Australian Government

Department of Agriculture, Fisheries and Forestry

Principles of epidemiological modelling

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Introduction

- Context
- What are epidemiological models
- Why use epidemiological models
- Steps in model building
- Types of models
- New approaches
- Conclusions

Context

- **Perspective**
- **Modelling**
- **Animal health policy and disease management**
- **Focus on emergency (foreign and emerging) diseases**
  - prevention and management

What are epidemiological models?

"A model is the representation of a physical process designed to increase appreciation and understanding of the process…..

In epidemiology … models are constructed to attempt to explain and predict patterns of disease occurrence and what is likely to happen if various alternative control strategies are adopted"

(Thrusfield 2007)

"Epidemiological models are usually defined as a mathematical and/or logical representation of the epidemiology of disease transmission and its associated processes."

(Dube et al. 2007)

Why use models?

- **Cost-effective way of studying disease spread and control**

- **Lack of experience with exotic and emerging diseases**
  - How to assess and plan?

- **Models are valuable tools**
  - to understand disease dynamics
  - to explore potential outbreak situations and different control options
  - provide decision support for policy makers and managers

Role of epidemiological models

- Study epidemiology of a disease - allow large amounts of information to be combined in a structured way
- Provide advice on emerging diseases and threats
- Contribute to risk management
- Potential size and economic impact of disease incursions
- Evaluate control strategies
- Support policy development - test ‘what if’ questions
- Inputs to training and exercises

Key elements of an epidemiological model

1. **Logic (conceptual understanding)**
   - Purpose and scope
   - How we represent the system under study
   - What is important to include/leave out

2. **Code**
   - Translating the logic into an effective (computer) program to deliver outputs

3. **Parameter values**
   - Reliable estimates of input values

Attention to all 3 elements are required for a reliable, robust model

Steps in model building

- Purpose
- Conceptual model
- Methodology / programming
- Data / parameterisation
- Validation / verification
- Communicating findings

Purpose

- **Why is the modelling study being done?**

- **This will affect:**

  1. Scale - the level at which the issue being studied
  2. Approach - what type of approach to use

Objectives

- **Descriptive** - better understanding of the disease process
- **Control –** assess effectiveness of various control options
- **Consequences** - evaluate (economic) impact of outbreaks
- **Support policy development and disease management** - training, response, decision support

Scale of modelling

- **Unit of interest**
  - animals
  - pens/sheds
  - farms
  - enterprises
- **On-farm dynamics vs between-farm dynamics**
- **Perspective**
  - local
  - regional
  - national
  - international

What type of model?

Models can take many different shapes, styles and levels of detail

Vary from simple deterministic mathematical models to complex spatially-explicit stochastic simulations

The approach used may vary depending on:

- **purpose of the study**
- **how well the epidemiology of a disease is understood**
- **the amount and quality of data available**
- **the background/training of the modellers**

Types of models cont'd

Models may be considered in terms of how they treat:

1. **Variability, chance and uncertainty**
   - **Deterministic vs stochastic**

2. **Time**
   - **Continuous vs discrete intervals**

3. **Space**
   - **Non-spatial vs spatial**

The approach taken should reflect the purpose of the study e.g. a broad understanding of disease dynamics or general action plan vs detailed understanding of disease behaviour under specific circumstances

Mathematical models

- **Been around for a long time and widely used to study human and animal diseases**

- **Range of approaches:**
  - Continuous time e.g. mass-action models
  - Discrete time e.g. chain binomial models
  - Markov chains and state-transition models

Mass Action models (Anderson-May)

- Population divided into compartments e.g. susceptible, infected, removed (S-I-R)
- Movement between compartments described by series of differential equations
- Deterministic
  - Stochastic variants
- Continuous time
- Trade off ‘realism’ for mathematical tractability
- Computationally simple, quick to develop
- Widely used to study infectious processes

$$\frac{dS}{dt} = B - \beta SI - dS;$$

$$\frac{dI}{dt} = \beta SI - gI - dI;$$

$$\frac{dR}{dt} = gI - dR;$$

Chain binomial models

$$C_{t+1} = S_t * (1 - q^{C_t})$$

- Assume that infection spreads within a population in discrete units of time, producing chains of infection

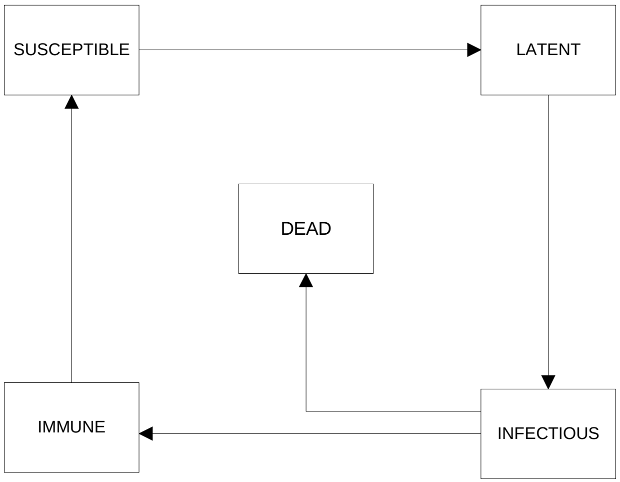
- Infection depends on susceptibles having ‘adequate contact’ with infecteds

- Probability of adequate contact is fixed and the same for all members of the population

