

Adding space to FMD and AI models

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April 2023

Why it is important to incorporate space

General considerations about space-and-time spread

Foot-and-mouth disease

Avian influenza

Metapopulation models

A few foot-and-mouth disease models

A few avian influenza models

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50 0 50 100 150 200
Yards

X Pump

• Deaths from cholera



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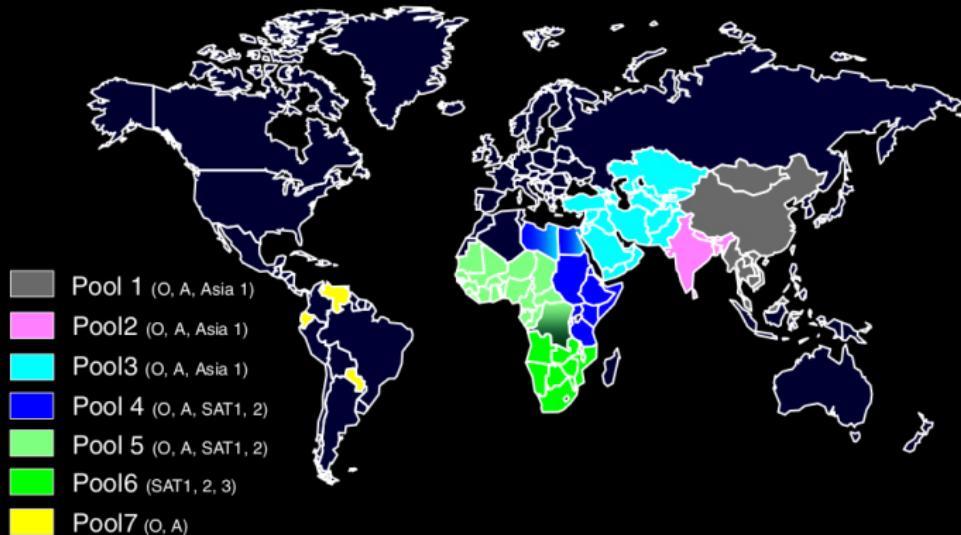


Figure 2 Geographical distribution of seven pools of foot-and-mouth disease viruses. Serotype O FMDV is the most widely distributed serotype of the virus (in 6 of the 7 indicated virus pools) whereas, in contrast, SAT3 is only present in pool 6 (within southern Africa). The Asia-1, SAT1 and SAT2 serotypes also have quite limited geographical distribution. However, individual countries can have multiple serotypes in circulation at the same time and hence it is necessary to be able to determine which serotype is responsible for an outbreak if vaccination is to be used. Countries which are normally free of the disease (marked in yellow) can still suffer incursions of the virus which can have high economic costs.

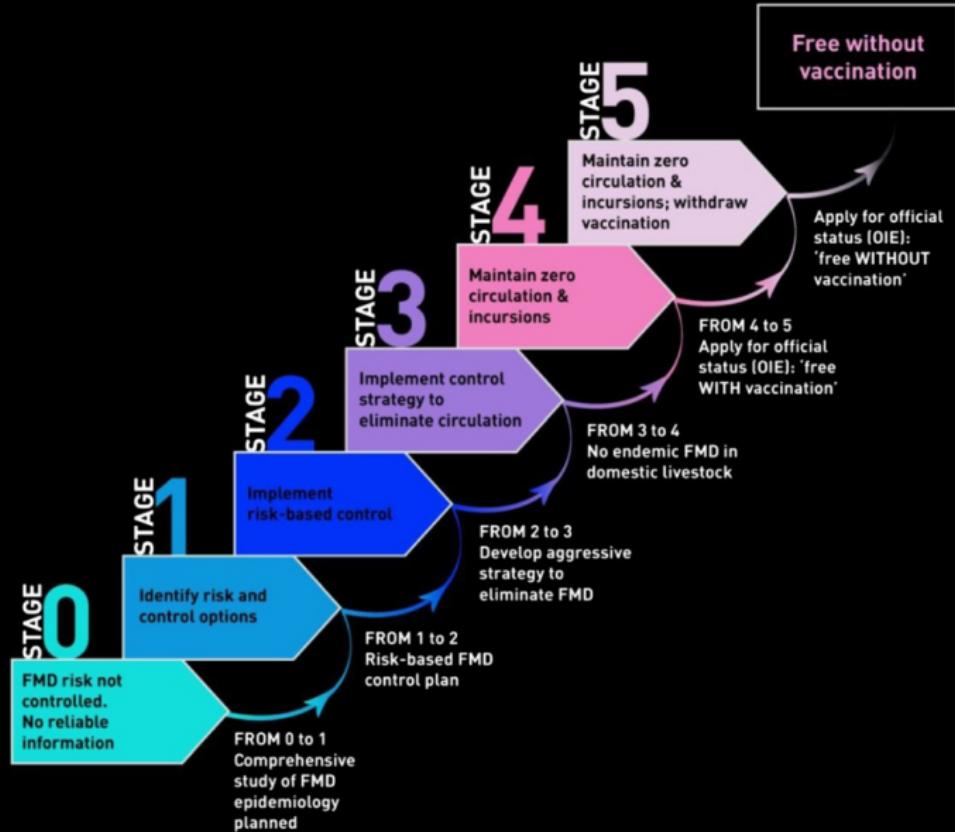


Figure 3 The FAO/EuFMD/OIE Progressive Control Pathway for FMD. The status of countries on the PCP-FMD is evaluated according to defined criteria. Countries with endemic disease are in stages 0 to 3 while countries with no endemic disease within livestock are at stage 4 or above. The image was kindly supplied by EuFMD.

