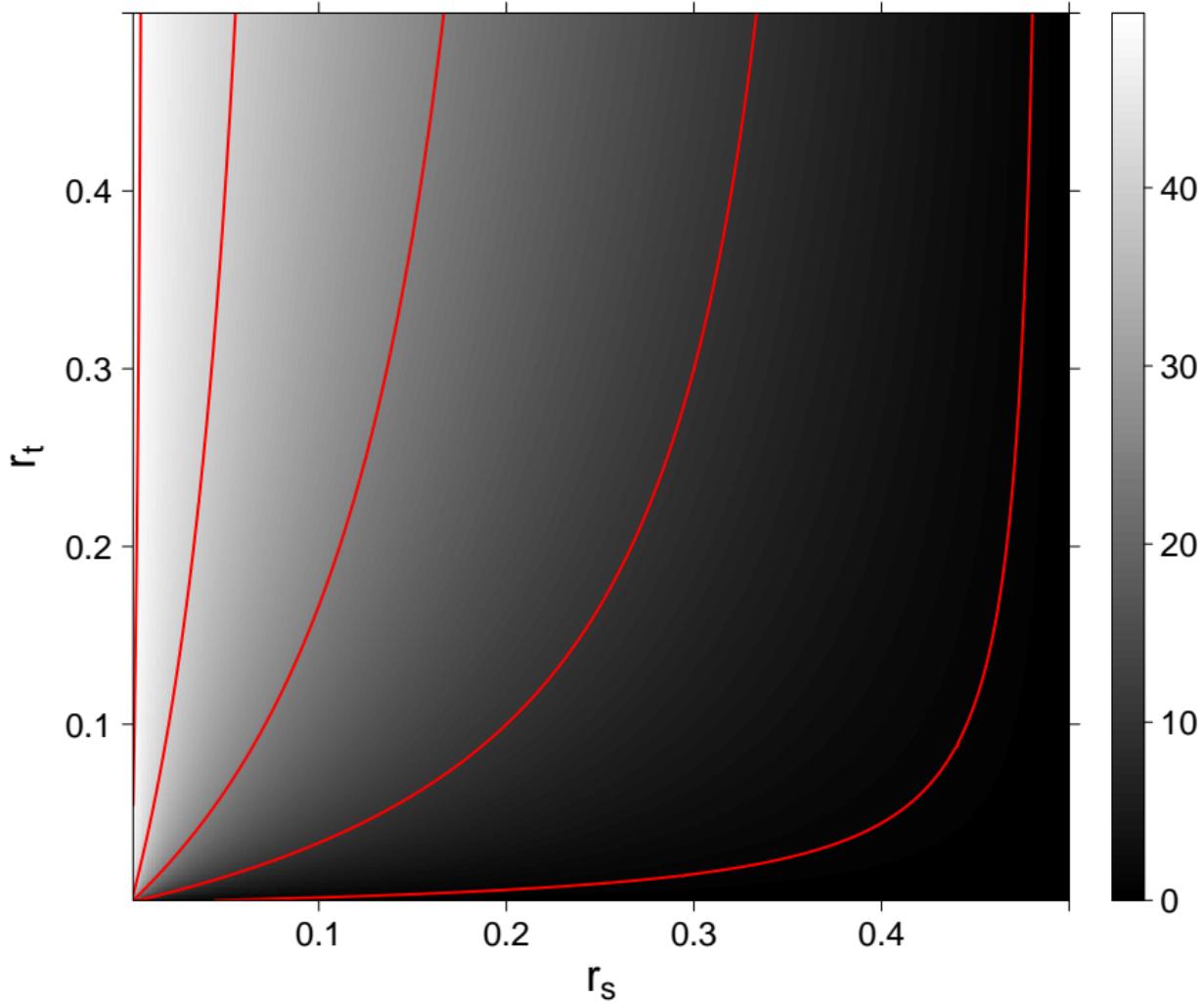
Suppose that  $S \in \{1, \dots, N - 1\}$ , that for  $i = 1, \dots, S$ ,  $r_i = r_s$  and that for  $i = S + 1, \dots, N$ ,  $r_i = r_t$

Then

$$S^c = \frac{mNr_t - r_s r_t}{m(r_s + r_t)} \quad (23)$$

If  $r_s = r_t = r$ , then

$$S^c = \frac{N}{2} - \frac{r}{2m} \quad (24)$$



## Proof of Prop 22 uses equitable partitions

Section 9.3 in *Algebraic Graph Theory*, Godsil & Royle (2013)

An **equitable partition**  $\pi$  splits a graph  $X$  into **cells**  $\mathcal{C}_i$ ,  $i = 1, \dots, r$ , s.t. for a vertex  $u$  in cell  $\mathcal{C}_i$ , the number of neighbours in cell  $\mathcal{C}_j$  is a constant  $b_{ij}$  that does not depend on  $u$

$\iff$  the subgraph of  $X$  induced by each cell is regular [vertices have same degree] and edges joining two distinct cells form a semiregular bipartite graph [vertices have same degree in each bipartite component]

The digraph with the  $r$  cells of  $\pi$  as vertices and the  $b_{ij}$  arcs from the  $i^{\text{th}}$  to the  $j^{\text{th}}$  cell of  $\pi$  is the **quotient**  $X/\pi$  of  $X$  on  $\pi$ . The adjacency matrix of  $X/\pi$  is  $A(X/\pi) = [b_{ij}]$

## Characterising an equitable partition

### Lemma 23 (A friendly characterisation)

$X$  graph,  $A(X)$  its adjacency matrix,  $\pi$  a partition of  $V(X)$  with characteristic matrix  $P$ . Then

$\pi$  equitable  $\iff$  column space of  $P$  is  $A$ -invariant

Write

$$J_{\text{PFE}}^S = \begin{pmatrix} m\mathbb{J} - Nm\mathbb{I} + r_s\mathbb{I} & m\mathbb{J} \\ m\mathbb{J} & m\mathbb{J} - Nm\mathbb{I} - r_t\mathbb{I} \end{pmatrix} \quad (25)$$

with  $\mathbb{J}$  matrix of all 1's

Consider (25) as the adjacency matrix of a digraph  $\mathcal{G}$

Suppose partition  $\pi$  splits  $\mathcal{G}$  in two cells,  $\{S_i\}_{i=1,\dots,s}$  (sources) and  $\{T_i\}_{i=s+1,\dots,N}$  (sinks)

The characteristic matrix of  $\pi$  is the  $N \times 2$ -matrix

$$C = \begin{pmatrix} \mathbf{1}_S & \mathbf{0}_S \\ \mathbf{0}_{N-S} & \mathbf{1}_{N-S} \end{pmatrix}$$

We have

$$J_{\text{PFE}}^S \mathbb{1} = J_{\text{PFE}}^S \begin{pmatrix} \mathbb{1}_S \\ \mathbb{1}_{N-S} \end{pmatrix} = \begin{pmatrix} r_s \mathbb{1}_S \\ -r_t \mathbb{1}_{N-S} \end{pmatrix}$$

Thus the column space of  $C$  is  $J_{\text{PFE}}^S$ -invariant  $\implies \pi$  is equitable

# Properties of equitable partitions

## Lemma 24

$\pi$  equitable partition of graph  $X$  with characteristic matrix  $P$ , and  $B = A(X/\pi)$ . Then  $AP = PB$  and  $B = (P^T P)^{-1} P^T AP$

## Theorem 25

$\pi$  equitable partition of graph  $X \implies$  characteristic polynomial of  $A(X/\pi)$  divides characteristic polynomial of  $A(X)$

$\implies$  the quotient matrix  $B_{\text{PFE}}^S$  satisfies

$$B_{\text{PFE}}^S = (C^T C)^{-1} C^T J_{\text{PFE}}^S C$$

$$\implies B_{\text{PFE}}^S = \begin{pmatrix} mS - mN + r_s & m(N - S) \\ mS & -(mS + r_s) \end{pmatrix}$$

And  $\sigma(B_{\text{PFE}}^S) \subset \sigma(J_{\text{PFE}}^S)$

$B_{\text{PFE}}^S$  essentially nonnegative (and clearly irreducible)

$$\implies \exists! \mathbf{v}_p \gg \mathbf{0} \text{ s.t. } B_{\text{PFE}}^S \mathbf{v}_p = \lambda_p \mathbf{v}_p = s(B_{\text{PFE}}^S) \mathbf{v}_p$$

Then  $J_{\text{PFE}}^S C = CB_{\text{PFE}}^S$

So

$$J_{\text{PFE}}^S C \mathbf{v}_p = CB_{\text{PFE}}^S \mathbf{v}_p = \lambda_p C \mathbf{v}_p$$

and  $C \mathbf{v}_p$  is an eigenvector of  $J_{\text{PFE}}^S$  that is also  $\gg \mathbf{0}$

As the only eigenvector  $\gg \mathbf{0}$  of  $J_{\text{PFE}}^S$  corresponds to  $s(J_{\text{PFE}}^S)$ , we have  $s(J_{\text{PFE}}^S) = s(B_{\text{PFE}}^S)$

To compute  $S^c$ , recall  $S^c$  is value of  $S$  where PFE loses stability

Consider  $B_{\text{PFE}}^S$ . We have  $\text{tr}(B_{\text{PFE}}^S) = -mN + r_s - r_t$  and

$$\det(B_{\text{PFE}}^S) = -mS(r_s + r_t) - r_s r_t + mNr_t$$

One shows easily that  $\det(\cdot)$  governs stability

$$\implies S^c = \frac{mNr_t - r_s r_t}{m(r_s + r_t)}$$



So..

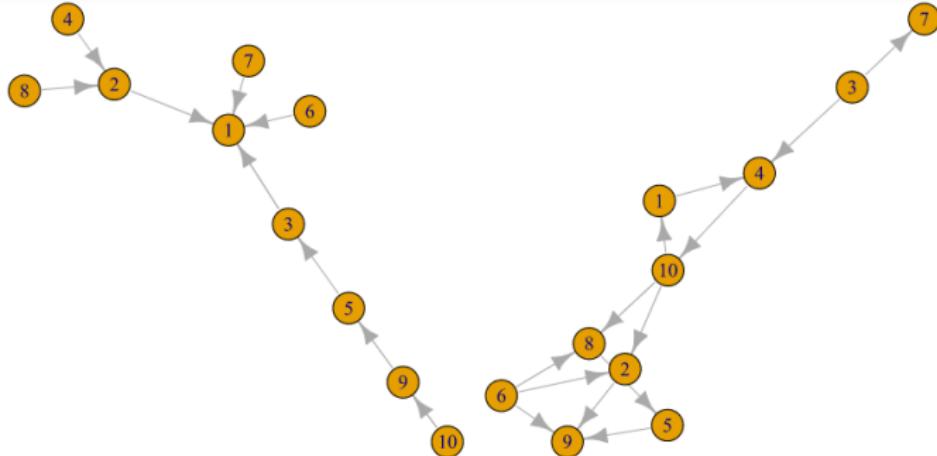
$\exists S_{int}$  (resp.  $S^C$ ), threshold interval (resp. number) of number of source locations s.t.

- ▶ Population likely (resp. assured) to go extinct below  $\min(S_{int})$  (resp.  $S^C$ )
- ▶ Population likely (resp. assured) to persist above  $\max(S_{int})$  (resp.  $S^C$ )

Strength of result depends on strong connectedness of location graph

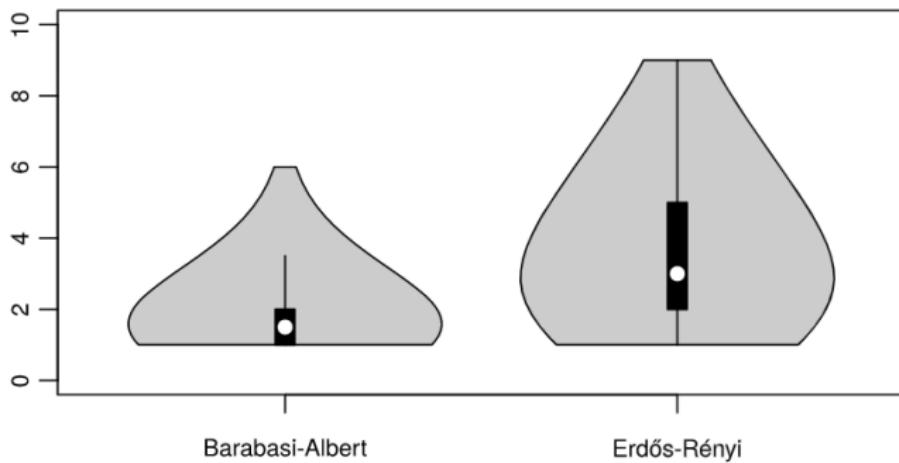
In case of strong connectedness, there is an  $\mathcal{R}_0$  type threshold

In case of complete graph with movement equal, we can actually find explicit expression for  $S^C$



**(a)** Barabasi-Albert digraph

**(b)** Erdős-Rényi digraph



**(c)** Values of  $S^c$

## A brief history of metapopulations

### The general context

### A metapopulation of sources and sinks with explicit movement

### Diseases in metapopulations

Mobility and the spatio-temporal spread of pathogens

Why use metapopulation models?

