Adding space to FMD and AI models

Julien Arino

April 2023

Why it is important to incorporate space

Metapopulation models

A few foot-and-mouth disease models

A few avian influenza models

- Why it is important to incorporate space
  - General considerations about space-and-time spread
  - Spatial aspects in animal diseases
  - Foot-and-mouth disease
  - Avian influenza

- Metapopulation models

- A few foot-and-mouth disease models

- A few avian influenza models

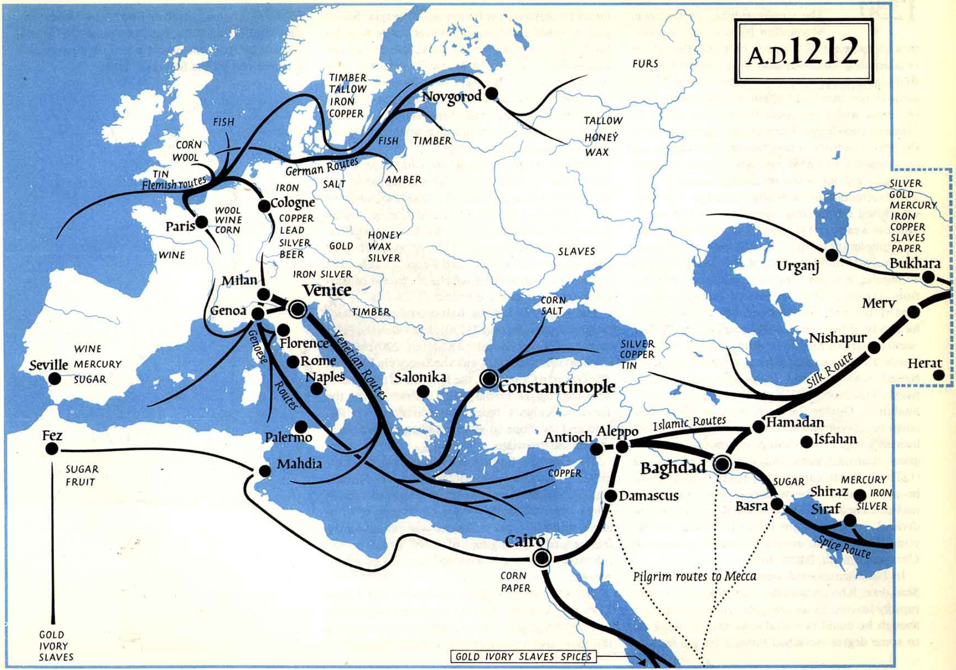
Why it is important to incorporate space

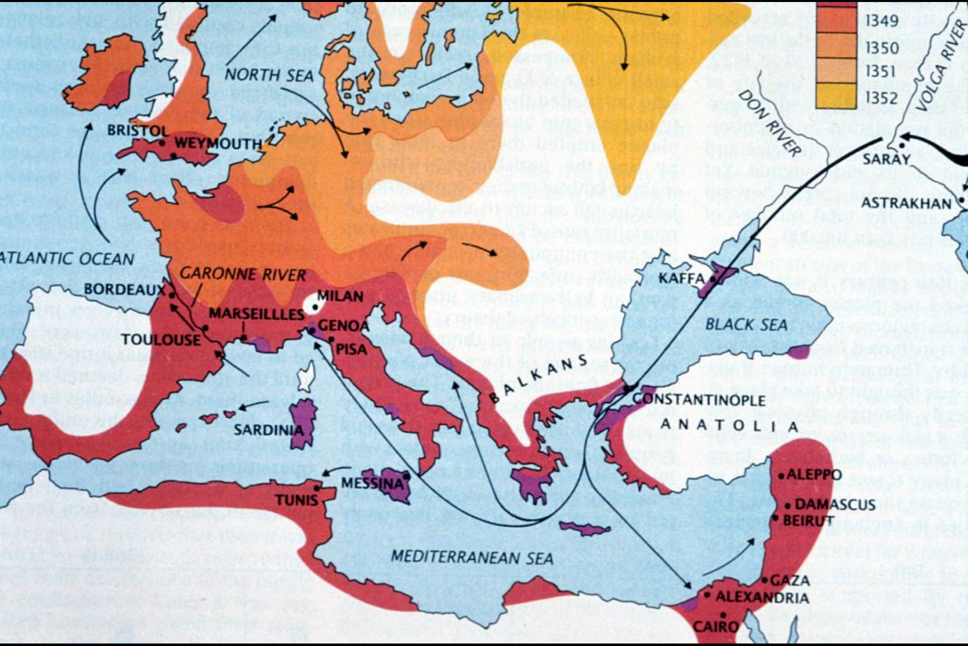
- General considerations about space-and-time spread
- Spatial aspects in animal diseases
- Foot-and-mouth disease
- Avian influenza

Metapopulation models

A few foot-and-mouth disease models

A few avian influenza models


A.D.1212
FURS
TIMBER
TALLOW
IRON
COPPER
Novgorod
FISH
CORN
WOOL
TIN
Flemish routes
German Routes
FISH
TIMBER
TALLOW
HONEY
WAX
AMBER
IRON
SALT
Cologne
COPPER
LEAD
SILVER
BEER
Paris
WOOL
WINE
CORN
WINE
GOLD
HONEY
WAX
SILVER
SLAVES
SILVER
GOLD
MERCURY
IRON
COPPER
SLAVES
PAPER
Urganj
Bukhara
IRON SILVER
Milan
Venice
Genoa
TIMBER
CORN
SALT
Merv
Nishapur
Herat
Silk Route
Genoese Routes
Venetian Routes
Florence
Rome
Naples
Salonika
Constantinople
SILVER
COPPER
TIN
WINE
Seville
MERCURY
SUGAR
Palermo
Fez
Mahdia
Antioch
Aleppo
Islamic Routes
Hamadan
Isfahan
SUGAR
FRUIT
COPPER
Baghdad
SUGAR
MERCURY
Shiraz
IRON
SILVER
Siraf
Basra
Damascus
Spice Route
Cairo
CORN
PAPER
Pilgrim routes to Mecca
GOLD
IVORY
SLAVES
GOLD IVORY SLAVES SPICES



1349
1350
1351
1352
VOLGA RIVER
DON RIVER
SARAY
ASTRAKHAN
NORTH SEA
BRISTOL
WEYMOUTH
ATLANTIC OCEAN
GARONNE RIVER
BORDEAUX
MILAN
MARSEILLLES
GENOA
TOULOUSE
PISA
KAFFA
BLACK SEA
BALKANS
CONSTANTINOPLE
ANATOLIA
SARDINIA
MESSINA
TUNIS
ALEPPO
DAMASCUS
BEIRUT
MEDITERRANEAN SEA
GAZA
ALEXANDRIA
CAIRO

The Black Death: a few facts

- First of the middle ages plagues to hit Europe
- Affected Afro-Eurasia from 1346 to 1353
- Europe 1347-1351
- Killed 75-200M in Eurasia & North Africa
- Killed 30-60% of European population

Plague control measures

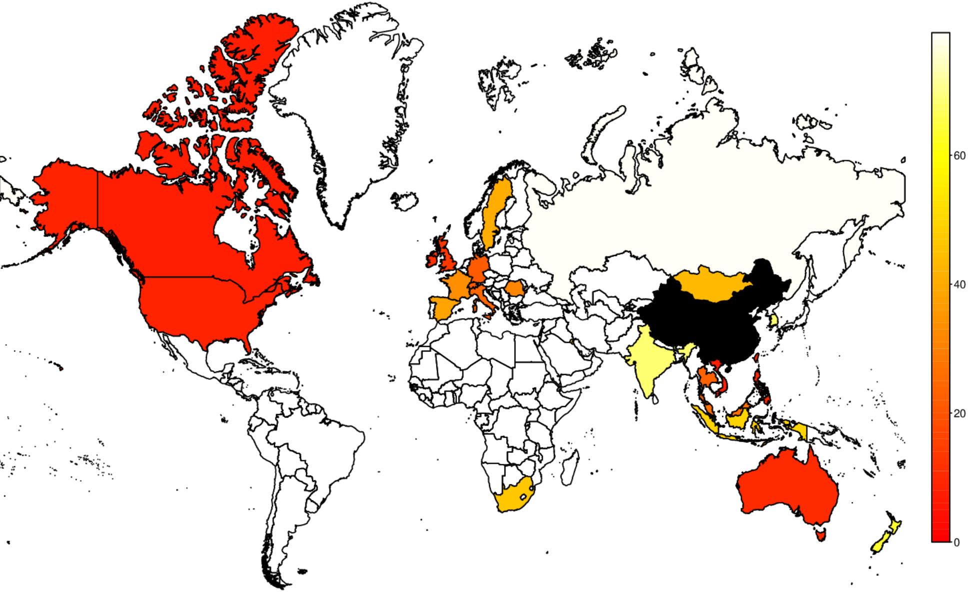
- Lazzarettos of Dubrovnik 1377 (30 days)
- Quarantena of Venice 1448 (40 days)
- Isolation of known or suspected cases as well as persons who had been in contact with them, at first for 14 days and gradually increased to 40 days
- Improvement of sanitation: development of pure water supplies, garbage and sewage disposal, food inspection
- Find and kill a snake, chop it into pieces and rub the various parts over swollen buboes. (Snake, synonymous with Satan, was thought to draw the disease out of the body as evil would be drawn to evil)