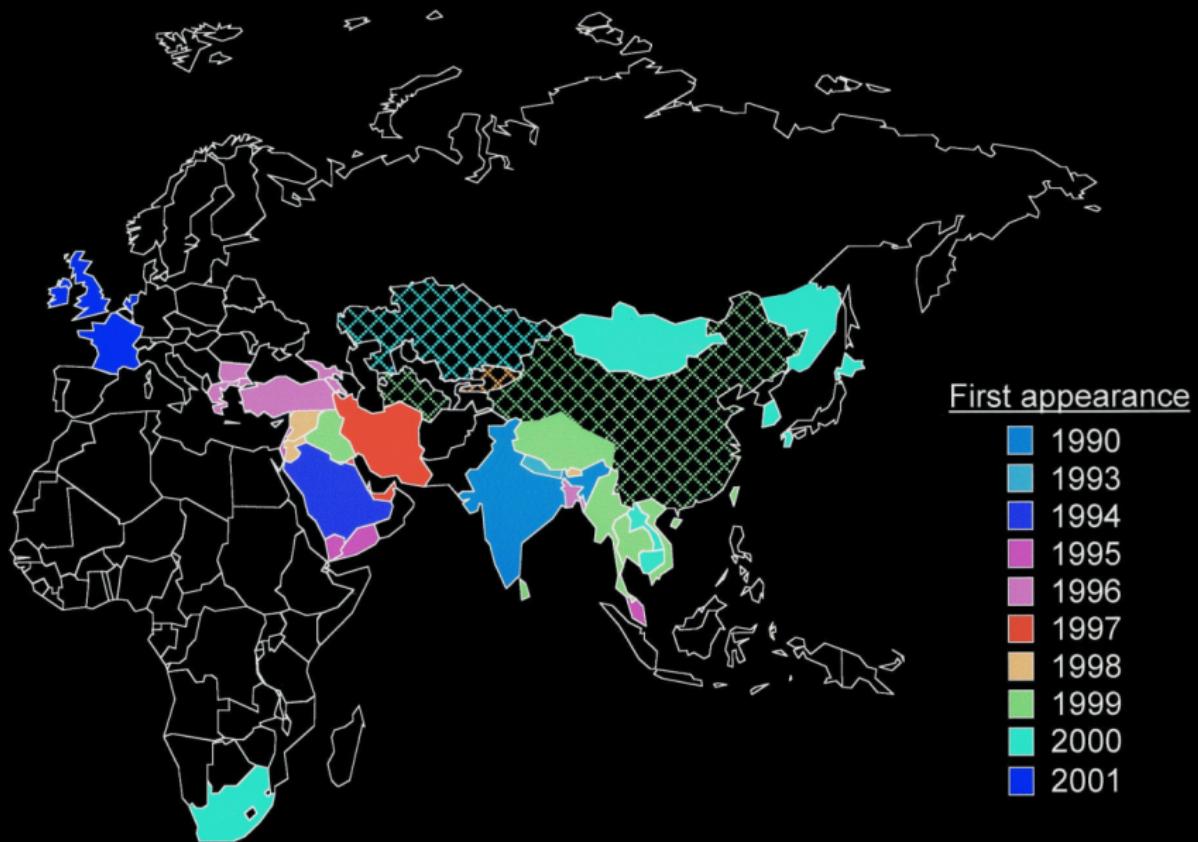
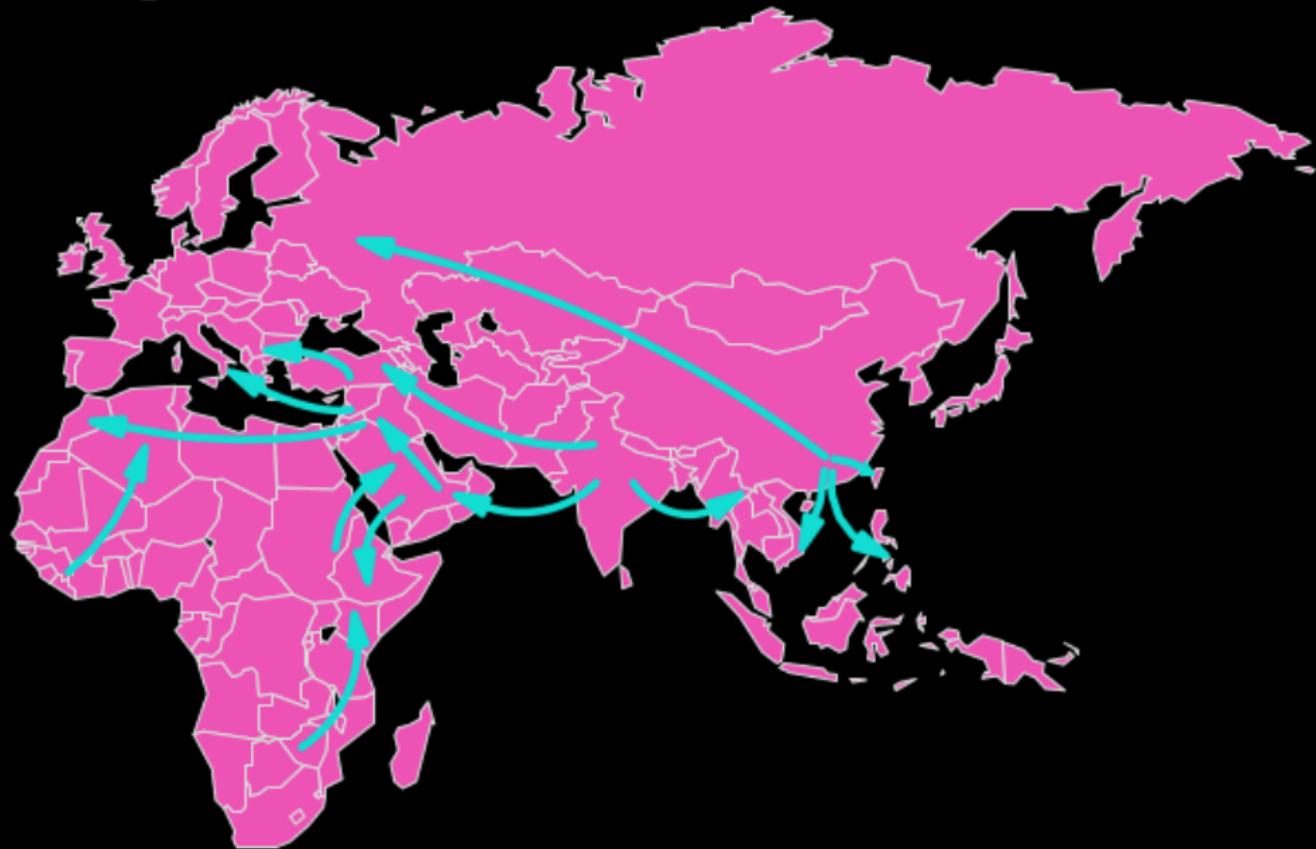


FIG. 4. The spread of the PanAsian strain of FMDV type O from its first appearance in India in 1990 until its appearance in the United Kingdom in 2001. Solid colors, PanAsian strain present; cross-hatched colors, type O present and PanAsian strain suspected. The data and map were compiled by Nick Knowles and can be found at www.iah.bbsrc.ac.uk/virus/picornaviridae/aphthovirus.