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

Bounds on  $\mathcal{R}_0$

To conclude on theory

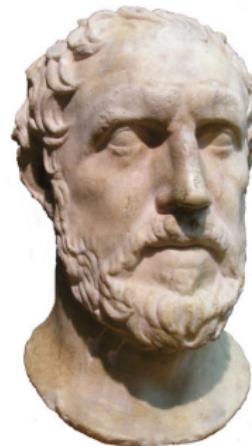
### Computational considerations

# 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



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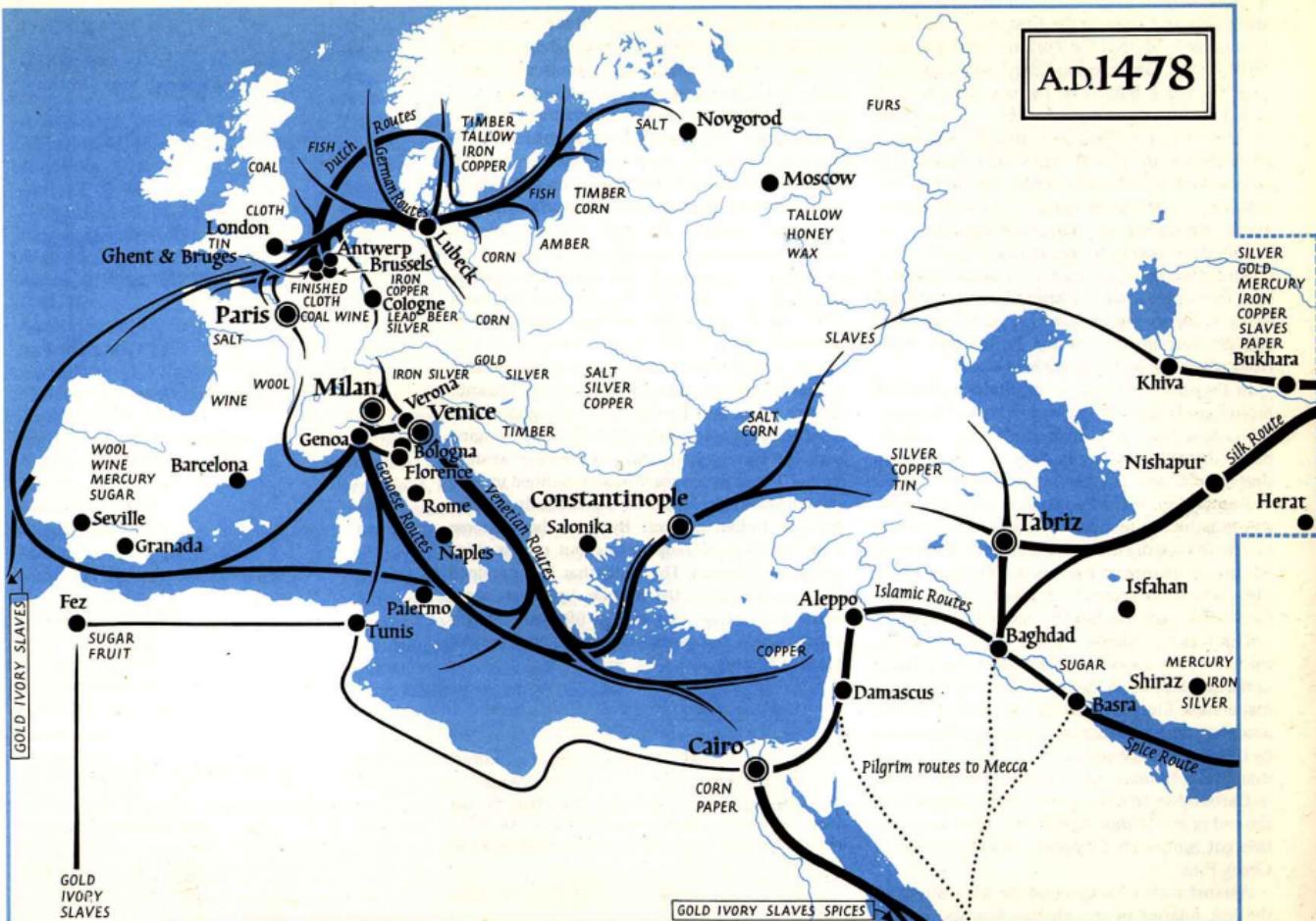
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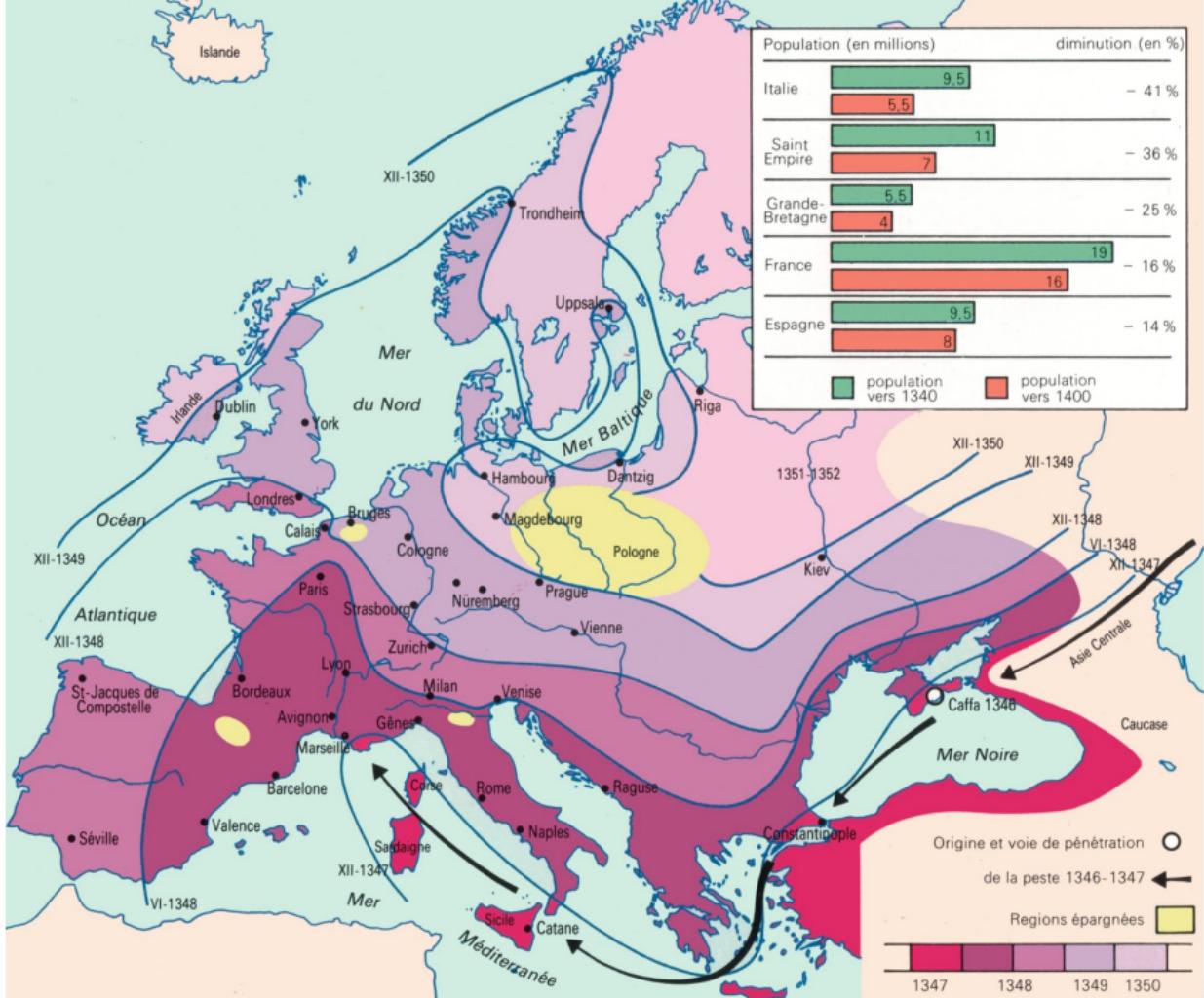
## Pathogen spread has evolved with mobility

Pathogens use trade routes

In ancient times, trade routes were “simple”

A.D.1478







Plague  
An Dom 1637  
Buried 515.  
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**  
**Liverpool to Winnipeg**  
PROVINCE OF MANITOBA

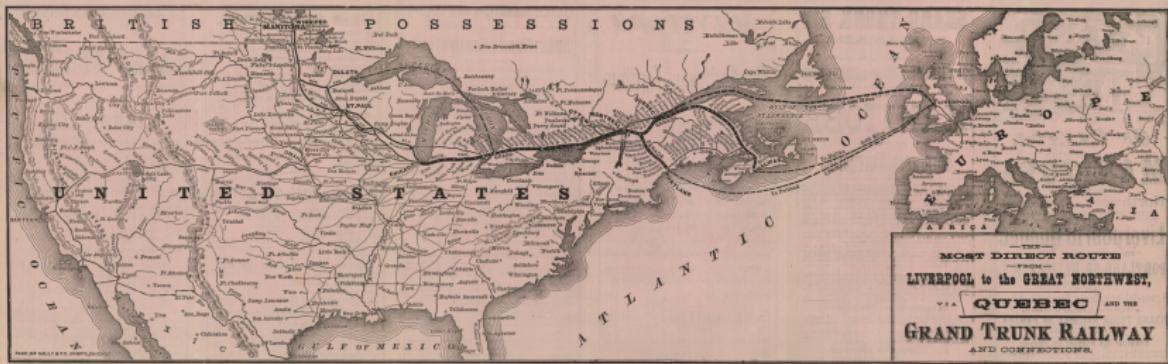
**MANITOBA** offers the most easily accessible  
land in the world, the most promising and productive  
lands in the world, the most abundant rainfall in the world,  
the most favorable climate in the world, the most  
fertile soil in the world, and within easy reach to the  
great centre of the Continent, which afford  
the greatest opportunities for life, health, gratitudo, and  
other 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**

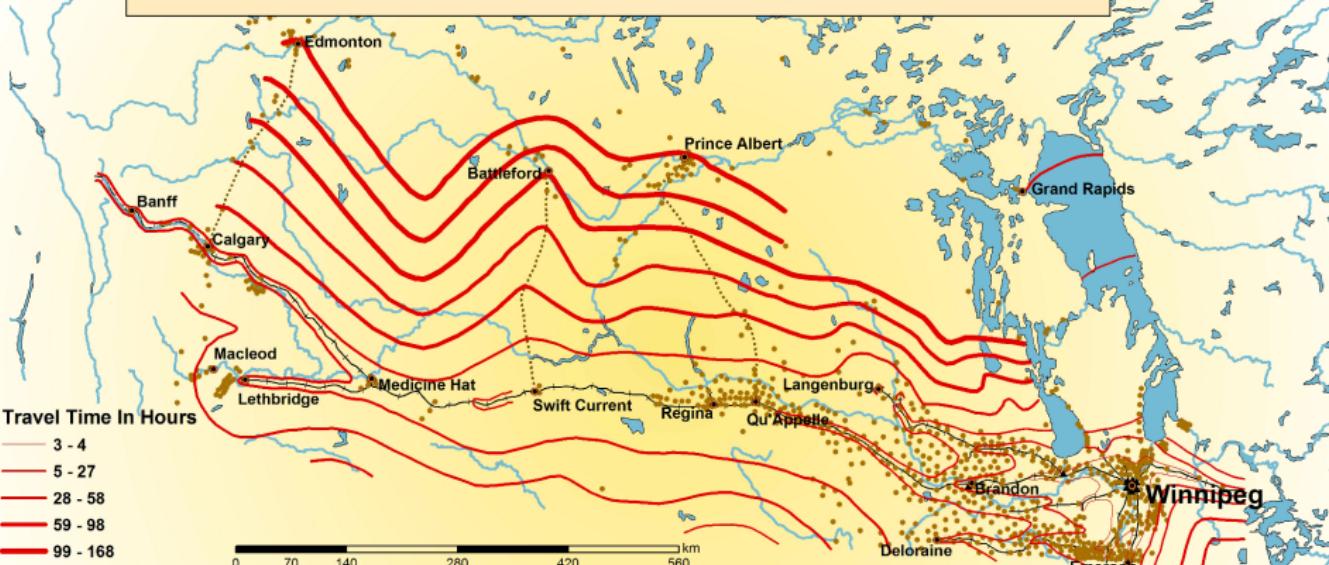
In one of the best fitted countries. Every square mile is vested  
in the Dominion Government, and every acre is held in trust for the  
people. A great deal of land has been sold, and it is believed  
that the rest will be sold at a very low price. The law is  
designed to encourage the people to settle on the land, and to  
make it available for the use of the people. The law is  
designed to encourage the people to settle on the land, and to  
make it available for the use of the people.



**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

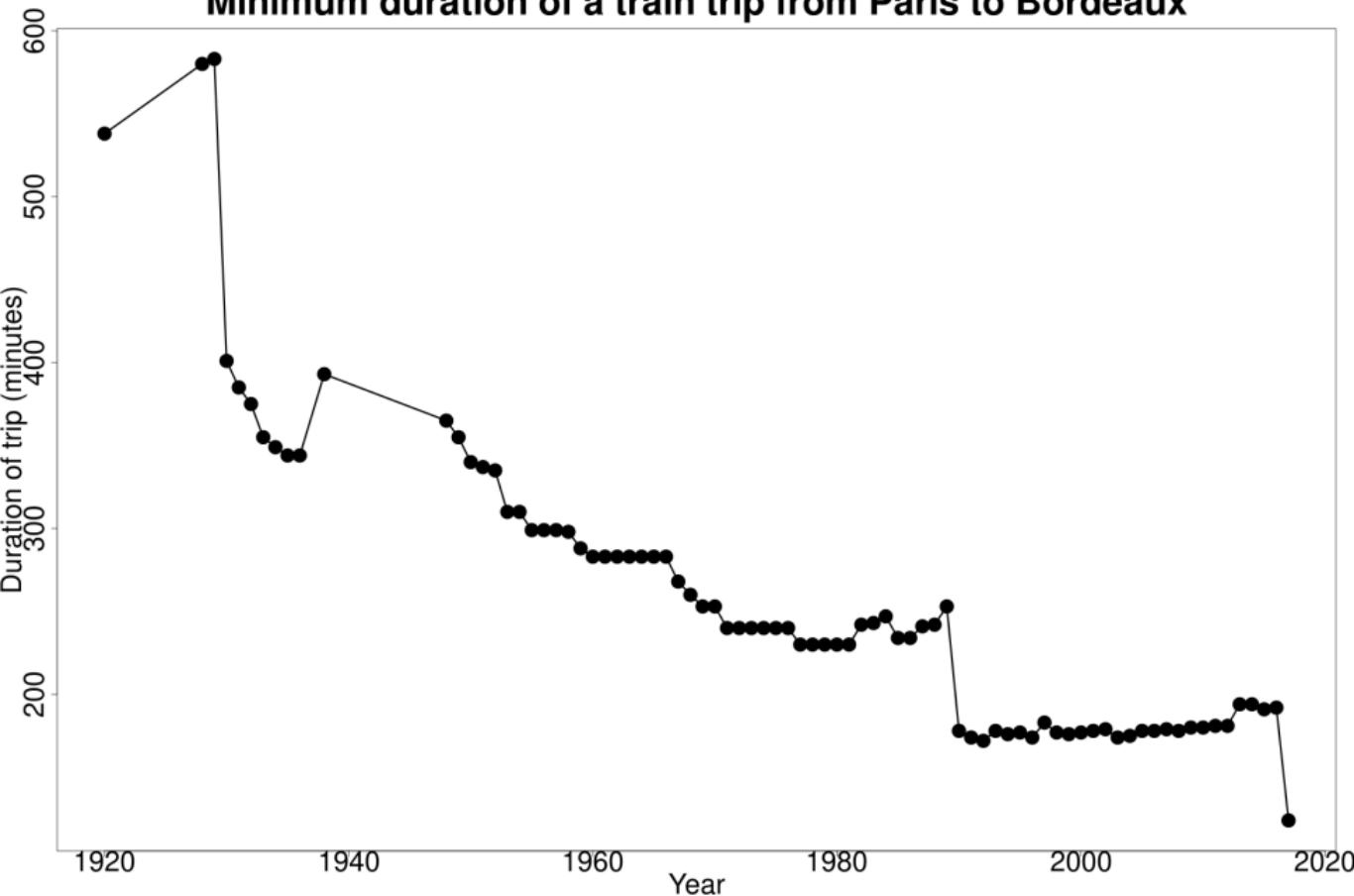


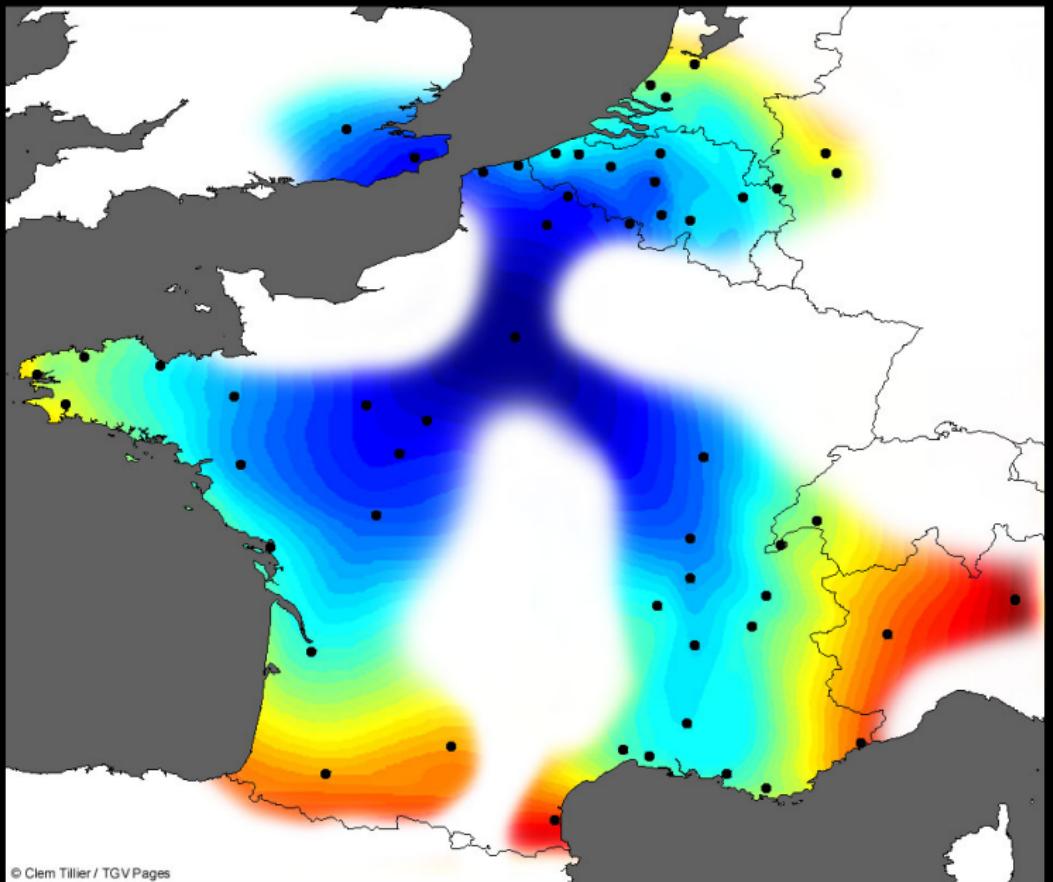
Compiled from maps prepared by John Warkentin "Western Canada 1886" in the Historical and Scientific Society of Manitoba, Series III No. 20 1963-1964