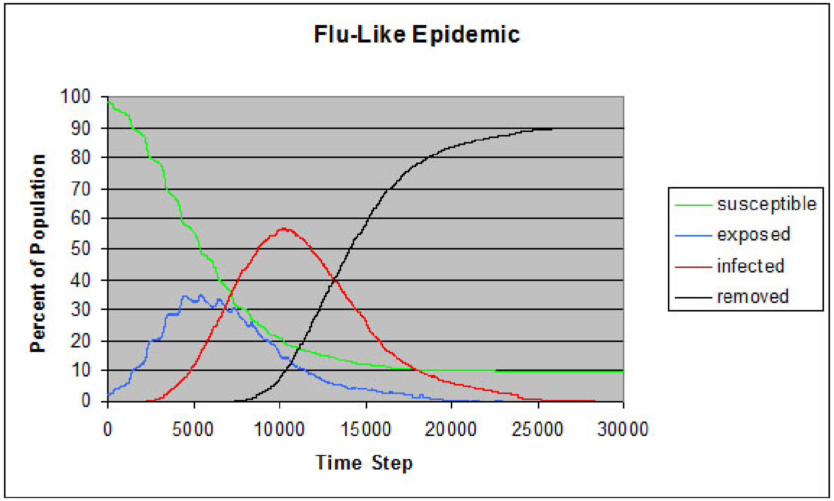
- Examples: Reed-Frost and Greenwood models

Markov chain and state-transition models

- **Discrete time models**
- **Used to analyse changes in disease status of the population over time**
- **Members of the population may be in one of several possible infection ‘states’**
- **During a time period an individual may stay in that change or move to another state (transition’)**
- **Transitions are based on probabilities**
  - **probabilities remain constant**



Conventional mathematical models



- **Use abstract representations**
  - relying on well-defined mathematical approaches (e.g. differential and partial differential equations)
- **Simplified populations**
- **Assume homogenous mixing of the population**
- **Simplified parameters to represent transmission**
- **Do not inherently account for spatial, environmental and social dimensions**

But from a disease manager's perspective…

- **Disease does not occur randomly in time and space**
- **Populations are not evenly distributed**
  - **e.g. clustering aids transmission, dispersal of individuals tends to reduce it.**
- **Infectiousness varies between individuals**
- **Environmental factors may influence disease expression – and its control**
- **The pattern of disease depends on:**
  - disease transmission processes
  - the environment in which transmission takes place
  - the contact structures

"Heterogeneity in host contact patterns profoundly shapes population-level disease dynamics"

Bansal et al. J. R. Soc. Interface (2007)

New paradigm

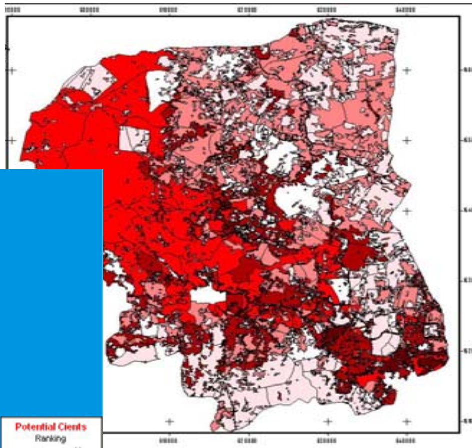
- While useful to study dynamics of infectious processes, simple mathematical approaches do have limitations
- Disease outbreaks occur in the context of physical, economic, technological, management and political infrastructures
- Spatial effects, population heterogeneity and social behaviour may profoundly affect transmission, persistence and control of disease.
- Increased interest to capture these complexities to better understand epidemiology of a disease

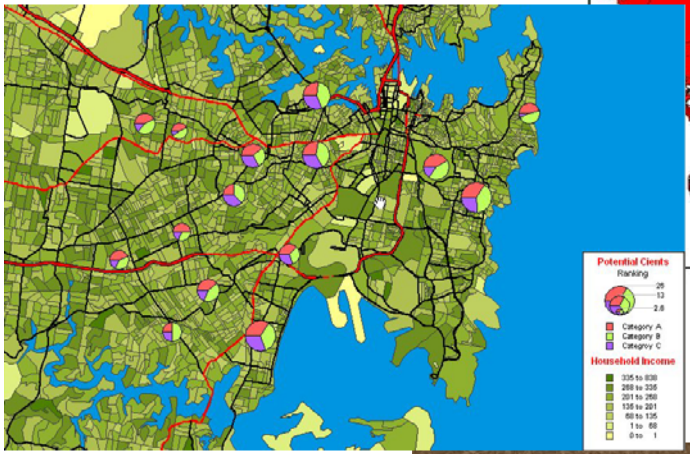
New technologies

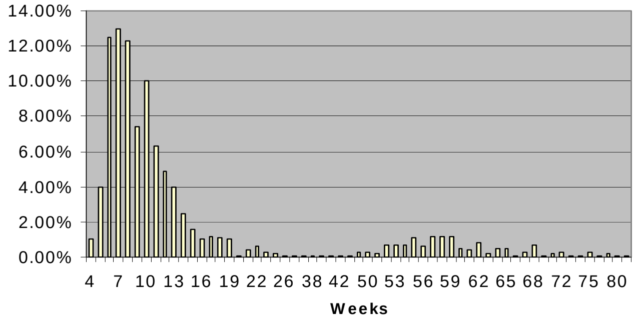
Developments in:

- Remote sensing
- Geographic information systems
- Data analytical methods
- Animal health economics
- Network theory
- Complex systems science

Multi-disciplinary approaches leading to new generation of epidemiological models