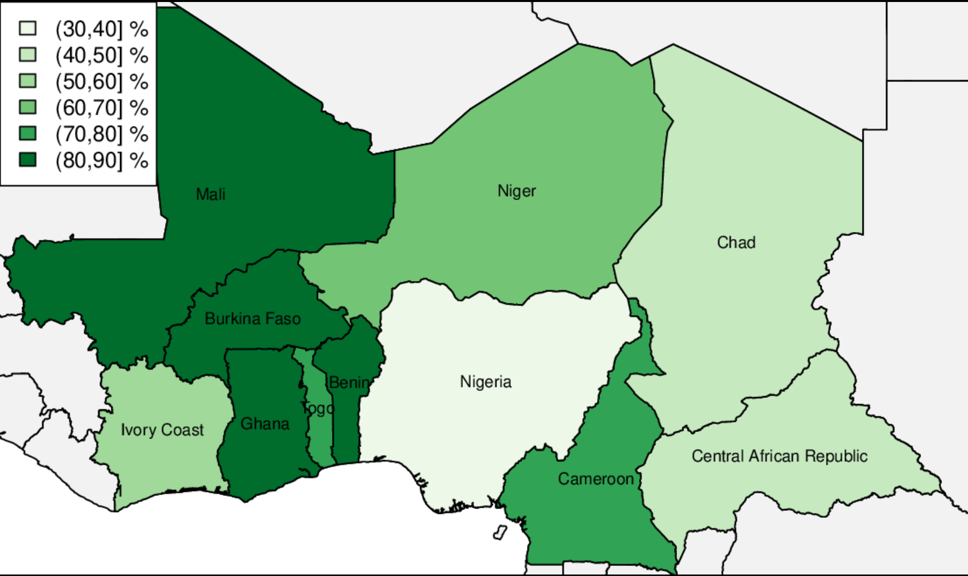
Pathogen spread has evolved with mobility

- Pathogens travel along trade routes
- In ancient times, trade routes were relatively easy to comprehend
- With acceleration and globalization of mobility, things have changed

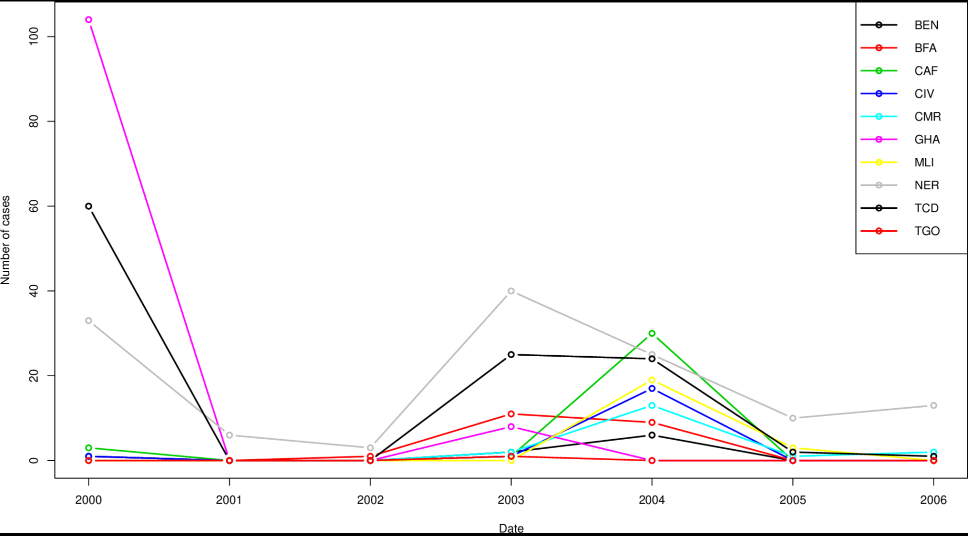

Yards
50
0
50
100
150
200
× Pump
• Deaths from cholera
OXFORD STREET
DEAN STREET
WARDOUR STREET
GT. MARLBOROUGH ST.
BROAD STREET
REGENT STREET
KING STREET
CONDUIT STREET
SAVILLE ROW
GOLDEN SQUARE
BREWER STREET
NEW BOND STREET
REGENTS QUADRANT
PICCADILLY

Countries with SARS cases (WHO/Dec 2003)

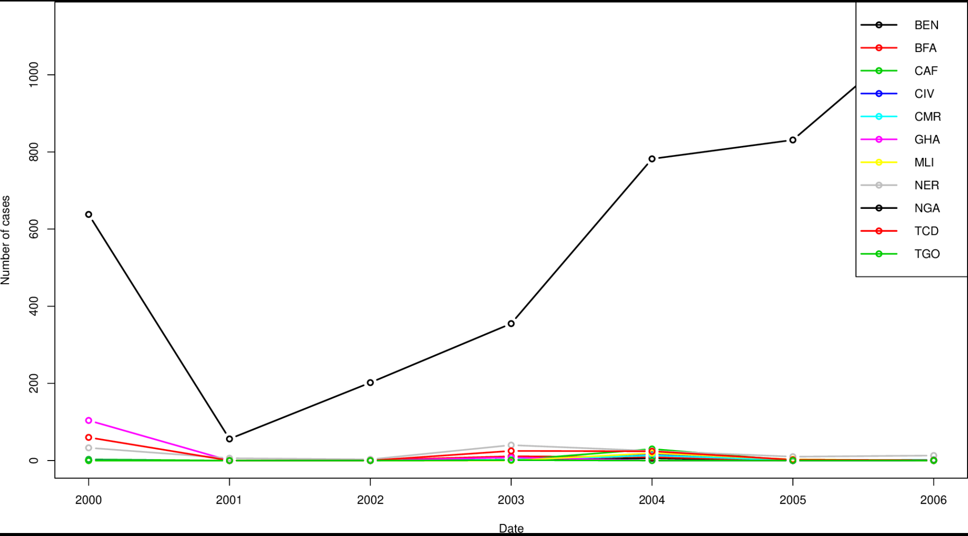




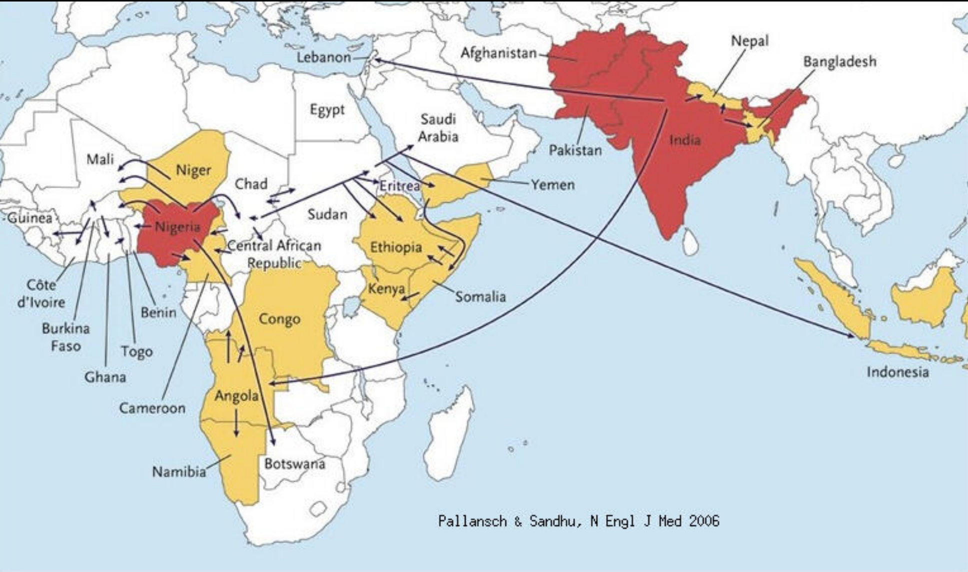
(30,40] %
(40,50] %
(50,60] %
(60,70] %
(70,80] %
(80,90] %
Mali
Niger
Chad
Burkina Faso
Benin
Nigeria
Togo
Ghana
Ivory Coast
Central African Republic
Cameroon



Number of cases
0
20
40
60
80
100
2000
2001
2002
2003
2004
2005
2006
Date
BEN
BFA
CAF
CIV
CMR
GHA
MLI
NER
TCD
TGO



BEN
BFA
CAF
CIV
CMR
GHA
MLI
NER
NGA
TCD
TGO
Number of cases
0
200
400
600
800
1000
2000
2001
2002
2003
2004
2005
2006
Date



Pallansch & Sandhu, N Engl J Med 2006

Why it is important to incorporate space

- General considerations about space-and-time spread
- Spatial aspects in animal diseases
- Foot-and-mouth disease
- Avian influenza