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



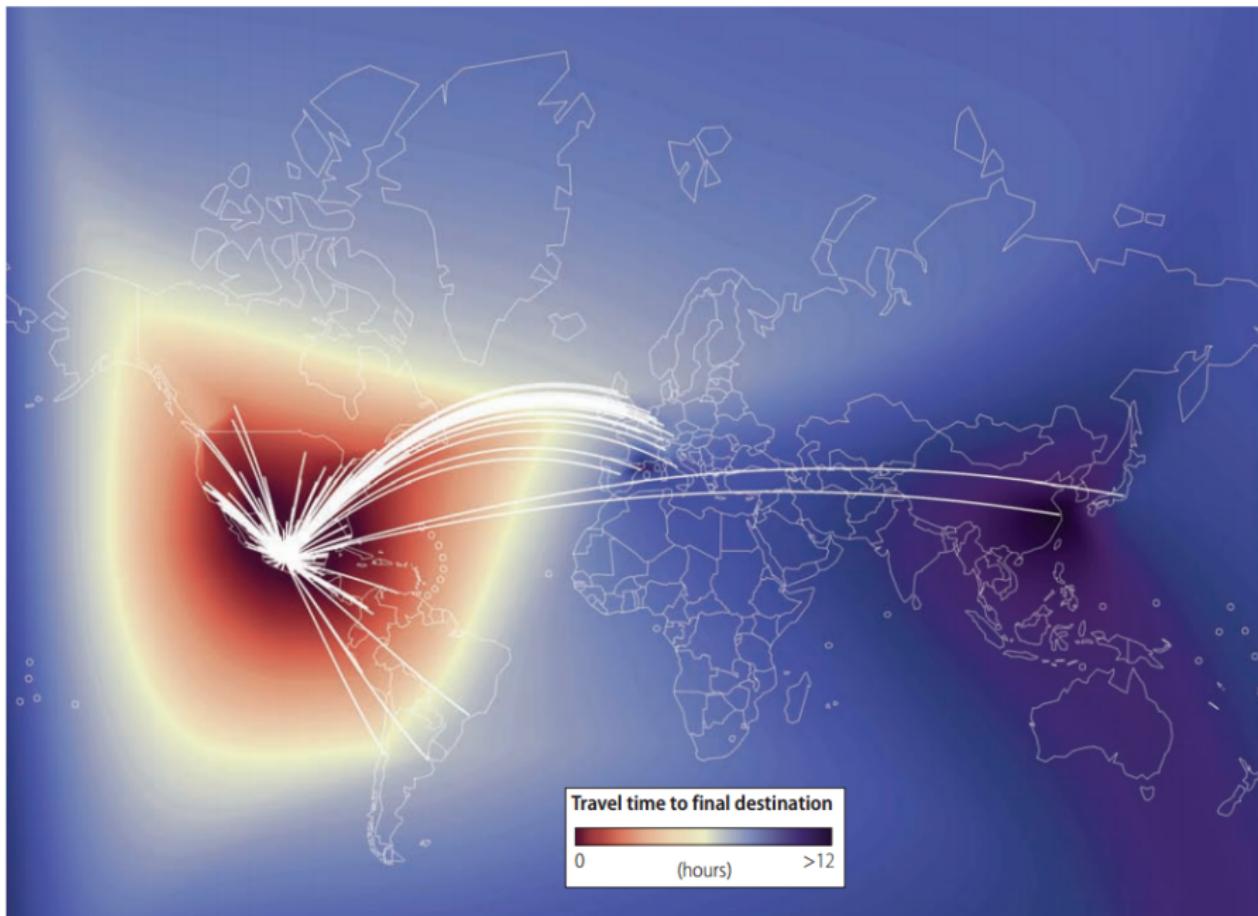


© Clem Tillier / TGV Pages



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

Fig. 2. International flights departing Mexico<sup>a</sup> and corresponding travel times, May 2009



<sup>a</sup> 82 international cities received flights directly from Mexico in May 2009.

# Scale of modern mobility difficult to apprehend

## Working definition

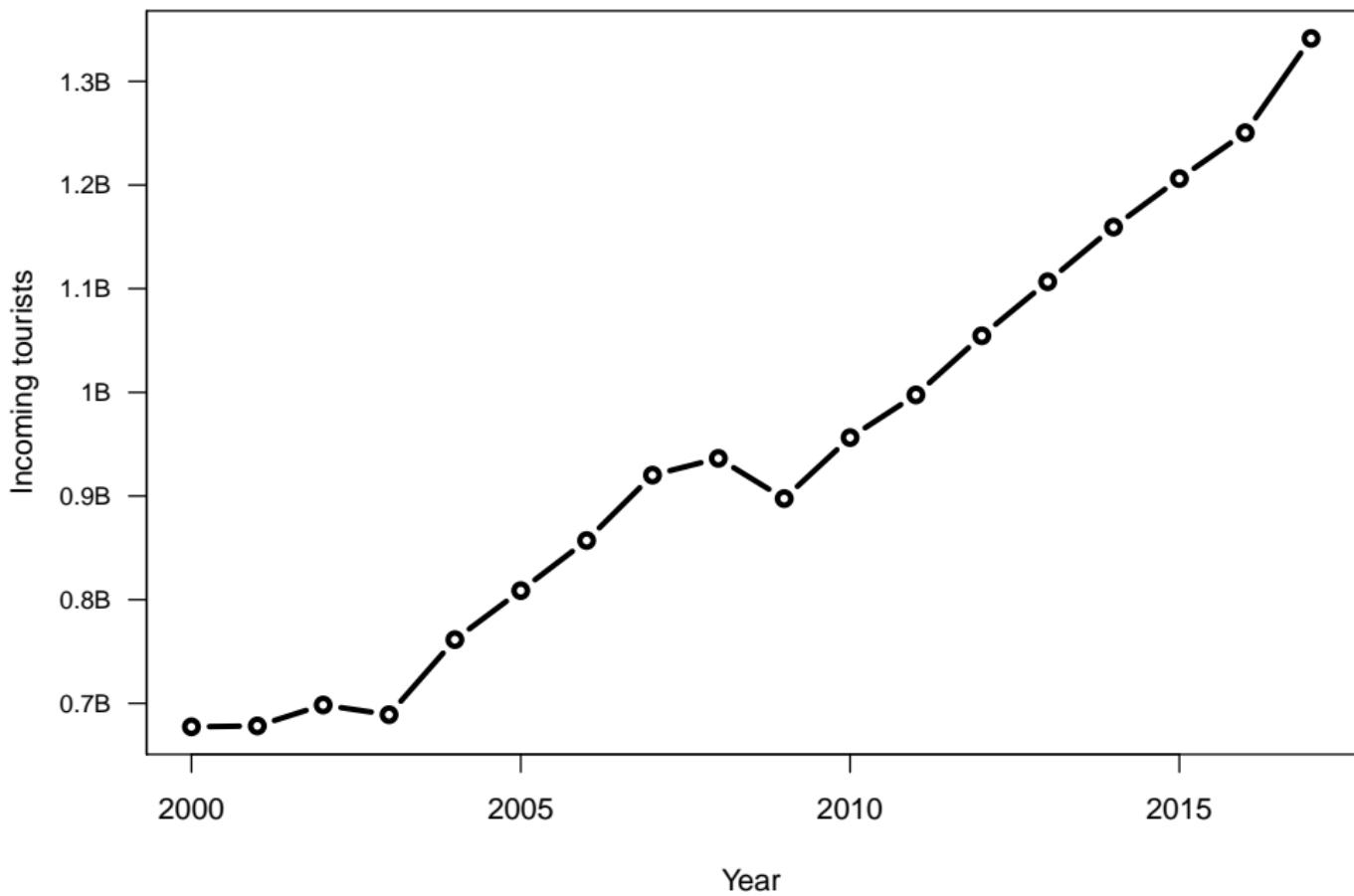
**Mobility** is the collection of processes through which individuals change their current location

Takes many different forms

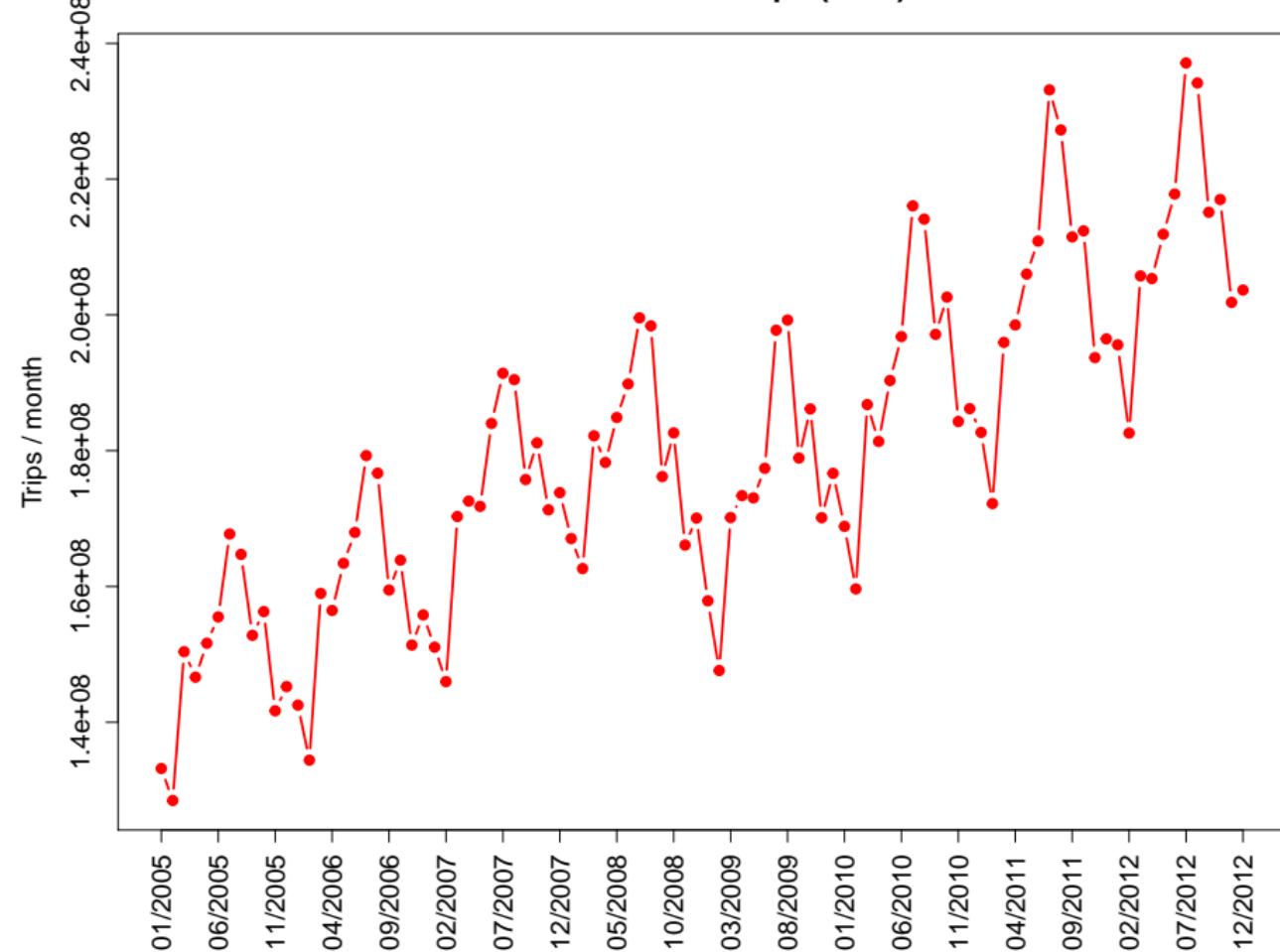
Evolves constantly

Numbers are .. colossal

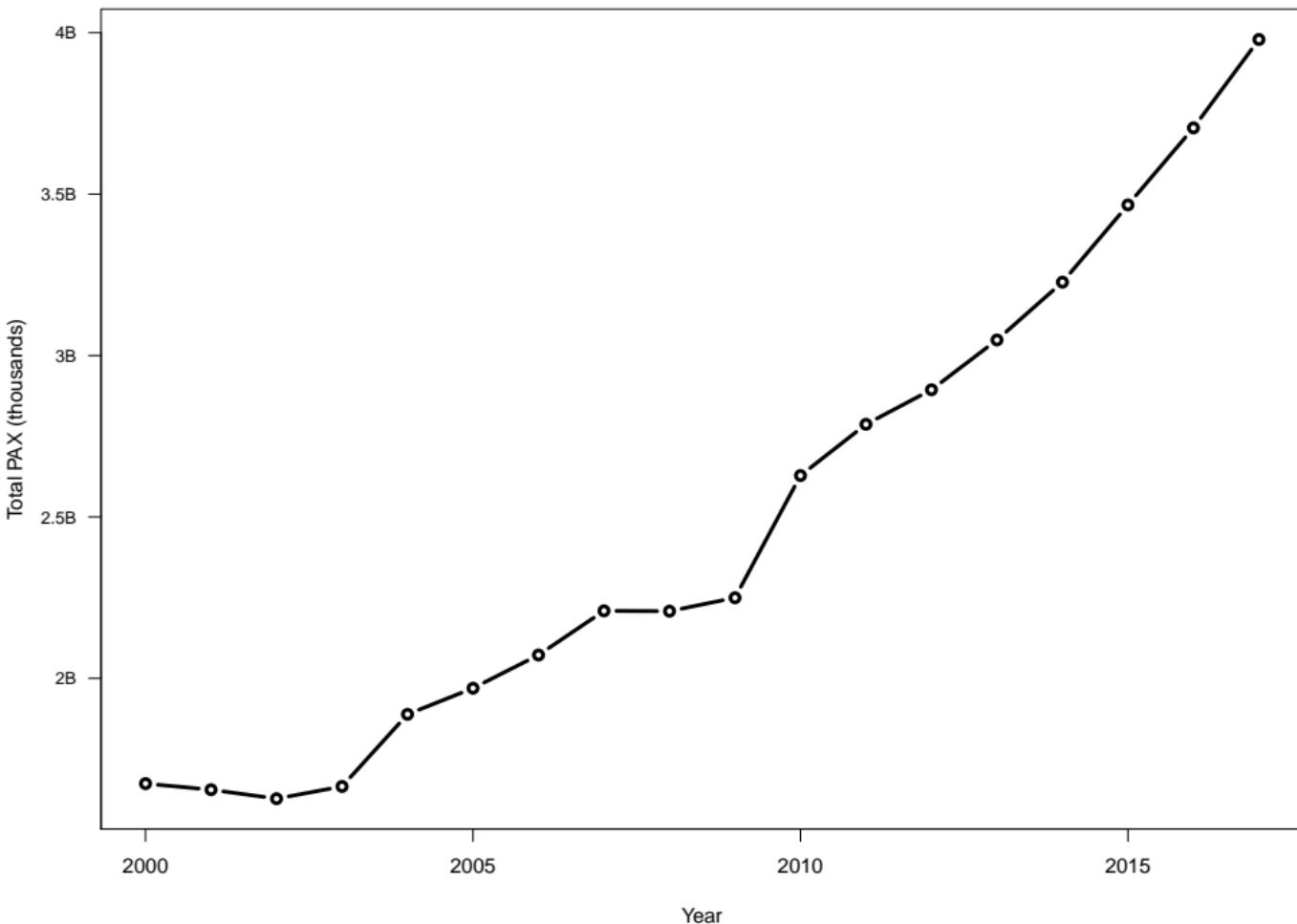
## Number of incoming tourists (all countries)