Spread of FMD in the old world



Source: WRL at IAH, Pirbright, UK

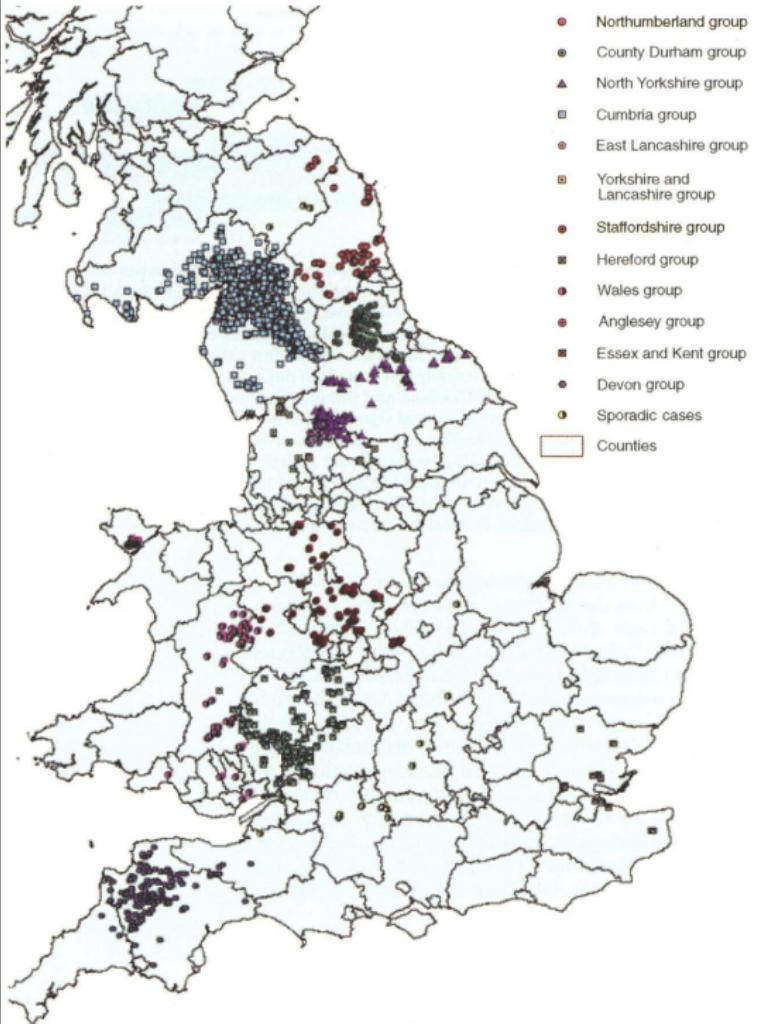
Descriptive epidemiology of the 2001 foot-and-mouth disease epidemic in Great Britain: the first five months

**J. C. GIBBENS, C. E. SHARPE, J. W. WILESMITH, L. M. MANSLEY, E. MICHALOPOULOU,
J. B. M. RYAN, M. HUDSON**

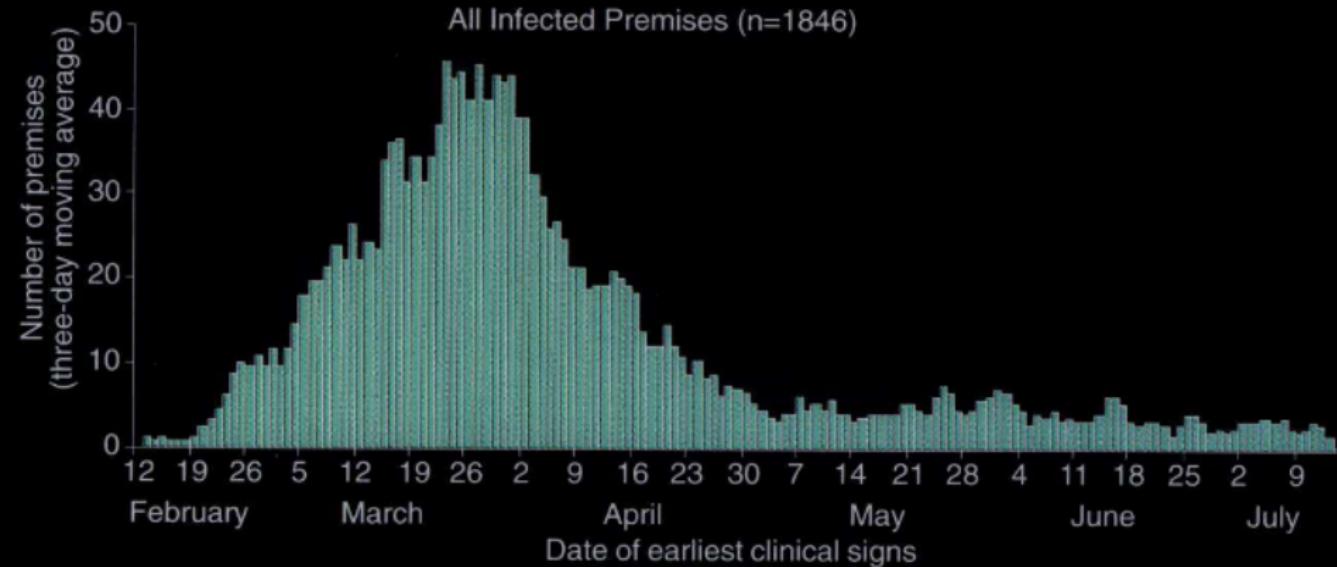
In February 2001, foot-and-mouth disease (FMD) was confirmed in Great Britain. A major epidemic developed, which peaked around 50 cases a day in late March, declining to under 10 a day by May. By mid-July, 1849 cases had been detected. The main control measures employed were livestock movement restrictions and the rapid slaughter of infected and exposed livestock. The first detected case was in south-east England; infection was traced to a farm in north-east England to which all other cases were linked. The epidemic was large as a result of a combination of events, including a delay in the diagnosis of the index case, the movement of infected sheep to market before FMD was first diagnosed, and the time of year. Virus was introduced at a time when there were many sheep movements around the country and weather conditions supported survival of the virus. The consequence was multiple, effectively primary, introductions of FMD virus into major sheep-keeping areas. Subsequent local spread from these introductions accounted for the majority of cases. The largest local epidemics were in areas with dense sheep populations and livestock dealers who were active during the key period. Most affected farms kept both sheep and cattle. At the time of writing the epidemic was still ongoing; however, this paper provides a basis for scientific discussion of the first five months.

