

## Metapopulation models – Part 2

### MATH 8xyz – Lecture 18

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The University of Manitoba campuses are located on original lands of Anishinaabeg, Ininew, Anisininew, Dakota and Dene peoples, and on the National Homeland of the Red River Métis.

We respect the Treaties that were made on these territories, we acknowledge the harms and mistakes of the past, and we dedicate ourselves to move forward in partnership with Indigenous communities in a spirit of Reconciliation and collaboration.

# Outline

Spatio-temporal spread of infectious pathogens

Metapopulations for disease spread modelling





**Spatio-temporal spread of infectious pathogens**

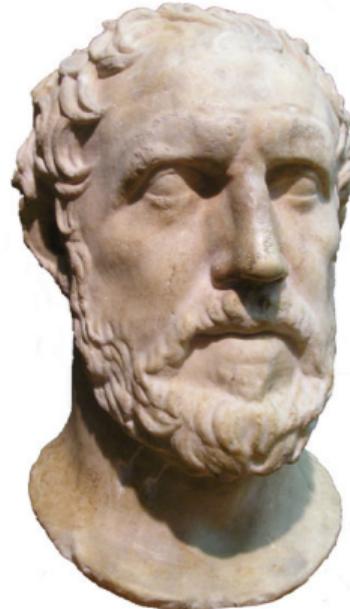
**Metapopulations for disease spread modelling**

# Diseases have been known to be mobile for a while

## The plague of Athens of 430 BCE

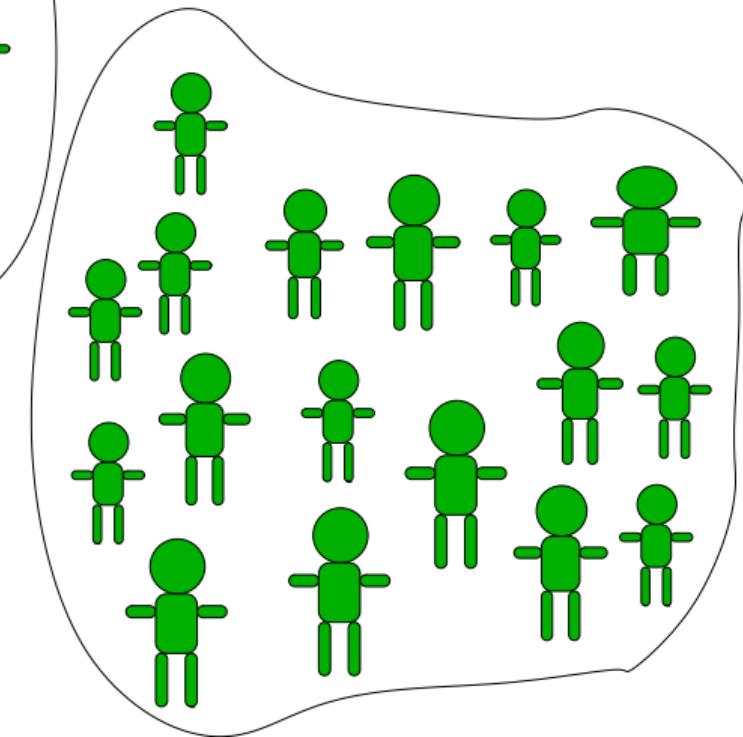
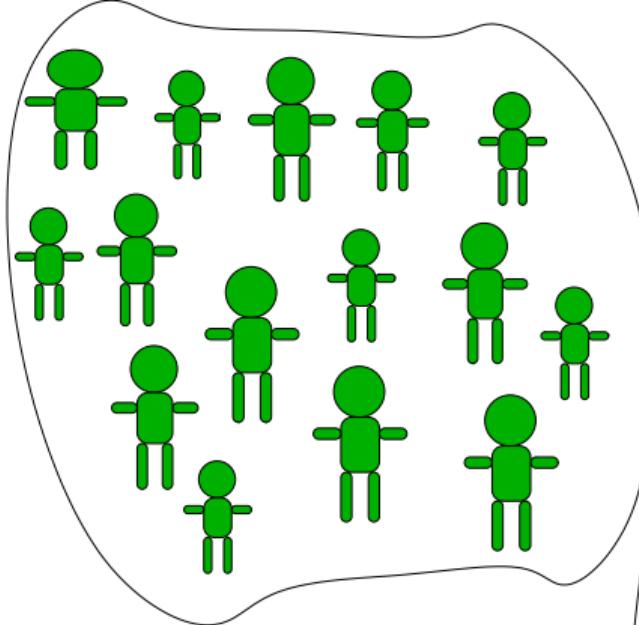
It first began, it is said, in the parts of Ethiopia above Egypt, and thence descended into Egypt and Libya and into most of the [Persian] King's country. Suddenly falling upon Athens, it first attacked the population in Piraeus [...] and afterwards appeared in the upper city, when the deaths became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

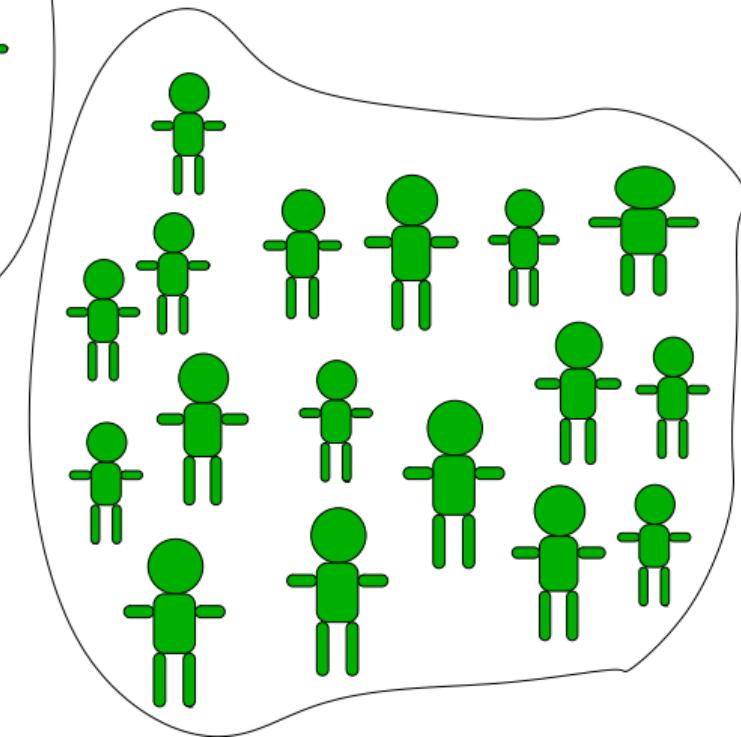
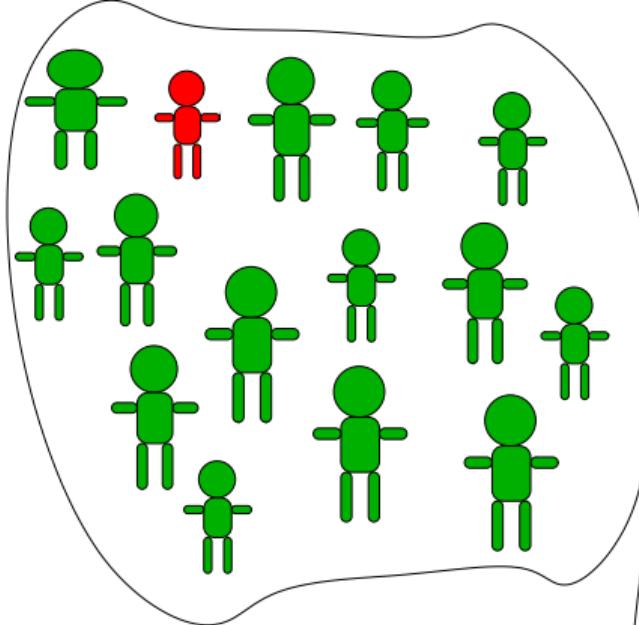
Thucydides (c. 460 BCE - c. 395 BCE)  
History of the Peloponnesian War

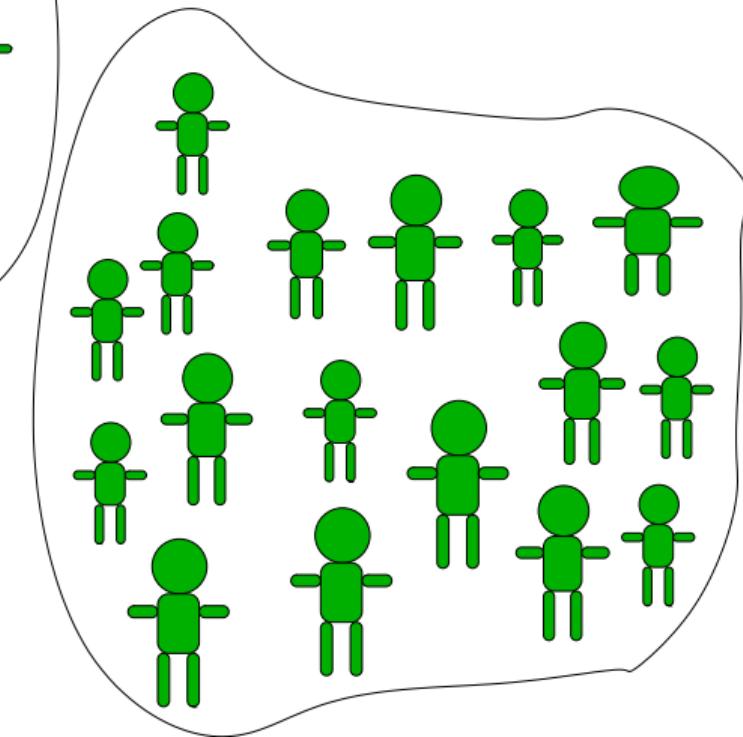
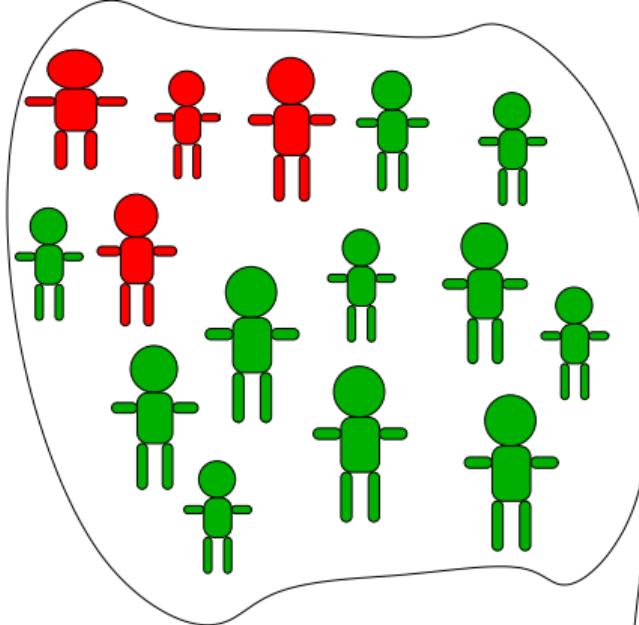