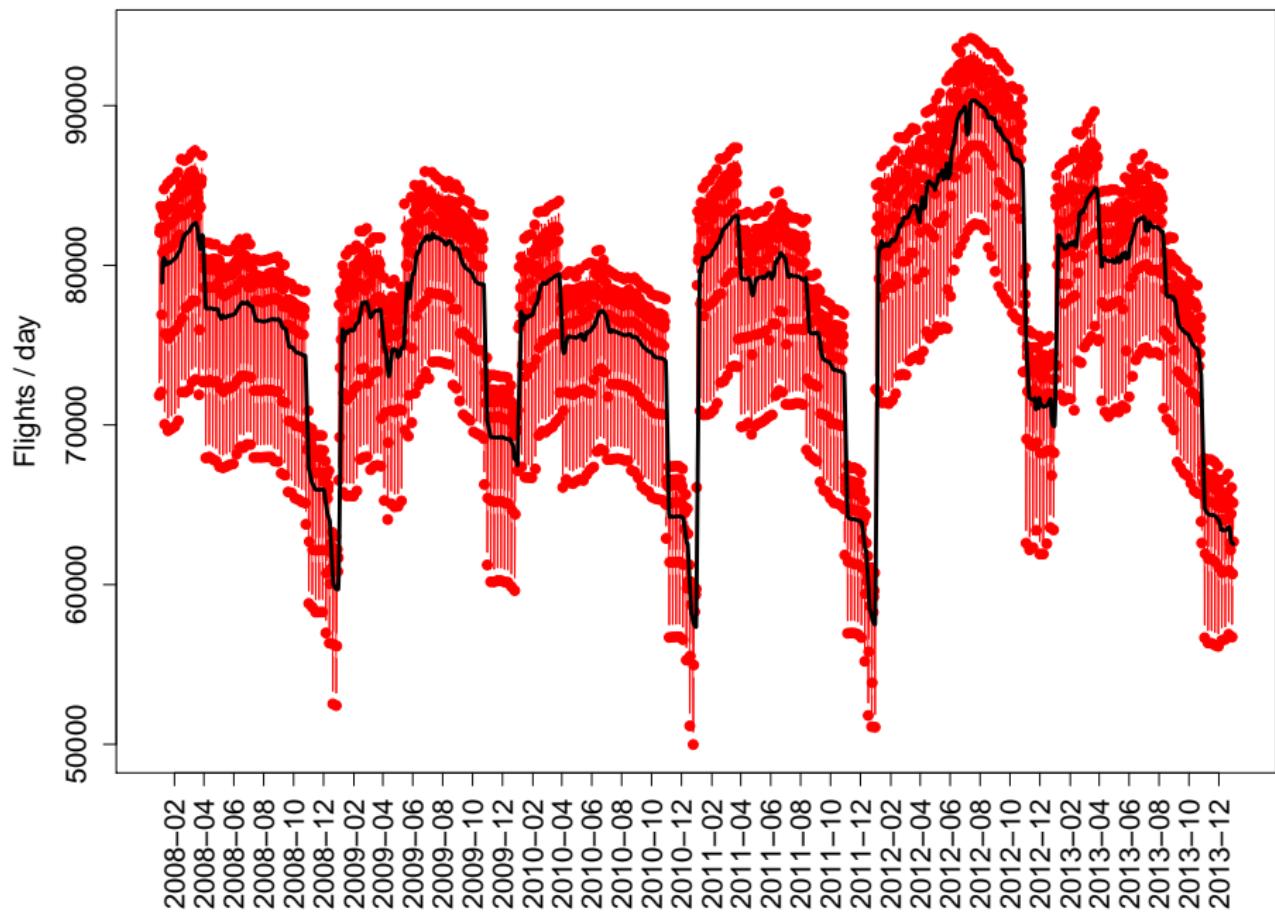
## Total number of trips (IATA)



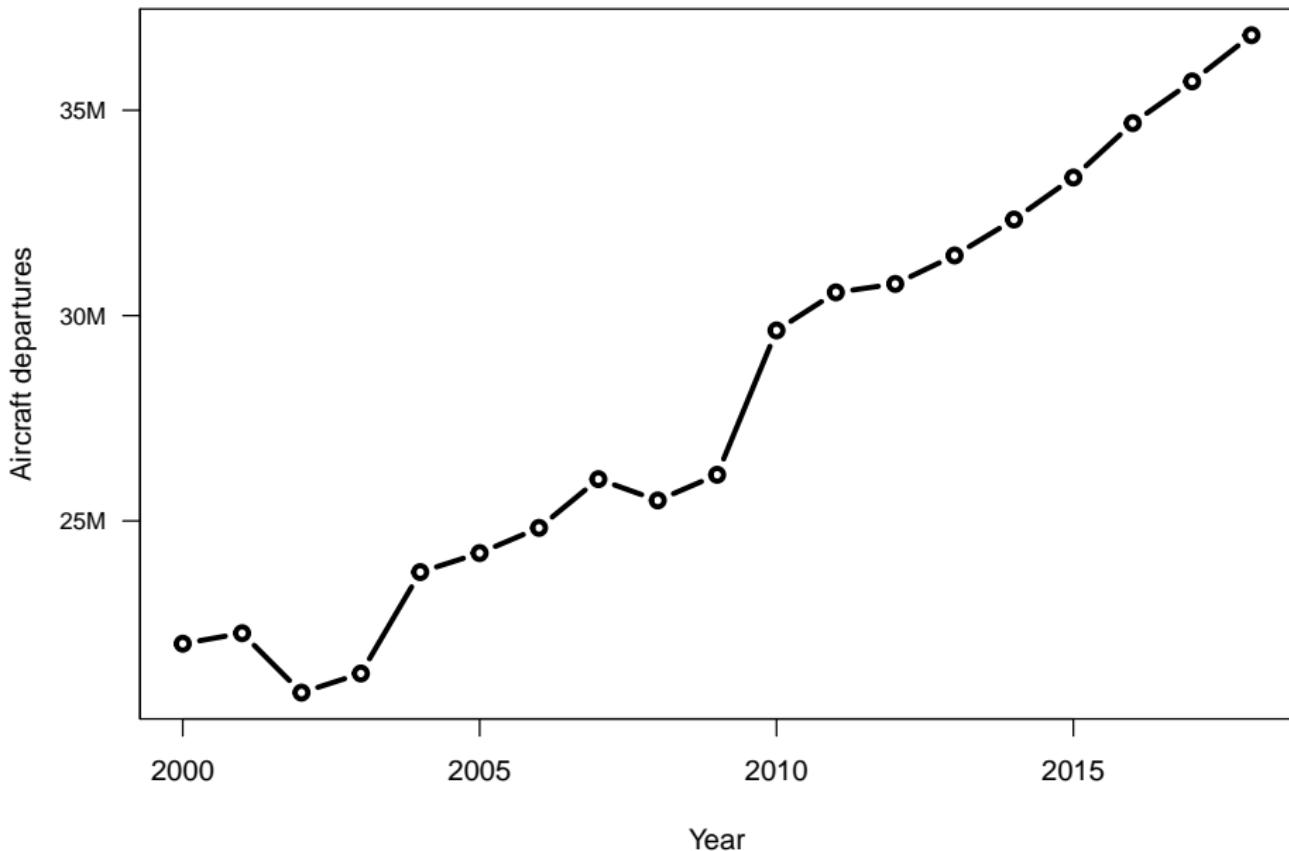
### Number of passengers transported (all countries)



## Number of flights (OAG)



## Number of aircraft departures (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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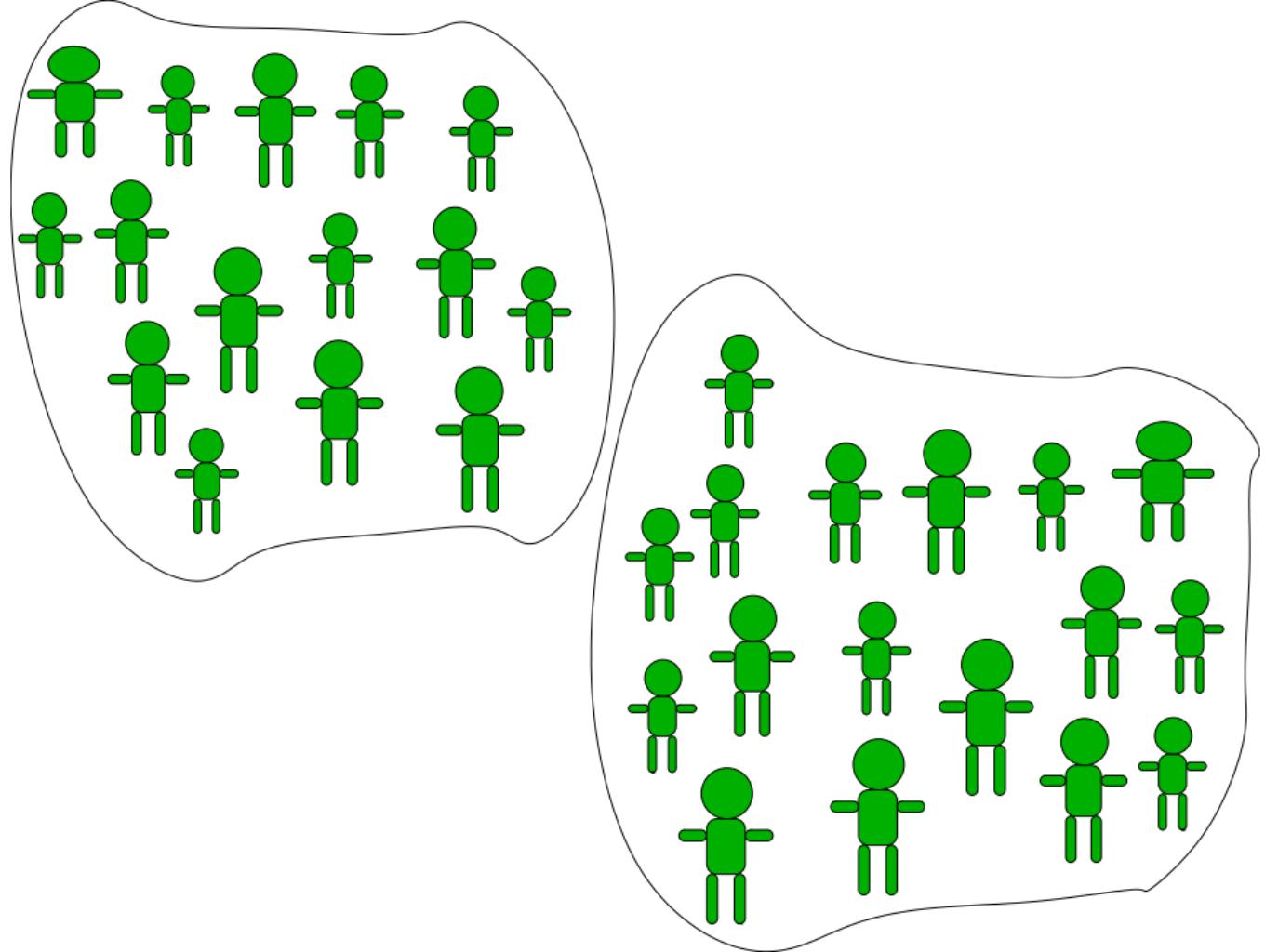
### Computational considerations

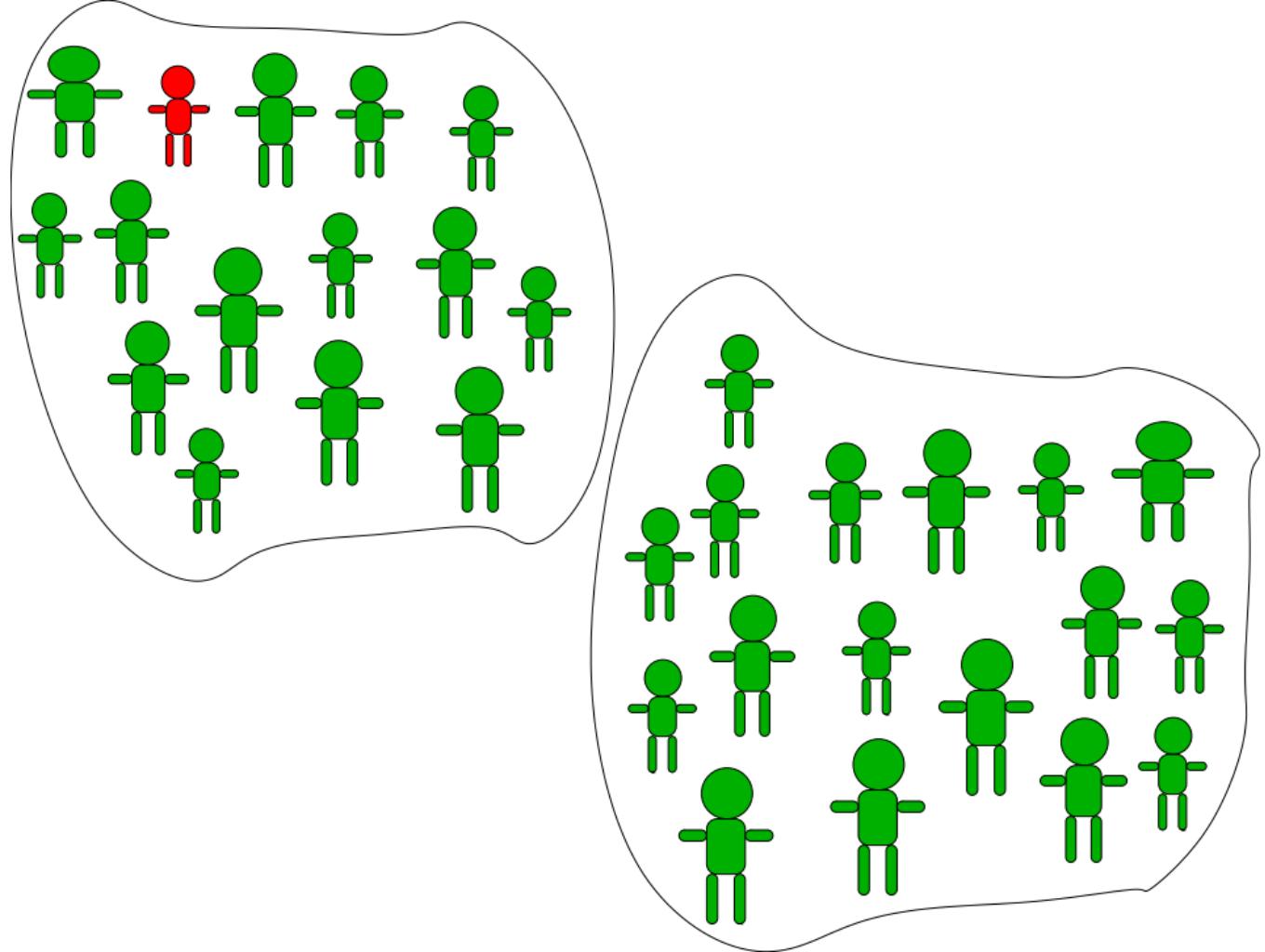
## Why use metapopulations for disease models?