Metapopulation models

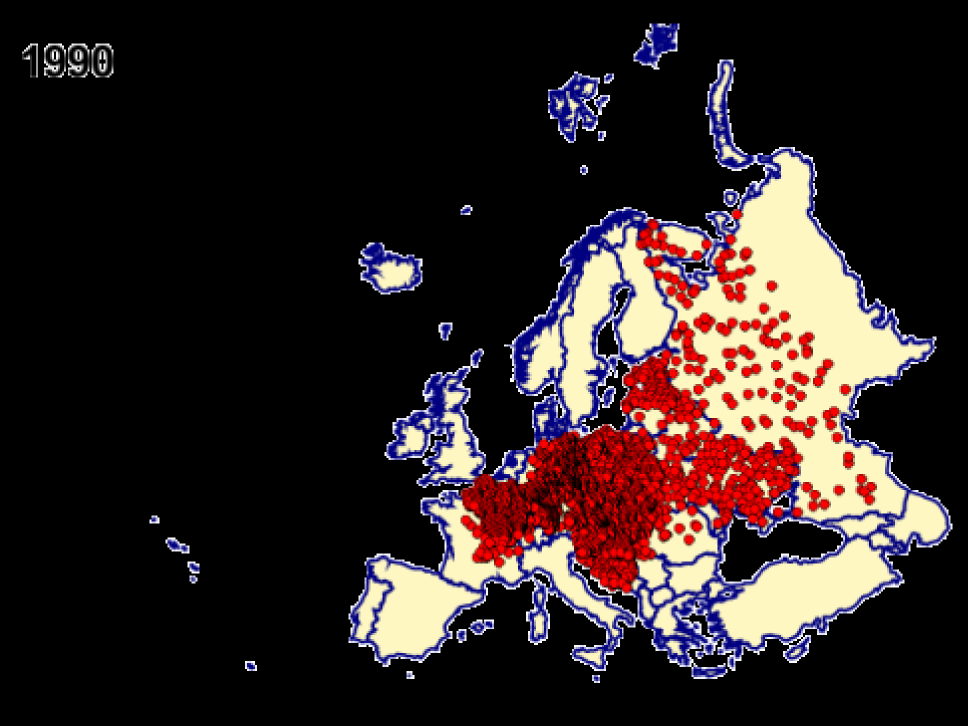
A few foot-and-mouth disease models

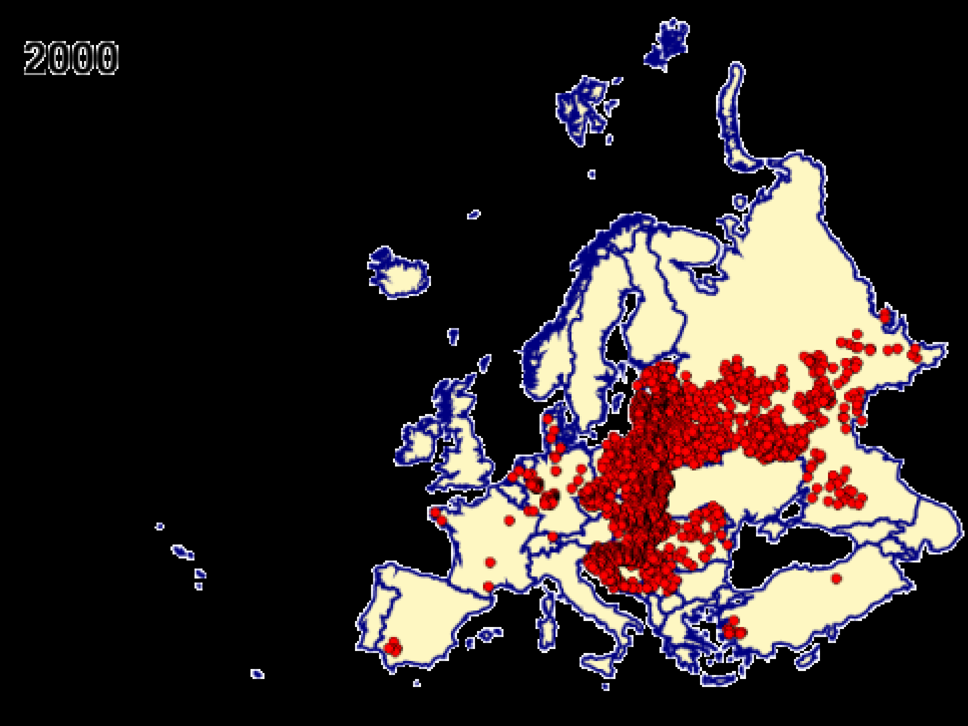
A few avian influenza models

Diseases in wild animals

Spread typically follows travelling wave patterns

Next slides: cases of rabies


1990


2000


2010

Diseases in livestock

Situation is more complicated

Why it is important to incorporate space

- General considerations about space-and-time spread
- Spatial aspects in animal diseases
- Foot-and-mouth disease
- Avian influenza

Metapopulation models

A few foot-and-mouth disease models

A few avian influenza models

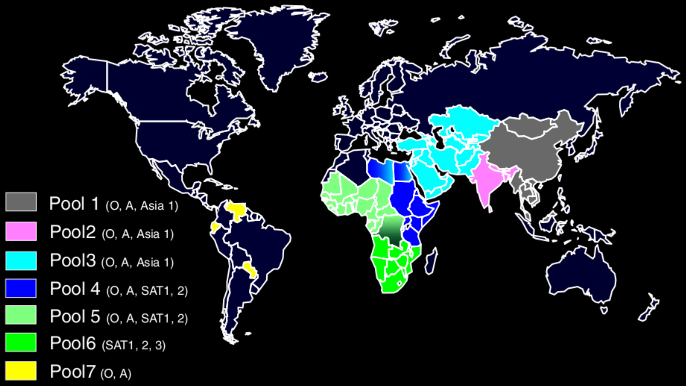


Figure 2 Geographical distribution of seven pools of foot-and mouth disease viruses. Serotype O FMDV is the most widely distributed serotype of the virus (in 6 of the 7 indicated virus pools) whereas, in contrast, SAT3 is only present in pool 6 (within southern Africa). The Asia-1, SAT1 and SAT2 serotypes 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.

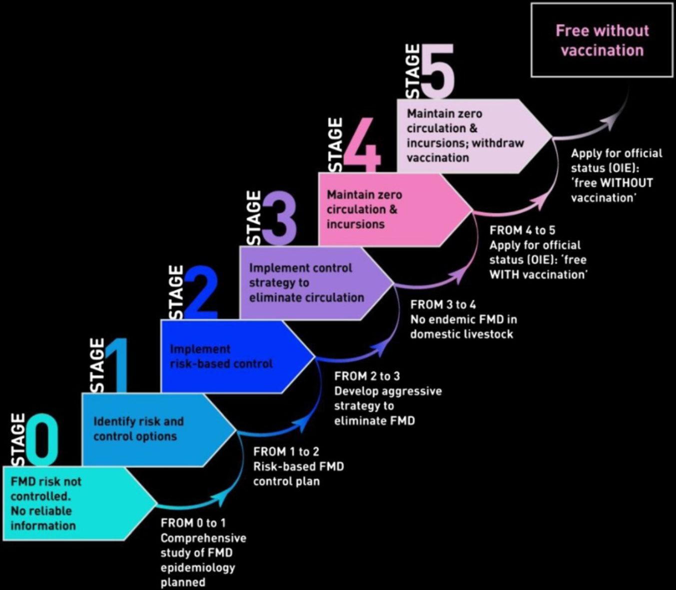


Figure 3 The FAO/EuFMD/OIE Progressive Control Pathway for FMD. The status of countries on the PCP-FMD is evaluated according to defined criteria. Countries with endemic disease are in stages 0 to 3 while countries with no endemic disease within livestock are at stage 4 or above. The image was kindly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

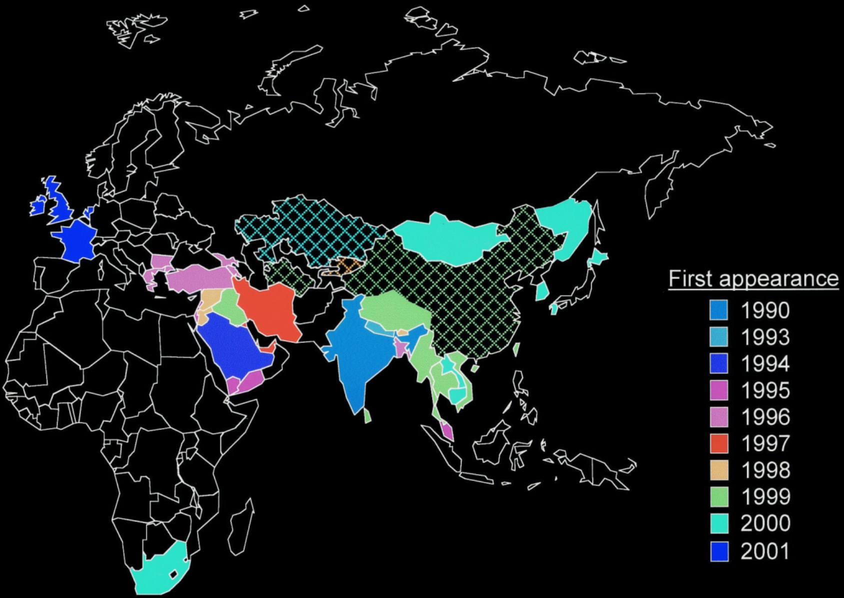
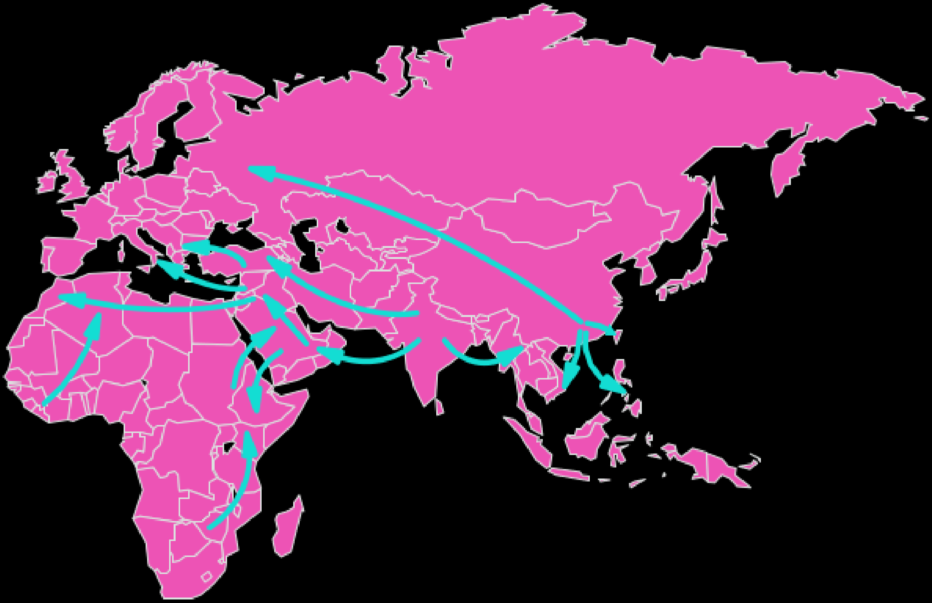