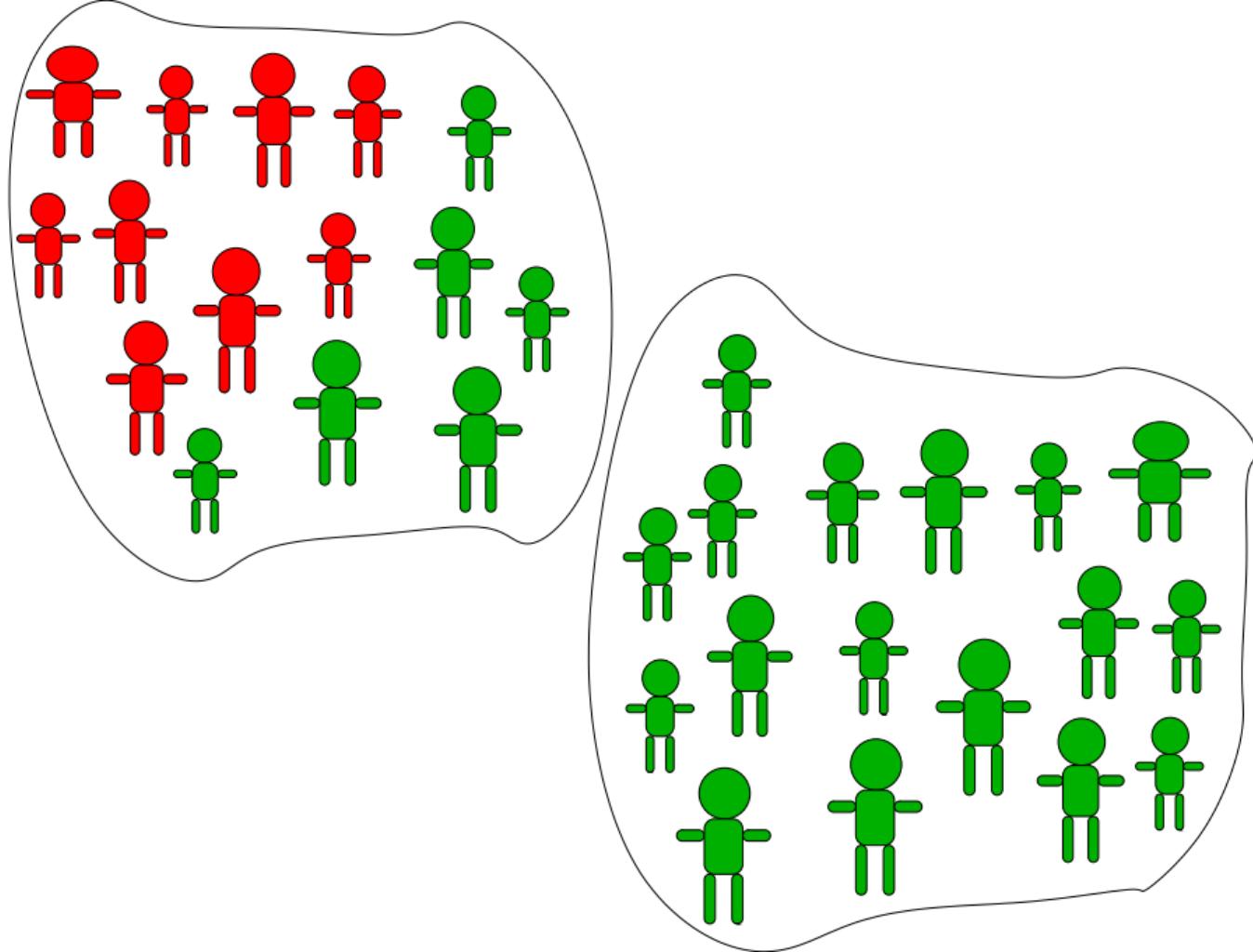
## How infectious pathogens become mobile

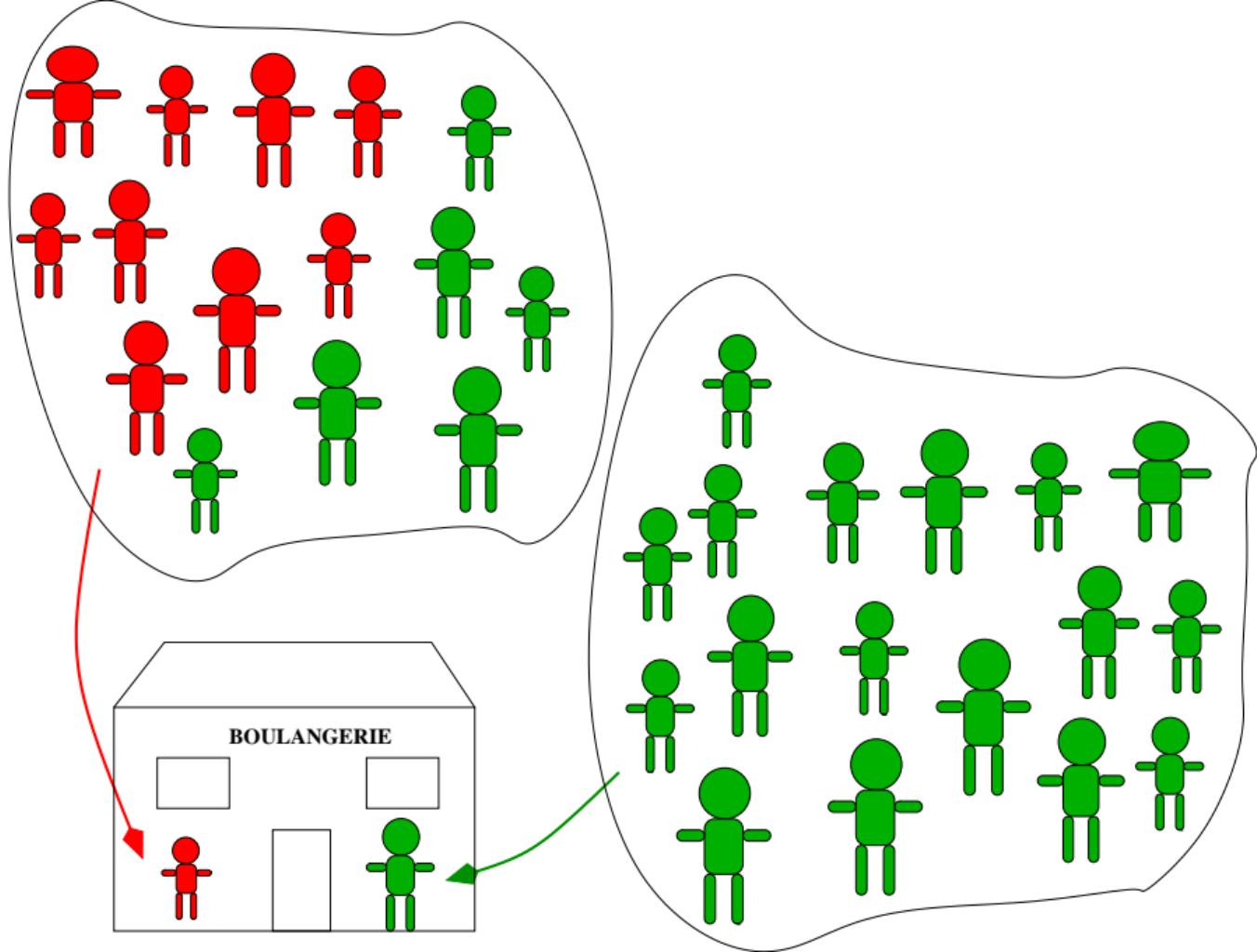
- ▶ I used to show the following set of figures to illustrate the spatialisation of spread
- ▶ I tried to get Gemini to do the same but the “returning home” part was not working at all
- ▶ So enjoy my fantastic skills instead

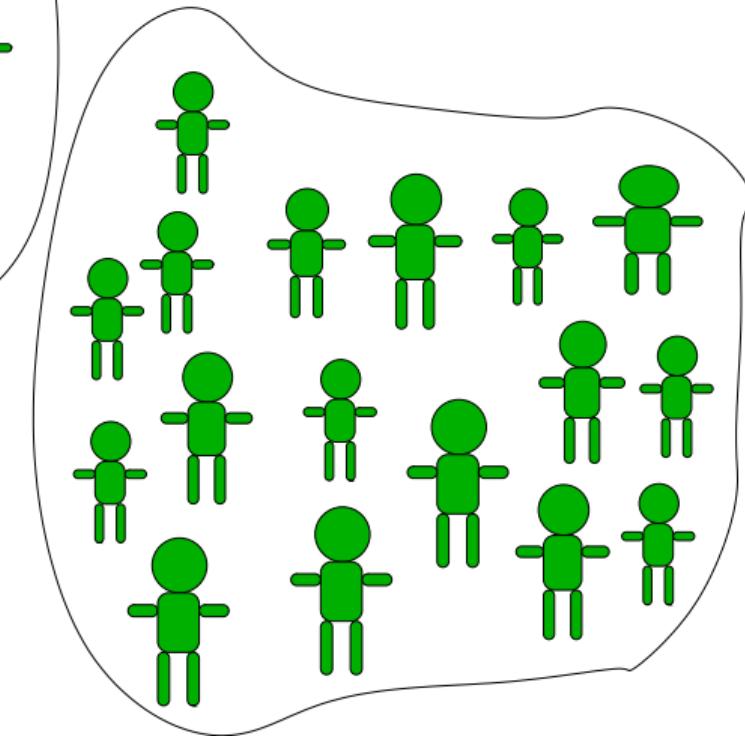
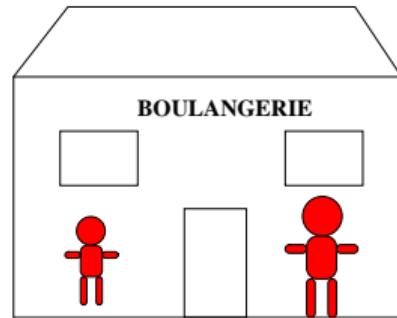
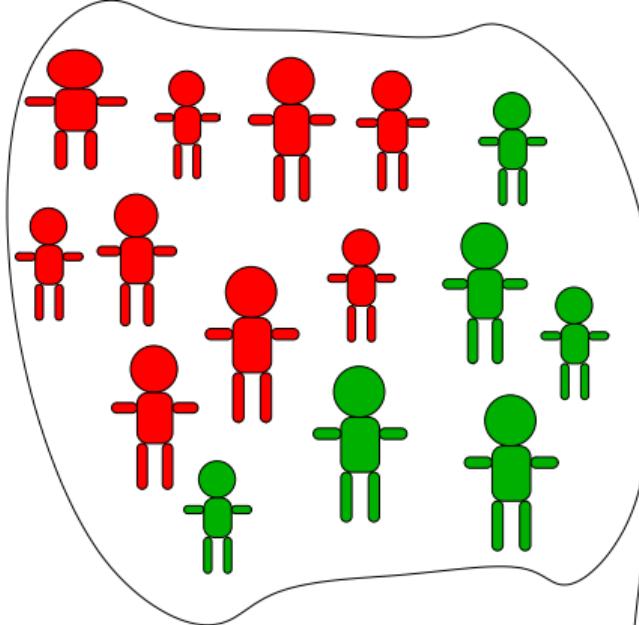