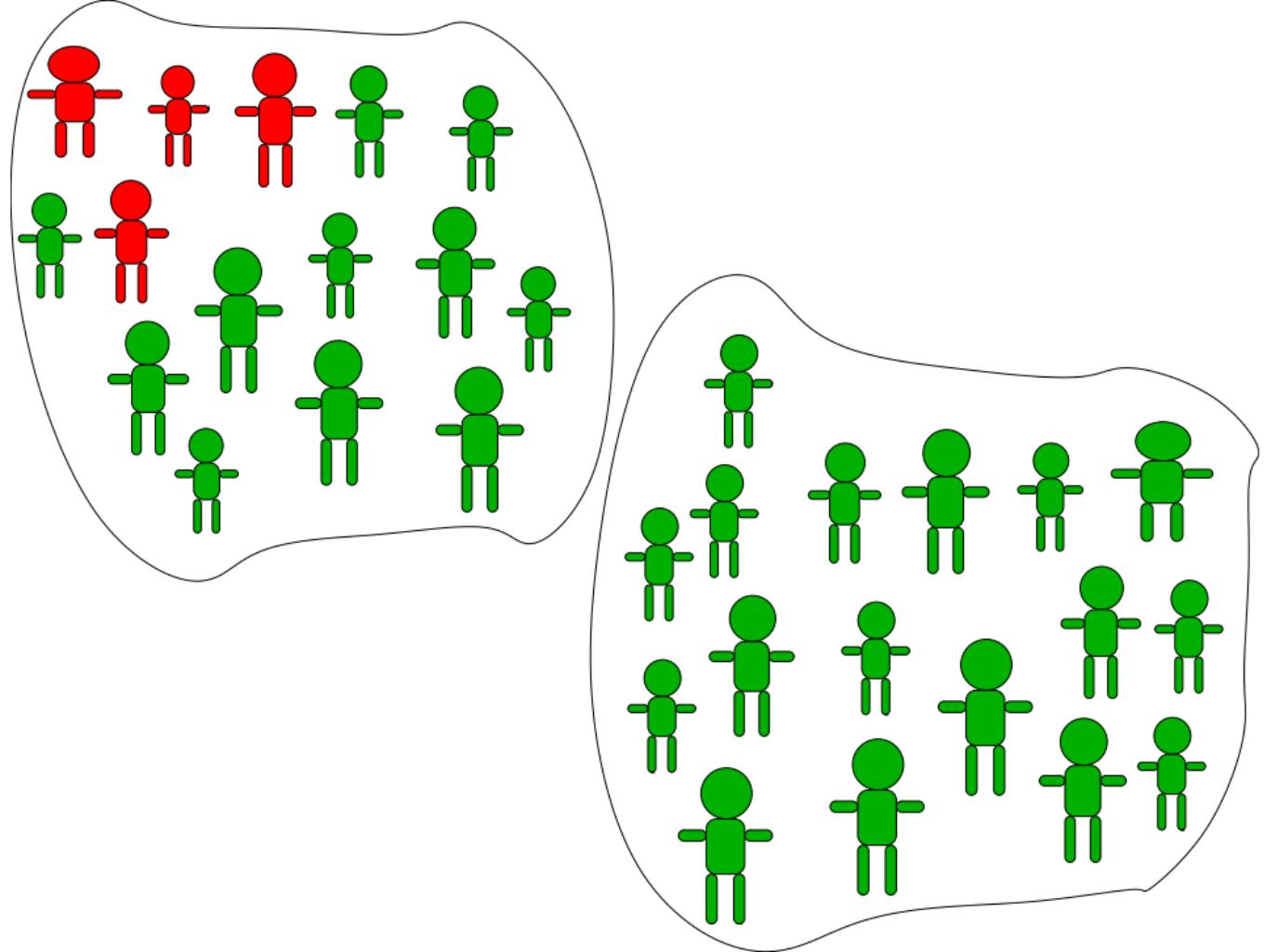
- ▶ Appropriate for the description of spatial spread of some diseases
- ▶ Ease of simulation
- ▶ Aggregation of data by governments is most often done at the jurisdictional level, very easy to reconcile with locations in metapopulations

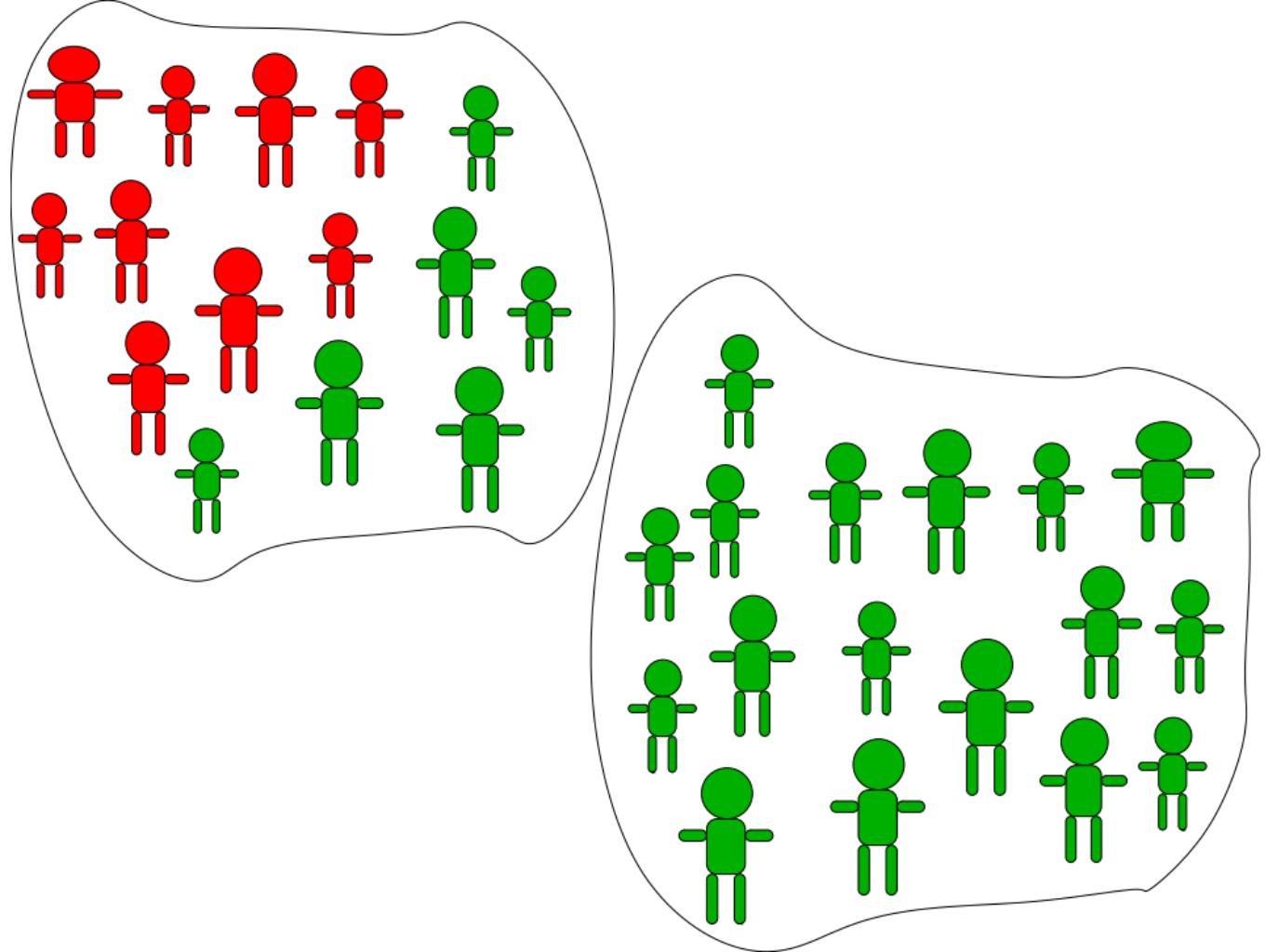
## A few pointers

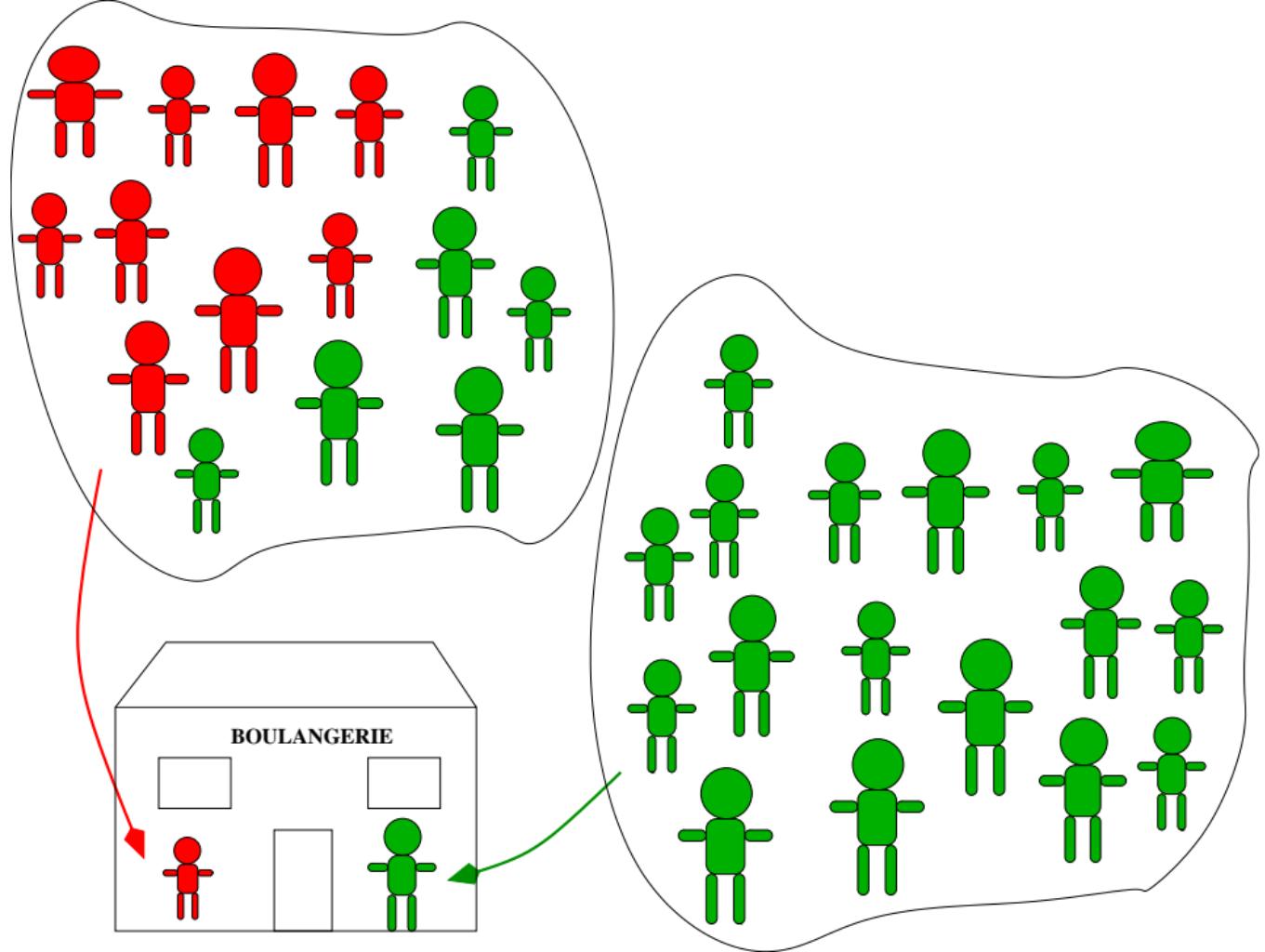
- ▶ JA & PvdD. Disease spread in metapopulations. *Fields Institute Communications* **48**:1-13 (2006)
- ▶ JA. Diseases in metapopulations. In *Modeling and Dynamics of Infectious Diseases*, World Scientific (2009)
- ▶ JA. Spatio-temporal spread of infectious pathogens of humans. *Infectious Disease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