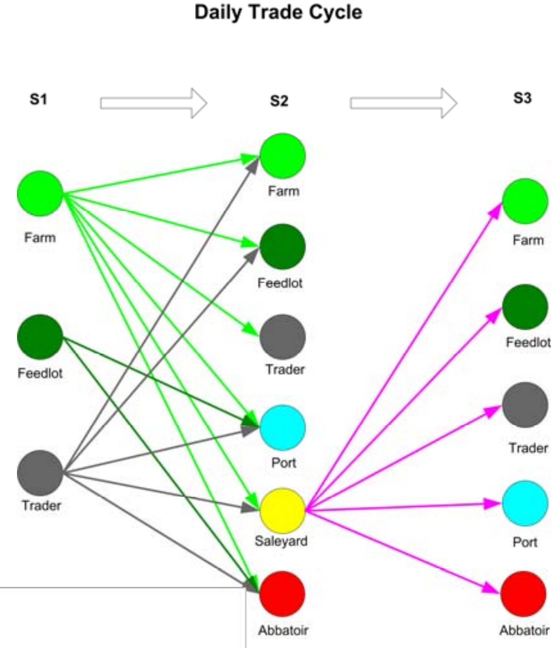


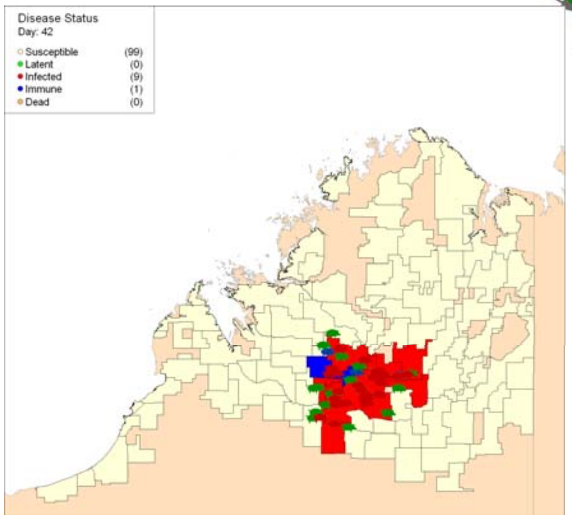




Newer approaches

- **Stochastic simulation**
- **Spatial modeling**
  - consider location and geographic dimensions
- **Network approaches**:
  - consider the social dimension: who has contact with who
- **Agent-based simulation**:
  - properties of individual entities or 'agents'





Simulation

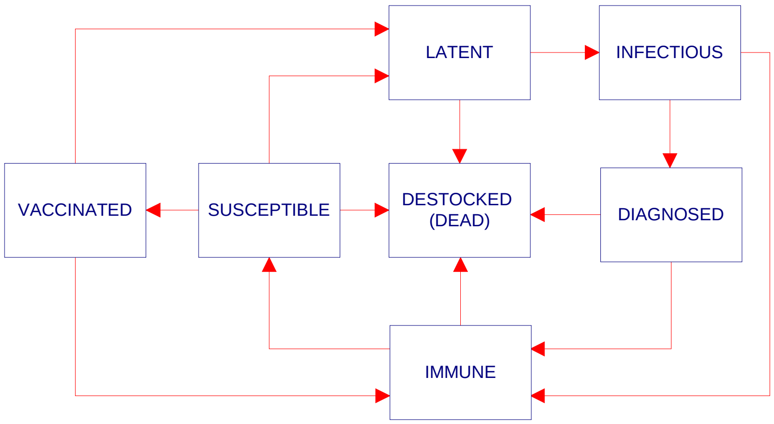
- A simulation model is a representation of a system or process that incorporates time and the changes that occur over time

- Based on the concepts of states, events, activities and processes

- State changes occur at discrete times called event times. When an event occurs, it may trigger new events, activities and processes.

Epidemic Model

States and Transitions



Epidemiological simulation models

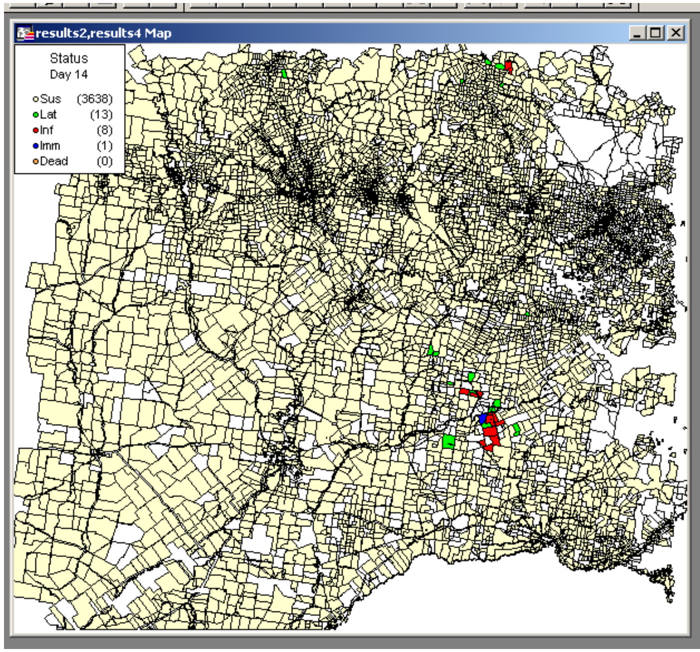
- **Population is made up of a series of <u>individual</u> units**
- **Commonly use modified state-transition structures**
  - stochastic, discrete time
  - transition probabilities may vary
- **Biological processes represented as series of probabilistic events**
- **'Monte Carlo' methods used to determine if events occur**
- **Can capture heterogeneity in individual attributes and in the network of interactions among them.**
- **More biologically 'real' but more complicated**
  - Can take considerable time to develop and validate
  - Not necessarily better than simpler models if conceptual understanding or data is lacking!

Spatial models

Many of the issues of interest to disease managers clearly have a spatial component

- What areas are at greater risk for disease introduction?
- Are there key locations from which disease may be spread?
- Where should I look?
- How large should control areas be?
- How wide should I make vaccination buffer zones?
- What is the size of the area that might be affected?
- If disease is introduced at “X”, will it spread to “Y” and if so how long might it take?
- If resources are limited, how and where should I apply them for greatest effect?