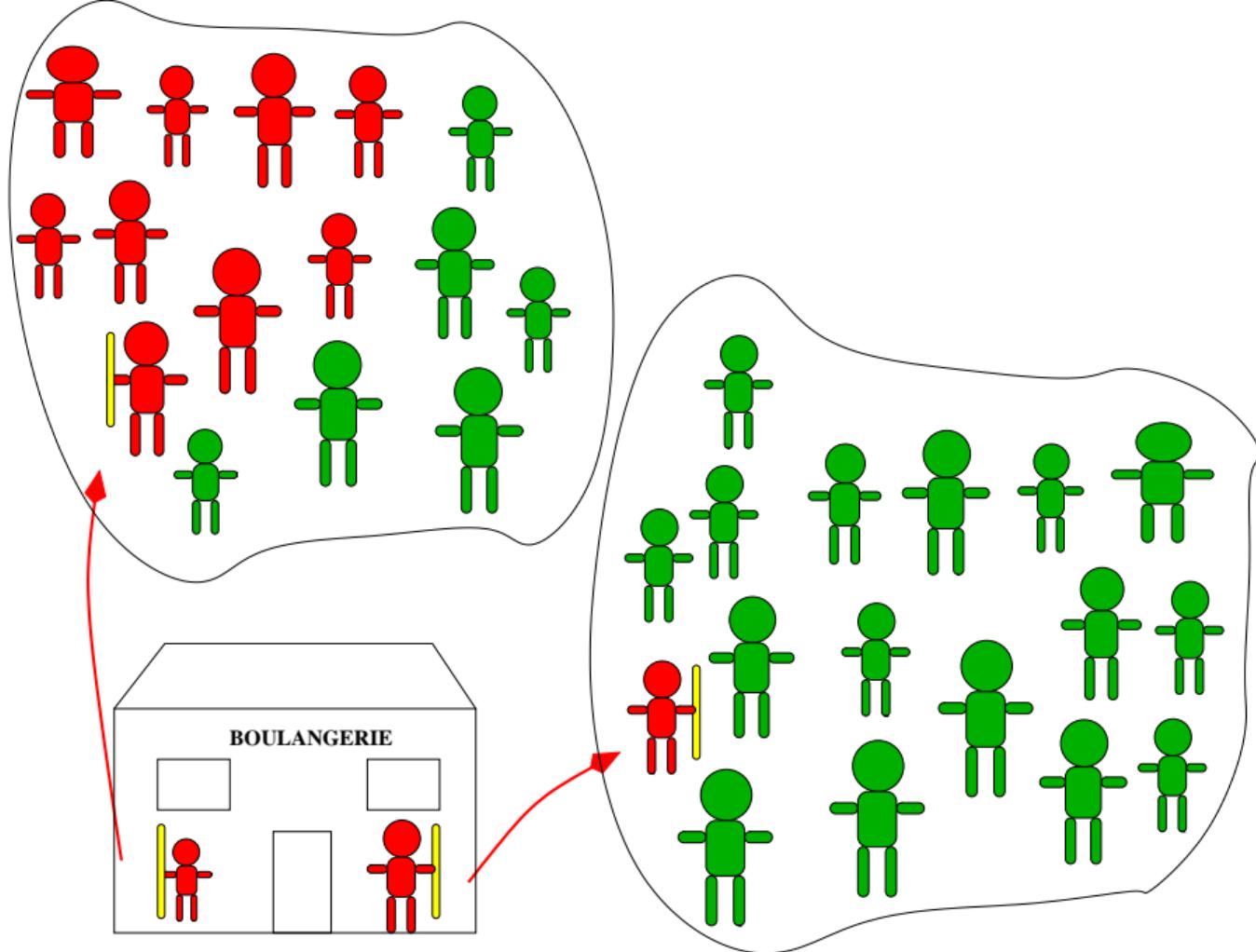


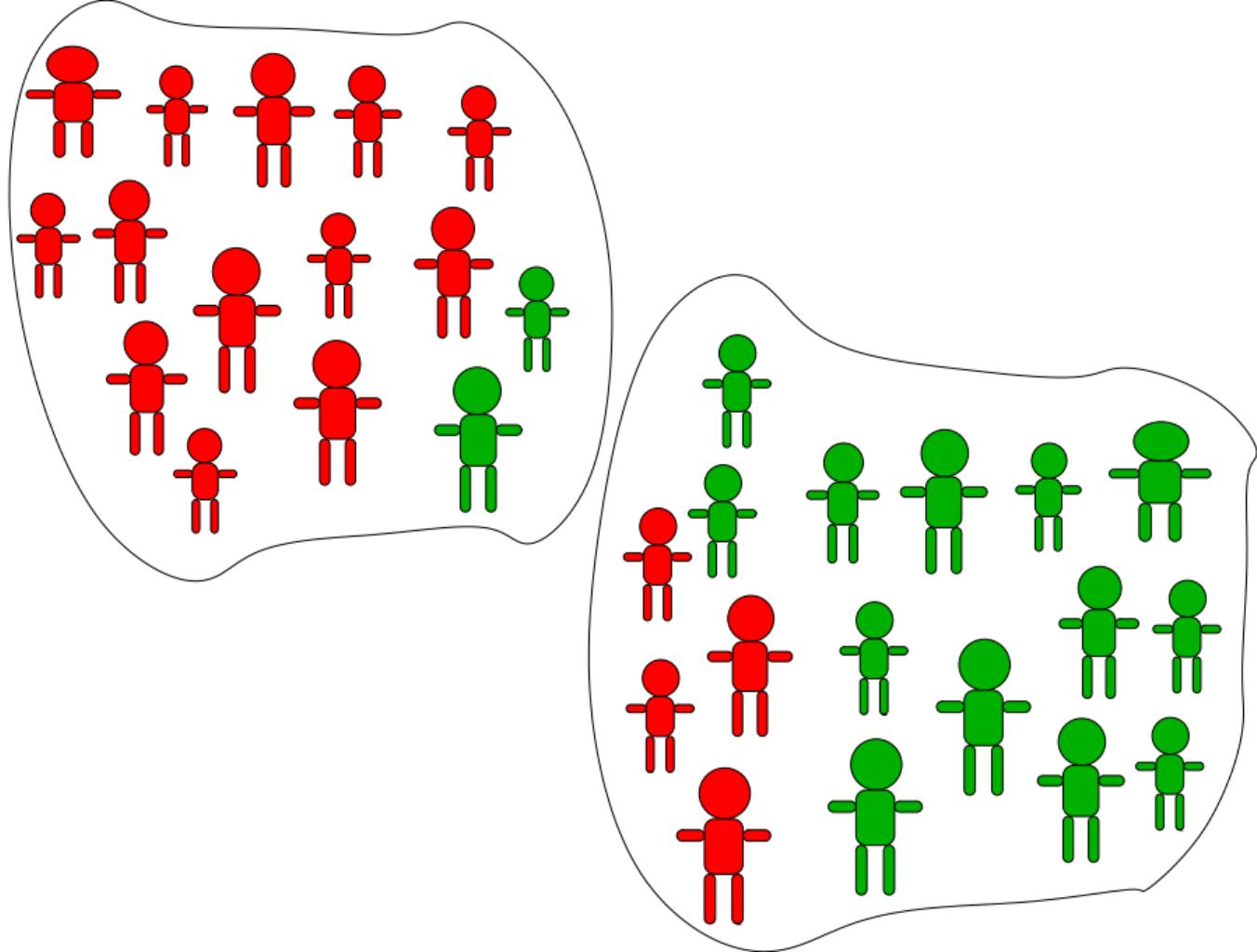


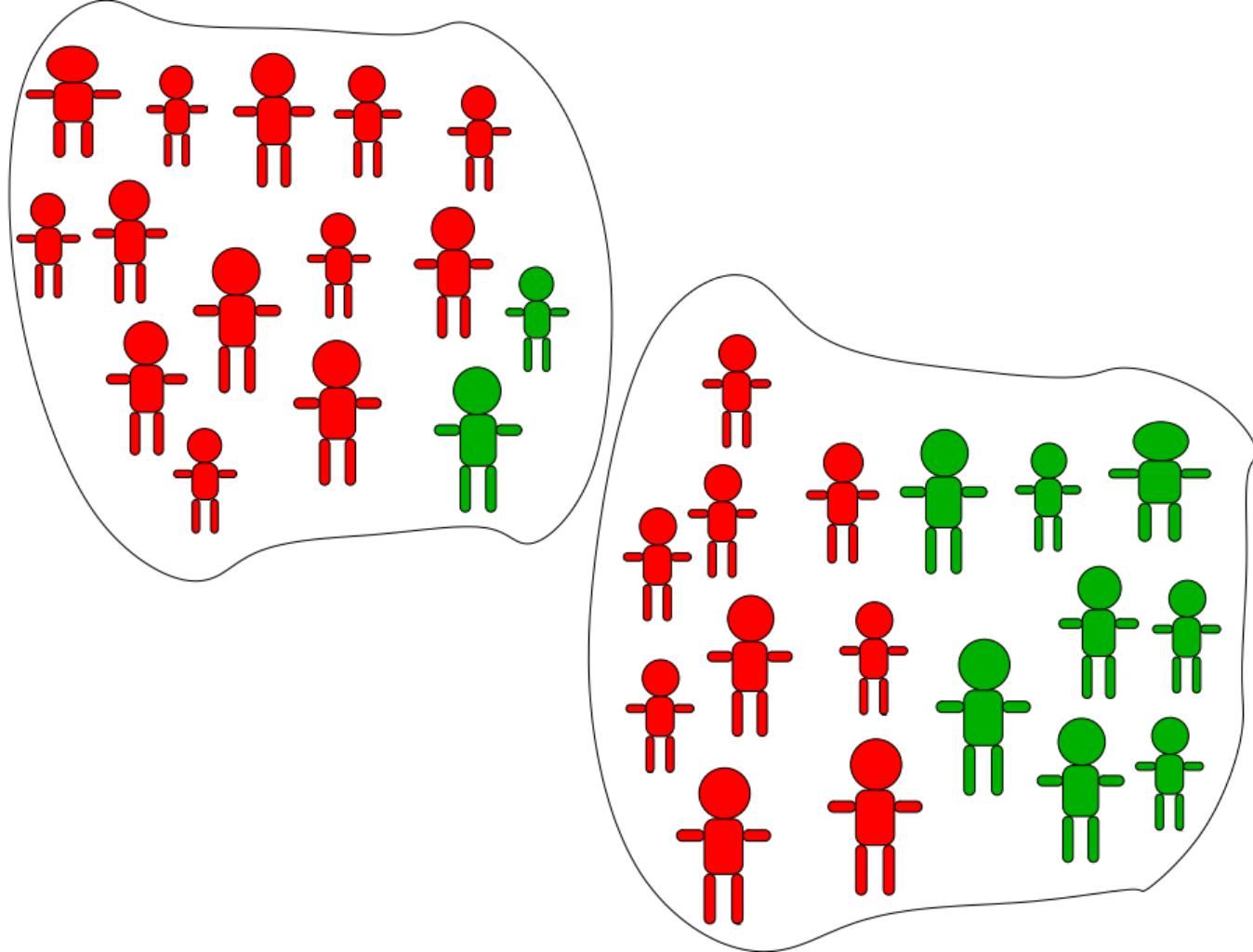






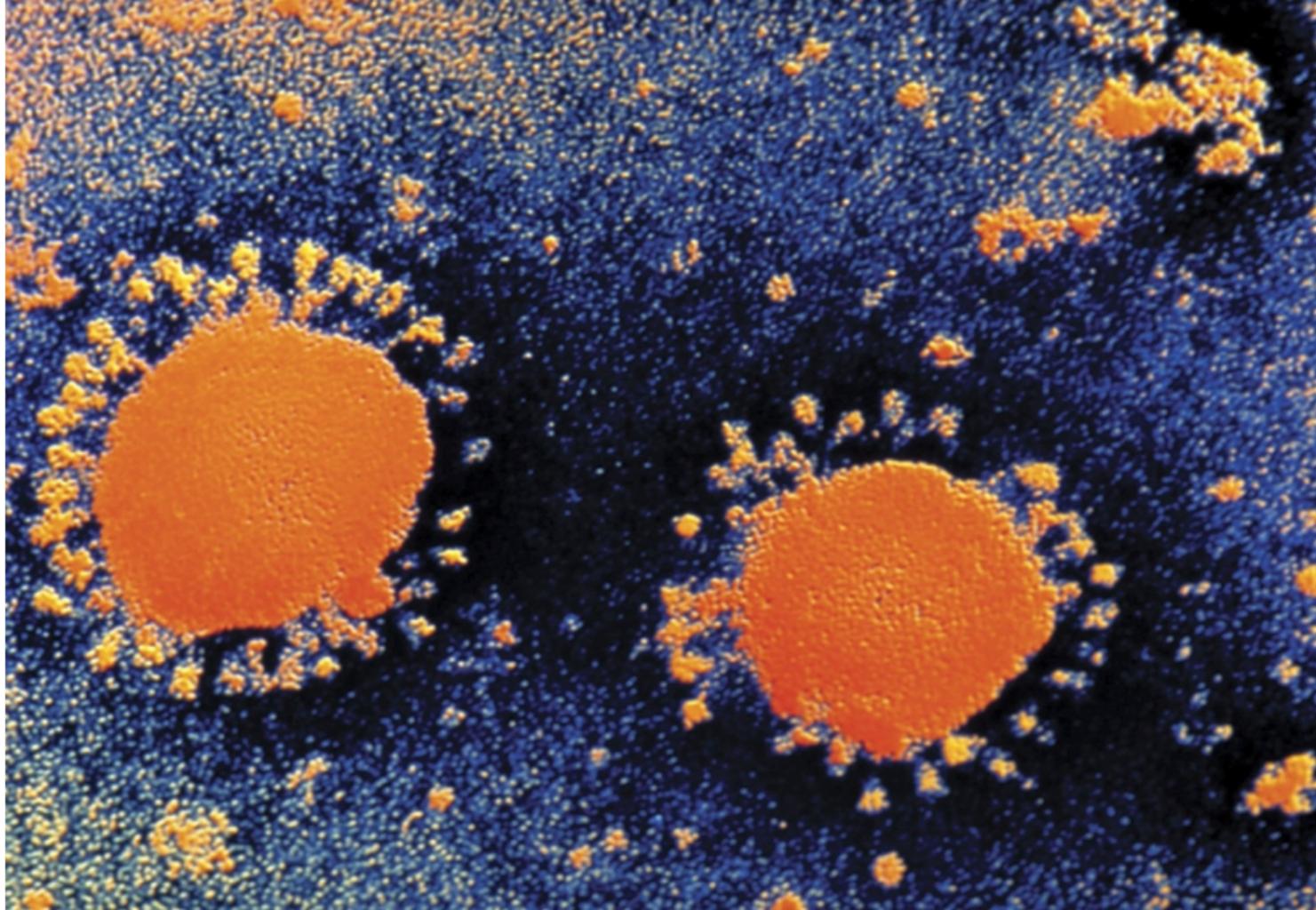




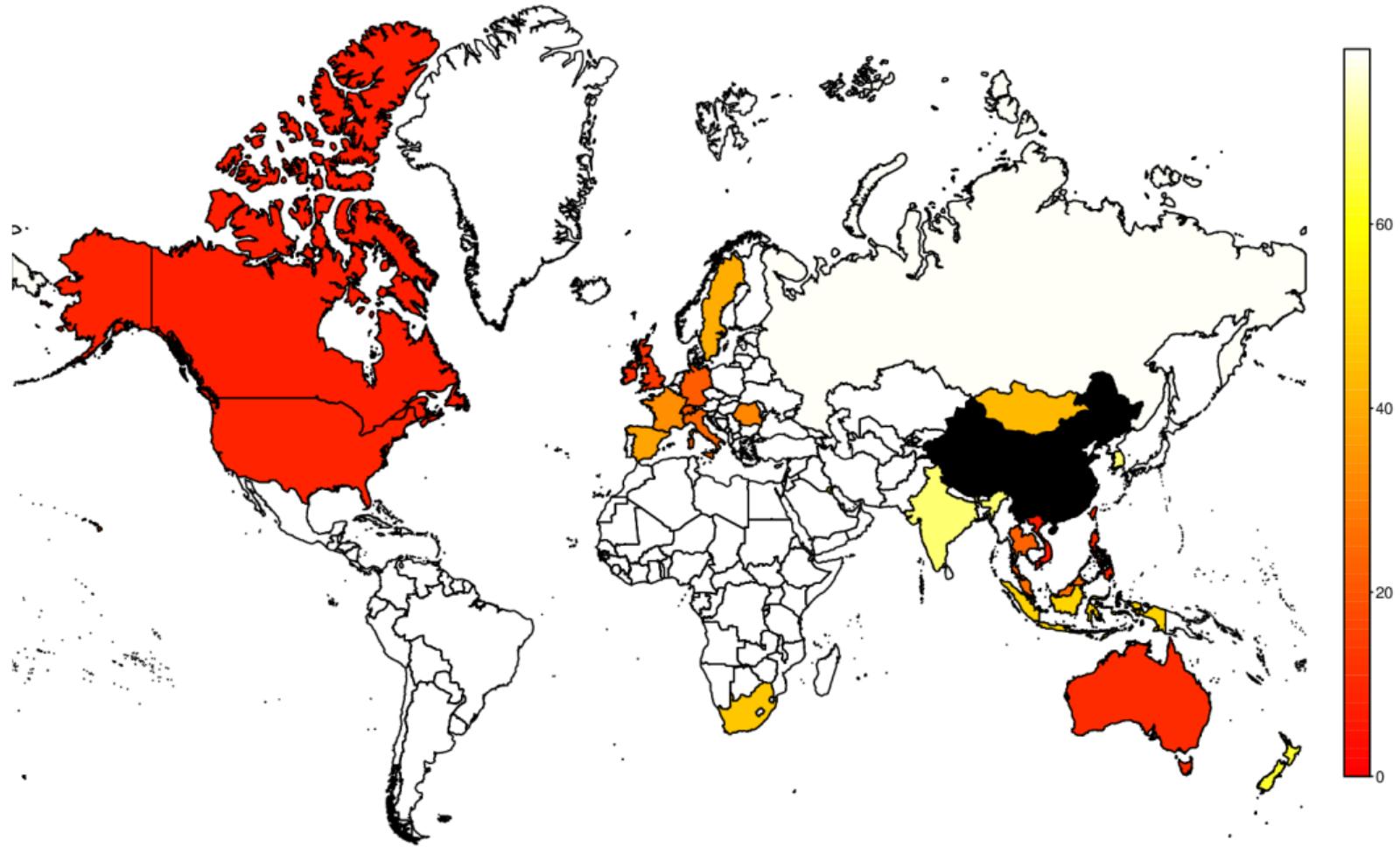


So...

- ▶ Bakery-driven pathogen spread
- ▶ Joke aside, let's consider two examples