FIG. 4. The spread of the PanAsian strain of FMDV type O from its first appearance in India in 1990 until its appearance in the United Kingdom in 2001. Solid colors, PanAsian strain present; cross-hatched colors, type O present and PanAsian strain suspected. The data and map were compiled by Nick Knowles 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

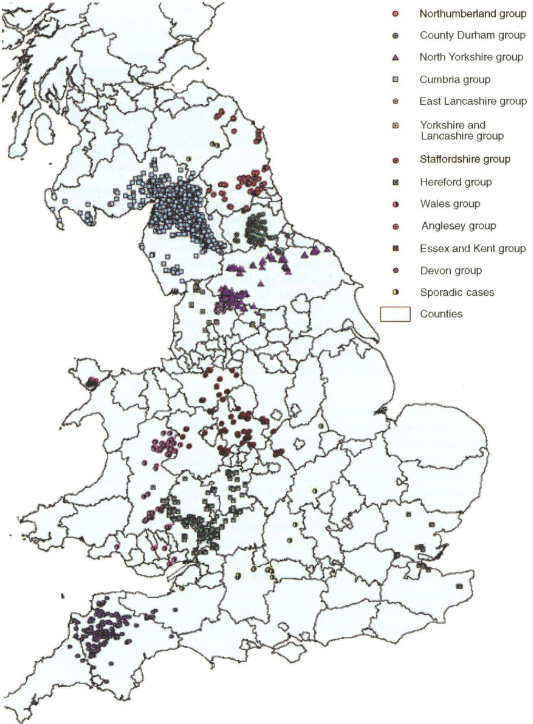
Descriptive epidemiology of the 2001 foot-and-mouth disease epidemic in Great Britain: the first five months

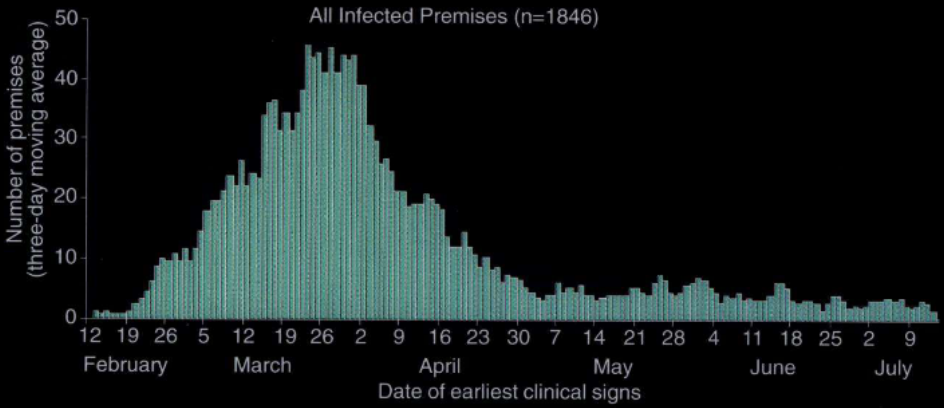
J. C. Gibbens, C. E. Sharpe, J. W. Wilesmith, L. M. Mansley, E. Michalopoulou, J. B. M. Ryan, M. Hudson

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

J. C. Gibbens, BVetMed, MSc, MSc, MRCVS,
J. W. Wilesmith, BVSc, MRCVS, HonMFPHM, State Veterinary Service, DEFRA, 1A Page Street, London SW1P 4PQ
C. E. Sharpe, BVetMed, MSc, MRCVS, State


Northumberland group
County Durham group
North Yorkshire group
Cumbria group
East Lancashire group
Yorkshire and Lancashire group
Staffordshire group
Hereford group
Wales group
Anglesey group
Essex and Kent group
Devon group
Sporadic cases
Counties



All Infected Premises (n=1846)
Number of premises
(three-day moving average)
50
40
30
20
10
0
12 19 26 5 12 19 26 2 9 16 23 30 7 14 21 28 4 11 18 25 2 9
February
March
April
May
June
July
Date of earliest clinical signs

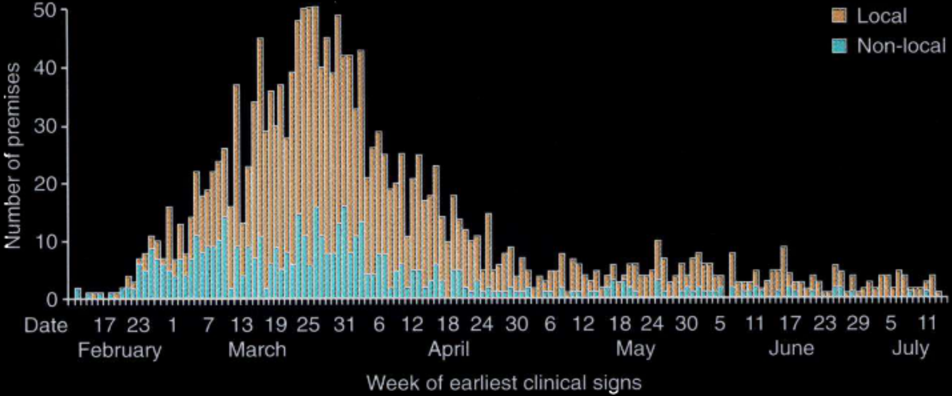


FIG 5: Epidemic curve to show number of foot-and-mouth disease infected premises with early disease each day, categorised to differentiate those within 3 km of an earlier case (local cases). (n=1847, Infected Premises with missing data excluded)

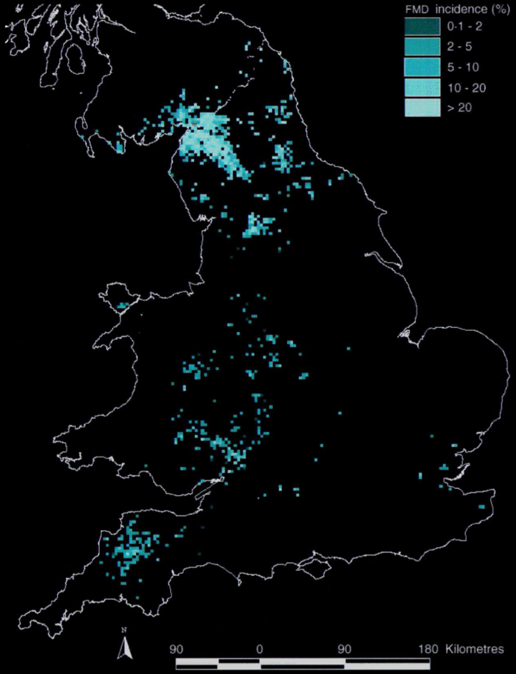


FIG 9: Cumulative incidence of foot-and-mouth disease (FMD) in Great Britain, February 20 to July 15, 2001

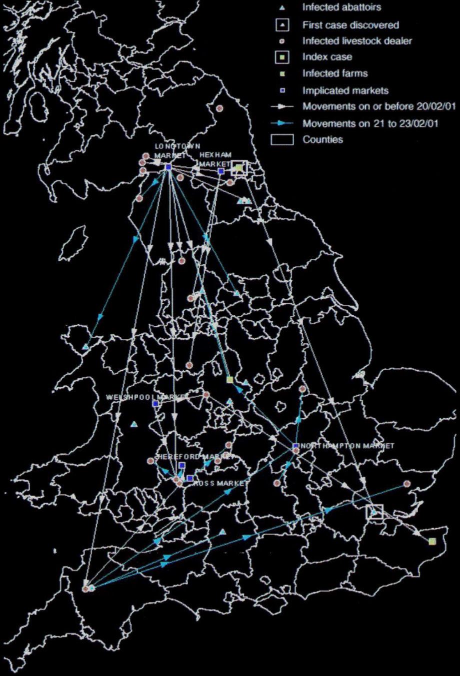


FIG 3: Movement of foot-and-mouth disease infected animals before February 23, 2001, and location of implicated markets, abattoirs and dealers (subject to information available on August 30, 2001)

2001 FMD epidemic in the UK

- Early February – Disease likely to have entered the UK
- 19th February – Foot-and-mouth disease first suspected
- 20th February – Foot-and-mouth disease confirmed
- 23rd February – Culling initiated of Infected Premises (IP) and Dangerous Contacts (DC). Movement restrictions are brought into force
- 15th March – Sheep, goats and pigs within 3km of an IP in Lockerbie, Carlisle and Solway are targeted for culling
- 23rd March – Contiguous Premises (CPs) are included in the cull
- 26th March – Epidemic reaches its maximum with 54 cases in one day
- 27th March – 3km cull begins in the Penrith valley, Cumbria
- 29th March – 24/48 hour policy begins, in which IPs are slaughtered within 24 hours, and DCs and CPs are culled within 48 hours
- 14th April – 3km cull in Cumbria reaches its height
- 26th April – Sheep, pigs and especially cattle from farms with high biosecurity may be exempt from culls
- 10th May – First case reported in the Settle area
- 20th June – First day with no reported cases

Why it is important to incorporate space

- General considerations about space-and-time spread
- Spatial aspects in animal diseases
- Foot-and-mouth disease
- Avian influenza