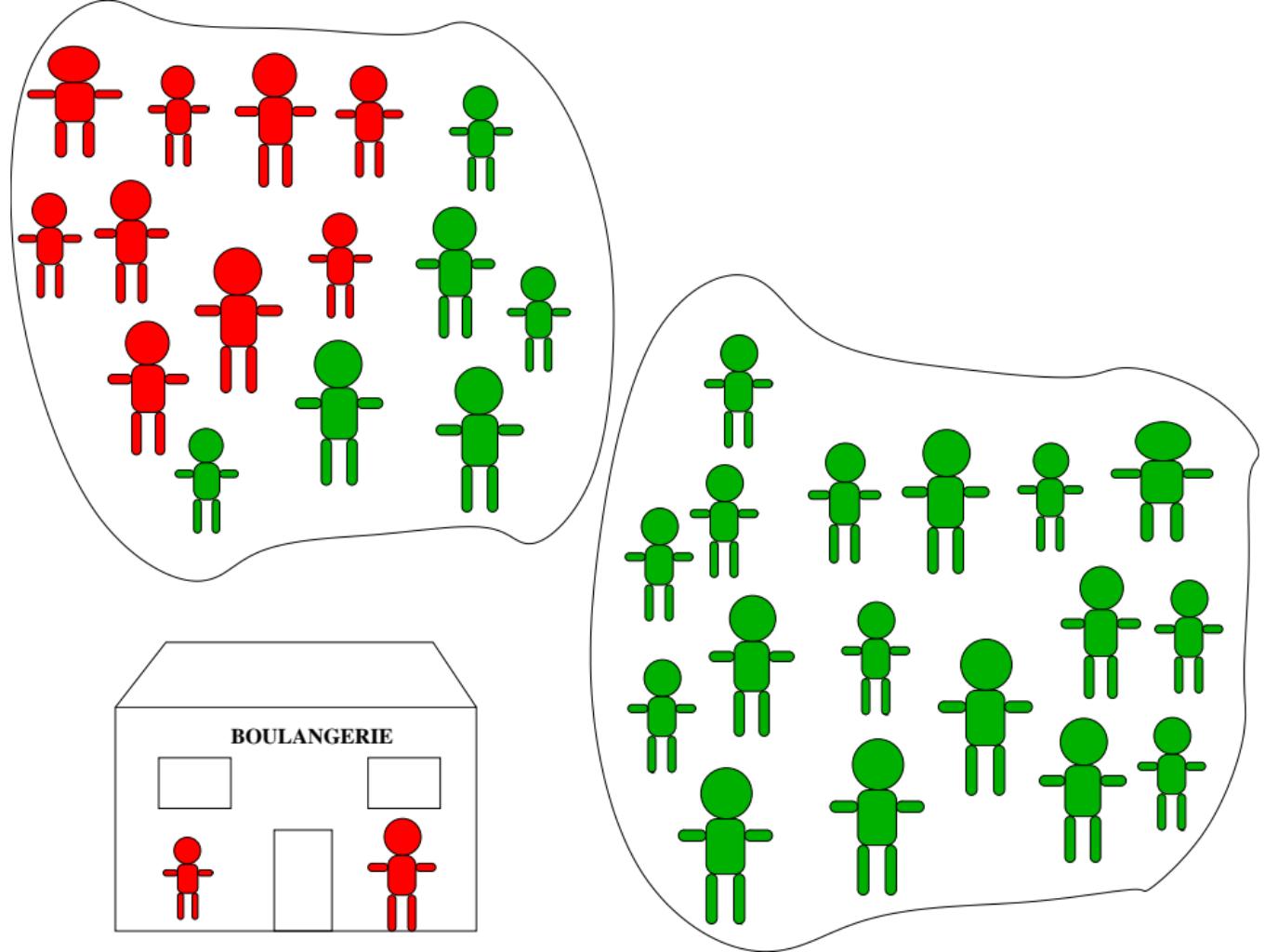


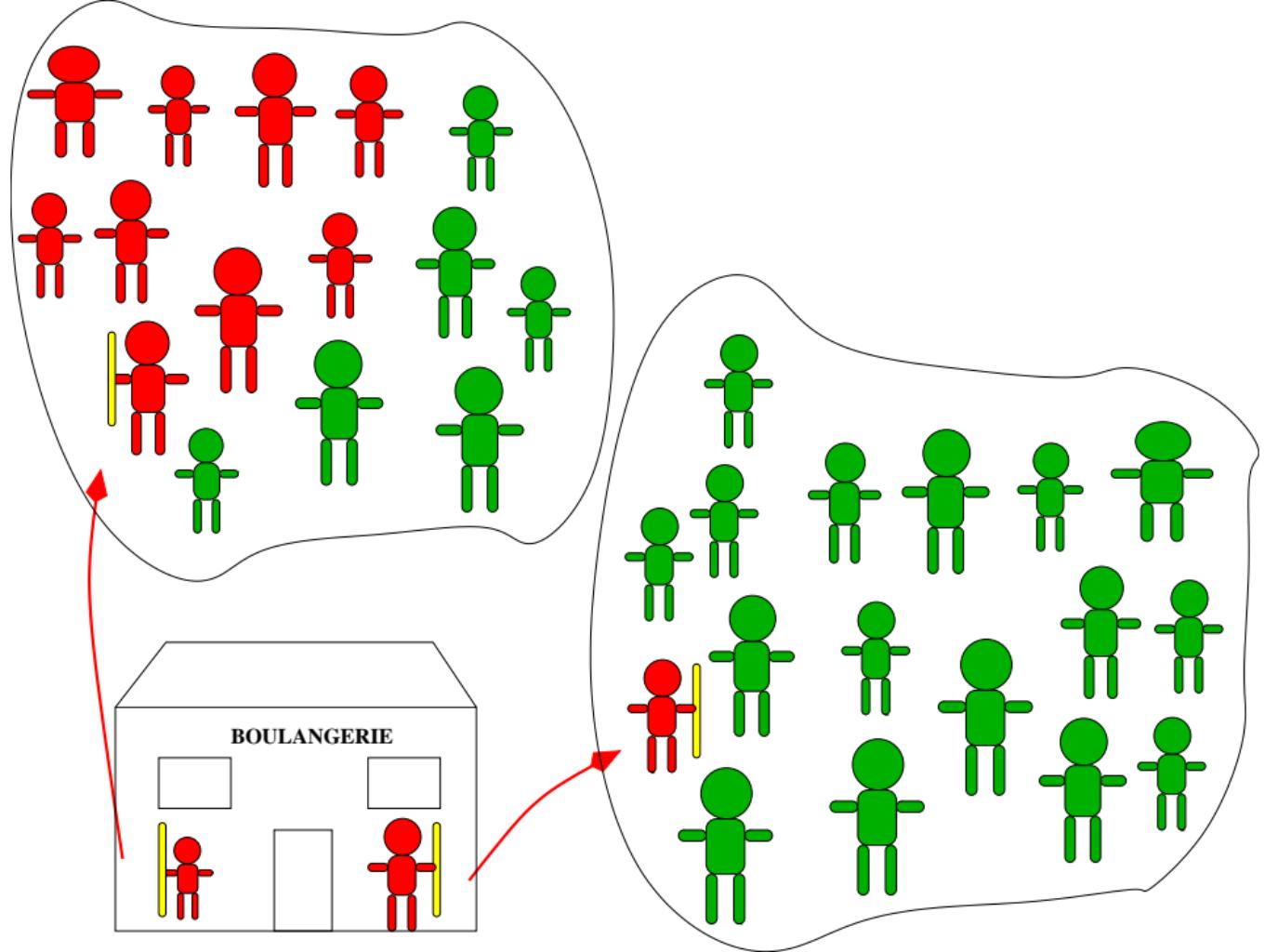


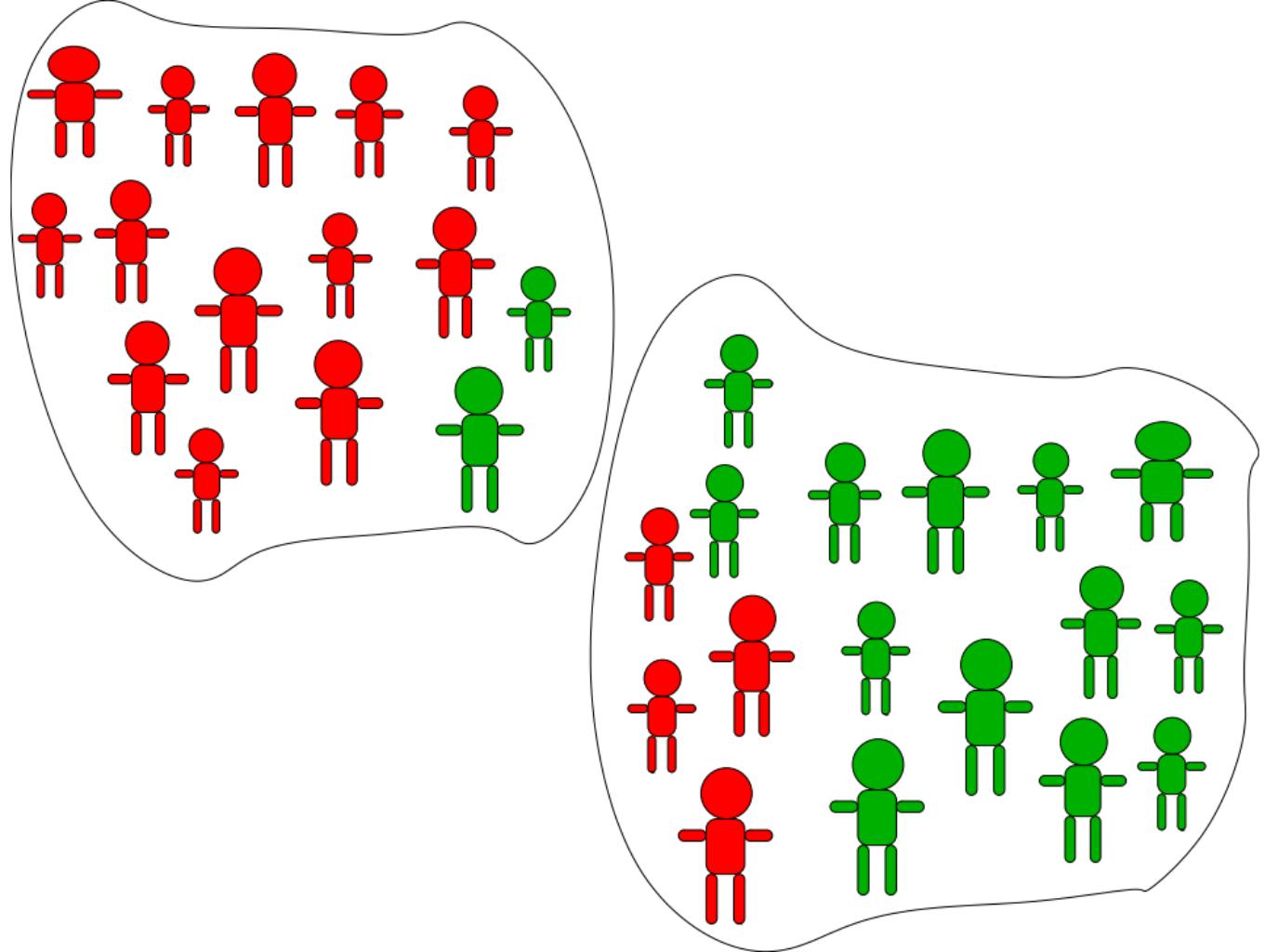


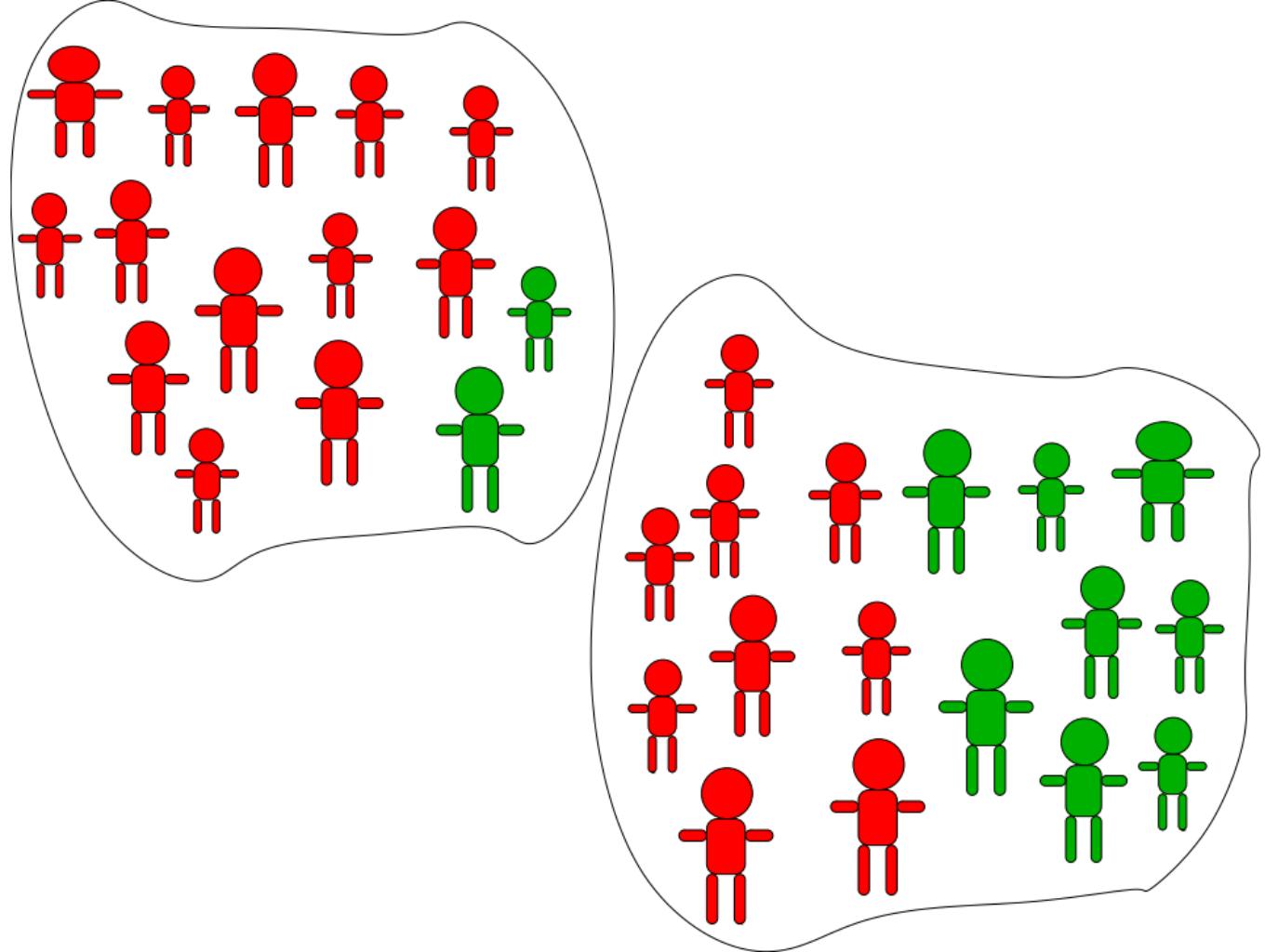


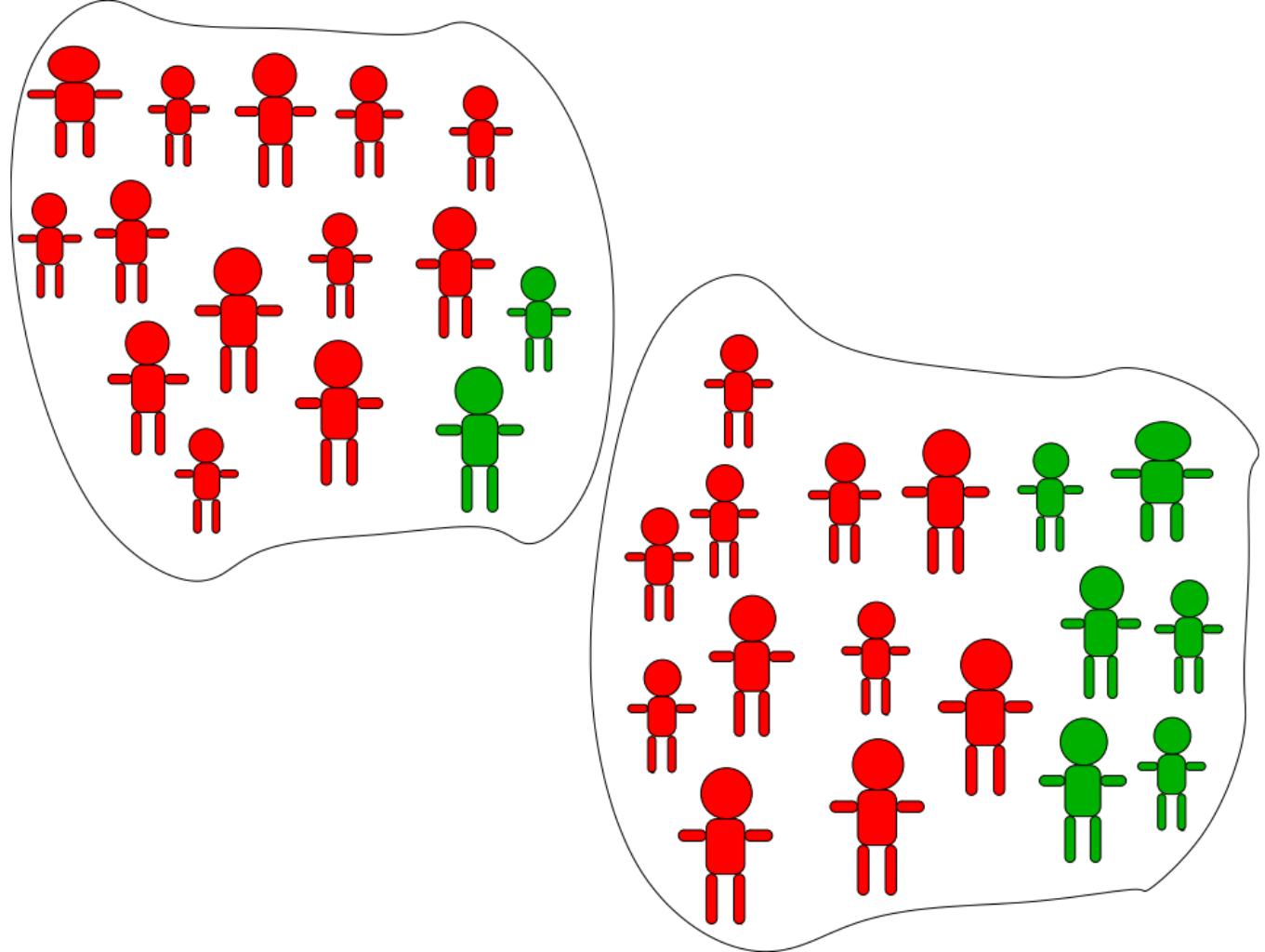












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Computation of a reproduction number