Spatial models cont'd



- **Concerned with spread of disease through space as well as time**
- **Don't assuming homogenous mixing of the population**
- **Consider locality: e.g. transmission more likely if closer**
- **Don't assume the environment is constant**
  - environmental factors may influence disease expression and its control
- **Adds a new dimension to studying spread and control of disease**
  - enable a more 'holistic' view of disease
- **An adjunct to more traditional approaches**

Modelling spatial processes

Can be classified by degree of abstraction of the spatial process e.g. French and White 2004*:

1. **Spatially abstract: spatial arrangement is considered but absolute distances or locations not required (e.g. lattice models)**
2. **Spatially explicit: spatial processes are represented by realistic patterns and separations but don’t refer to specific locations.**
3. **Spatially specific: input variables and simulated model output refer to specific geographic locations**

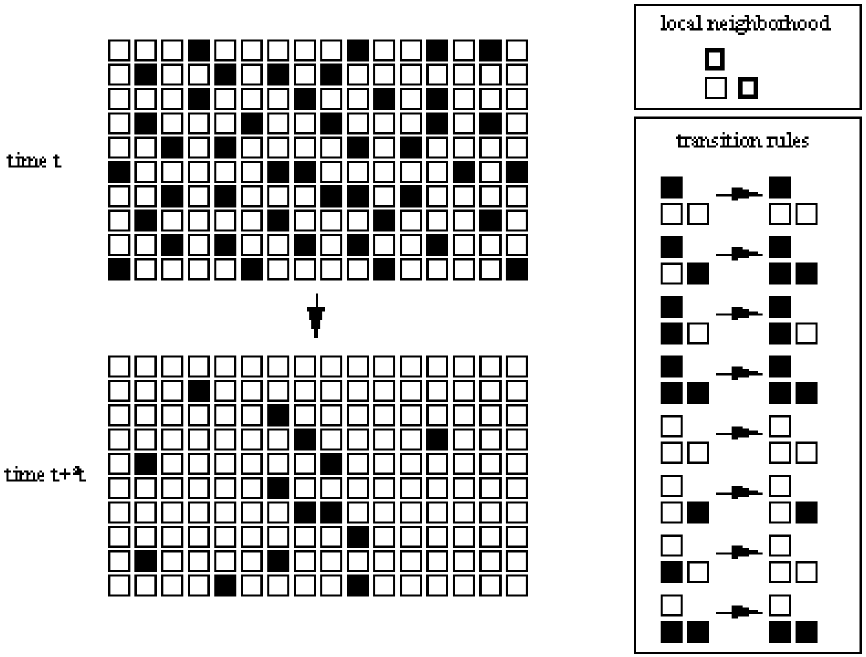
Like time, space may be treated as discrete or continuous

**French and White (2004)The use of GIS in modelling the temporal and spatial spread of animal diseases. In P. Durr and A Gatrell (eds) GIS and Spatial Analysis in Veterinary Science. CABI Publishing, Wallingford.*

Examples

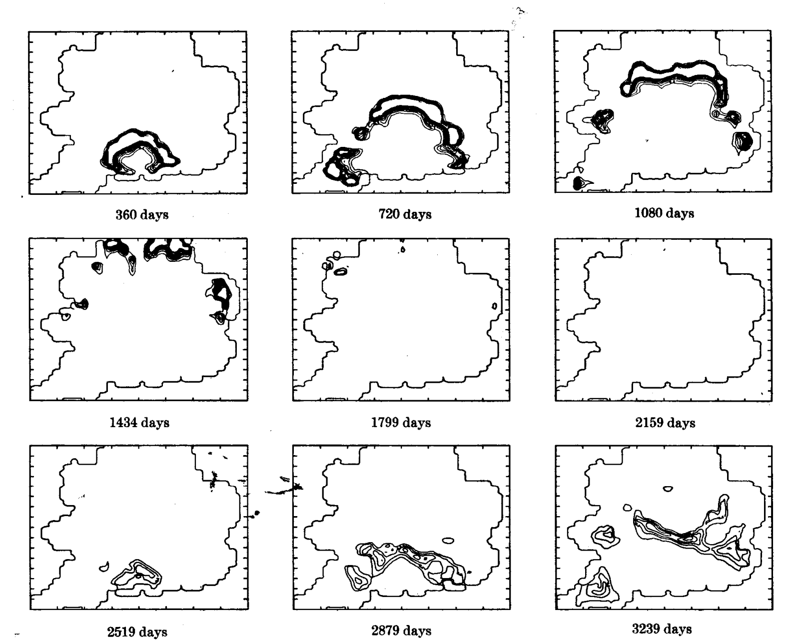
1. Discrete space models:

Lattice /grid cell/cellular automata

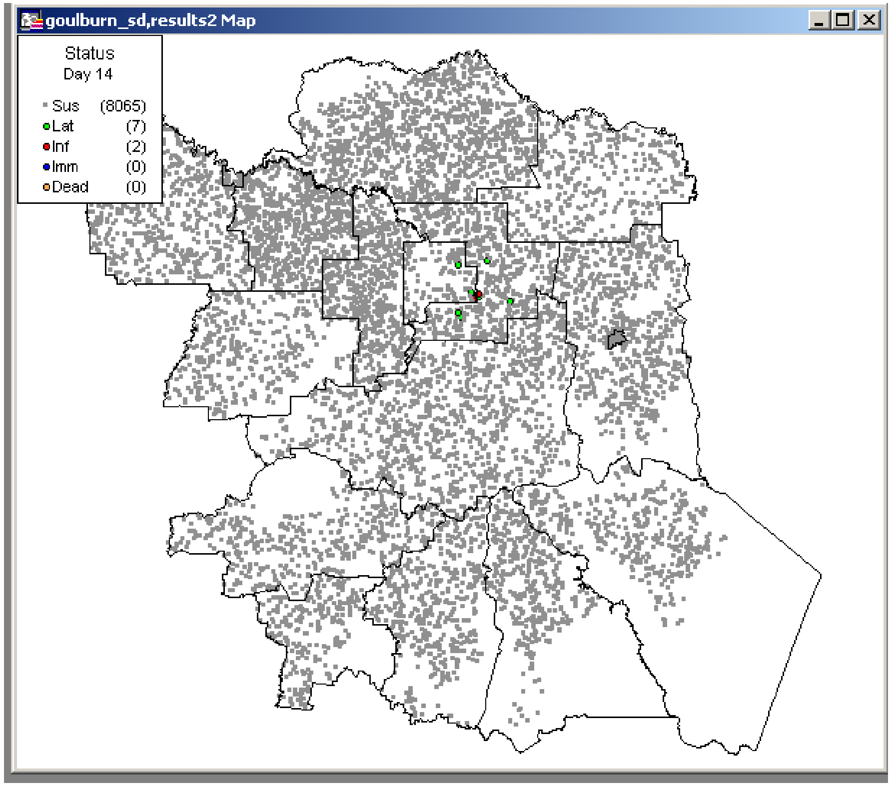


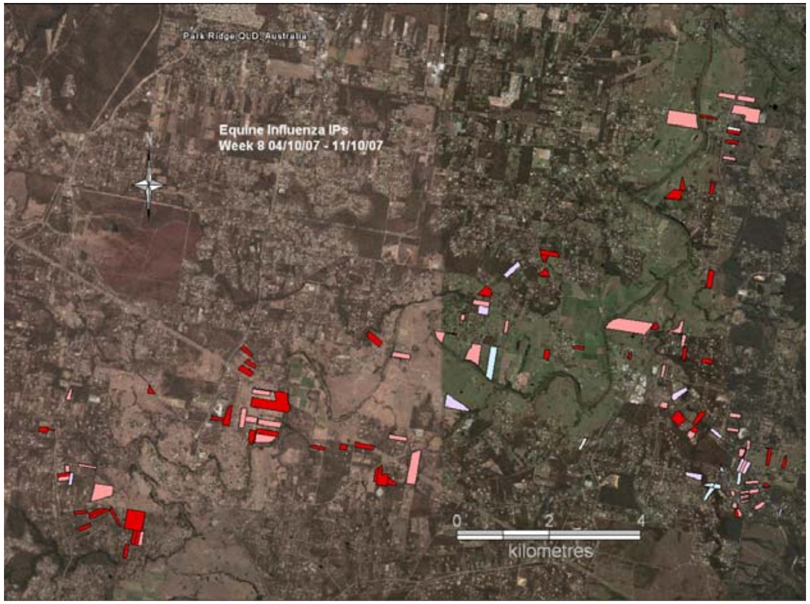
2. Continuous space:

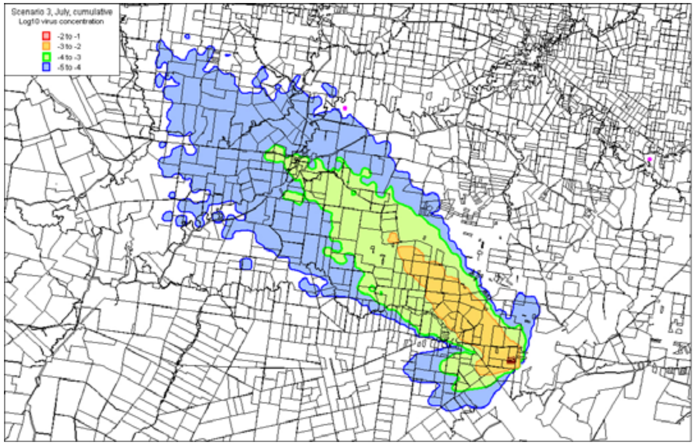
Diffusion/dispersal models - treat space, time and populations as continuous entities