Veterinary Record (2001)
149, 729-743

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All Infected Premises (n=1846)



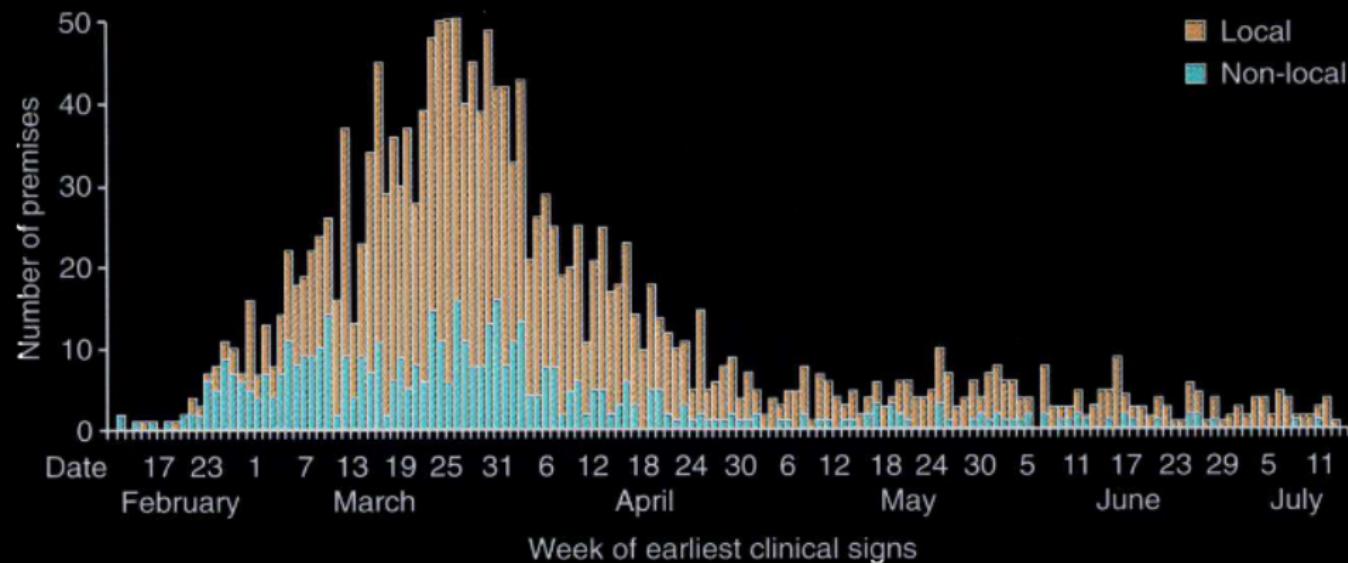


FIG 5: Epidemic curve to show number of foot-and-mouth disease infected premises with early disease each day, categorised to differentiate those within 3 km of an earlier case (local cases). (n=1847, Infected Premises with missing data excluded)

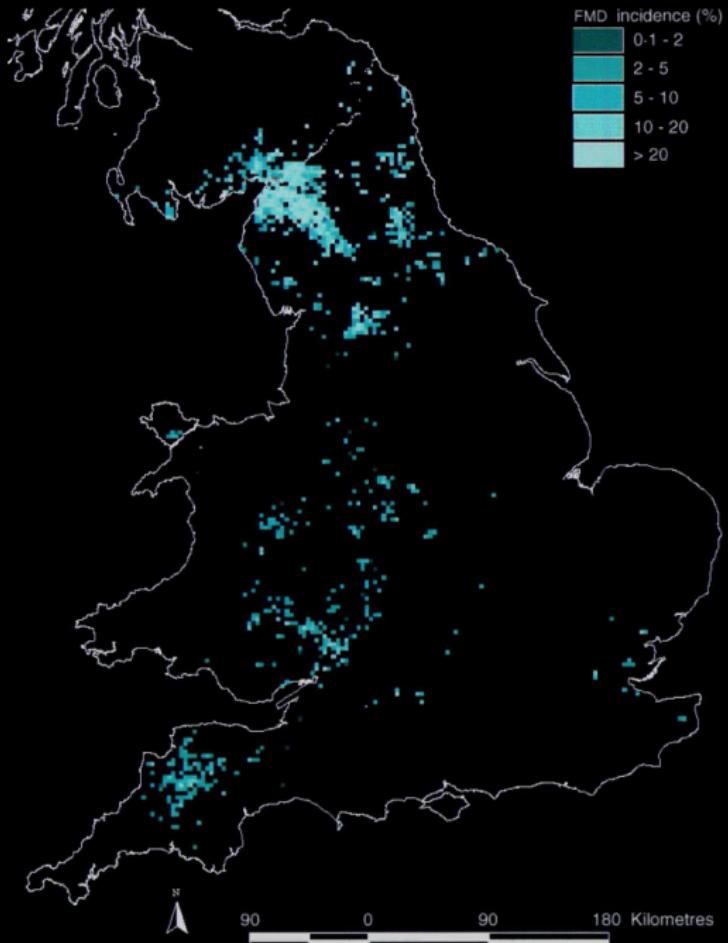


FIG 9: Cumulative incidence of foot-and-mouth disease (FMD) in Great Britain, February 10 to July 15, 2001

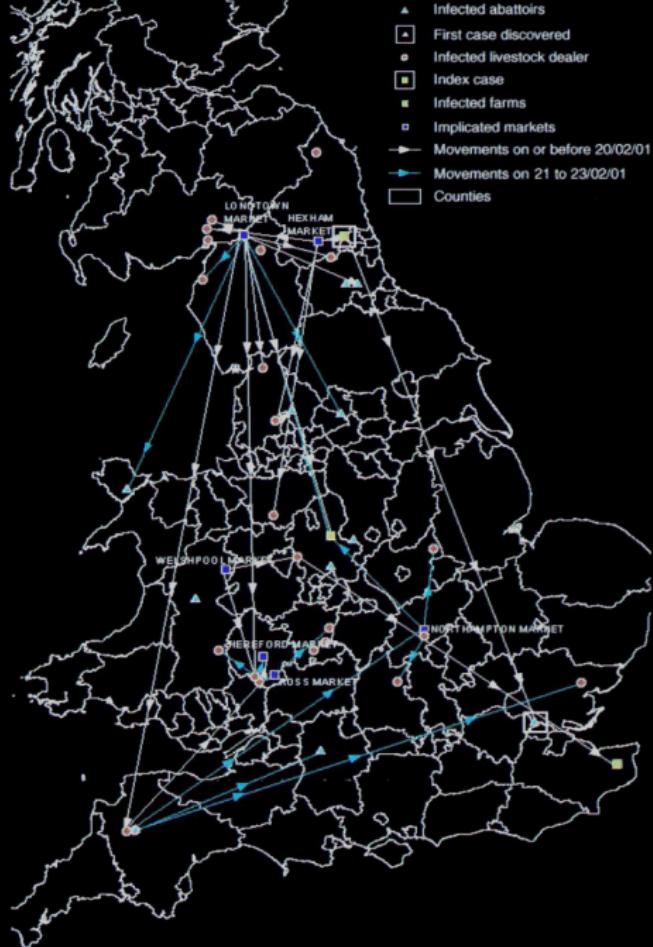


FIG 3: Movement of foot-and-mouth disease infected animals before February 23, 2001,
and location of implicated markets, abattoirs and dealers (subject to information
available on August 30, 2001)