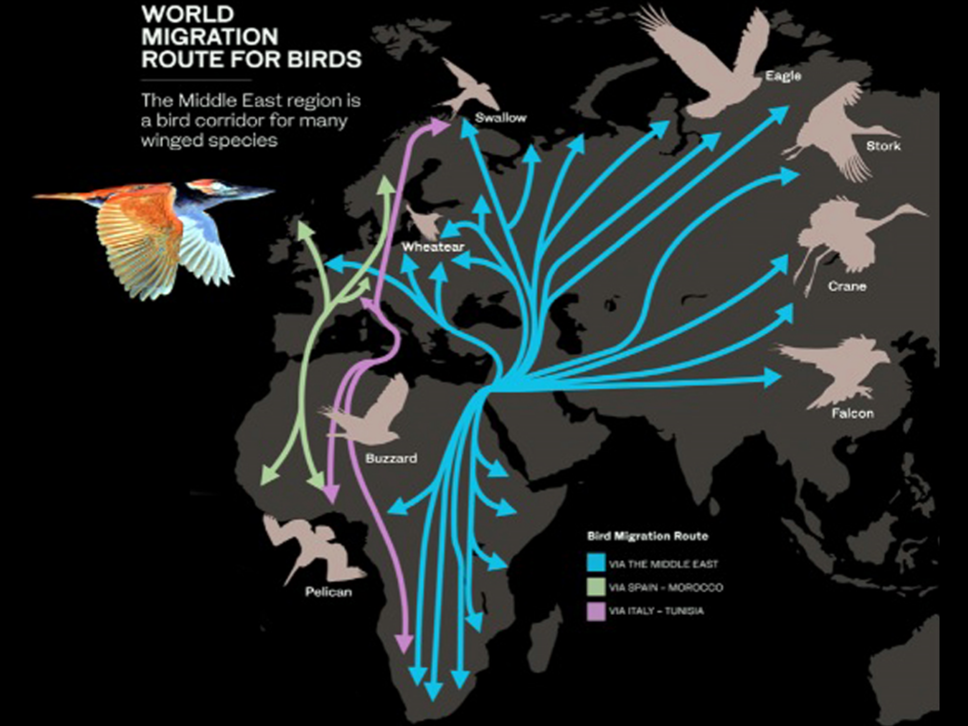
Metapopulation models

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
Swallow
Eagle
Stork
Wheatear
Crane
Falcon
Buzzard
Pelican
Bird Migration Route
VIA THE MIDDLE EAST
VIA SPAIN - MOROCCO
VIA ITALY - TUNISIA

NATIONAL GEOGRAPHIC

CELEBRATING THE YEAR OF THE BIRD

Navigating by Nature

The length and timing of bird migrations vary greatly, with long-distance journeys requiring extraordinary energy reserves and navigational abilities. These migratory patterns, shown here for the Eastern Hemisphere, often are ingrained, triggered by seasonal shifts in day length, but also by temperature and food availability—factors that can be heavily influenced by climate and environmental change.

SHORE AND WADING BIRDS

Shore and wading birds often complete their migrations in several long-distance stages, traveling between suitable stop-over areas for refueling. Many migratory bird populations have declined in recent decades because of hunters and loss of habitat.

LAND BIRDS

Migration distances vary by bird type and species. Corncrakes fly long distances from northern Eurasia to southern Africa, while orange-bellied parrots range only from the south coast of Australia to Tasmania.

Northern wheatear 1
Oenanthe oenanthe
Length: 6 in
Breeds: Eurasia, Alaska, Greenland
Winters: Sahel region and eastern Africa

WATERFOWL

Unlike many other birds, waterfowl can molt so quickly that they enter a flightless stage. They may first migrate to safe molting areas with abundant food, then continue on weeks later, once flight feathers grow in.

Bar-headed geese, the highest recorded migrators, can fly over the Himalaya.

SEABIRDS

Some species – including most gulls and terns – prefer shallower inland and coastal waters. Sabine's gull is a trans-equatorial migrant that also flies between the Eastern and Western Hemispheres.

BIRDS OF PREY

Large birds such as eagles can save energy by riding thermal updrafts that form only over land. Falcons and other birds that rely more on flapping their wings to power their journeys can make long sea crossings.

SWIMMING AND WALKING

With short, strong wings, penguins appear to fly underwater. Some young seabirds, such as auks, can swim before they can fly. Flightless birds, such as emus and penguins, and sometimes even flight-capable birds walk long distances.

Emperor penguin

Emu

PREPARATIONS FOR FLIGHT

Before migrating, birds may molt and regrow feathers and exhibit a combination of changes in their hormones, metabolism, and diet, building up their fat stores and flight muscles. Some forgo sleep during nonstop travel; a few may rest one hemisphere of their brain mid-flight.

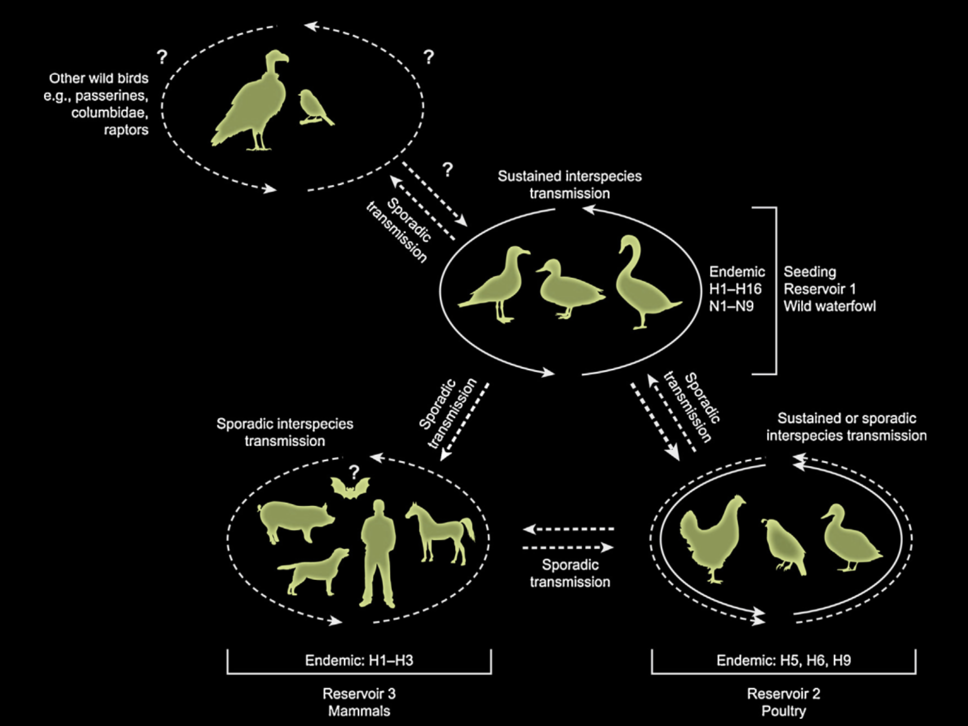
Increased fat reserves to fuel migration

NAVIGATION METHODS

Birds flying locally rely on wind patterns as well as visual, olfactory, and auditory cues to find their way. Long-distance migrants also use the sun, stars, and magnetic fields as compasses to navigate their routes.

HUMAN IMPACTS

Migrators face many dangers, but humans may be their greatest threat. For example, collisions with man-made structures – especially those lit up at night – kill millions of birds a year; development and agriculture destroy habitats.


Other wild birds
e.g., passerines,
columbidae,
raptors
?
?
?
Sporadic
transmission
Sustained interspecies
transmission
Endemic
H1–H16
N1–N9
Seeding
Reservoir 1
Wild waterfowl
Sporadic
transmission
Sporadic
transmission
Sporadic interspecies
transmission
?
Sustained or sporadic
interspecies transmission
Sporadic
transmission
Endemic: H1–H3
Reservoir 3
Mammals
Endemic: H5, H6, H9
Reservoir 2
Poultry

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

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:

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

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 $f_p : \mathbb{R}^{n_p} \to \mathbb{R}^{n_p}$
- 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 $g_p : \mathbb{R}^{n_p} \times \mathbb{R}^{n_q} \to \mathbb{R}^{n_p}$

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

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

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

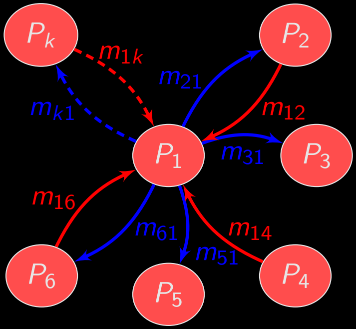
Split continuous space into N discrete geographical locations (*ptatches*)

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

Explicit movement (focus on P_1)



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

or

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

Graph setting

Suppose

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

Graph is a digraph: movement is not always symmetric

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

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

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

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

Connection matrix

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

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

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

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

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 $\mathcal{G}_c$

Srong connectedness and irreducibility

Definition 3 (Reducible/irreducible matrix)

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

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

Theorem 4

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

Notation

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

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

Then

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

Vector form of the system

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

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

with

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

Definitions and notation for matrices

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

The movement matrix

The matrix

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

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* $\mathrm{diag}(D)\gg\mathbf{0}$, *then* $D-\mathcal{M}$ *invertible M-matrix and* $(D-\mathcal{M})^{-1}>\mathbf{0}$
4. $\mathcal{M}$ *irreducible and* $\mathrm{diag}(D)>\mathbf{0}\implies D-\mathcal{M}$ *nonsingular irreducible M-matrix and* $(D-\mathcal{M})^{-1}\gg\mathbf{0}$

Behaviour of the mobility component

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

$$\mathbf{N}_c' = \mathcal{M}_c \mathbf{N}_c \tag{7}$$

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

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

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

$$T_p' = D_p(T_p) + \sum_{c \in \mathcal{C}} \sum_{q \in \mathcal{P}} m_{cpq} N_{cq} \tag{8}$$

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

In what follows, assume

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

Vector / matrix form of the equation

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

$$\mathbf{T}' = \mathbf{b} - \mathbf{d}\mathbf{T} + \sum_{c \in \mathcal{C}} \mathcal{M}_c \mathbf{N}_c \tag{10}$$

where

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

The nice case

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

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

Then

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

Equilibria

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

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 $\mathbf{T}^\star = (\mathbf{d} - \mathcal{M})^{-1}\mathbf{b}$ unique