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

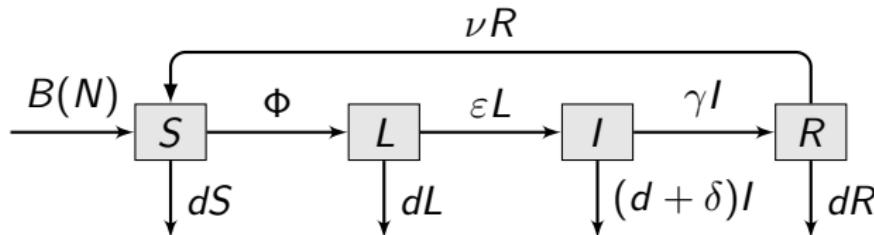
Metapopulation-specific problems

Bounds on  $\mathcal{R}_0$

To conclude on theory

### Computational considerations

## The toy SLIRS model in patches



$$S' = \mathcal{B}(N) + \nu R - \Phi - dS \quad (26a)$$

$$L' = \Phi - (\varepsilon + d)L \quad (26b)$$

$$I' = \varepsilon L - (\gamma + d + \delta)I \quad (26c)$$

$$R' = \gamma I - (\nu + d)R \quad (26d)$$

$\Phi$  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

$$S'_p = \mathcal{B}_p(N_p) + \nu_p R_p - \Phi_p - d_p S_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (27a)$$

$$L'_p = \Phi_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q \quad (27b)$$

$$I'_p = \varepsilon_p L_p - (\gamma_p + d_p) I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (27c)$$

$$R'_p = \gamma_p I_p - (\nu_p + d_p) R_p + \sum_{q \in \mathcal{P}} m_{Rpq} R_q \quad (27d)$$

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (27e)$$

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

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

$$S'_{sp} = \mathcal{B}_{sp}(N_{sp}) + \nu_{sp}R_{sp} - \Phi_{sp} - d_{sp}S_{sp} + \sum_{q \in \mathcal{P}} m_{sspq}S_{sq} \quad (28a)$$

$$L'_{sp} = \Phi_{sp} - (\varepsilon_{sp} + d_{sp})L_{sp} + \sum_{q \in \mathcal{P}} m_{Lspq}L_{sq} \quad (28b)$$

$$I'_{sp} = \varepsilon_{sp}L_{sp} - (\gamma_{sp} + d_{sp})I_{sp} + \sum_{q \in \mathcal{P}} m_{Ispq}I_{sq} \quad (28c)$$

$$R_{sp} = \gamma_{sp}I_{sp} - (\nu_{sp} + d_{sp})R_{sp} + \sum_{q \in \mathcal{P}} m_{Rspq}R_{sq} \quad (28d)$$

with incidence

$$\Phi_{sp} = \sum_{k \in \mathcal{S}} \beta_{skp} \frac{S_{sp}I_{kp}}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (28e)$$

- ▶ 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)

$$S'_{pq} = \mathcal{B}_{pq}(N_p^r) + \nu_{pq}R_{pq} - \Phi_{pq} - d_{pq}S_{pq} + \sum_{k \in \mathcal{P}} m_{Spqk}S_{pk} \quad (29a)$$

$$L'_{pq} = \Phi_{pq} - (\varepsilon_{pq} + d_{pq})L_{pq} + \sum_{k \in \mathcal{P}} m_{Lpqk}L_{pk} \quad (29b)$$

$$I'_{pq} = \varepsilon_{pq}L_{pq} - (\gamma_{pq} + d_{pq})I_{pq} + \sum_{k \in \mathcal{P}} m_{Ipqk}I_{pk} \quad (29c)$$

$$R'_{pq} = \gamma_{pq}I_{pq} - (\nu_{pq} + d_{pq})R_{pq} + \sum_{k \in \mathcal{P}} m_{Rpqk}R_{pk} \quad (29d)$$

with incidence

$$\Phi_{pq} = \sum_{k \in \mathcal{P}} \beta_{pqk} \frac{S_{pq}I_{kq}}{N_p^{q_q}}, \quad q_q = \{0, 1\} \quad (29e)$$

- ▶ 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  $\mathcal{B}_p(N_p) = \mathcal{B}_p$

$$S'_p = \mathcal{B}_p - \Phi_p - d_p S_p + \nu_p R_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (30a)$$

$$L'_p = \Phi_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q \quad (30b)$$

$$I'_p = \varepsilon_p L_p - (\gamma_p + d_p) I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (30c)$$

$$R'_p = \gamma_p I_p - (\nu_p + d_p) R_p + \sum_{q \in \mathcal{P}} m_{Rpq} R_q \quad (30d)$$

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (30e)$$

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

## A brief history of metapopulations

### The general context

A metapopulation of sources and sinks with explicit movement

### Diseases in metapopulations

Mobility and the spatio-temporal spread of pathogens

Why use metapopulation models?

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

Bounds on  $\mathcal{R}_0$

To conclude on theory

### Computational considerations

## Disease free equilibrium

The model is at equilibrium if the time derivatives are zero

### Definition 26 (Metapopulation DFE)

In the case of system (30), 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 (28), replace  $L_p$  with  $L_{sp}$  and  $I_p$  with  $I_{sp}$ , for (29), replace  $L_p$  by  $L_{pp}$  and  $I_p$  by  $I_{pp}$ . To simplify notation, we could write  $L_\bullet$  and  $I_\bullet$ )

Assume (30) 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:

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

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

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 ( $\mathbf{d}, \nu$  diagonal)

## R at DFE

Recall second equation:

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

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

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

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

## **S** at the DFE

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

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

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

So DFE makes sense with

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

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To conclude on theory

### Computational considerations

- ▶ 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.  $\Xi$ :

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

Note that

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

whenever  $k \neq p$ , so

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

## 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

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

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

Inverse of  $V$  easy ( $2 \times 2$  block lower triangular):

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

where

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

## $\mathcal{R}_0$ 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

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

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 27

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

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

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 27 is exact

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

Indeed, by Theorem 15(3) and more importantly (often  $\mathcal{M}$  is irreducible), Theorem 15(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

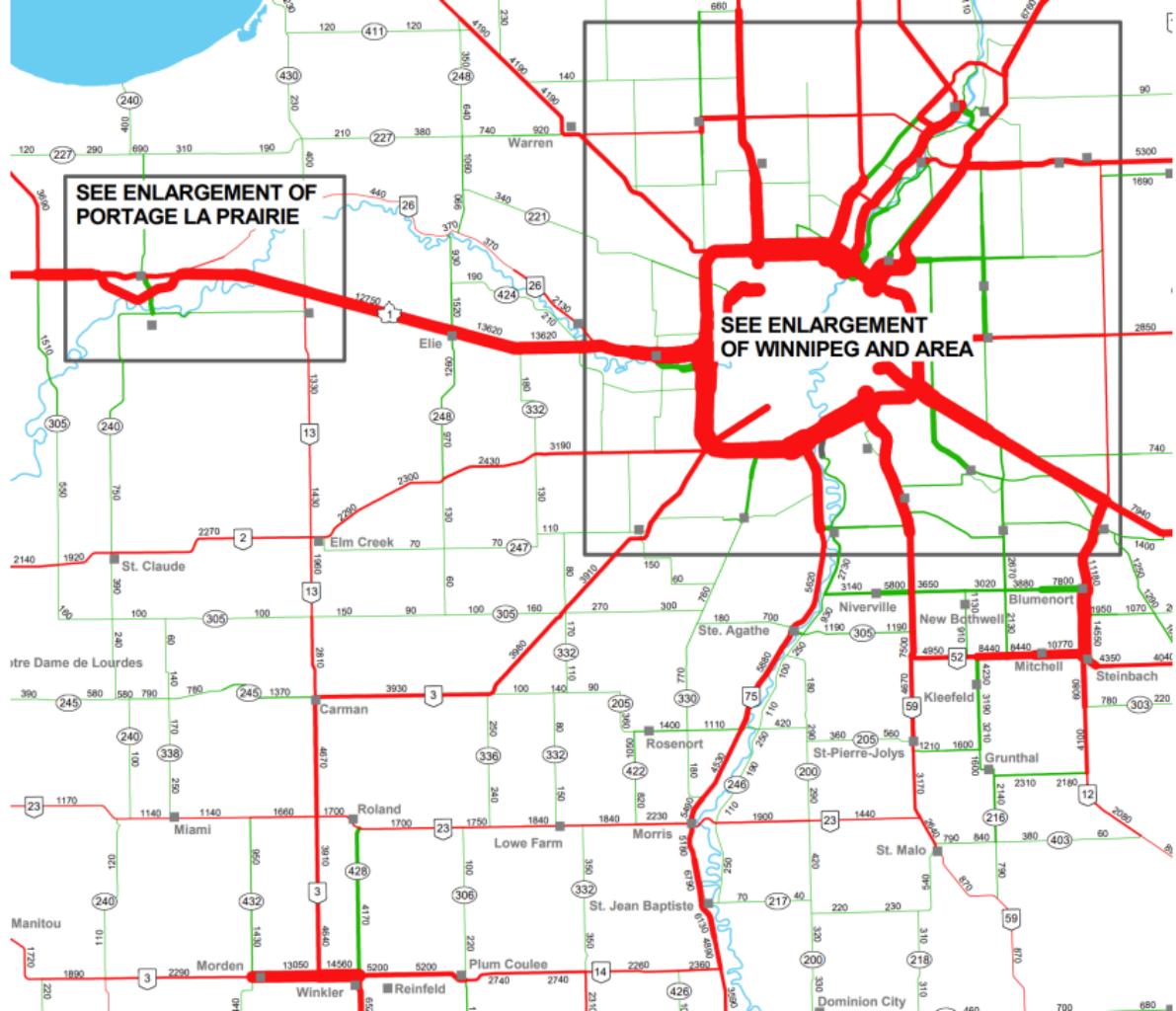
# Do not in $\mathcal{R}_0$ put all your .. interpretation?

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

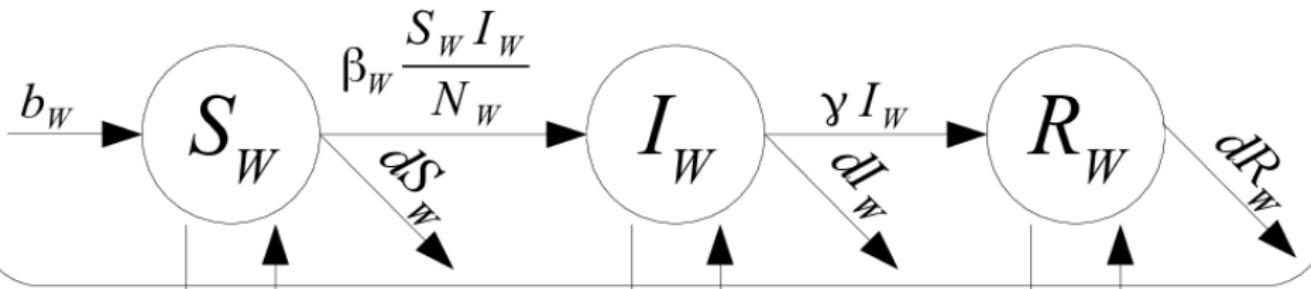
JA & S Portet. Epidemiological implications of mobility between a large urban centre and smaller satellite cities. *Journal of Mathematical Biology* 71(5):1243-1265 (2015)



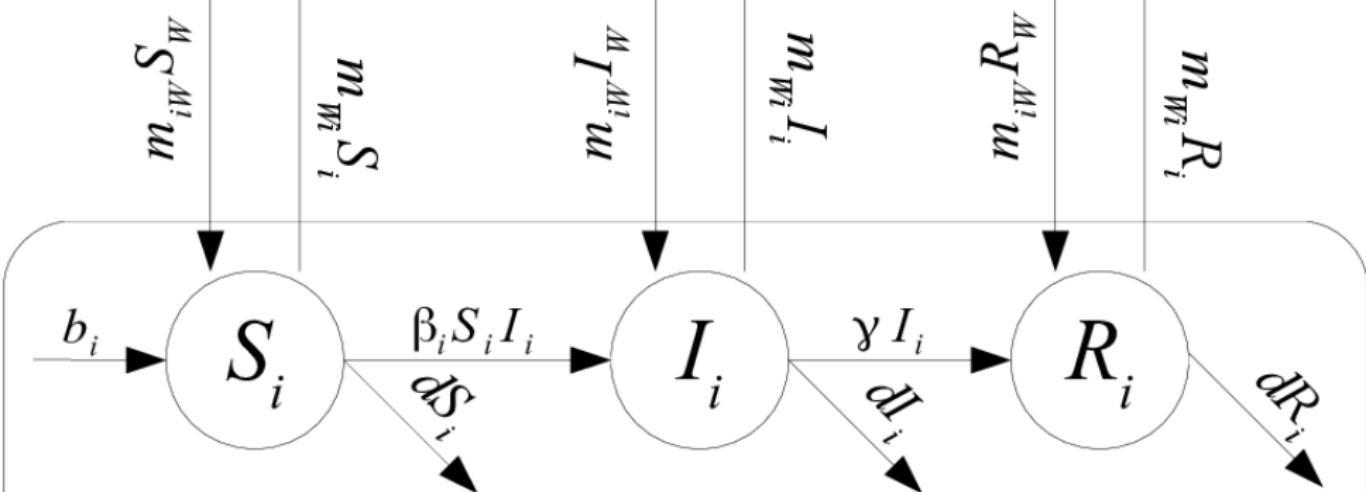
## Known and estimated quantities

City	Pop. (2014)	Pop. (now)	Dist.	Avg. trips//
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.,

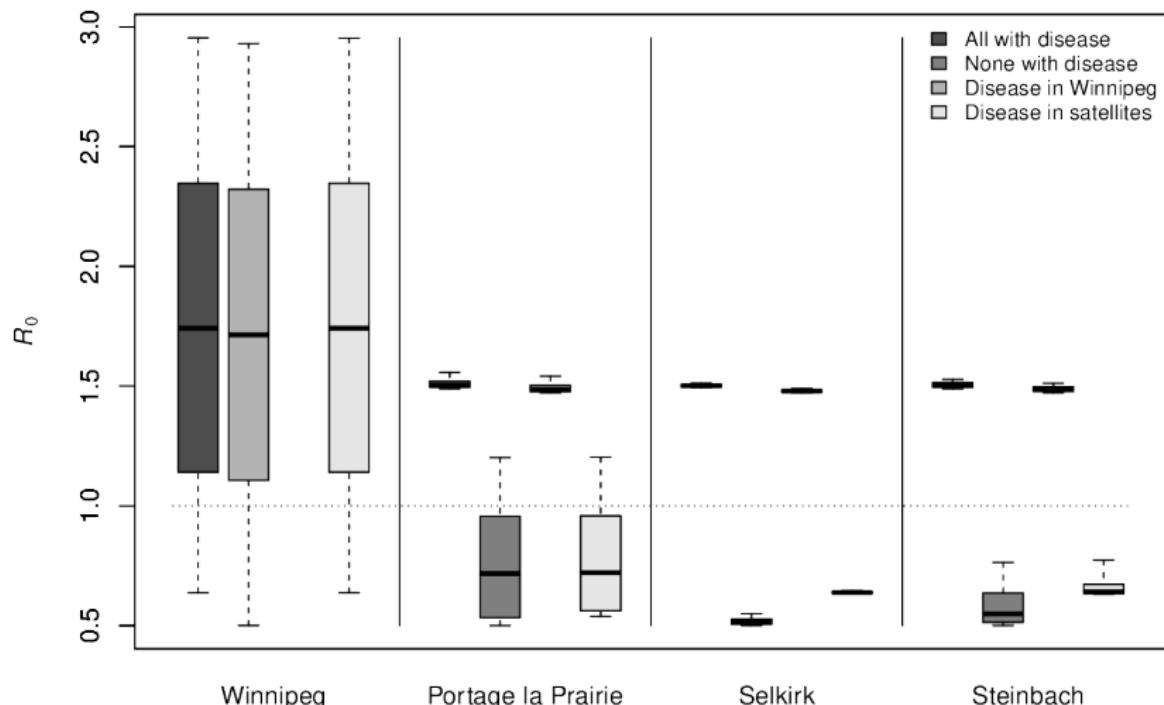
$$m_{yx} = -\ln \left( \frac{N_x(1)}{N_x(0)} \right)$$