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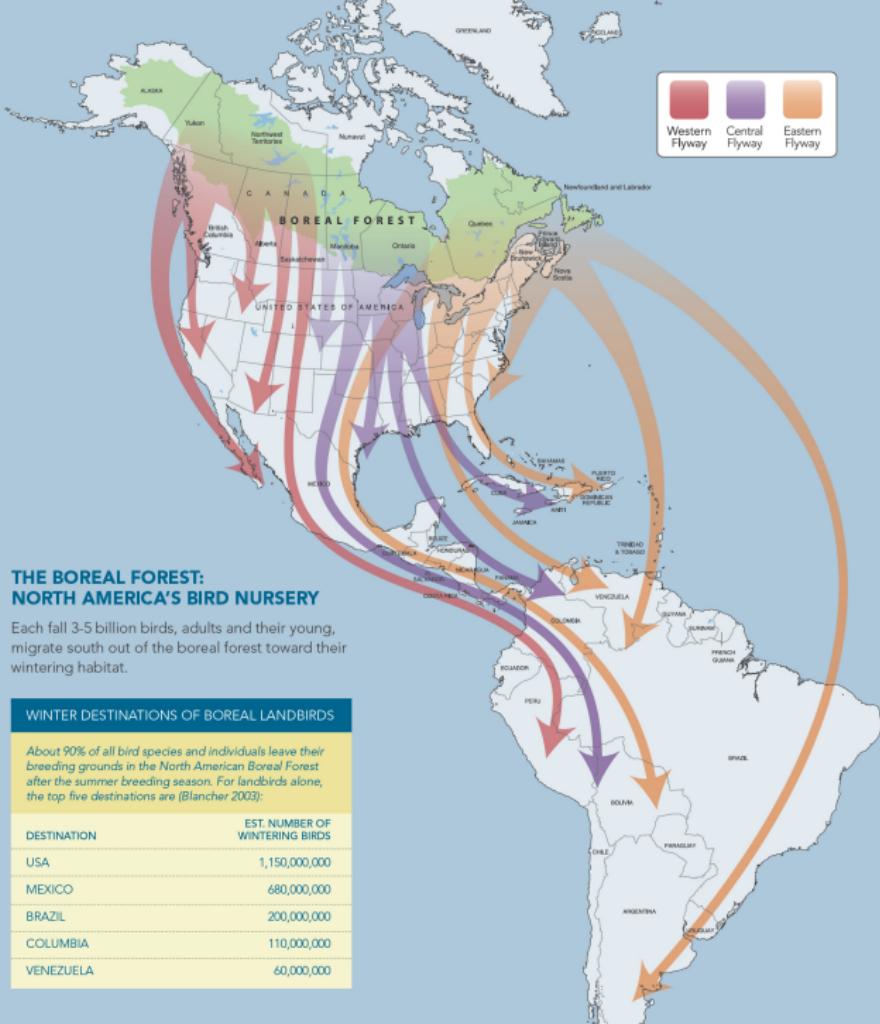
Avian influenza

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A few foot-and-mouth disease models

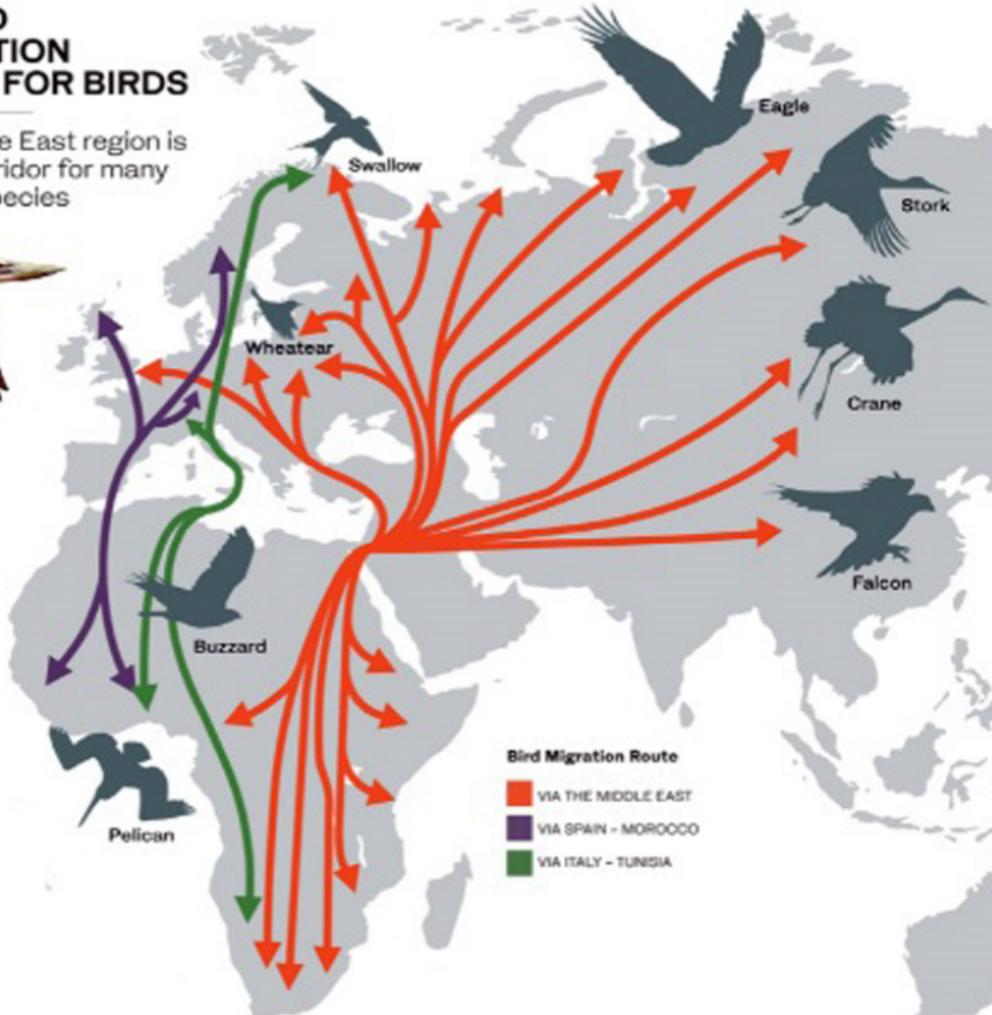
A few avian influenza models

- ▶ Avian Influenza global concern because it involves multiple bird species, both wild and livestock
- ▶ The thing with wild birds is that they fly... :)