3. Spatially-explicit:

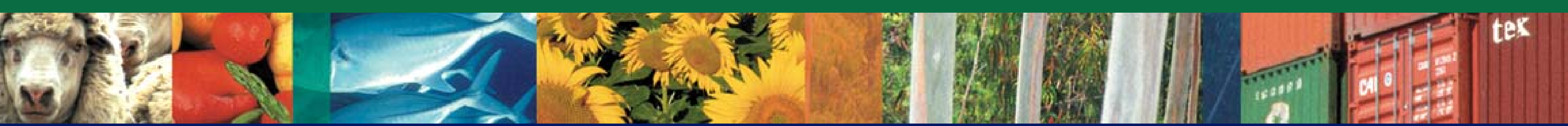


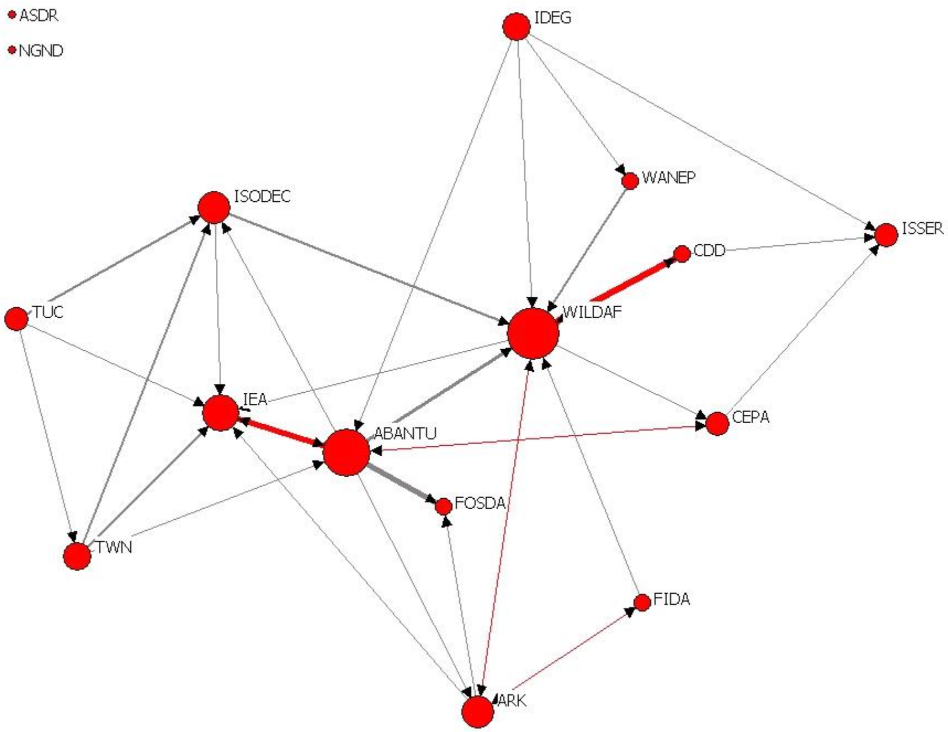




Contact network models

- Mix probability theory and graph theory
- Recognise that all susceptible individuals do not face the same risk of contracting a disease
- Borrow from sociological approaches - account for the points of connection between individuals.
- Each individual within the population is represented as a point (node) in a contact network
- Links connect individuals and represent interactions that take place, e.g. in the home, at school or work, while at a hospital, in public places, etc.
- Captures the diversity of contacts that underlie the spread of disease.

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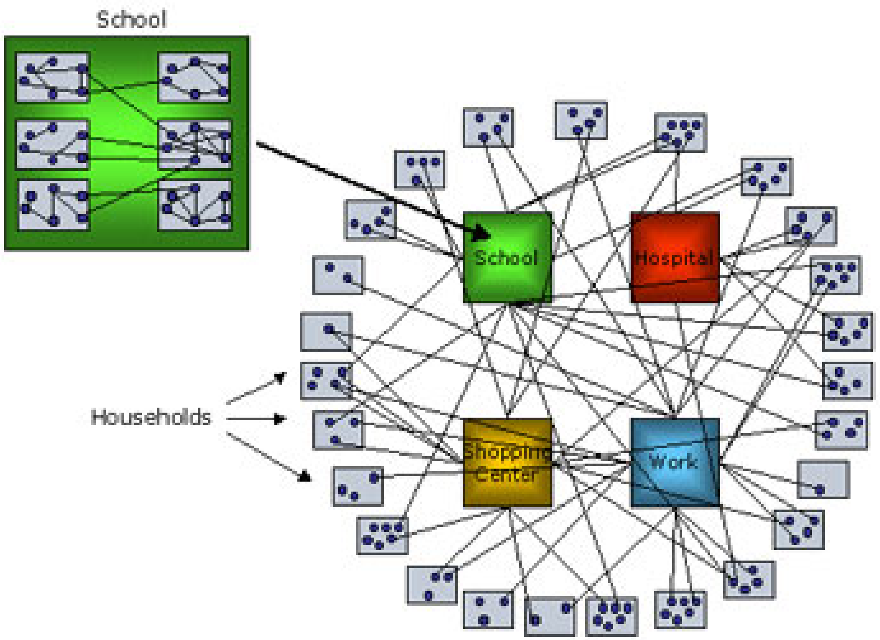
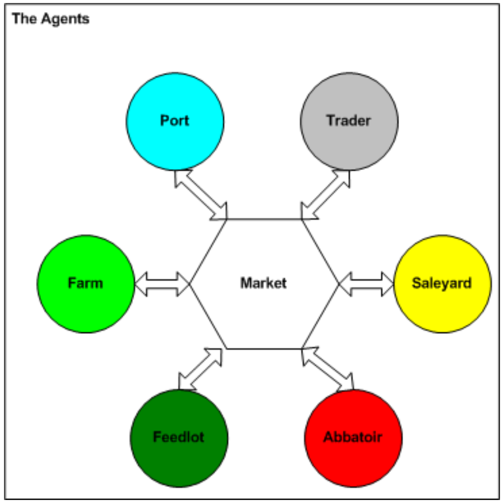