Behaviour of the total population

Equal irreducible movement case

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

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

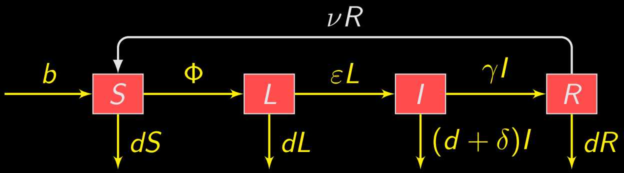
Indeed, we have

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

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 $\to \mathbf{T}^\star \gg 0$ (provided $\mathbf{b} > \mathbf{0}$, of course)

The toy SLIRS model in patches



$$S' = b + \nu R - \Phi - dS \tag{12a}$$
$$L' = \Phi - (\varepsilon + d)L \tag{12b}$$
$$I' = \varepsilon L - (\gamma + d + \delta)I \tag{12c}$$
$$R' = \gamma I - (\nu + d)R \tag{12d}$$

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

$$
\begin{aligned}
S_p' &= b_p + \nu_p R_p - \Phi_p - d_p S_p + \sum_{q\in\mathcal{P}} m_{Spq} S_q && \text{(13a)}\\
L_p' &= \Phi_p - (\varepsilon_p + d_p)\, L_p + \sum_{q\in\mathcal{P}} m_{Lpq} L_q && \text{(13b)}\\
I_p' &= \varepsilon_p L_p - (\gamma_p + d_p) I_p + \sum_{q\in\mathcal{P}} m_{Ipq} I_q && \text{(13c)}\\
R_p' &= \gamma_p I_p - (\nu_p + d_p)\, R_p + \sum_{q\in\mathcal{P}} m_{Rpq} R_q && \text{(13d)}
\end{aligned}
$$

with incidence

$$
\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \qquad q_p \in \{0,1\} \tag{13e}
$$

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

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

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

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

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

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

with incidence

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

- 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)

$$
\begin{aligned}
S'_{pq} &= b_{pq} + \nu_{pq} R_{pq} - \Phi_{pq} - d_{pq} S_{pq} + \textstyle\sum_{k\in\mathcal{P}} m_{Spqk} S_{pk} && \text{(15a)} \\
L'_{pq} &= \Phi_{pq} - (\varepsilon_{pq} + d_{pq}) L_{pq} + \textstyle\sum_{k\in\mathcal{P}} m_{Lpqk} L_{pk} && \text{(15b)} \\
I'_{pq} &= \varepsilon_{pq} L_{pq} - (\gamma_{pq} + d_{pq}) I_{pq} + \textstyle\sum_{k\in\mathcal{P}} m_{Ipqk} I_{pk} && \text{(15c)} \\
R'_{pq} &= \gamma_{pq} I_{pq} - (\nu_{pq} + d_{pq}) R_{pq} + \textstyle\sum_{k\in\mathcal{P}} m_{Rpqk} R_{pk} && \text{(15d)}
\end{aligned}
$$

with incidence

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

- 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

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

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

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

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

with incidence

$$\Phi_p = \beta_p \frac{S_p I_p}{N_p^{q_p}}, \qquad q_p \in \{0,1\} \tag{16e}$$

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

$\implies$ Good case of large-scale system

(matrix analysis is your friend)

Existence and uniqueness

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

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

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

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

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

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

R at DFE

Recall second equation:

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

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

We have been here before!

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

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

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

$\implies$ 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

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

Computing the basic reproduction number $\mathcal{R}_0$

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

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

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

Differentiate w.r.t. Ξ:

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

Note that

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

whenever $k \neq p$, so

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

Evaluate $D\mathcal{F}$ at DFE

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

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

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

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

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

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

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

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

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

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

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

where

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

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

Next generation matrix

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

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

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

i.e.,

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

Local asymptotic stability of the DFE

Theorem 9

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

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

Then the DFE

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

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

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

Some remarks about $\mathcal{R}_0$

The expression for $\mathcal{R}_0$ in Theorem 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*