WORLD MIGRATION ROUTE FOR BIRDS

The Middle East region is a bird corridor for many winged species



Navigating by Nature



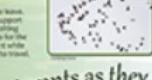
yway

.....Highways in the sky connect Alaska to the world

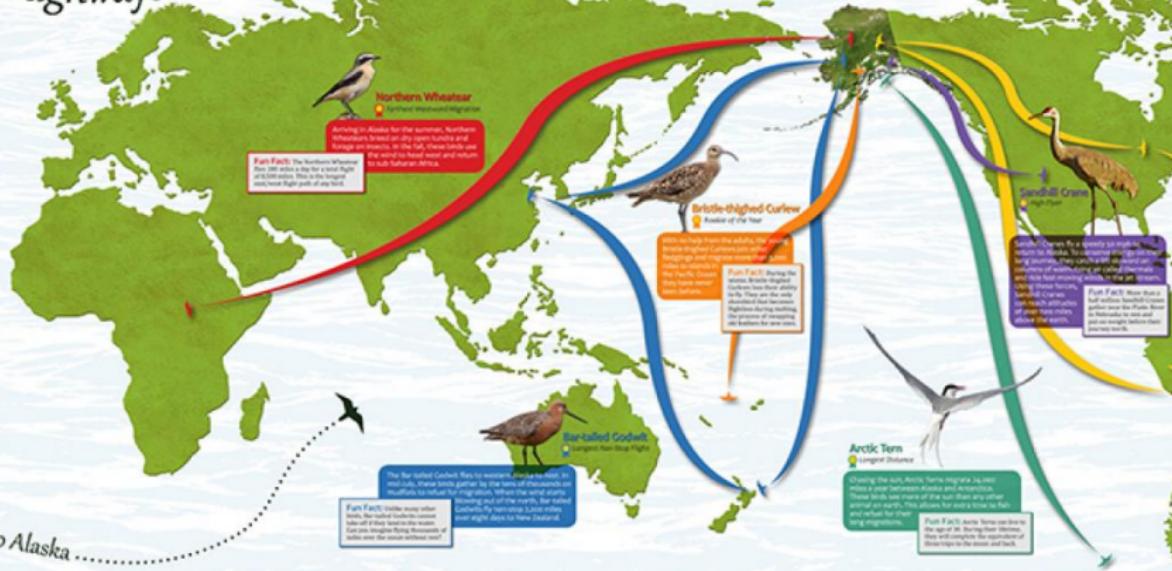


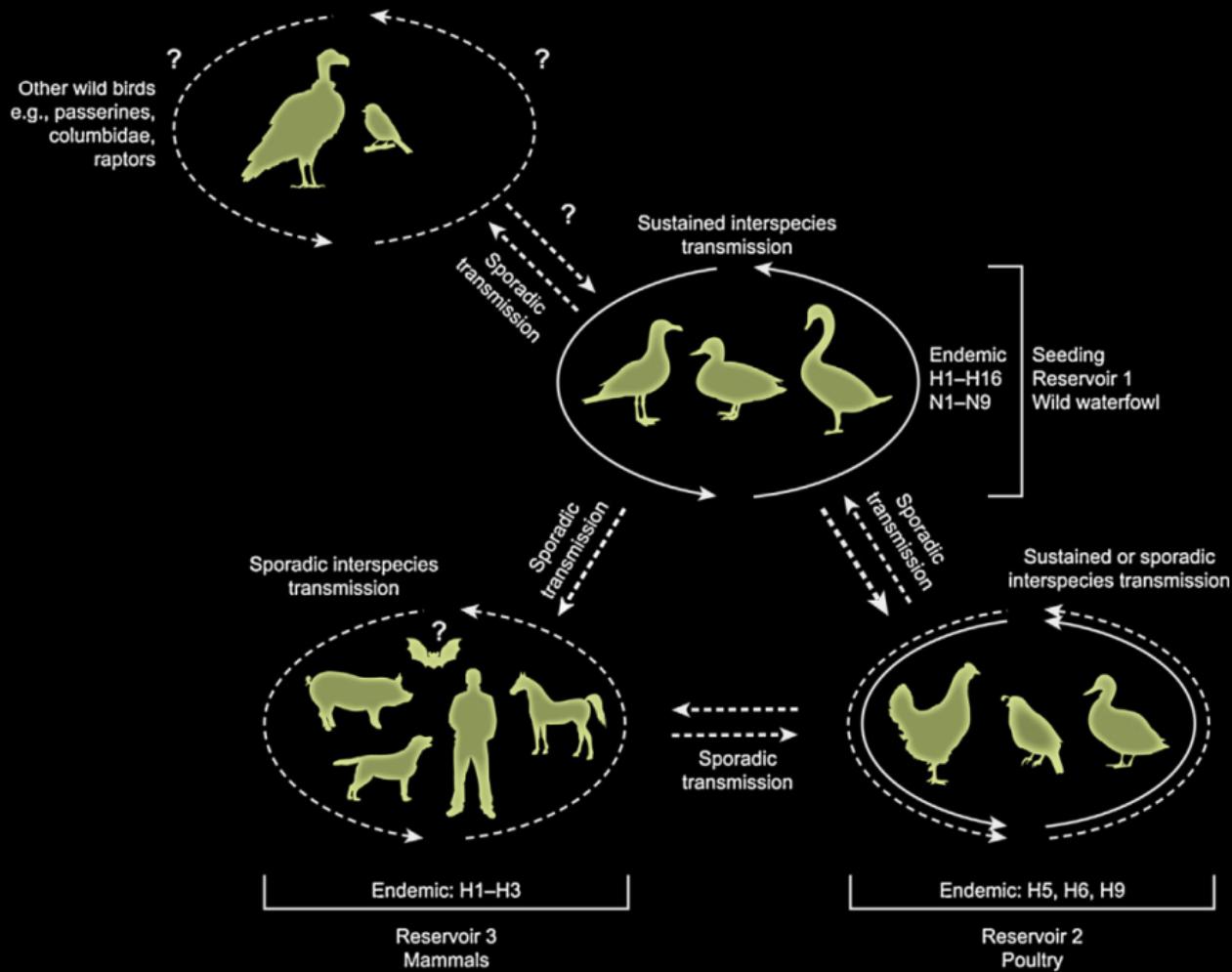
es with avian life!

here are eight identified flyways, while more than four of the eight flyways converge in Alaska, home to billions of birds every year.



migrants as they fly to Alaska





Why it is important to incorporate space

Metapopulation models

Metapopulations à la Levins

Metapopulations à la Levin

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Generic model

The movement matrix

Behaviour of the mobility component

A few sample models

Existence of a DFE

Computation of a reproduction number

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What are metapopulations?