# Countries with SARS cases (WHO/Dec 2003)



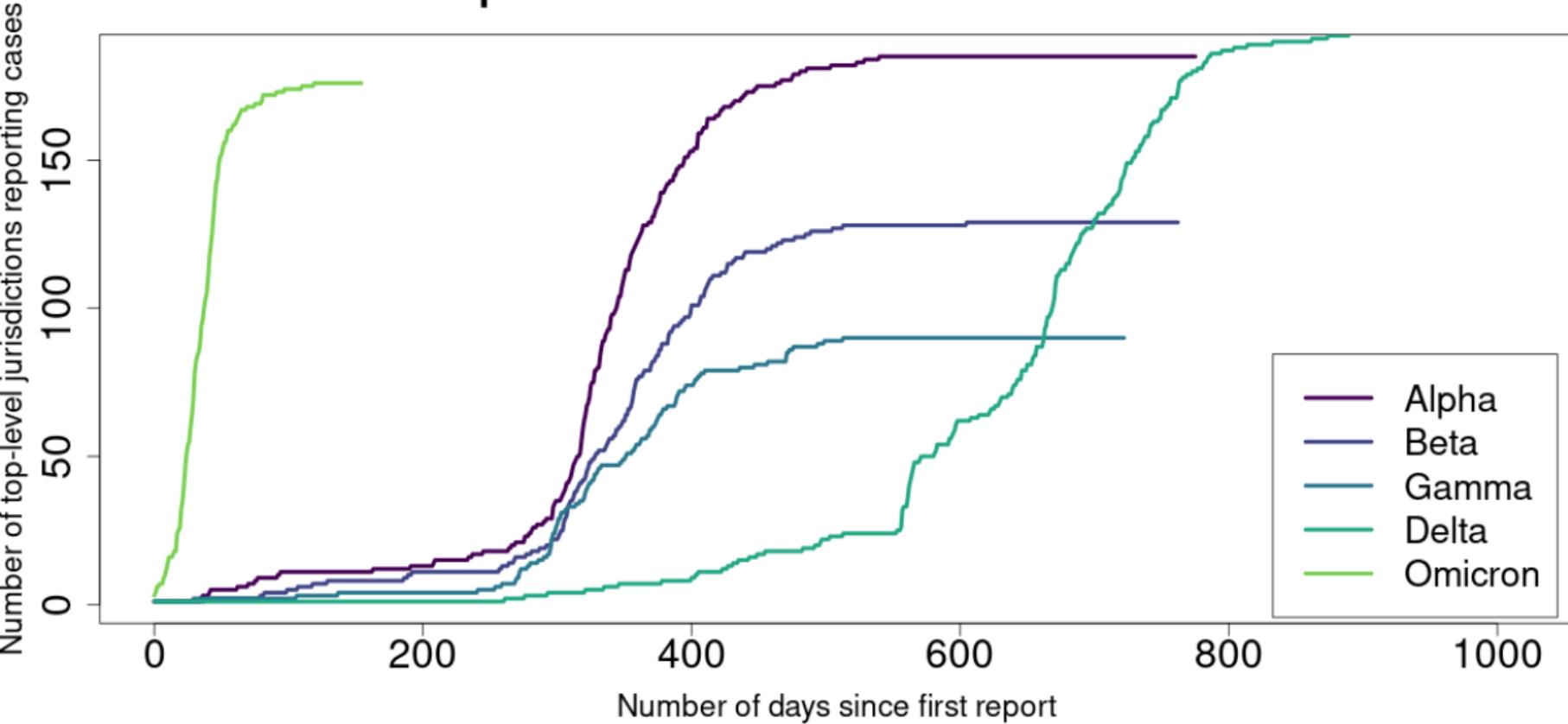
## Spatial spread of pH1N1 in 2009

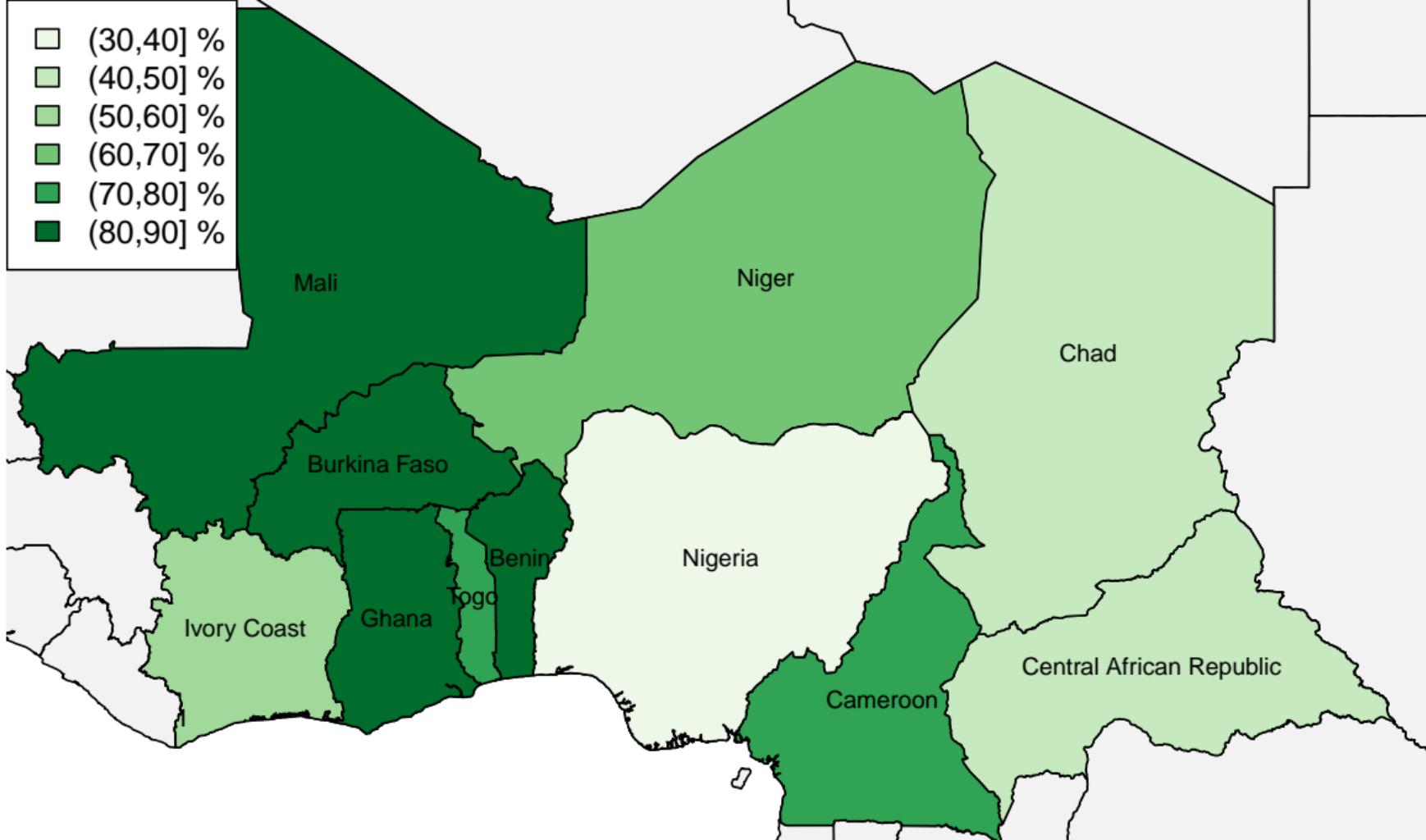
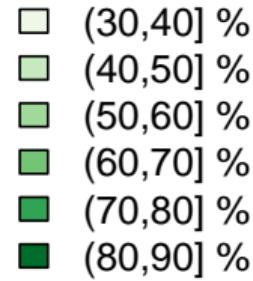
In March and April 2008 (used as surrogate for 2009 data),