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))
```

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

Write down indices of the different state variable types

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

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

Set up IC and time

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

Set up β to avoid blow up

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

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

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

Define the vector field

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

And now call the solver

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

One little trick (case with demography)

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

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

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

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

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

Word of warning about that trick, though..

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

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

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

Why it is important to incorporate space

Metapopulation models

A few foot-and-mouth disease models

- Woolhouse and collaborators
- Ringa & Bauch

A few avian influenza models

Why it is important to incorporate space

Metapopulation models

A few foot-and-mouth disease models

- Woolhouse and collaborators
- Ringa & Bauch

A few avian influenza models

Models à la Levins

Space is implicit: count infected herds

IMA Journal of Mathematics Applied in Medicine & Biology (1997) **14**, 1–9

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

D. T. HAYDON† AND M. E. J. WOOLHOUSE
Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS, UK

R. P. KITCHING
Institute for Animal Health, Pirbright Laboratory, Pirbright, Surrey GU24 0NF, UK

The model

$$\Delta S(t) = -\beta(t)S(t)I(t) \tag{17a}$$
$$\Delta L(t) = \beta(t)S(t)I(t) - \beta(t-\sigma)S(t-\sigma)I(t-\sigma) \tag{17b}$$
$$\begin{aligned}\Delta I(t) = {} & \beta(t-\sigma)S(t-\sigma)I(t-\sigma) \\ & - \beta(t-\sigma-\nu)S(t-\sigma-\nu)I(t-\sigma-\nu)\end{aligned} \tag{17c}$$
$$\Delta R(t) = \beta(t-\sigma=\nu)S(t-\sigma-\nu)I(t-\sigma-\nu) \tag{17d}$$

where $\Delta X(t) = X(t+1) - X(t)$, σ is the fixed latent period and ν is the fixed infectious period

Reproduction number

Provided $N \gg 1$,

$$\mathcal{R}_0 = \frac{\beta(0)N}{\nu}$$

Estimates of $\beta(t)$ obtained using

$$\beta(t) = \frac{\Delta L(t) + \beta(t-\sigma)S(t-\sigma)I(t-\sigma)}{S(t)I(t)}$$

Used for the 1967-1968 UK epidemic, time unit of 1 day, $\sigma = 5$ days, $\nu = 4$ days and $N = 16,507$ herds

Here, space is purely implicit, in the sense that the only source of spatiality is the fact that the data comes from farms that are spatially located

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

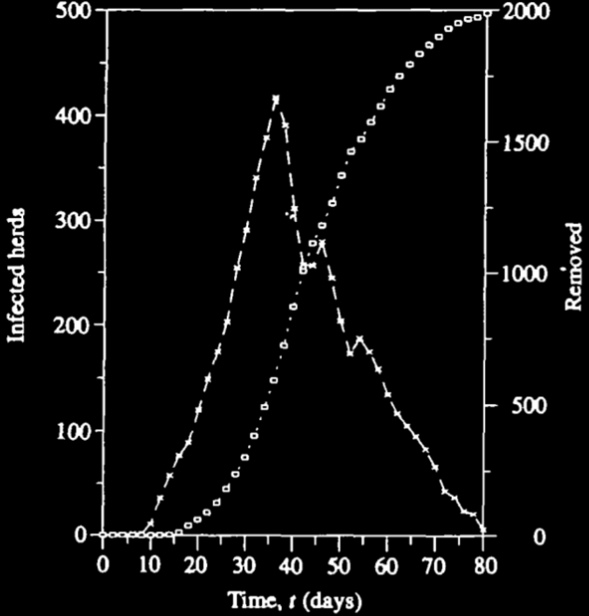


FIG. 1. (–□–) Cumulative numbers of the herds removed, $R(t)$, and (✶) the reconstructed number of infectives calculated from equation (3) during the 1967–68 UK (FMD) epidemic.

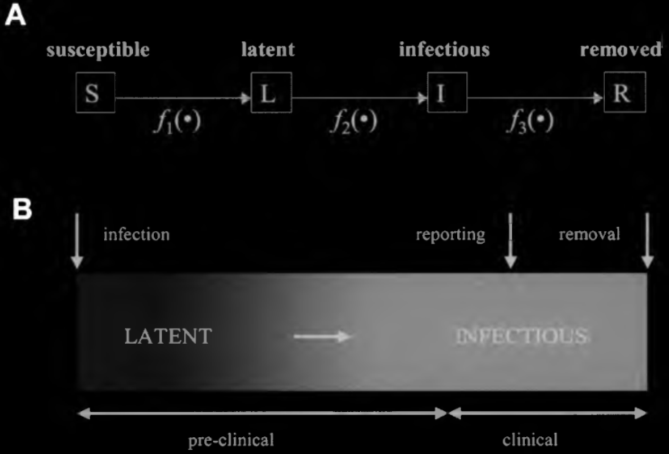


Figure 1. Compartments, in theory and practice. A) A diagrammatic representation of a simple SLIR model showing the flow of hosts between susceptible, latent infected, infectious and removed compartments. The numbers (or fractions or densities) of hosts in these compartments are represented by the variables S, L, I and R respectively. The rate of flow is specified by three expressions: $f_1(\bullet)$, the rate at which susceptible hosts become infected; $f_2(\bullet)$, the rate at which latently infected hosts become infectious; and $f_3(\bullet)$, the rate at which infectious hosts are removed. Different models use different mathematical expressions, representing different levels of detail and incorporating different numbers of parameters. B) A diagrammatic representation of the course of a FMD infection in a single host (or single farm). Note that the transition between latent and infectious does not correspond to the appearance of clinical signs: animals may be infectious before clinical signs appear. In practice, there is inevitably a further delay before clinical signs are observed and reported.

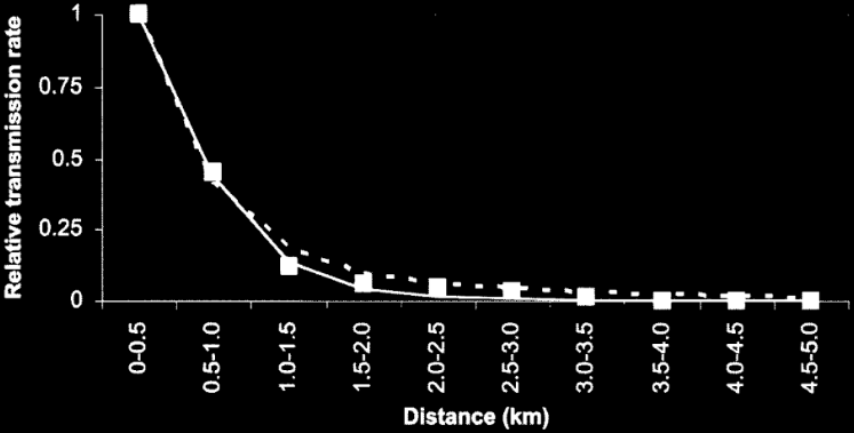


Figure 3. Examples of transmission kernels, relative per capita rate of transmission as a function of distance between farms. Empirical results (symbols) derived using data tracing studies carried out during the UK 2001 epidemic after the imposition of a national ban on livestock movements (Keeling *et al.*, 2001) are compared with two standard functions: 1) k/d^2 with k=0.41 (broken line); and 2) $g\exp[-hd]$ with g=4.8 and h=2.4 (solid line). All functions show per capita transmission rates relative to that over distances of 0 to 0.5km. The constants k, g and h were fitted using the least squares method. The empirically-derived transmission kernel equates to 70% of transmission occurring over distances up to 3km. Note that function (1) overestimates transmission rates at longer distances, whereas function (2) underestimates these.

Dynamics of the 2001 UK Foot and Mouth Epidemic: Stochastic Dispersal in a Heterogeneous Landscape

Matt J. Keeling,[1]* Mark E. J. Woolhouse,[2] Darren J. Shaw,[2] Louise Matthews,[2] Margo Chase-Topping,[2] Dan T. Haydon,[3] Stephen J. Cornell,[1] Jens Kappey,[1] John Wilesmith,[4] Bryan T. Grenfell[1]

Foot-and-mouth is one of the world's most economically important livestock diseases. We developed an individual farm–based stochastic model of the current UK epidemic. The fine grain of the epidemiological data reveals the infection dynamics at an unusually high spatiotemporal resolution. We show that the spatial distribution, size, and species composition of farms all influence the observed pattern and regional variability of outbreaks. The other key dynamical component is long-tailed stochastic dispersal of infection, combining frequent local movements with occasional long jumps. We assess the history and possible duration of the epidemic, the performance of control strategies, and general implications for disease dynamics in space and time.

Incorporating space

Transmission between farms determined by number and type of livestock and distance between susceptible and infectious farms

Probability that a susceptible farm i becomes infected a given day

$$\mathbb{P} = 1 - \exp\left(-SN_i \sum_{j \in \text{infectious}} TN_j K(d_{ij})\right) \tag{18}$$

K infection kernel, d_{ij} distance between farms i and j

Table 1. Results from the stochastic spatial model (*2, 10*) considering a variety of control options. The total reported cases (on an individual farm basis) for each control policy and the total cull (including IP slaughtering, DC, and CP culls) are given as a percentage of the results from the full model using the observed control policy, including the extended 3-km and welfare culls. The total number of farms vaccinated is given as a percentage of the total cull in the full model. All of the control policies tested below ignore the extended 3-km and welfare culls used in some locations. The standard control policy follows the timing and level of the observed measure. The prompt cull follows the level of the observed measures but achieves a 24/48-hour delay from reporting to slaughter/cull throughout the epidemic. The intensive cull follows the timing of the observed measures but matches the levels achieved in the latter stages of the epidemic. The 3-km ring cull removes infected premises and all other farms within a 3-km radius. The next three measures include vaccination of cattle (at 90% coverage) within a 3-km ring around all infected premises in addition to the slaughter and cull policy. Vaccination of all species gives somewhat better, but qualitatively similar, results. Finally, we consider barrier vaccination (as in Fig. 3D) at 90% coverage. More details about the various control measures are given in the supplementary material (*10*).

Control measure	Total cases	Total cull	Total vaccinated
Standard	105%	84%	0%
IP cull only	927%	342%	0%
Prompt cull (24/48-hour delay throughout)	57%	54%	0%
Intensive cull (high levels throughout)	45%	73%	0%
3-km ring cull only	47%	142%	0%
Standard + 90% vaccination	84%	72%	76%
Standard + vaccination from May	97%	81%	8%
IP only + vaccination	784%	156%	453%
Standard + barrier vaccination	70%	69%	251%

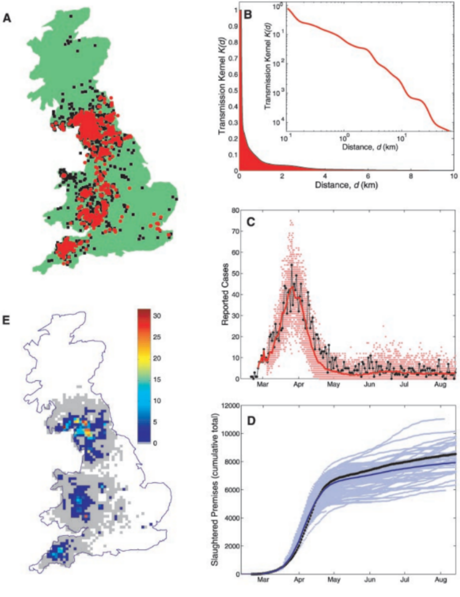
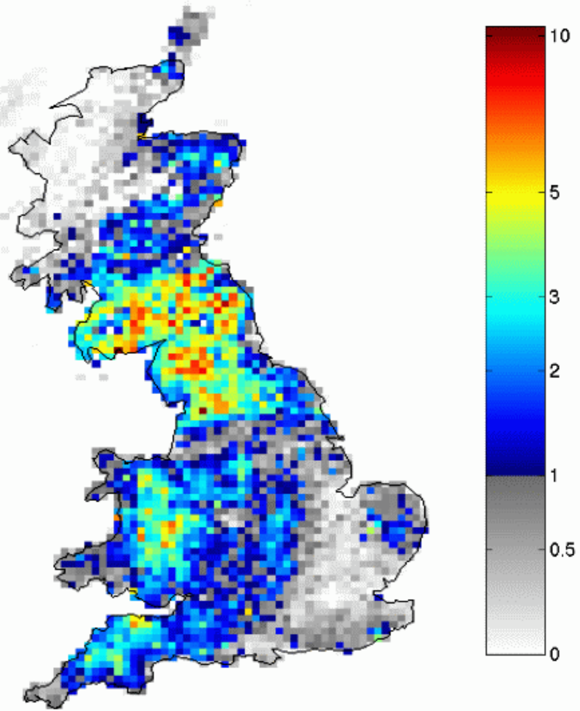


Fig. 1. A comparison between the observed epidemic and 100 replicates of the stochastic model. Simulations start on 23 February 2001 (when movement restrictions were fully in place) and use the reported cases to that date and the position of all susceptible farms as initial conditions. (**A**) The actual spatial distribution of IPs (red) and culled premises (black). (**B**) The transmission kernel *K* as a function of distance (*d*), calculated from the distance between sources of infectious and their secondary cases. (**C**) Comparison of the number of infected premises. (**D**) Comparison of the cumulative total of culled or slaughtered premises. Black dots show the actual number, pale dots (red or blue) show the results from simulations, and solid lines (red or blue) show the average of the simulations. (**E**) The average number of simulated cases in 10-km-by-10-km squares. The model results shown are from 100 simulations.


10
5
3
2
1
0.5
0

THE ROYAL SOCIETY

Received 7 February 2003
Accepted 14 April 2003
Published online 7 July 2003

Neighbourhood control policies and the spread of infectious diseases

L. Matthews[1*], D. T. Haydon[2], D. J. Shaw[1], M. E. Chase-Topping[1], M. J. Keeling[3,4] and M. E. J. Woolhouse[1]