Metapopulations are *populations of populations*.

Two main 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

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 :

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

β immigration rate between *locations*, T total number of locations
and μ 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

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

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Levins-type vs Explicit movement

Levins model and its offspring: movement is implicit

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

β 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

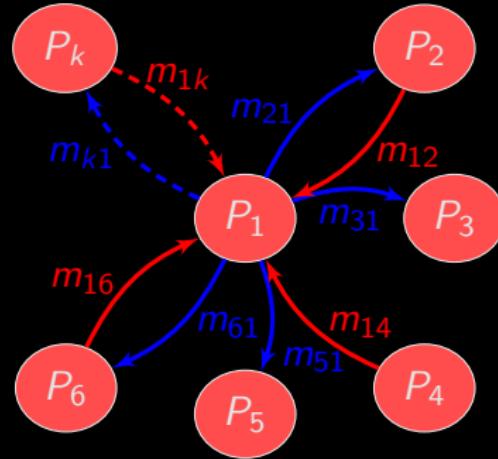
Split continuous space into N discrete geographical locations (*ptatches*)

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

Strongly connected multi-digraph

Definition 1 (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 2 (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 3 (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 4

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

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Notation

- ▶ $N_{cp}(t)$ number of individuals of compartment c in location p at time t
- ▶ $\mathbf{N}_c = (N_{c1}, \dots, N_{c|\mathcal{P}|})^T$ distribution of individuals of compartment $c \in \mathcal{C}$ among the different locations
- ▶ $\mathbf{N}^p = (N_1^p, \dots, N_{|\mathcal{P}|}^p)^T$ composition of the population in location $p \in \mathcal{P}$

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

$$m_{cpp} = - \sum_{\substack{q \in \mathcal{P} \\ q \neq p}} m_{cqp} \quad (3)$$

Then

$$N'_s = f_{cp}(N^p) + \sum_{q \in \mathcal{P}} m_{cpq} N_{cq} \quad (4)$$

Vector form of the system

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

$$\mathbf{N}'_c = f(\mathbf{N}) + \mathcal{M}_c \mathbf{N}_c \quad (5)$$

with

$$\mathcal{M}_c = \begin{pmatrix} -\sum_{k \in \mathcal{P}} m_{ck1} & m_{c12} & \cdots & m_{c1|\mathcal{P}|} \\ m_{c|\mathcal{P}|1} & m_{c|\mathcal{P}|2} & \cdots & -\sum_{k \in \mathcal{P}} m_{ck|\mathcal{P}|} \end{pmatrix} \quad (6)$$

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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 $m_{ij} > 0 \quad \forall i, j = 1, \dots, n$. 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

$$\mathcal{M}_c = \begin{pmatrix} -\sum_{k \in \mathcal{P}} m_{ck1} & m_{c12} & \cdots & m_{c1|\mathcal{P}|} \\ m_{c|\mathcal{P}|1} & m_{c|\mathcal{P}|2} & \cdots & -\sum_{k \in \mathcal{P}} m_{ck|\mathcal{P}|} \end{pmatrix} \quad (6)$$

is the **movement matrix**

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

\mathcal{M}_c describes

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

Properties of the movement matrix \mathcal{M}

First, remark $-\mathcal{M}_c$ is a Laplacian matrix

Lemma 5

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

For complete proof of Lemma 5 and Proposition 6 (next page), see Arino, Bajeux & Kirkland, BMB 2019

Proposition 6 (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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Assume no within-location dynamics, just movement. Then (5) takes the form

$$\mathbf{N}'_c = \mathcal{M}_c \mathbf{N}_c \quad (7)$$

Theorem 7

For a given compartment $c \in \mathcal{C}$, suppose that the movement matrix \mathcal{M}_c is irreducible. Then for any $\mathbf{N}_c(0) > 0$, (7) satisfies

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

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

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

$$T'_p = D_p(T_p) + \sum_{c \in \mathcal{C}} \sum_{q \in \mathcal{P}} m_{cpq} N_{cq} \quad (8)$$

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

$$D_p(T_p) = b_p - d_p T_p \tag{9}$$

Vector / matrix form of the equation

Assuming demography is of the form (9), write (8) in vector form

$$\mathbf{T}' = \mathbf{b} - \mathbf{dT} + \sum_{c \in \mathcal{C}} \mathcal{M}_c \mathbf{N}_c \quad (10)$$

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.,

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

Then

$$\begin{aligned}\mathbf{T}' &= \mathbf{b} - \mathbf{dT} + \mathcal{M} \sum_{c \in \mathcal{C}} \mathbf{N}_c \\ &= \mathbf{b} - \mathbf{dT} + \mathcal{M} \mathbf{T}\end{aligned}\tag{11}$$

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 6(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 6(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)

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Existence of a DFE

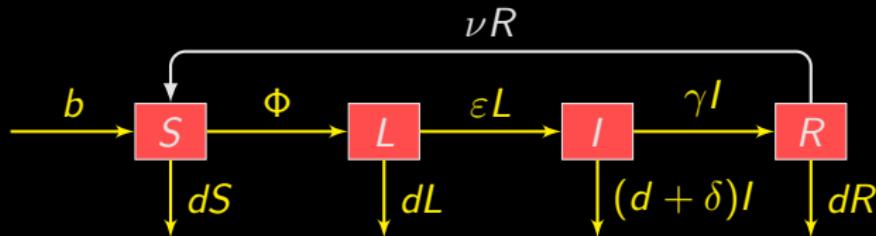
Computation of a reproduction number

Computational considerations

A few foot-and-mouth disease models

A few avian influenza models

The toy SLIRS model in patches



$$S' = b + \nu R - \Phi - dS \quad (12a)$$

$$L' = \Phi - (\varepsilon + d)L \quad (12b)$$

$$I' = \varepsilon L - (\gamma + d + \delta)I \quad (12c)$$

$$R' = \gamma I - (\nu + d)R \quad (12d)$$

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

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

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

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

$$S'_p = b_p + \nu_p R_p - \Phi_p - d_p S_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (13a)$$

$$L'_p = \Phi_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q \quad (13b)$$

$$I'_p = \varepsilon_p L_p - (\gamma_p + d_p) I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (13c)$$

$$R'_p = \gamma_p I_p - (\nu_p + d_p) R_p + \sum_{q \in \mathcal{P}} m_{Rpq} R_q \quad (13d)$$

