

IF EPIDEMIOLOGICAL MODELS ARE SIMPLIFICATIONS OF REAL SYSTEMS, WHY ARE THEY SO HARD TO UNDERSTAND?



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INTRODUCTION



- What are epidemiological models?
 - Mathematical/logical representations of disease transmission and associated processes (Dube et al., 2007)
 - Almost always simplified in some way (Taylor 2003)
 - Useful if “real” studies impractical
 - Validity limited by understanding of the system and data
 - Address “what might happen if... ?” questions

“Prediction is difficult, especially about the future”

Neils Bohr



INTRODUCTION

- Decision makers can have confidence in a model if it is:
 - **Conceptually valid**
 - appropriate logical/mathematical representation of the real system
 - **Verified**
 - correctly implemented as equations/code
 - **Operationally valid**
 - produce outputs that are sufficiently accurate and precise for objectives
 - **Built with good quality data**
 - **Sensitivity analysis is conducted**
 - investigation uncertain assumptions and parameter estimates important



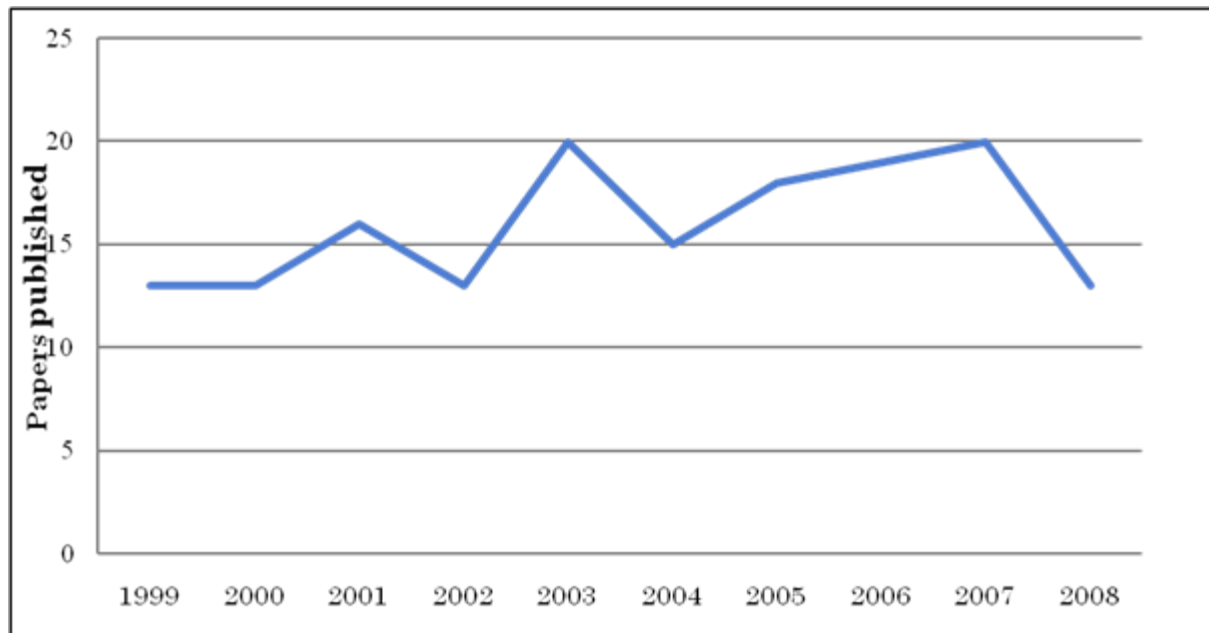
METHODS

- Systematic review of published modelling studies 1999-2008
- Inclusion criteria:
 - Process models to investigate temporal dynamics of infection
 - viral, bacterial or prion agents
 - domestic terrestrial animal species
- Exclusion criteria:
 - associative models (solely fit to data)
 - wildlife models
 - no mention of a specific agent in title/abstract
- Multiple papers of the same model evaluated together



PAPERS AND MODELS...

- 350+ papers identified in searches
- 166 papers met inclusion criteria
- 111 models
- Mean 1.5 papers per model



OBJECTIVES OF MODELLING STUDIES

- Insight into epidemiology of infection
 - Generate hypotheses
 - Identify vulnerabilities
 - Identify uncertainties for empirical studies
- Understand potential likelihood and consequences of infection
- Evaluate different management strategies
 - Future resource planning
 - Economic assessment
 - Accuracy/timeliness of surveillance systems
 - Retrospective analysis of past epidemics
- Training/education
- (Real time prediction and decision support)



CONSIDERATIONS IN MODEL DESIGN

- Objectives of the study affect the scale and design of a model
- Data availability/quality also a factor
- What is the unit of interest?
 - Animal
 - Sub-population (e.g. shed)
 - Farm/herd
 - Nested approaches (e.g. on farm and between farm spread)
- How should the units be represented?
 - Individual (increased data requirements)
 - Continuous (limits number of host attributes)