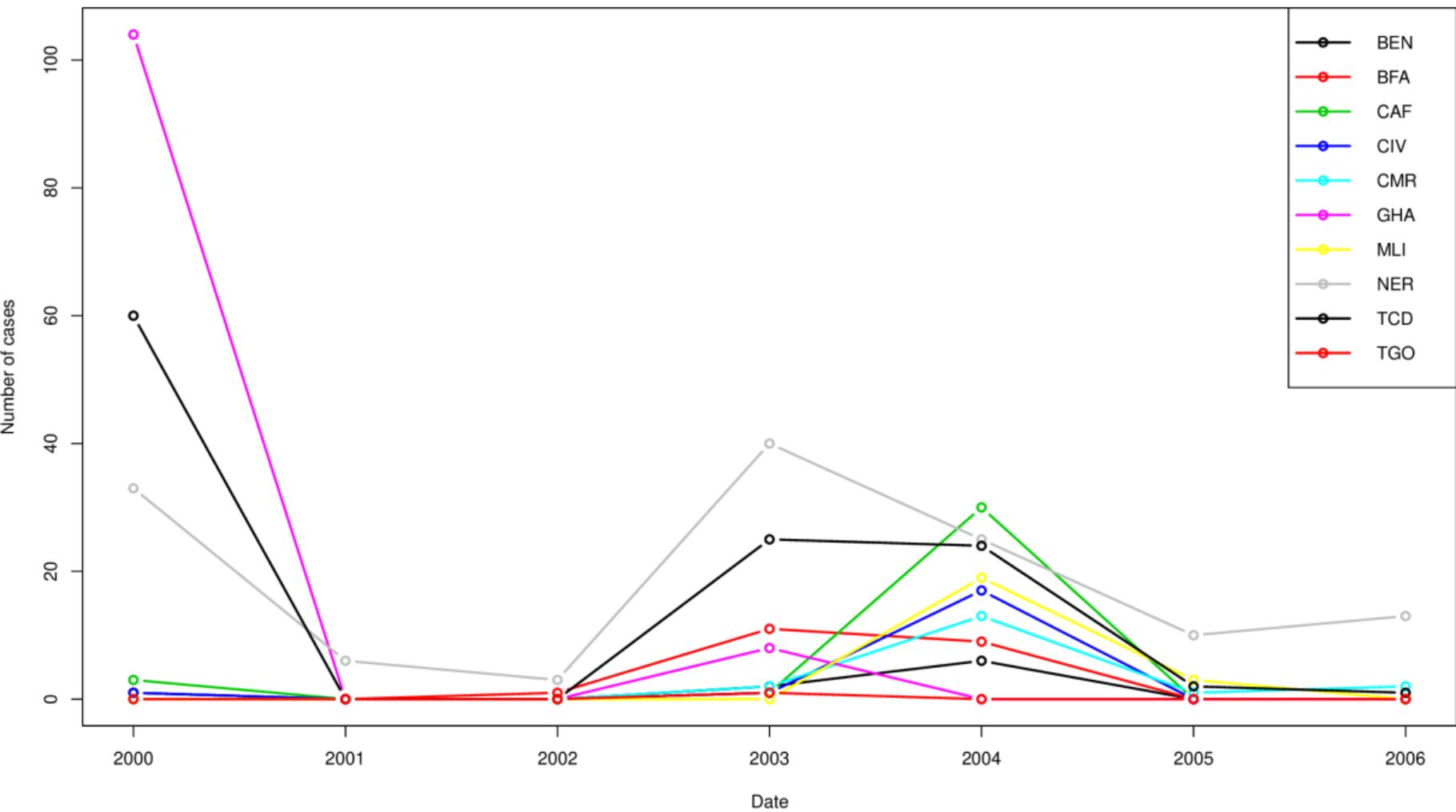
- ▶ 2.35 million passengers flew from MX to 1018 cities in 164 countries
- ▶ 80.7% flew to US and Canada, 8.8% South and Central America, 8.7% Europe
- ▶ of 20 countries with highest volumes of passengers arriving from MX, 16 had confirmed importations from MX on 5/25
- ▶ ROC curve of relationship between international air-traffic flows and H1N1 importation: countries receiving more than 1400 passengers from MX at significantly elevated risk for importation
- ▶ Use this passenger threshold: international air-traffic volume  $> 92\%$  sensitive and  $> 92\%$  specific in predicting importation (area under ROC curve 0.97)

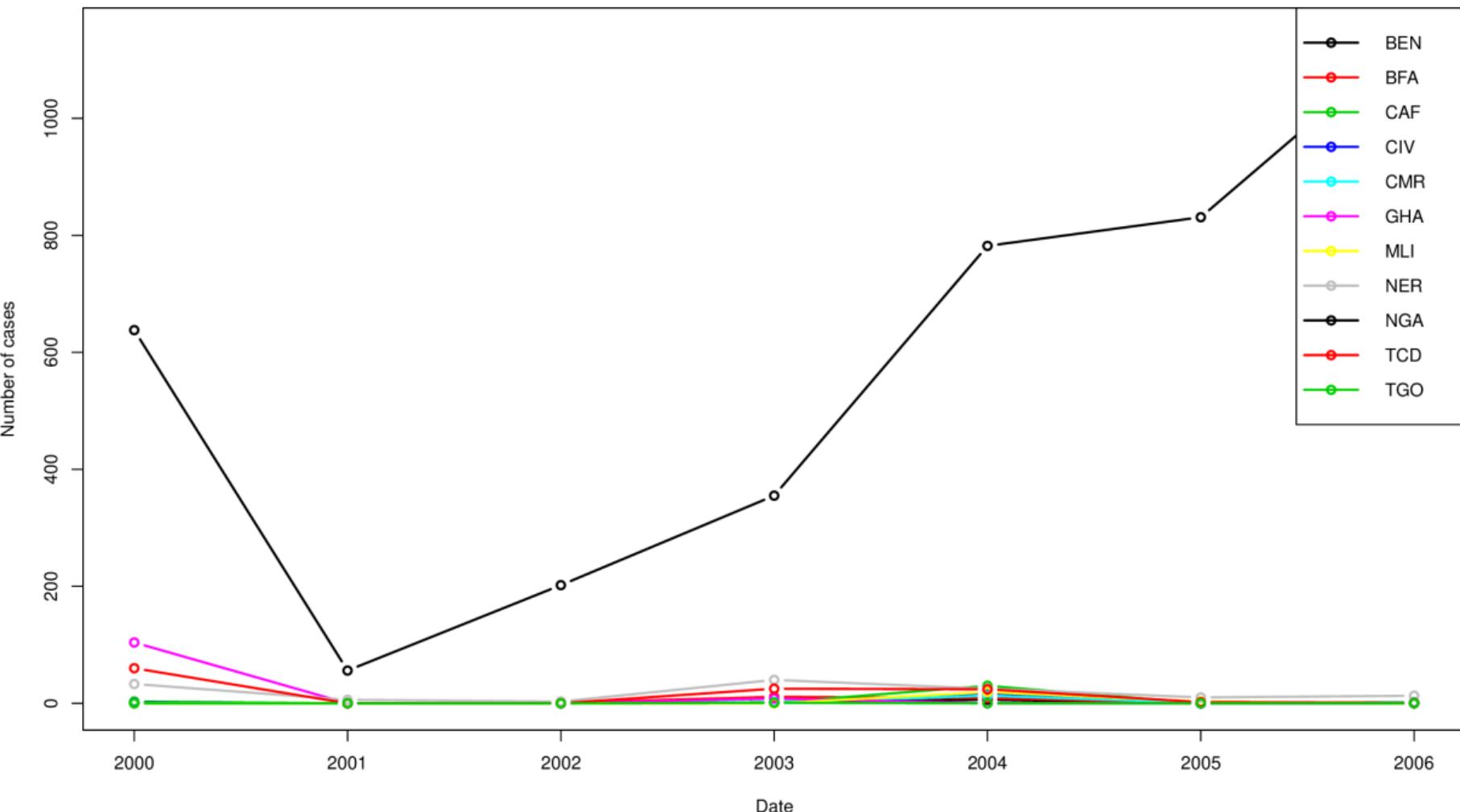
Khan, JA, Hu et al, New England Journal of Medicine, 2009

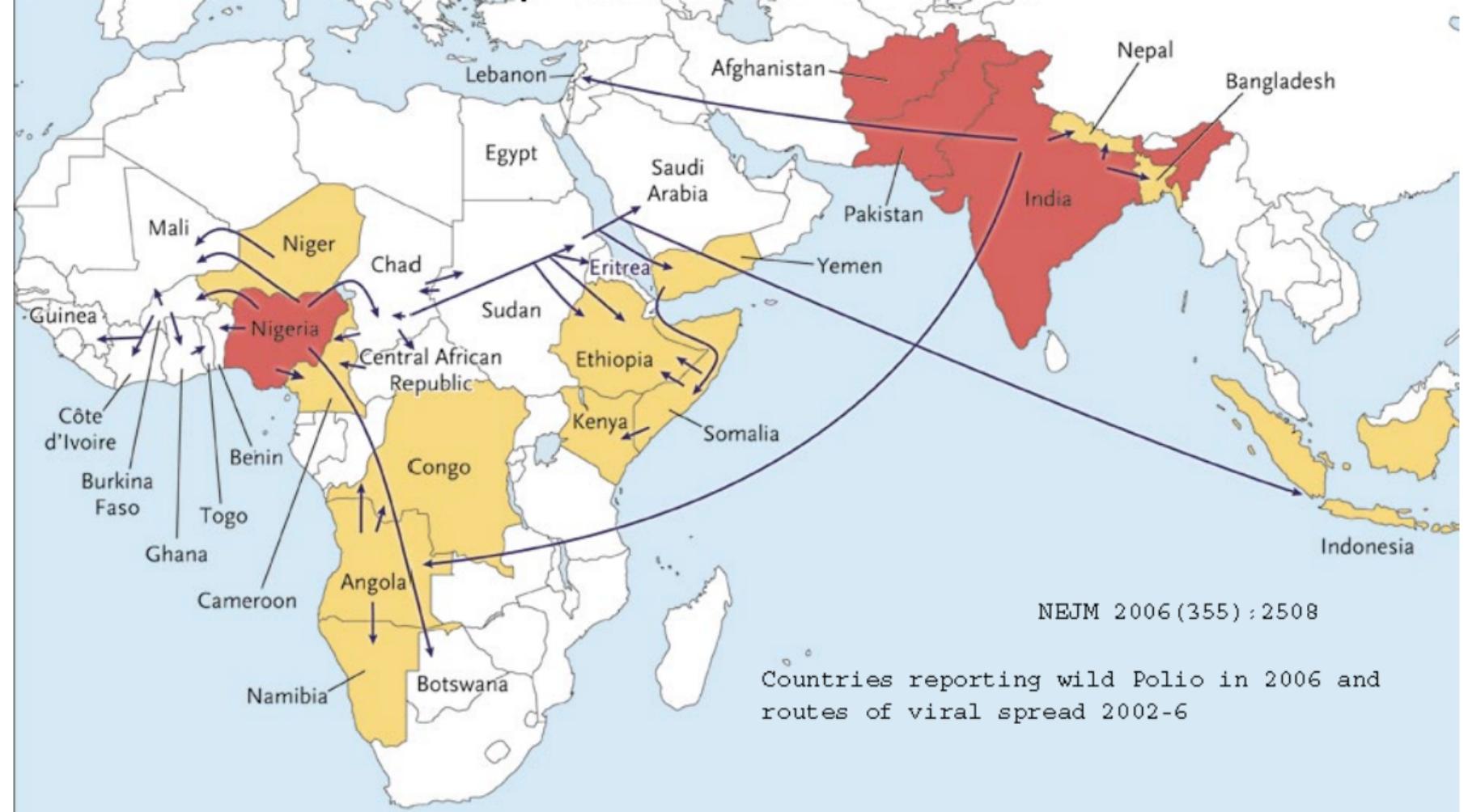
## Spread of COVID-19 variants of concern











## In a globalised world

- ▶ Public health policy decisions are taken at the jurisdictional level, typically national (ISO 3166-1) or first-level sub-national (ISO 3166-2) – extremely rarely supra-nationally  
(International Health Regulations (IHR) define processes regarding reporting of disease outbreaks, make recommendations about handling of travellers, etc. See COVID-19: even those of the rules that were somewhat prescriptive were not followed)
- ▶ Individuals are mobile and thus so are the pathogens they harbour
- ▶ Policy decisions have consequences outside the jurisdictions where they are taken!
- ▶ COVID-19 was a single outbreak, not one outbreak per country it affected

Spatio-temporal spread of infectious pathogens

Metapopulations for disease spread modelling

# Metapopulations for disease spread modelling

Why use metapopulation models?