School
School
Hospital
Households
Shopping Center
Work

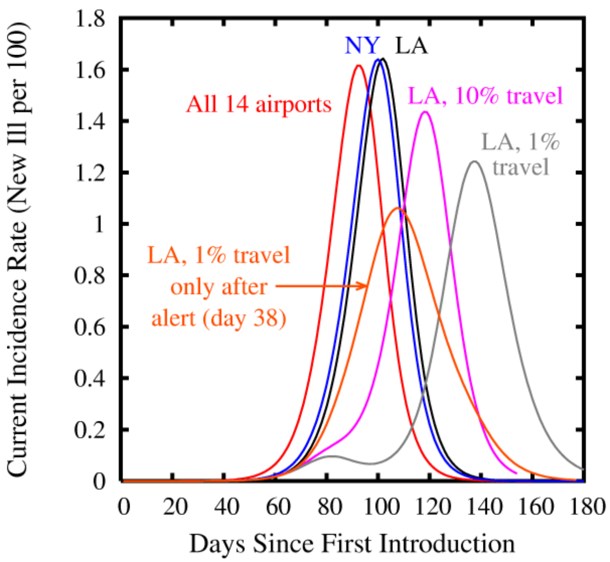
Agent-based simulation

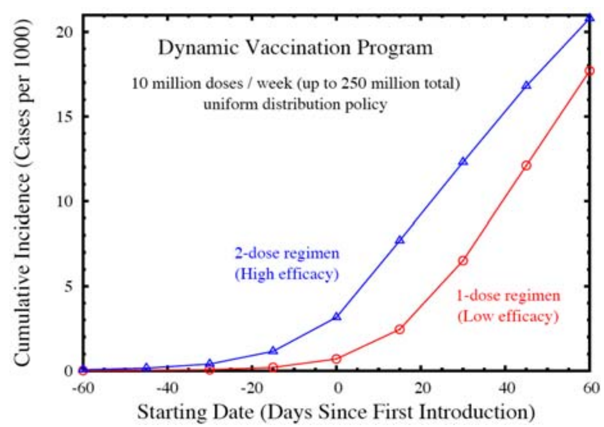
- representation of a system or process that incorporates time and the changes that occur over time
- consists of individual entities (agents)
- possess an internal *state* and set of behaviors or *rules* which determine how the agent's state is updated from one time-step to the next
- rules determine sequencing of actions in the model.
- emergent behaviour
- In Australia agent-based models being used to model national livestock movements
- Massive agent-based models are being used to study diseases like pandemic influenza at a national scale e.g. Los Alamos NL: EpiCast



EpiCast

- A stochastic agent-based simulation model of the United States population of 281 million individuals (implemented on parallel supercomputers), to predict the nationwide spread of infectious diseases and to assess various mitigation strategies.





Data/parameterisation

"One considerable challenge to any modelling study is parameterization, in particular assessing the many unknown and unmeasurable parameters that allow the model to capture the observed outbreak."

Tildesley et al. Proc Royal Soc. B, 2008

- **Modelling invariably involves trade-offs**
  - Model complexity vs lack of data
  - Specificity (time and space) – applicability to other locations/times

- **Particularly difficult for a country with no recent experience of the disease under study**
  - Overseas outbreaks/historical findings
  - Detailed data analysis
  - Expert opinion

But …

- **Need to interpret findings from overseas with caution due to differences in:**
  - Environment including weather, livestock densities, etc
  - Production systems
  - Marketing systems

- **May have to adjust key parameters to reflect differences**
  - Validation?

- **Findings from one outbreak cannot necessarily be used to infer behaviour of the next one**

“ … reconstructing piece by piece a past outbreak is certainly useful, but we may have to admit that it may be useless to anticipate the next outbreak …”

Francois Moutou, EUFMD 2003

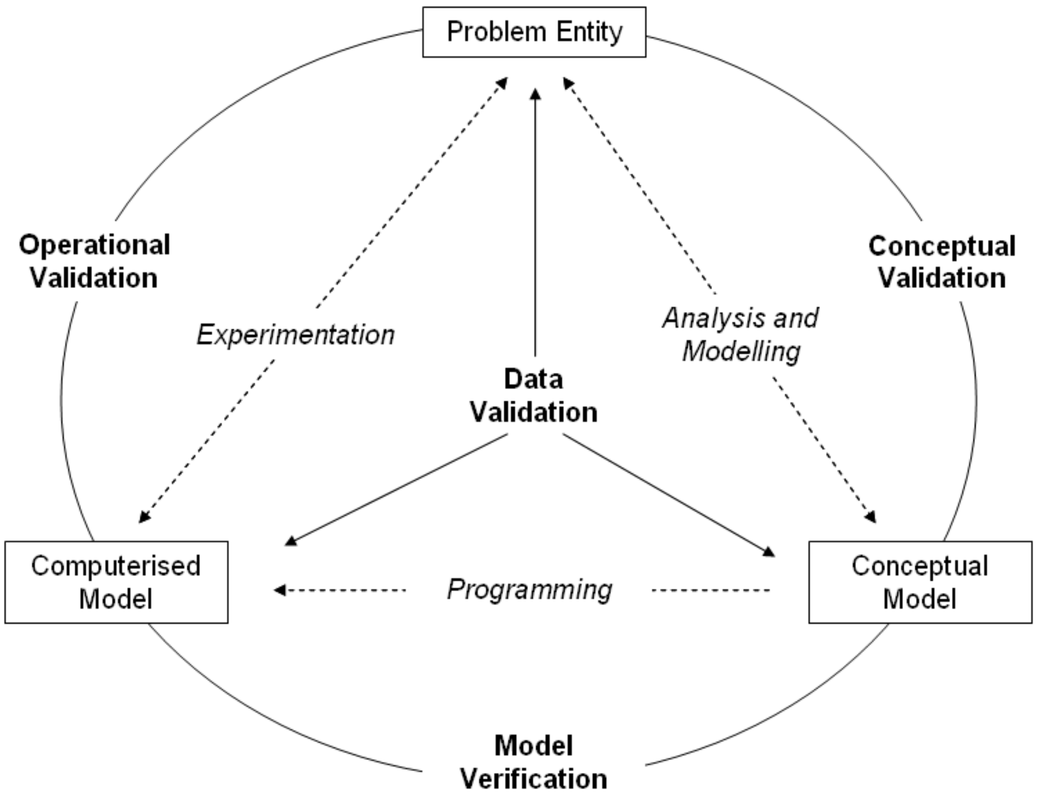
Validation and verification

Validation:

- **Assessing the accuracy of model output and ensuring its usefulness and relevance for the intended purpose**

Verification:

- **Ensuring the logic, formulae and computer code has been correctly written and represented**



Using and communicating the outputs

- **Modern epidemiological models are specialised tools**
  - Training in their use and good understanding of strengths and limitations of particular approaches is essential

- **Findings need to be interpreted with awareness of limitations and data quality**
  - Commonsense
  - Assist decision-making, not replace it!

- **Importance of sensitivity analyses**
  - How sensitive is the model to individual parameters and assumptions?