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

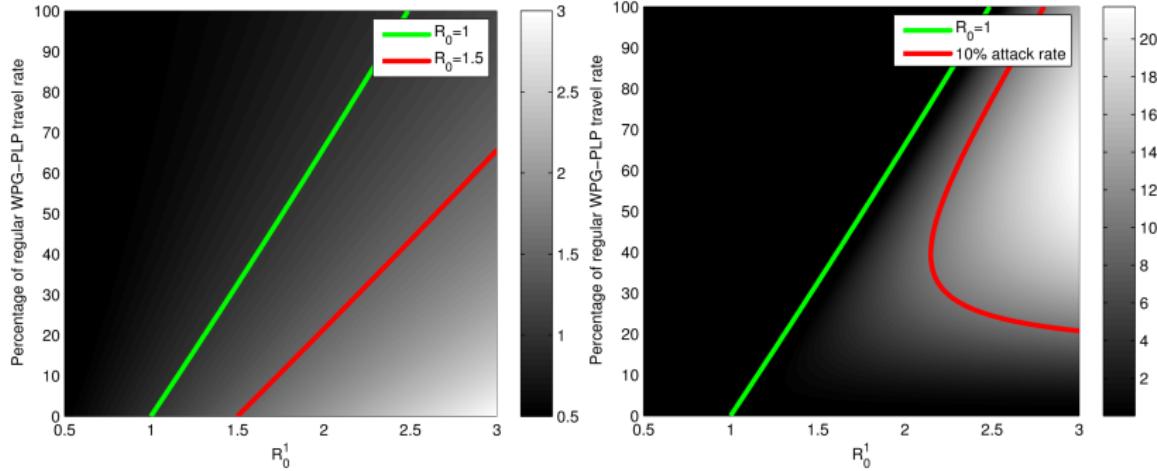
This is due to the movement rate: if  $M = 0$ , then

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

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

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To conclude on theory

### 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 28

Let  $\mathcal{R}_0$  be defined as in Theorem 27 and use proportional incidence  $\Phi_p = \beta_p S_p I_p / N_p$ . If  $\mathcal{R}_0 < 1$ , then the DFE of system (30) is globally asymptotically stable

## Proof

Since  $S_i \leq N_i$ ,  $\Phi_i \leq \beta_i N_i I_i / N_i$ , and equation (30b) gives the inequality

$$L'_p \leq \beta_p I_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q \quad (31)$$

For comparison, define a linear system given by (31) with equality and equation (30c), namely

$$L'_p = \beta_p I_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q$$

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

- ▶ This system linear has coefficient matrix  $F - V$ , and so by the argument in the proof of Theorem 27, satisfies  $\lim_{t \rightarrow \infty} L_p = 0$  and  $\lim_{t \rightarrow \infty} I_p = 0$  for  $\mathcal{R}_0 = \rho(FV^{-1}) < 1$
- ▶ Using a comparison theorem and noting (31), it follows that these limits also hold for the nonlinear system (30b) and (30c)
- ▶ That  $\lim_{t \rightarrow \infty} R_i = 0$  and  $\lim_{t \rightarrow \infty} S_i = N_i^*$  follow from (30d) and (30a)

Thus for  $\mathcal{R}_0 < 1$ , the disease free equilibrium is globally asymptotically stable and the disease dies out



## $|\mathcal{S}| |\mathcal{P}|$ -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 28 to show that if  $\mathcal{R}_0 < 1$ , then the DFE of the  $|\mathcal{S}| |\mathcal{P}|$ -SLIRS (28) is globally asymptotically stable.

### Theorem 29

*For system (28) 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*

## Proof of Theorem 29

To establish the global stability of the DFE, consider the nonautonomous system consisting of (28b)-(28d), with (28b) written as

$$\begin{aligned} L'_{sp} = & \sum_{j \in S} \beta_{sjp} (N_{sp} - L_{sp} - I_{sp} - R_{sp}) \frac{I_{jp}}{N_{jp}} \\ & - (d_{sp} + \varepsilon_{sp}) L_{sp} + \sum_{q \in P} m_{spq} L_{sq} \end{aligned} \tag{32}$$

in which  $S_{sp}$  has been replaced by  $N_{sp} - L_{sp} - I_{sp} - R_{sp}$ , and  $N_{sp}$  is a solution of (??) (dynamics of  $N_{sp}$ )

Write this system as the nonautonomous system

$$x' = f(t, x) \quad (33)$$

where  $x$  is the  $3|\mathcal{C}||\mathcal{P}|$  dimensional vector consisting of the  $L_{sp}$ ,  $I_{sp}$  and  $R_{sp}$

The DFE of (28) corresponds to the equilibrium  $x = 0$  in (33)

System (??) can be solved for  $N_{sp}(t)$  independently of the epidemic variables, and Theorem ?? implies that the time dependent functions  $N_{sp}(t) \rightarrow N_{sp}^*$  as  $t \rightarrow \infty$

Substituting this large time limit value  $N_{sp}^*$  for  $N_{sp}$  in (32) gives

$$\begin{aligned} L'_{sp} = & \sum_{j=1}^s \beta_{sjp} (N_{sp}^* - L_{sp} - I_{sp} - R_{sp}) \frac{I_{jp}}{N_{jp}^*} \\ & - (d_{sp} + \varepsilon_{sp}) L_{sp} + \sum_{q \in \mathcal{P}} m_{spq} L_{sq} \end{aligned} \quad (34)$$

Therefore, system (33) is asymptotically autonomous, with limit equation

$$x' = g(x) \quad (35)$$

To show that 0 is a globally asymptotically stable equilibrium for the limit system (35), consider the linear system

$$x' = Lx \quad (36)$$

where  $x$  is the  $3|\mathcal{S}||\mathcal{P}|$  dimensional vector consisting of the  $L_{sp}$ ,  $I_{sp}$  and  $R_{sp}$ . In  $L$ , we replace  $S_{sp}/N_{jp}$  with  $N_{sp}^*/N_{jp}^*$ . Equations (28c) and (28d) are not affected by this transformation, whereas (28b) takes the form

$$L'_{sp} = \sum_{j \in \mathcal{S}} \beta_{sjp} \frac{N_{sp}^*}{N_{jp}^*} I_{jp} - (d_{sp} + \varepsilon_{sp}) L_{sp} + \sum_{q \in \mathcal{P}} m_{spq} L_{sq} \quad (37)$$

Comparing (34) and (37), we note that

$$\forall x \in \mathbb{R}_+^{3|\mathcal{S}||\mathcal{P}|}, \quad g(x) \leq Lx$$

In system (36), equations for  $L_{sp}$  and  $I_{sp}$  do not involve  $R_{sp}$

Let  $\tilde{x}$  be the part of the vector  $x$  corresponding to the variables  $L_{sp}$  and  $I_{sp}$ , and  $\tilde{L}$  be the corresponding submatrix of  $L$

The method of proof used to prove LAS can also be applied to study the stability of the  $\tilde{x} = 0$  equilibrium of the subsystem  $\tilde{x}' = \tilde{L}\tilde{x}$ , with  $\tilde{L} = F - V$

Therefore, if  $\mathcal{R}_0 < 1$ , then the equilibrium  $\tilde{x} = 0$  of the subsystem  $\tilde{x}' = \tilde{L}\tilde{x}$  is stable. When  $\tilde{x} = 0$ , (28d) takes the form

$$R'_s = (\mathcal{M}_s - D_s)R_s$$

with  $R_s = (R_{s1}, \dots, R_{s|\mathcal{P}|})^T$  and  $D_s$  is the diagonal matrix with  $p$ th diagonal entry equal to  $d_{sp}$

We know from Lemma 14 and Proposition 15:

- ▶  $-\mathcal{M}_s$  is a singular M-matrix
- ▶  $-\mathcal{M}_s + D_s$  is a nonsingular M-matrix for each  $D_s$

Thus the equilibrium  $R_s = 0$  of this linear system in  $R_s$  is stable

As a consequence, the equilibrium  $x = 0$  of (36) is stable when  $\mathcal{R}_0 < 1$

Using a standard comparison theorem, it follows that 0 is a globally asymptotically stable equilibrium of (35)

For  $\mathcal{R}_0 < 1$ , the linear system (37) and (28c) has a unique equilibrium (the DFE) since its coefficient matrix  $F - V$  is nonsingular

The proof of global stability is completed using results on asymptotically autonomous equations



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To conclude on theory

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## 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

$$s'_{kp} = f_{kp}(S_p, I_p) \quad (38a)$$

$$i'_{\ell p} = g_{\ell p}(S_p, I_p) \quad (38b)$$

with known properties, what is known of

$$s'_{kp} = f_{kp}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{kpq} s_{kq} \quad (39a)$$

$$i'_{\ell p} = g_{\ell p}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{\ell pq} i_{\ell q} \quad (39b)$$

- ▶ 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  $\{\mathcal{R}_0 < 1 \implies \text{DFE GAS}, \mathcal{R}_0 > 1 \implies 1 \text{ GAS EEP}\}$  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 30 (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 31 (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 32

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 33

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  $c \in \mathcal{C}$

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# SEIRS with residency location

For convenience, write

$$\frac{\partial \Phi_{ik}^D}{\partial I_{jk}} := \left. \frac{\partial \Phi_{ik}}{\partial I_{jk}} \right|_{DFE}.$$

## Theorem 34

Let  $v_m^{-1}$  and  $v_M^{-1}$  be the minimum and maximum column sums of the  $(2,1)$  block  $\bigoplus_{p=1}^{|\mathcal{P}|} (A_p C_p^{-1} B_p)$  in matrix  $V^{-1}$  defined by (??). Then there holds that

$$|\mathcal{P}| \left( \min_{i,j,k=1,\dots,|\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{jk}} \right) v_m^{-1} \leq \mathcal{R}_0 \leq |\mathcal{P}| \left( \max_{i,j,k=1,\dots,|\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{jk}} \right) v_M^{-1}. \quad (40)$$

## Proof

The  $i,j$  block of  $G$  ( $\oplus(A_p C_p^{-1} B_p)^{-1}$ ) is  $G_{ij}(A_j C_j^{-1} B_j)^{-1}$  for all  $i,j$ . As  $G_{ij}$  is diagonal, left multiplication with  $(A_j C_j^{-1} B_j)^{-1}$  amounts to multiplying row  $q = 1, \dots, |\mathcal{P}|$  of  $(A_j C_j^{-1} B_j)^{-1}$  by the  $q^{\text{th}}$  diagonal entry of  $G_{ij}$ , that is,  $\partial\Phi_{iq}^D/\partial I_{jq}$ . Let  $v_{kl}^{-1}(j)$  denote the  $(k,l)$  entry of  $(A_j C_j^{-1} B_j)^{-1}$ , for  $k,l = 1, \dots, |\mathcal{P}|$ . Then a given block  $G_{ij}(A_j C_j^{-1} B_j)^{-1}$  takes the form

Thus, for the whole matrix,

$$\mathbb{1}^T G (\oplus (A_p C_p^{-1} B_p)^{-1}) = \left( \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{1k}} v_{k1}^{-1}(1), \dots, \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{|\mathcal{P}|k}} v_{k|\mathcal{P}|}^{-1}(1) \right) \quad (41)$$

Define

$$\frac{\partial \Phi_{i_m k_m}^D}{\partial I_{j_m k_m}} = \min_{i, j, k=1, \dots, |\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{jk}}$$

and

$$\frac{\partial \Phi_{i_M k_M}^D}{\partial I_{j_M k_M}} = \max_{i, j, k=1, \dots, |\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{jk}}.$$

Then, for any column  $c$  in the  $j^{\text{th}}$  block of columns, there holds

$$\begin{aligned}
 & \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} \frac{\partial \Phi_{i_m k_m}^D}{\partial I_{j_m k_m}} v_{kc}^{-1}(j) \leq \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{jk}} v_{kc}^{-1}(j) \leq \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} \frac{\partial \Phi_{i_M k_M}^D}{\partial I_{j_M k_M}} v_{kc}^{-1}(j) \\
 \Leftrightarrow & \frac{\partial \Phi_{i_m k_m}^D}{\partial I_{j_m k_m}} \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} v_{kc}^{-1}(j) \leq \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{jk}} v_{kc}^{-1}(j) \leq \frac{\partial \Phi_{i_M k_M}^D}{\partial I_{j_M k_M}} \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} v_{kc}^{-1}(j) \\
 \Leftrightarrow & |\mathcal{P}| \frac{\partial \Phi_{i_m k_m}^D}{\partial I_{j_m k_m}} \sum_{k=1}^{|\mathcal{P}|} v_{kc}^{-1}(j) \leq \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{jk}} v_{kc}^{-1}(j) \leq |\mathcal{P}| \frac{\partial \Phi_{i_M k_M}^D}{\partial I_{j_M k_M}} \sum_{k=1}^{|\mathcal{P}|} v_{kc}^{-1}(j).
 \end{aligned} \tag{42}$$

Defining  $v_m^{-1}$  and  $v_M^{-1}$  as in the theorem, it follows that for all  $c, j = 1, \dots, |\mathcal{P}|$ ,

$$|\mathcal{P}| \frac{\partial \Phi_{i_m k_m}^D}{\partial I_{j_m k_m}} v_m^{-1} \leq \sum_{i=1}^{|\mathcal{P}|} \sum_{k=1}^{|\mathcal{P}|} \frac{\partial \Phi_{ik}^D}{\partial I_{jk}} v_{kc}^{-1}(j) \leq |\mathcal{P}| \frac{\partial \Phi_{i_M k_M}^D}{\partial I_{j_M k_M}} v_M^{-1},$$

and thus

$$|\mathcal{P}| \frac{\partial \Phi_{i_m k_m}^D}{\partial I_{j_m k_m}} v_m^{-1} \leq \mathbb{1}^T G (\oplus (A_p C_p^{-1} B_p)^{-1}) \leq |\mathcal{P}| \frac{\partial \Phi_{i_M k_M}^D}{\partial I_{j_M k_M}} v_M^{-1}.$$

Using a standard result on the localization of the dominant eigenvalue of a nonnegative matrix, which states that the dominant eigenvalue of a nonnegative matrix is bounded below and above by the minimum and maximum of its column sums, the result then follows.

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## Interesting (IMHO) problems

More is needed on inheritance problem, in particular GAS part (Li, Shuai, Kamgang, Sallet, and older stuff: Michel & Miller, Šiljak)

Incorporate travel time (delay) and events (infection, recovery, death ..) during travel

What is the minimum complexity of the movement functions  $m$  below

$$s'_{kp} = f_{kp}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{kpq}(S, I) s_{kq}$$
$$i'_{\ell p} = g_{\ell p}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{\ell pq}(S, I) i_{\ell q}$$

required to observe a metapopulation-induced behaviour?

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Diseases in metapopulations

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 $\beta$ to avoid blow up

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

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

```
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  $\mathbf{N}^* = (\mathbf{d} - \mathcal{M})^{-1}\mathbf{b}$

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

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

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

Then

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

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