Metapopulations with explicit movement

The graph setting

The models considered

Going to vector form

The movement matrix

Behaviour of the mobility component

Existence of a DFE

Computation of a reproduction number

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

Metapopulation-specific problems

Computational aspects of metapopulation models

## 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)
- ▶ JA, Bajeux & Kirkland. Number of source patches required for population persistence in a source-sink metapopulation. *Bulletin of Mathematical Biology* **81**: 1916–1942 (2019)

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## Metapopulations with explicit movement

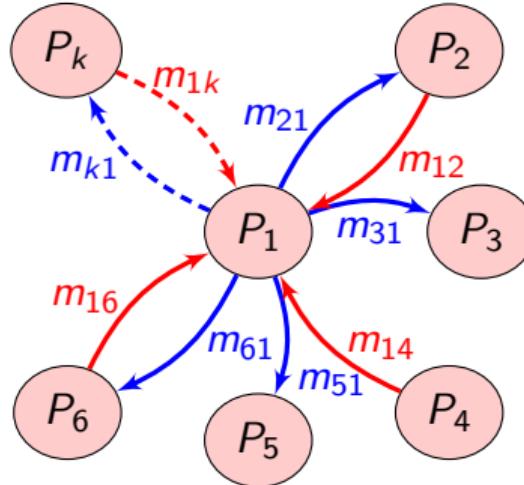
Split continuous space into  $N$  discrete geographical locations (*ptatches*)

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

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

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

## Explicit movement (focus on $P_1$ )



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

or

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

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## Graph setting

Suppose

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

Graph is a digraph: movement is not always symmetric

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

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

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

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

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

## Connection matrix

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

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

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

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

## Strong connectedness and irreducibility

### Definition 1 (Reducible/irreducible matrix)

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

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

### Theorem 2

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

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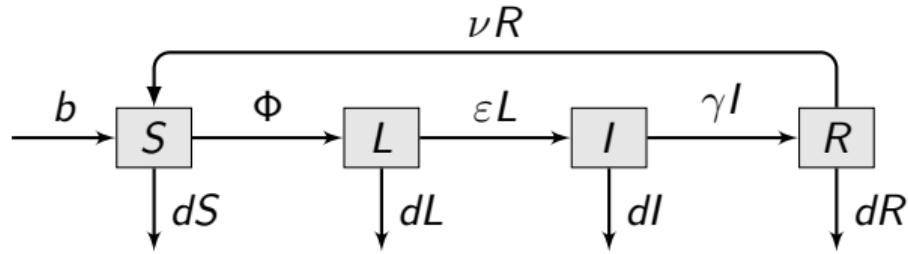
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## The prototype SLIRS used in patches



$$S' = b + \nu R - \Phi - dS \quad (1a)$$

$$L' = \Phi - (\varepsilon + d)L \quad (1b)$$

$$I' = \varepsilon L - (\gamma + d)I \quad (1c)$$

$$R' = \gamma I - (\nu + d)R \quad (1d)$$

$\Phi$  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

$$S'_p = b_p + \nu_p R_p - \Phi_p - d_p S_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (2a)$$

$$L'_p = \Phi_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q \quad (2b)$$

$$I'_p = \varepsilon_p L_p - (\gamma_p + d_p) I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (2c)$$

$$R'_p = \gamma_p I_p - (\nu_p + d_p) R_p + \sum_{q \in \mathcal{P}} m_{Rpq} R_q \quad (2d)$$

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (2e)$$

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

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

$$S'_{sp} = b_p + \nu_{sp} R_{sp} - \Phi_{sp} - d_{sp} S_{sp} + \sum_{q \in \mathcal{P}} m_{Sspq} S_{sq} \quad (3a)$$

$$L'_{sp} = \Phi_{sp} - (\varepsilon_{sp} + d_{sp}) L_{sp} + \sum_{q \in \mathcal{P}} m_{Lspq} L_{sq} \quad (3b)$$

$$I'_{sp} = \varepsilon_{sp} L_{sp} - (\gamma_{sp} + d_{sp}) I_{sp} + \sum_{q \in \mathcal{P}} m_{Ispq} I_{sq} \quad (3c)$$

$$R_{sp} = \gamma_{sp} I_{sp} - (\nu_{sp} + d_{sp}) R_{sp} + \sum_{q \in \mathcal{P}} m_{Rspq} R_{sq} \quad (3d)$$

with incidence

$$\Phi_{sp} = \sum_{k \in \mathcal{S}} \beta_{skp} \frac{S_{sp} I_{kp}}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (3e)$$

- ▶ 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)

$$S'_{pq} = b_p + \nu_{pq} R_{pq} - \Phi_{pq} - d_{pq} S_{pq} + \sum_{k \in \mathcal{P}} m_{Spqk} S_{pk} \quad (4a)$$

$$L'_{pq} = \Phi_{pq} - (\varepsilon_{pq} + d_{pq}) L_{pq} + \sum_{k \in \mathcal{P}} m_{Lpqk} L_{pk} \quad (4b)$$

$$I'_{pq} = \varepsilon_{pq} L_{pq} - (\gamma_{pq} + d_{pq}) I_{pq} + \sum_{k \in \mathcal{P}} m_{Ipqk} I_{pk} \quad (4c)$$

$$R'_{pq} = \gamma_{pq} I_{pq} - (\nu_{pq} + d_{pq}) R_{pq} + \sum_{k \in \mathcal{P}} m_{Rpqk} R_{pk} \quad (4d)$$

with incidence

$$\Phi_{pq} = \sum_{k \in \mathcal{P}} \beta_{pqk} \frac{S_{pq} I_{kq}}{N_p^{q_q}}, \quad q_q = \{0, 1\} \quad (4e)$$

- ▶ 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  $\mathcal{B}_p(N_p) = b_p$

$$S'_p = b_p - \Phi_p - d_p S_p + \nu_p R_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (5a)$$

$$L'_p = \Phi_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q \quad (5b)$$

$$I'_p = \varepsilon_p L_p - (\gamma_p + d_p) I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (5c)$$

$$R'_p = \gamma_p I_p - (\nu_p + d_p) R_p + \sum_{q \in \mathcal{P}} m_{Rpq} R_q \quad (5d)$$

with incidence

$$\Phi_p = \beta_p S_p I_p \quad (5e)$$

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)

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## Notation

- ▶  $X_{cp}(t)$  number of individuals of compartment  $c$  in location  $p$  at time  $t$   
(Here and elsewhere: omit dependence on  $t$  unless it causes confusion)
- ▶  $\mathbf{X}_c = (X_{c1}, \dots, X_{c|\mathcal{P}|})^T$  distribution of individuals of compartment  $c \in \mathcal{C}$  among the different locations  
[E.g., for (5),  $\mathbf{X}_S = (S_1, \dots, S_{|\mathcal{P}|})^T$ ]
- ▶  $\mathbf{X}^p = (X_1^p, \dots, X_{|\mathcal{P}|}^p)^T$  composition of the population in location  $p \in \mathcal{P}$   
[E.g., for (5),  $\mathbf{X}^p = (S_p, L_p, I_p, R_p)^T$ ]

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

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

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

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

more compact, denote the rate of leaving location  $p$  as

$$m_{cpp} = - \sum_{\substack{q \in \mathcal{P} \\ q \neq p}} m_{cqp} \tag{6}$$

Then

$$X'_{cp} = f_{cp}(\mathbf{X}^p) + \sum_{q \in \mathcal{P}} m_{cpq} X_{cq} \tag{7}$$

## Vector form of the system

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

$$\mathbf{X}'_c = f(\mathbf{X}) + \mathcal{M}_c \mathbf{X}_c \quad (8)$$

with

$$\mathcal{M}_c = \begin{pmatrix} -\sum_{k \in \mathcal{P}} m_{ck1} & m_{c12} & \cdots & m_{c1|\mathcal{P}|} \\ m_{c|\mathcal{P}|1} & m_{c|\mathcal{P}|2} & \cdots & -\sum_{k \in \mathcal{P}} m_{ck|\mathcal{P}|} \end{pmatrix} \quad (9)$$

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## Definitions and notation for matrices

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

## The movement matrix

The matrix

$$\mathcal{M}_c = \begin{pmatrix} -\sum_{k \in \mathcal{P}} m_{ck1} & m_{c12} & \cdots & m_{c1|\mathcal{P}|} \\ m_{c|\mathcal{P}|1} & m_{c|\mathcal{P}|2} & \cdots & -\sum_{k \in \mathcal{P}} m_{ck|\mathcal{P}|} \end{pmatrix} \quad (9)$$

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 weighted Laplacian matrix (using out-degrees)

### Lemma 3

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 3 and Proposition 4 (next page), see Arino, Bajer & Kirkland, BMB 2019

## Proposition 4 ( $D$ a diagonal matrix)

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

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## Behaviour of the mobility component – No demography

Assume no within-location dynamics, just movement. Then (8) takes the form

$$\mathbf{X}'_c = \mathcal{M}_c \mathbf{X}_c \quad (10)$$

### Theorem 5

For a given compartment  $c \in \mathcal{C}$ , suppose that the movement matrix  $\mathcal{M}_c$  is irreducible. Then for any  $\mathbf{X}_c(0) > 0$ , (10) satisfies

$$\lim_{t \rightarrow \infty} \mathbf{X}_c(t) = \mathbf{X}_c^* \gg 0$$

Note that  $\mathbf{X}_c^*$  depends on  $\langle \mathbb{1}, \mathbf{X}_c(0) \rangle$

## Reduction to total population per location – Demography

Let

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

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

$$T'_p = D_p(T_p) + \sum_{c \in \mathcal{C}} \sum_{q \in \mathcal{P}} m_{cpq} X_{cq} \quad (11)$$

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

## Nature of the demography

Most common types of demographic functions

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

We have assumed (since birth term is  $b_p$ )

$$D_p(T_p) = b_p - d_p T_p \tag{12}$$

## Vector / matrix form of the equation

Assuming demography is of the form (12), write (11) in vector form

$$\mathbf{T}' = \mathbf{b} - \mathbf{dT} + \sum_{c \in C} \mathcal{M}_c \mathbf{X}_c \quad (13)$$

where

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

## The nice case

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

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

(stronger than the property of movement being *similar for all compartments*, which only requires zero/nonzero patterns in all  $\mathcal{M}_c$ ,  $c \in \mathcal{C}$ , to be the same)

Then

$$\begin{aligned}\mathbf{T}' &= \mathbf{b} - \mathbf{dT} + \mathcal{M} \sum_{c \in \mathcal{C}} \mathbf{N}_c \\ &= \mathbf{b} - \mathbf{dT} + \mathcal{M} \mathbf{T}\end{aligned}\tag{14}$$

## Equilibria

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

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

Is it?