- **By definition models are simplifications of more complex systems**
  - May be realistic, but are not reality
  - What <u>could</u> happen, not what <u>will</u> happen

Perspective from the UK

- For the first time models were developed and used to direct control policy during an actual outbreak
- Varying views on their value

  "... surely the FMD experience should have made the modellers appreciate the limitations of their science and accept at least some responsibility for the misery and expense that their models initiated" (Kitching 2004)

- DEFRA review (Taylor 2003*)
  - Most appropriate use - tools in peacetime to aid retrospective analysis of real epidemics to gain insights.
  - Hypothetical epidemics can be modelled to better understand the relative merits of different strategies in different situations

*DEFRA-commissioned review on use of models to inform disease control policy

Use of epidemiological models for management of animal diseases*

- Models need to be fit for purpose and appropriately verified and validated.

- For informing disease control policy, modelling will be most useful when used pre-outbreak

- Recent experience (e.g. UK 2001) suggests that predictive modelling during actual outbreaks needs to be used cautiously.

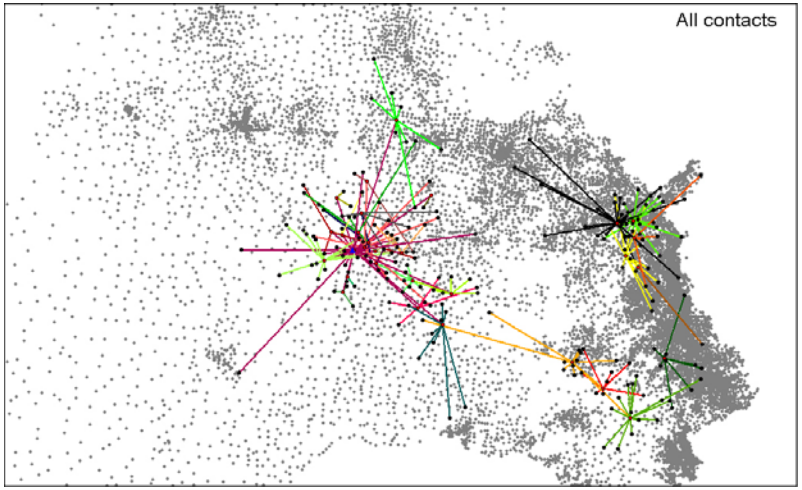
- Models are just one tool for providing scientific advice, and should not be considered in isolation to experimental studies, and analysis of epidemiological data.

**Dube et al. 2007 Discussion paper for 75th General Session of the OIE, May 2007*

Using epidemiological models for managing outbreaks

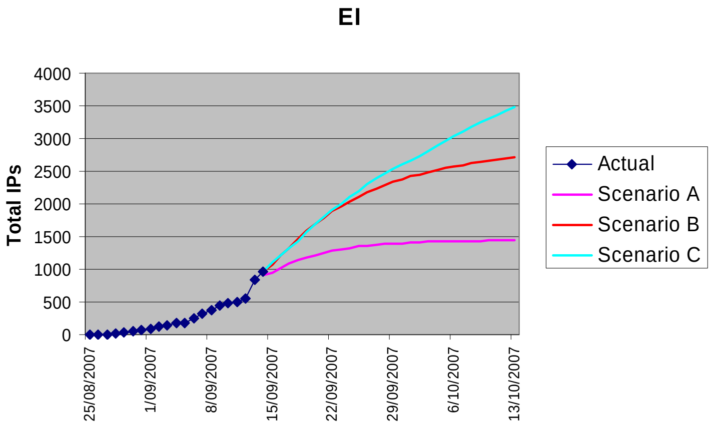
1. Pre-outbreak (preparedness)

- risk assessments i.e. to identify areas, sub-populations, production systems etc., that might be at greater risk
- evaluating effectiveness of various surveillance and control strategies
- underpinning economic impact studies
- providing scenarios for preparedness/training exercises.



2. During an outbreak (response)

- **Assist resource planning**
- **Investigate alternate control measures**
- **Outbreak predictions**
  - **more problematic (parameter estimation)**



"Prediction is very difficult, especially if it is about the future"

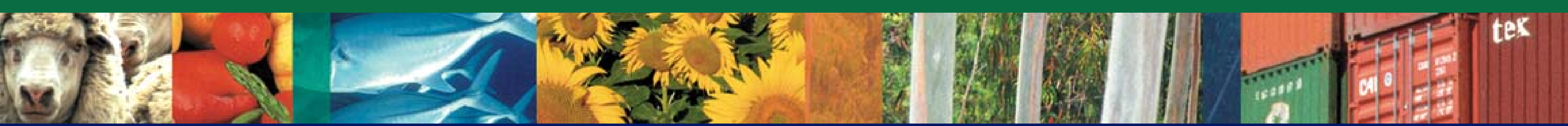
Niels Bohr, Danish physicist, 1885 - 1962

Conclusions

- Epidemiological models are valuable tools to assist policy development on disease prevention and control:
  - investigate disease dynamics
  - study introduction scenarios
  - analyse impacts
  - test mitigation strategies
  - assist decision-making

- Multidisciplinary approaches using a range of technologies means it is becoming possible to build increasingly sophisticated models of animal and human disease

- New generation epidemiological models enable disease to be studied in the context of geo-spatial, economic, technological, management and political infrastructures



Conclusions cont’d

- **Models need to be fit for purpose and appropriately verified and validated**

- **Best approaches are likely to result when epidemiologists, modellers and disease managers work together rather than in isolation**

- **Modern epidemiological models are specialised tools**
  - **Training in their use and good understanding of strengths and limitations is essential in order to interpret the outputs**

- **Models are just one tool for providing scientific advice, and the findings should not be considered in isolation to experimental studies and field data**

Thank You

Questions?