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (13e)$$

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

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

$$S'_{sp} = b_{sp} + \nu_{sp}R_{sp} - \Phi_{sp} - d_{sp}S_{sp} + \sum_{q \in \mathcal{P}} m_{Sspq}S_{sq} \quad (14a)$$

$$L'_{sp} = \Phi_{sp} - (\varepsilon_{sp} + d_{sp})L_{sp} + \sum_{q \in \mathcal{P}} m_{Lspq}L_{sq} \quad (14b)$$

$$I'_{sp} = \varepsilon_{sp}L_{sp} - (\gamma_{sp} + d_{sp})I_{sp} + \sum_{q \in \mathcal{P}} m_{Isdq}I_{sq} \quad (14c)$$

$$R_{sp} = \gamma_{sp}I_{sp} - (\nu_{sp} + d_{sp})R_{sp} + \sum_{q \in \mathcal{P}} m_{Rspq}R_{sq} \quad (14d)$$

with incidence

$$\Phi_{sp} = \sum_{k \in \mathcal{S}} \beta_{skp} \frac{S_{sp} I_{kp}}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (14e)$$

- ▶ 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)

$$S'_{pq} = b_{pq} + \nu_{pq} R_{pq} - \Phi_{pq} - d_{pq} S_{pq} + \sum_{k \in \mathcal{P}} m_{Spqk} S_{pk} \quad (15a)$$

$$I'_{pq} = \Phi_{pq} - (\varepsilon_{pq} + d_{pq}) I_{pq} + \sum_{k \in \mathcal{P}} m_{Lpqk} L_{pk} \quad (15b)$$

$$L'_{pq} = \varepsilon_{pq} L_{pq} - (\gamma_{pq} + d_{pq}) I_{pq} + \sum_{k \in \mathcal{P}} m_{Ipqk} I_{pk} \quad (15c)$$

$$R'_{pq} = \gamma_{pq} I_{pq} - (\nu_{pq} + d_{pq}) R_{pq} + \sum_{k \in \mathcal{P}} m_{Rpqk} R_{pk} \quad (15d)$$

with incidence

$$\Phi_{pq} = \sum_{k \in \mathcal{P}} \beta_{pqk} \frac{S_{pq} I_{kq}}{N_p^{q_q}}, \quad q_q = \{0, 1\} \quad (15e)$$

- ▶ 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

$$S'_p = b_p - \Phi_p - d_p S_p + \nu_p R_p + \sum_{q \in \mathcal{P}} m_{Spq} S_q \quad (16a)$$

$$L'_p = \Phi_p - (\varepsilon_p + d_p) L_p + \sum_{q \in \mathcal{P}} m_{Lpq} L_q \quad (16b)$$

$$I'_p = \varepsilon_p L_p - (\gamma_p + d_p) I_p + \sum_{q \in \mathcal{P}} m_{Ipq} I_q \quad (16c)$$

$$R'_p = \gamma_p I_p - (\nu_p + d_p) R_p + \sum_{q \in \mathcal{P}} m_{Rpq} R_q \quad (16d)$$

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \quad q_p \in \{0, 1\} \quad (16e)$$

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

Why it is important to incorporate space

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Metapopulations à la Levin

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Disease free equilibrium

The model is at equilibrium if the time derivatives are zero

Definition 8 (Metapopulation DFE)

In the case of system (16), 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 (14), replace L_p with L_{sp} and I_p with I_{sp} , for (15), replace L_p by L_{pp} and I_p by I_{pp} . To simplify notation, we could write L_\bullet and I_\bullet)

Assume (16) 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:

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

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

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}, ν 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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Computing the basic reproduction number \mathcal{R}_0

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

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

Differentiate w.r.t. Ξ :

$$D\mathcal{F} = \begin{pmatrix} \frac{\partial \Phi_1}{\partial L_1} & \dots & \frac{\partial \Phi_1}{\partial L_{|\mathcal{P}|}} & \frac{\partial \Phi_1}{\partial l_1} & \dots & \frac{\partial \Phi_1}{\partial l_{|\mathcal{P}|}} \\ \vdots & & \vdots & \vdots & & \vdots \\ \frac{\partial \Phi_{|\mathcal{P}|}}{\partial L_1} & \dots & \frac{\partial \Phi_{|\mathcal{P}|}}{\partial L_{|\mathcal{P}|}} & \frac{\partial \Phi_{|\mathcal{P}|}}{\partial l_1} & \dots & \frac{\partial \Phi_{|\mathcal{P}|}}{\partial l_{|\mathcal{P}|}} \\ 0 & \dots & 0 & 0 & \dots & 0 \\ \vdots & & \vdots & \vdots & & \vdots \\ 0 & \dots & 0 & 0 & \dots & 0 \end{pmatrix}$$

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 (2×2 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

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

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

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 9

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

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

Then the DFE

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

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

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

Some remarks about \mathcal{R}_0

The expression for \mathcal{R}_0 in Theorem 9 is exact

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

Indeed, by Theorem 6(3) and more importantly (often \mathcal{M} is irreducible), Theorem 6(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

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

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

Theorem 10

Let \mathcal{R}_0 be defined as in Theorem 9 and use proportional incidence
 $\Phi_p = \beta_p S_p I_p / N_p$. If $\mathcal{R}_0 < 1$, then the DFE of system (16) is
globally asymptotically stable

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

In the case in which movement is equal for all compartments and there is no disease death, a comparison theorem argument can be used as in Theorem 10 to show that if $\mathcal{R}_0 < 1$, then the DFE of the $|\mathcal{S}| |\mathcal{P}|$ -SLIRS (14) is globally asymptotically stable.

Theorem 11

For system (14) 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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Set up parameters

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

Work out movement matrix

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

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

Write down indices of the different state variable types

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

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

Set up IC and time

```
# Set initial conditions. For example, we start with 2
# infectious individuals in Canada.

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

Set up β to avoid blow up

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

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

```
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

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Woolhouse and collaborators

Ringa & Bauch

A few avian influenza models

Models à la Levins

Space is implicit: count infected herds

An analysis of foot-and-mouth-disease epidemics in the UK

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From: Foot-and-Mouth Disease: Current Perspectives. Edited by: Francisco Sobrino and Esteban Domingo

Chapter 13

Mathematical Models of the Epidemiology and Control of Foot-and-Mouth Disease

Mark E. J. Woolhouse

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Dynamics and control of foot-and-mouth disease in endemic countries: A pair approximation model



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HIGHLIGHTS

- Traditional models of FMD focus on control and dynamics in disease-free settings.
- We analyze long-term dynamics and control of FMD in endemic countries.
- Success of vaccination depends on rates of vaccine and natural immunity waning.
- Prophylactic vaccination performs better than ring vaccination.
- More mathematical models applicable to FMD-endemic countries need to be developed.

Why it is important to incorporate space

Metapopulation models

A few foot-and-mouth disease models

A few avian influenza models

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Highly pathogenic avian influenza H5N8 in south-west France 2016–2017: A modeling study of control strategies



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