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

Using the spectrum shift of Theorem 4(1)

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

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

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

## Behaviour of the total population

Equal irreducible movement case

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

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

Indeed, we have

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

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

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

## Behaviour of total population (equal *reducible* movement)

### Theorem 6

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

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

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

## The not-so-nice case

Recall that

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

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

Let

$$\underline{\mathcal{M}} = \left[ \min_{c \in \mathcal{C}} m_{cpq} \right]_{pq, p \neq q} \quad \overline{\mathcal{M}} = \left[ \max_{c \in \mathcal{C}} m_{cpq} \right]_{pq, p = q}$$

and

$$\underline{\mathcal{M}} = \left[ \max_{c \in \mathcal{C}} m_{cpq} \right]_{pq, p \neq q} \quad \overline{\mathcal{M}} = \left[ \min_{c \in \mathcal{C}} m_{cpq} \right]_{pq, p = q}$$

Cool, no? No!

Then we have

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

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

Me, roughly 10 minutes after making 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..

We can still do stuff, however more on a case-by-case basis

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## Disease free equilibrium

The model is at equilibrium if the time derivatives are zero

### Definition 7 (Metapopulation DFE)

In the case of system (5), 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 (3), replace  $L_p$  with  $L_{sp}$  and  $I_p$  with  $I_{sp}$ , for (4), replace  $L_p$  by  $L_{pp}$  and  $I_p$  by  $I_{pp}$ . To simplify notation, we could write  $L_\bullet$  and  $I_\bullet$ )

Assume (5) at metapopulation DFE. Then  $\Phi_p = 0$  and

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

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

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

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

## $\mathbf{R}$ at DFE

Recall second equation:

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

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

We have been here before!

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

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

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

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

## S at the DFE

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

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

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

- ▶  $d - M^S$  invertible
- ▶  $d - M^S$  nonsingular M-matrix

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

So DFE makes sense with

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

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- ▶ Linear stability of the disease free equilibrium can be investigated by using the next generation matrix method of [?]
- ▶ 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

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

## Evaluate $D\mathcal{F}$ at DFE

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

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

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

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

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

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

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

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

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

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

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

where

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

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

Next generation matrix

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

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

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

i.e.,

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

## Local asymptotic stability of the DFE

### Theorem 8

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

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

Then the DFE

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

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

From PvdD & Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Bulletin of Mathematical Biology* 180(1-2): 29-48 (2002)

## Some remarks about $\mathcal{R}_0$

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

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

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

However, numerically, this works easy unless conditioning is bad

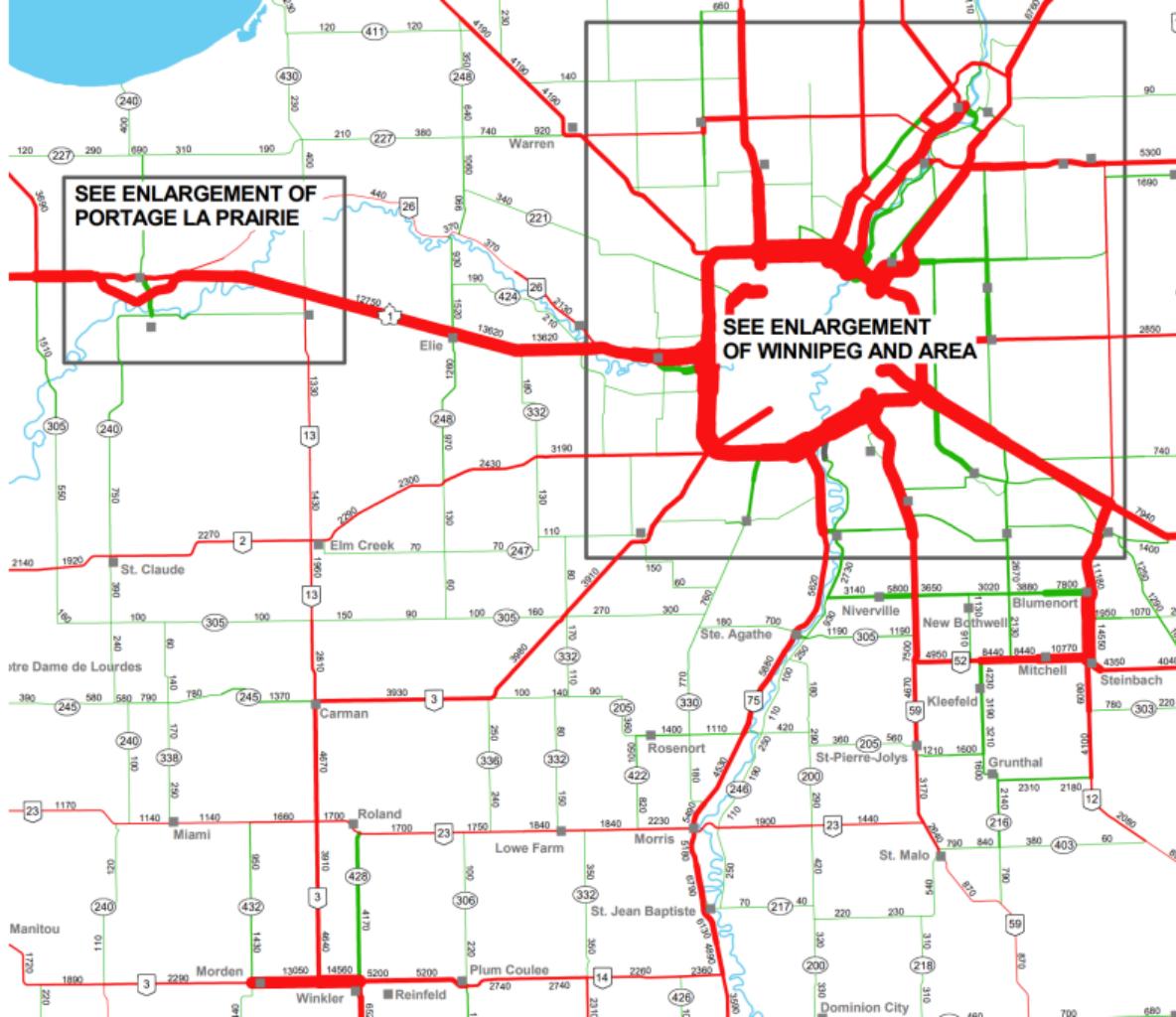
## Do not in $\mathcal{R}_0$ put all your .. interpretation?

An urban centre and satellite cities

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

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

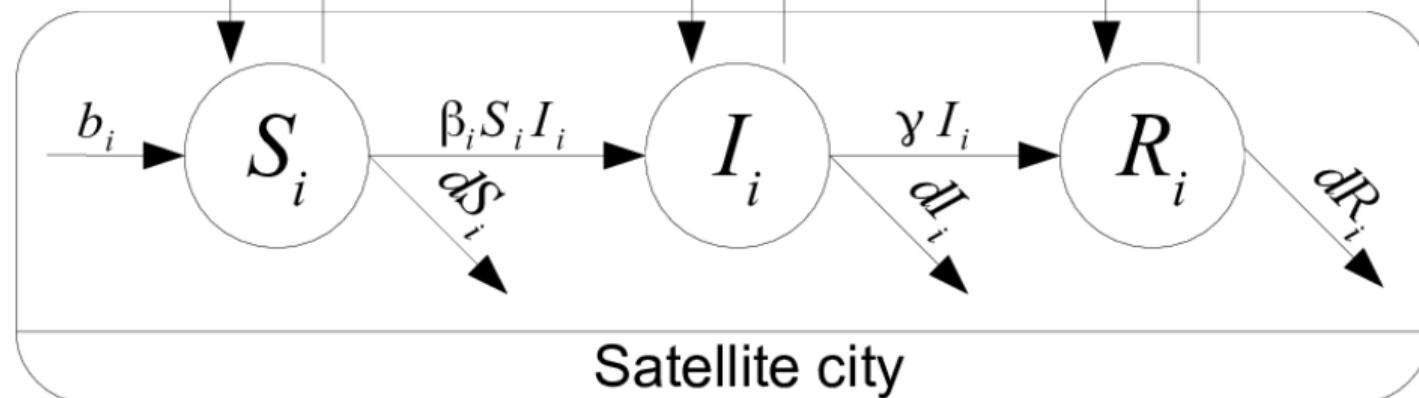
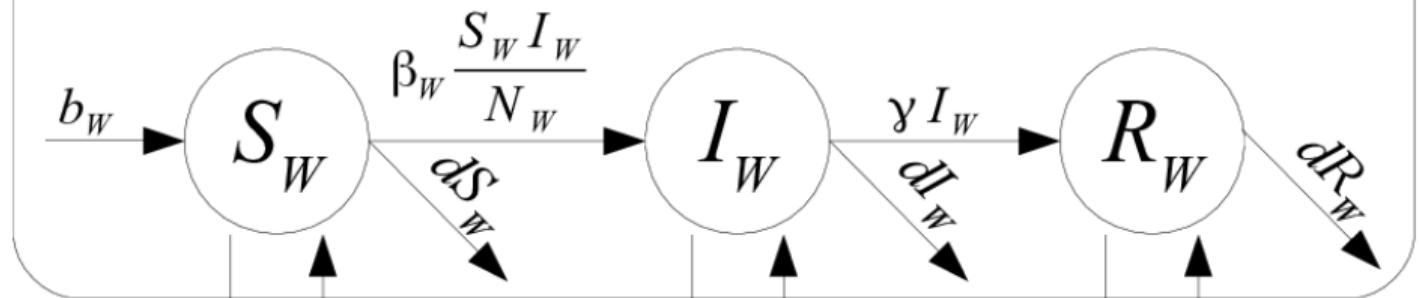
JA & S Portet. Epidemiological implications of mobility between a large urban centre and smaller satellite cities. *Journal of Mathematical Biology* 71(5):1243-1265 (2015)



## Known and estimated quantities

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



## 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.,

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

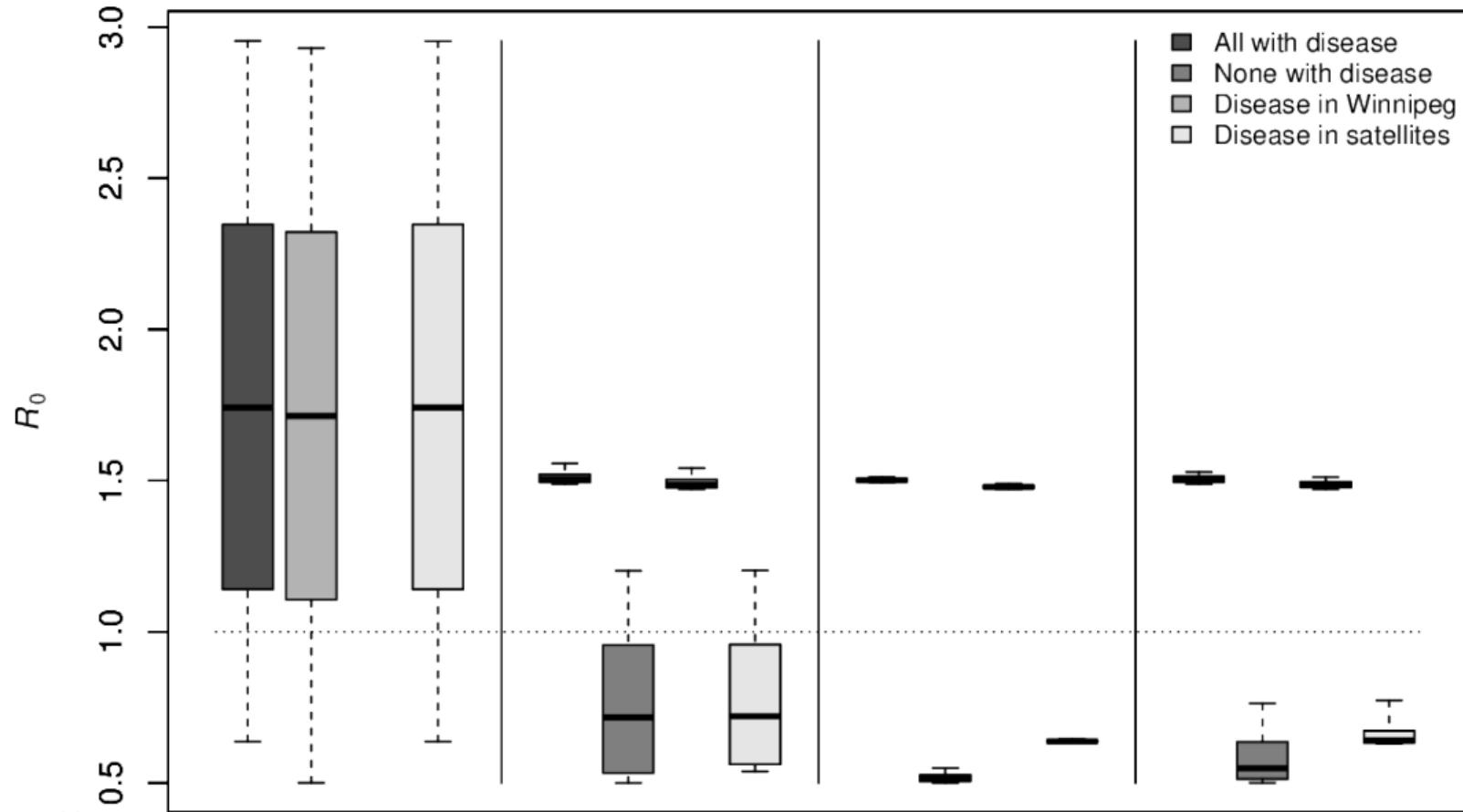
Now,  $N_x(1) = N_x(0) - T_{yx}$ , where  $T_{yx}$  number of individuals going from  $x$  to  $y$  / day.