[1]*Centre for Tropical Veterinary Medicine, University of Edinburgh, Easter Bush, Roslin EH25 9RG, UK*
[2]*Department of Zoology, University of Guelph, Guelph, Ontario N1G 2W1, Canada*
[3]*Mathematics Institute, and* [4]*Department of Biological Sciences, University of Warwick, Gibbet Hill, Coventry CV4 7AL, UK*

Another model

$$S' = -\beta(1-f(c))\frac{SI}{N} - c\frac{SI}{N} \tag{19a}$$

$$I' = \beta(1-f(c))\frac{SI}{N} - \sigma I \tag{19b}$$

$$R' = \sigma I + c\frac{SI}{N} \tag{19c}$$

$f(c)$ proportion of exposed holdings removed, c the removal rate (level of control)

$\mathcal{R}_0 = \beta/\sigma$ and

$$\mathcal{R}_c = \beta\frac{1-f}{\sigma} = (1-f)\mathcal{R}_0$$

Then consider a metapopulation version

Break down susceptible population into clusters of holdings within which short-range transmission occurs, and between which long-range transmission occurs

Transmission rate β broken down into a short-range transmission rate, β_s, corresponding to infections generated within the cluster, and a long-rangetransmission rate,β_l, corresponding to infections generated outside the cluster in question

Modelling vaccination strategies against foot-and-mouth disease

M. J. Keeling*, M. E. J. Woolhouse†, R. M. May‡, G. Davies§ & B. T. Grenfell||

** Department of Biological Science & Mathematics Institute, University of Warwick, Gibbet Hill Road, Coventry, CV4 7AL, UK*
† Centre for Infectious Diseases, College of Medicine and Veterinary Medicine, University of Edinburgh, Easter Bush, Roslin, Midlothian, EH25 9RG, UK
‡ Department of Zoology, University of Oxford, Oxford, OX1 3PS, UK
§ Zinnia, Kettlewell Hill, Woking, Surrey, GU21 4JJ, UK
|| Department of Zoology, University of Cambridge, Downing Street, Cambridge, CB2 3EJ, UK

Vaccination has proved a powerful defence against a range of infectious diseases of humans and animals. However, its potential to control major epidemics of foot-and-mouth disease (FMD) in livestock is contentious. Using an individual farm-based model, we consider either national prophylactic vaccination campaigns in advance of an outbreak, or combinations of reactive vaccination and culling strategies during an epidemic. Consistent with standard epidemiological theory, mass prophylactic vaccination could reduce greatly the potential for a major epidemic, while the targeting of high-risk farms increases efficiency. Given sufficient resources and preparation, a combination of reactive vaccination and culling might control ongoing epidemics. We also explore a reactive strategy, 'predictive' vaccination, which targets key spatial transmission loci and can reduce markedly the long tail that characterizes many FMD epidemics. These analyses have broader implications for the control of human and livestock infectious diseases in heterogeneous spatial landscapes.

The basic model

The model used throughout this paper is a spatial stochastic simulation, where the infectious state of every livestock farm in Britain is predicted on a daily basis. The rate, r, at which farm i (which is currently susceptible) is infected is given by,

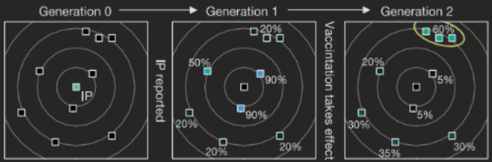
$$R_{\mathrm{i}} = \sum_{L \in \text{livestock}} S_L N_L^{\mathrm{i}} \times \sum_{j \in \text{infectious}} \sum_{L \in \text{livestock}} T_L N_L^{\mathrm{j}} \times K(d_{\mathrm{ij}})$$

where N_L^{i} is the number of livestock of type L within farm i; S_L is the susceptibility of livestock L; T_L is the transmission rate of livestock L; d_{ij} is the distance between farms i and j; and K is the transmission kernel. Once infected, farms are assumed to remain in an exposed (but not infectious) state for 4 days, after which they become infectious and can transmit the virus to other farms. Nine days after infection, after the appearance of clinical signs, the presence of the disease is reported; after a further delay of between 1 and 3 days (depending of the stage of the epidemic) the animals on the infected farm are slaughtered and the appropriate neighbourhood cull is performed (see Supplementary Information). It was estimated that around 40% of dangerous contacts were infected. More details of the parameter estimation and model validation can be found elsewhere[7].

Predictive vaccination

Schematic diagrams showing the probability of being infected in each generation. In generation 0 the central farm is infected (it is an IP), whereas the surrounding farms are assumed susceptible. At the end of generation 1, the animals in the IP show signs and the farm reports infection — at this stage vaccination should occur. In generation 1, farms are infected in relation to their distance from the IP. The two farms that are closest have very high probabilities of already being infected, and therefore are unlikely to be infected in the next generation. It is the cluster of farms (circled blue) that have the greatest chance of being infected in generation 2 because: there is a 99% chance that at least one of them is still susceptible in generation 1; they can get infected in generation 2 from farms close to the original IP; and there is a 49% chance that at least one of them got infected in generation 1, subsequent spread to the remainder in generation 2 is then likely. Therefore, in response to the IP, the circled cluster of farms should be vaccinated with the highest priority as here the vaccine has the maximal effect — vaccinating the nearest farms would be futile as they will already be infected before the vaccine takes effect.

The efficacy of predictive vaccination depends on how reliably risk factors for infection and transmission can be identified. Here we have assumed complete knowledge of those risk factors (although the actual outcome is still stochastic in nature). The effectiveness of the strategy will be less if risk factors are less well known.



Why it is important to incorporate space

Metapopulation models

A few foot-and-mouth disease models

- Woolhouse and collaborators
- Ringa & Bauch

A few avian influenza models

Journal of Theoretical Biology 357 (2014) 150–159

Contents lists available at ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/yjtbi

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

N. Ringa [a,*], C.T. Bauch [a,b]

[a] Department of Mathematics and Statistics, University of Guelph, 50 Stone Rd E, Guelph, Canada ON N1G 2W1
[b] Department of Applied Mathematics, University of Waterloo, 200 University Avenue West Waterloo, Canada ON N2L 3G1

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 that ring vaccination.
- More mathematical models applicable to FMD-endemic countries need to be developed.

Pair approximation models

Suppose farms are in status X or Y (e.g., susceptible and infected). Pair approximation models consider the *expected number* $[XY]$ of pairs of the form X and Y at time t

A sample derivation (appendix in the paper)

The dynamics of $[SI]$ are governed by the equation

$$g'(t) = \sum r(\varepsilon)\Delta g(\varepsilon)$$

where $g(t)$ state variable of interest ($[SI]$ here), $r(\varepsilon)$ rate of event ε and $\Delta g(\varepsilon)$ change this event causes in $g(t)$

We're interested in transformation of edges, e.g., infection through an $S - I$ edge converts S into E, i.e. $SI \mapsto EI$ ($\mapsto$ means "transformed to")

What affects $[SI]'$

- Infection of susceptible farm by infectious farm in the $S-I$ edge converts S into E, i.e. $SI \mapsto EI$. Adds $-\tau[SI]$, since this "destroys" $S-I$ edges
- Infection of susceptible farm "from the left" in a triple $I-S-I$, i.e. $I \leftrightarrow SI$ gives rise to $SI \mapsto EI$, i.e., $-\tau[ISI]$
- Latent period $1/\nu$, so $SE \mapsto SI$, "creating" an $S-I$
- Infectious farm recovers at rate σ, therefore $SI \mapsto SR$ contributes $\sigma[SI]$
- Ring vaccination (vaccination of E and S farms with links with I farms) in the S farm in a pair $S-I$, at rate ψ_r converts $S-I$ to $I-V$ and adds $\psi_r[SI]$
- Ring vaccination in the susceptible farm in a triple $I-S-I$, at rate ψ_r converts $S-I$ to $I-V$ and adds $\psi_r[ISI]$
- A recovered farm in an $I-R$ pair loses natural immunity at rate ω to form an $S-I$ pair, thus adding $\omega[IR]$
- A vaccinated farm in an $I-V$ pair loses vaccine protection at rate θ to form an $S-I$ pair, thus adding $\theta[IV]$

Therefore the equation of motion for $[SI]$ is

$$\begin{aligned}[SI]' = &-\tau([ISI] + [SI]) + \nu[SE] - \sigma[SI] - \psi_r([SI] + [ISI]) \\ &- \psi_p[SI] + \omega[IR] + \theta[IV]\end{aligned}$$

Why it is important to incorporate space

Metapopulation models

A few foot-and-mouth disease models

A few avian influenza models

- Andronico *et al*

Why it is important to incorporate space

Metapopulation models

A few foot-and-mouth disease models

A few avian influenza models

- Andronico *et al*

Epidemics 28 (2019) 100340

Contents lists available at ScienceDirect

Epidemics

journal homepage: www.elsevier.com/locate/epidemics

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

Alessio Andronico[a,*], Aurélie Courcoul[b,1], Anne Bronner[c], Axelle Scoizec[d], Sophie Lebouquin-Leneveu[d], Claire Guinat[e], Mathilde C. Paul[e], Benoît Durand[b], Simon Cauchemez[a]

[a] Mathematical Modelling of Infectious Diseases Unit, Institut Pasteur, UMR2000, CNRS, 75015, Paris, France
[b] Epidemiology Unit, Paris-Est University, Laboratory for Animal Health, French Agency for Food, Environment and Occupational Health and Safety (ANSES), Maisons-Alfort, France
[c] Direction générale de l'Alimentation, Paris, 75015, France
[d] Anses, Laboratoire de Ploufragan-Plouzané, Unité d'épidémiologie et bien-être en aviculture et cuniculture, Ploufragan, 22440, France
[e] IHAP, Université de Toulouse, INRA, ENVT, Toulouse, France

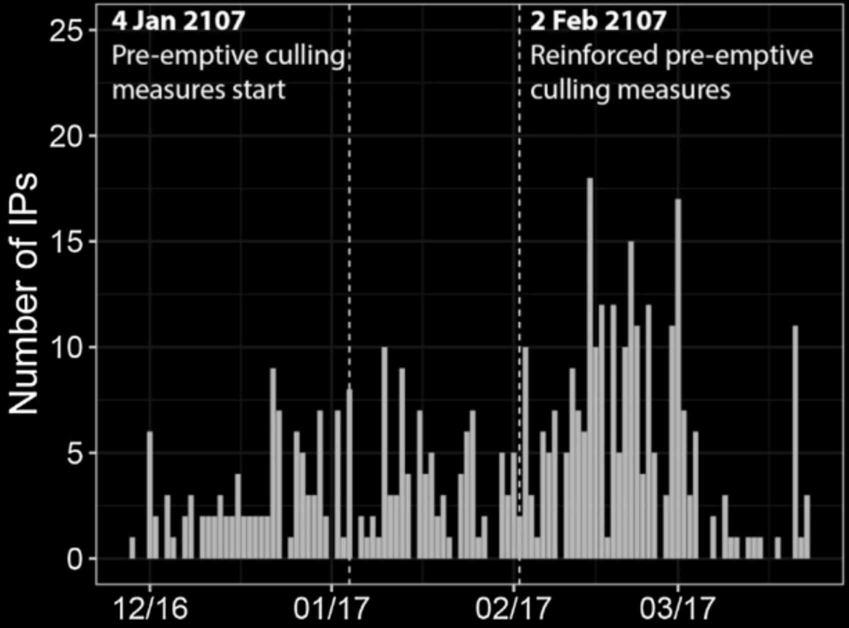


Fig. 1. Epidemic curve. Daily number of IPs by date of suspicion.