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 $\mathcal{R}_0^x \in [0.5, 3]$



Lower connectivity can drive  $\mathcal{R}_0$

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

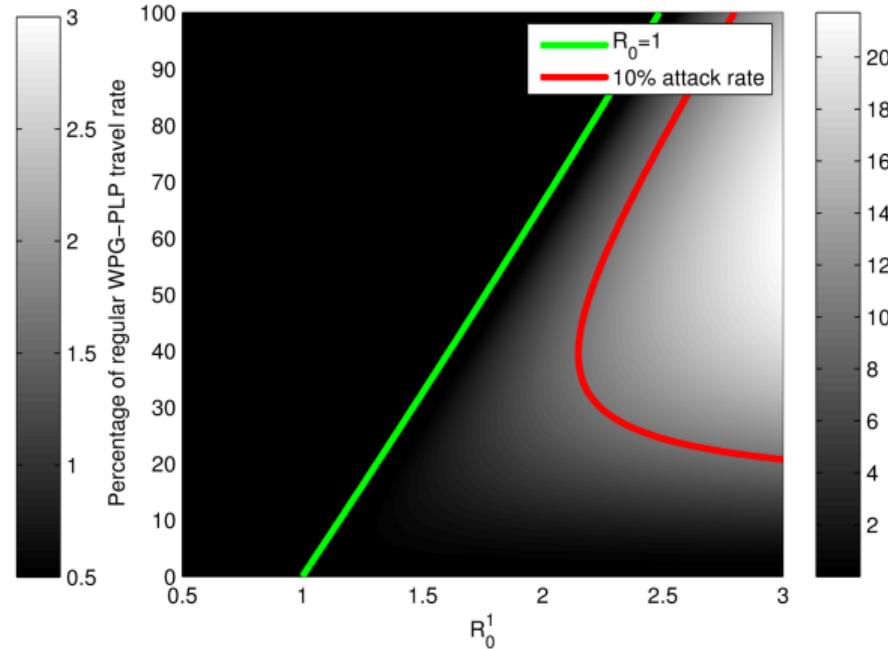
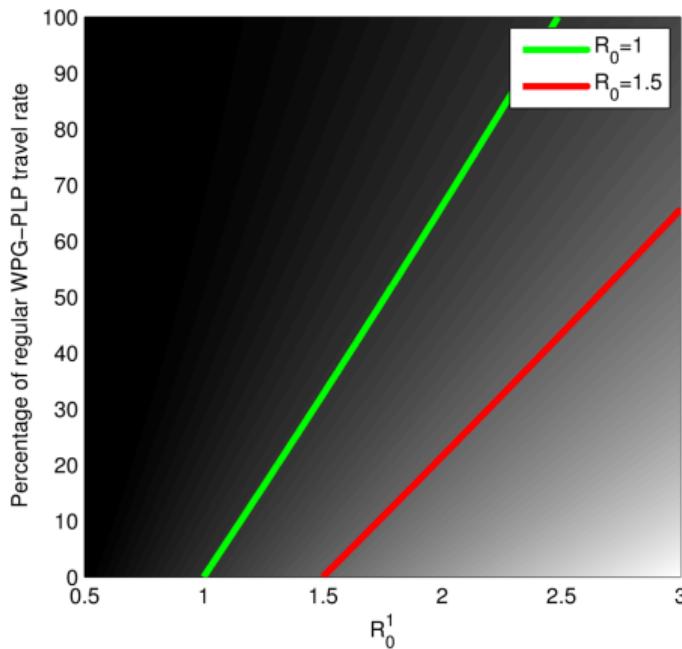
This is due to the movement rate: if  $\mathcal{M} = 0$ , then

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

since  $FV^{-1}$  is then block diagonal

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

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



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

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

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

### Theorem 9

Let  $\mathcal{R}_0$  be defined as in Theorem 8 and use proportional incidence  $\Phi_p = \beta_p S_p I_p / N_p$ . If  $\mathcal{R}_0 < 1$ , then the DFE of system (5) is globally asymptotically stable

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

In the case in which movement is equal for all compartments and there is no disease death, a comparison theorem argument can be used as in Theorem 9 to show that if  $\mathcal{R}_0 < 1$ , then the DFE of the  $|\mathcal{S}| |\mathcal{P}|$ -SLIRS (3) is globally asymptotically stable.

### Theorem 10

*For system (3) with  $|\mathcal{S}|$  species and  $|\mathcal{P}|$  locations, with movement equal for all compartments, define  $\mathcal{R}_0$  appropriately and use proportional incidence. If  $\mathcal{R}_0 < 1$ , then the DFE is globally asymptotically stable*

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## Metapopulation-specific problems – 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

$$s'_{kp} = f_{kp}(S_p, I_p) \quad (15a)$$

$$i'_{\ell p} = g_{\ell p}(S_p, I_p) \quad (15b)$$

with known properties, what is known of

$$s'_{kp} = f_{kp}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{kpq} s_{kq} \quad (16a)$$

$$i'_{\ell p} = g_{\ell p}(S_p, I_p) + \sum_{q \in \mathcal{P}} m_{\ell pq} i_{\ell q} \quad (16b)$$

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

## An inheritance problem – Backward bifurcations

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

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

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

## Metapopulation-induced behaviours ?

“Converse” problem to inheritance problem. Given

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

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

with known properties, does

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

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

exhibit some behaviours not observed in the uncoupled system?

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

## Mixed equilibria

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

This is the problem of **mixed equilibria**

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

## Types of equilibria

### Definition 11 (Location level EP)

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

### Definition 12 (Metapopulation level EP)

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

## Mixed equilibria

### Definition 13

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

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

E.g.,

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

is mixed and so is

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

Notation is specific here:  $p \in \mathcal{P}$ ,  $\mathcal{A}(p)$  and  $\mathcal{D}(p)$  are the ancestry and descendants of  $p$  in the movement digraph

### Theorem 14

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

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

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

# Metapopulations for disease spread modelling

Why use metapopulation models?

Metapopulations with explicit movement

The graph setting

The models considered

Going to vector form

The movement matrix

Behaviour of the mobility component

Existence of a DFE

Computation of a reproduction number

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

Metapopulation-specific problems

**Computational aspects of metapopulation models**

- ▶ 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)
```

## Computing birth and death rates

Average life expectancy at birth (years): 81.30, 78.59, 67.74, 66.43, 72.19

```
pop = c(34.017, 1348.932, 1224.614, 173.593, 93.261) * 1e+06
countries = c("Canada", "China", "India", "Pakistan", "Philippines")
death_rates = 1/(365.25*c(81.30, 78.59, 67.74, 66.43, 72.19))
birth_rates = pop*death_rates
```

## Work out movement matrix

Use the approximation explained in Arino & Portet (JMB 2015)

```
p = list()
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))
```

For simplicity, let's assume all movement rates are equal

```
p$P = dim(p$M)[1]
p$epsilon = rep((1/1.5), p$P)
p$gamma = rep((1/5), p$P)
p$nu = rep((1/365.25), p$P)
p$b = birth_rates
p$d = death_rates
# 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$idx_R = (3*p$P+1):(4*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)
R0 = mat.or.vec(p$P, 1)
I0[1] = 2
S0 = pop - (L0 + I0 + R0)
# Vector of initial conditions to be passed to ODE solver.
IC = c(S = S0, L = L0, I = I0, R = R0)
# Time span of the simulation (5 years here)
tspan = seq(from = 0, to = 100, by = 0.1)
```

## Computing $\mathcal{R}_0$ in patches in isolation to set up $\beta$

Useful to know  $\mathcal{R}_{0p}$ , basic reproduction number for patch  $p \in \mathcal{P}$  disconnected from the network

In the absence of movement, system in  $p \in \mathcal{P}$  is

$$S'_p = b_p - \beta_p S_p I_p - d_p S_p + \nu_p R_p \quad (17a)$$

$$L'_p = \beta_p S_p I_p - (\varepsilon_p + d_p) L_p \quad (17b)$$

$$I'_p = \varepsilon_p L_p - (\gamma_p + d_p) I_p \quad (17c)$$

$$R'_p = \gamma_p I_p - (\nu_p + d_p) R_p \quad (17d)$$

DFE is clearly  $(S_p, L_p, I_p, R_p) = (b_p/d_p, 0, 0, 0)$

Infected variables are  $\mathcal{I} = \{L, I\}$

$$\mathcal{F} = (\beta_p S_p I_p, 0)^T \text{ and } \mathcal{V} = ((\varepsilon_p + d_p)L_p, -\varepsilon_p L_p + (\gamma_p + d_p)I_p)$$

so

$$\mathcal{F} = \begin{pmatrix} 0 & \beta_p \frac{b_p}{d_p} \\ 0 & 0 \end{pmatrix} \text{ and } \mathcal{V} = \begin{pmatrix} \varepsilon_p + d_p & 0 \\ -\varepsilon_p & \gamma_p + d_p \end{pmatrix}$$

Thus

$$\mathcal{R}_{0p} = \rho(\mathcal{F}\mathcal{V}^{-1}) = \rho \left( \begin{pmatrix} 0 & \beta_p \frac{b_p}{d_p} \\ 0 & 0 \end{pmatrix} \frac{1}{(\varepsilon_p + d_p)(\gamma_p + d_p)} \begin{pmatrix} \gamma_p + d_p & 0 \\ \varepsilon_p & \varepsilon_p + d_p \end{pmatrix} \right)$$

and it follows that

$$\mathcal{R}_{0p} = \frac{\beta_p}{\gamma_p + d_p} \frac{\varepsilon_p}{\varepsilon_p + d_p} \frac{b_p}{d_p} \tag{18}$$

Set up  $\beta$  to avoid blow up

Let us take  $\mathcal{R}_{0p} = 1.5$  for patches in isolation. Solve (18) for  $\beta_p$ :

$$\beta_p = \frac{\mathcal{R}_{0p}(\gamma_p + d_p)(\varepsilon_p + d_p)d_p}{\varepsilon_p b_p}$$

```
for (i in 1:p$P) {  
  p$beta[i] =  
    R_0[i] *(p$gamma[i]+p$d[i]) * (p$epsilon[i]+p$d[i]) * p$d[i] /  
    (p$epsilon[i]*p$d[i])  
}
```

## Define the vector field

```
SLIRS_metapop_rhs <- function(t, x, p) {  
  with(as.list(p), {  
    S = x[idx_S]  
    L = x[idx_L]  
    I = x[idx_I]  
    R = x[idx_R]  
    Phi = beta*S*I  
    dS = b - d*S - Phi + M%*%S  
    dL = Phi - (epsilon+d)*L + M%*%L  
    dI = epsilon*L - (gamma+d)*I + M%*%I  
    dR = gamma*I - (nu+d)*R + M%*%R  
    return(list(c(dS, dL, dI, dR)))  
  })  
}
```

And now call the solver

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

## One little trick (case with demography)

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

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

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

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

Then

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

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

Word of warning about that trick, though..

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

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

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

⇒ use this for numerics, not for the mathematical analysis

# Bibliography I