CONSIDERATIONS IN MODEL DESIGN

- How should time be represented?
 - Discrete time steps
 - Solved for each step based on previous step's results
 - Time step should be appropriate to the dynamics of infection, desired precision of results and available data
 - Discrete event
 - Events scheduled in a queue
 - Events simulated in order of occurrence
 - Continuous time
 - Differential equation models (calculus)



CONSIDERATIONS IN MODEL DESIGN

- How to represent the course of infection?
 - Most model types use a Markov chain/state transition approach
 - Units can exist in mutually exclusive states
 - Transition between states as “events” occur



CONSIDERATIONS IN MODEL DESIGN

- Are chance or uncertain elements important?
 - **Deterministic** parameters – fixed
 - **Stochastic** parameters – probability distributions
- Are spatial factors important?
 - Non-spatial
 - Pseudo-spatial (grids/lattices)
 - Spatially explicit (distances/points/regions)

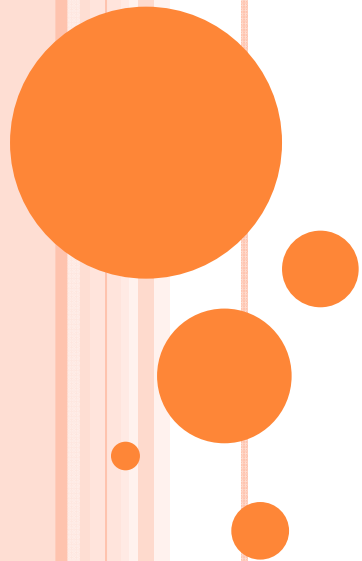


CONSIDERATIONS IN MODEL DESIGN

- How will the model determine a solution?
 - Mathematical
 - Use differential equations/difference equations/linear algebra to find a closed form solution
 - Simulation
 - Uses numerical substitution to estimate results
 - Usually more complex, more parameters

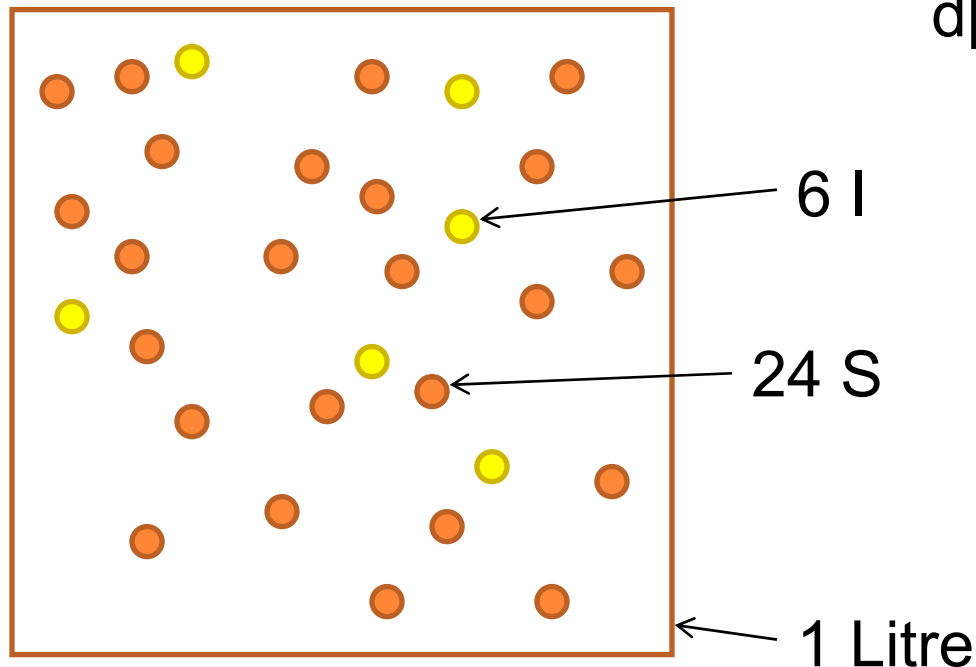


MATHEMATICAL APPROACHES TO REPRESENTING THE TRANSMISSION INFECTION



MASS ACTION MODELS

- Based on chemical law of mass action



$$d[I]/dt = k[S][I]$$

$$= k \times 24 \times 6/1L$$

- But what is a good analogy of the [S] and [I] in a population?? Frequency/density??



MASS ACTION MODELS

- Continuous time
- Continuous unit
- Deterministic
 - Stochastic variants
- Homogeneous mixing
- Easily fitted to data, quick to develop
- Modified to add other pathways:
 - Vertical transmission
 - vectors etc.

$$\frac{dS}{dt} = b - \beta SI - dS$$

$$\frac{dI}{dt} = \beta SI - \gamma I - dI$$

$$\frac{dR}{dt} = \gamma I - dR$$

Where:

S=density of susceptible individuals

I=density of infectious individuals

R=density of removed individuals

β =transmission coefficient

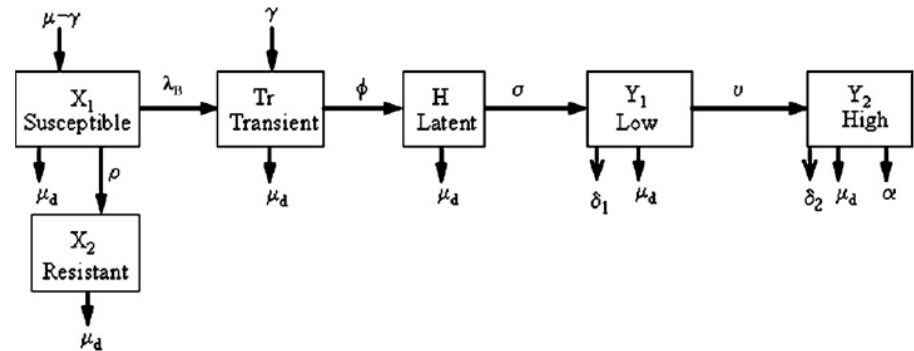
γ =recovery rate

b=birth rate

d=death rate

DISCRETE TIME MARKOV CHAIN/STATE TRANSITION APPROACHES

- Discrete time
- Continuous unit
- Deterministic/stochastic
- Homogeneous mixing
- Equations represent the transitions between each state for each time step
- Equations and parameters constant over time



CHAIN BINOMIAL MODELS

- Reed-Frost model is most common example
- Discrete time
- Continuous/discrete entity
- Deterministic/stochastic approaches

- Homogeneous mixing
- Each susceptible unit has an equal probability of “effective contact” with a single infectious unit per time period

$$I_t = S_{t-1}(1-(1-p)^{I_{t-1}})$$

$$R_t = R_{t-1} + I_{t-1}$$

$$S_t = S_{t-1} - S_{t-1}(1-(1-p)^{I_{t-1}})$$

Where:

I_t =Number of infectious units at time t

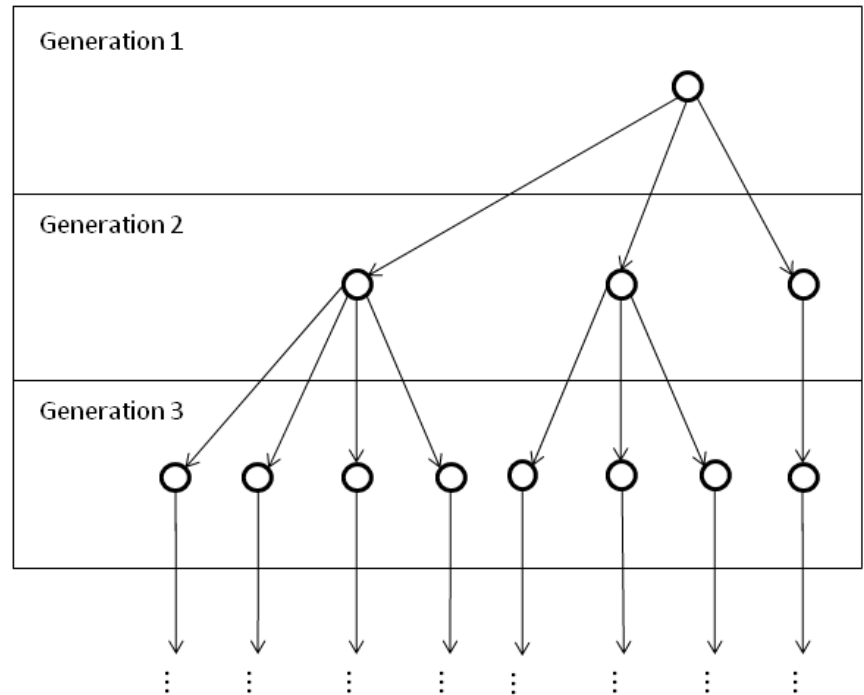
S_t =Number of susceptible units at time t

p=probability of an effective contact



BRANCHING PROCESS MODELS

- Continuous unit, discrete/continuous time
- Infectious units generated spontaneously from other infectious units
- Often assume infinite susceptible population (no burn-out)
- Secondary cases independently distributed
- Deterministic/stochastic
- Limited parameter requirements
 - case reproduction rate
 - generation time
 - detection time



$$I_{t+1} = \sum_{k=0}^{I_t} \xi_k$$

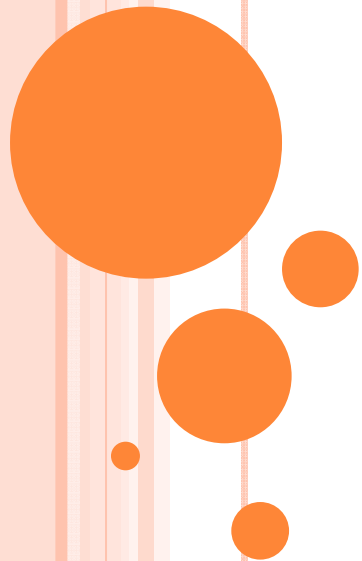
Where:

I_t = Number of infectious units at time t

ξ_k = Stochastic estimate of case

reproduction ratio

SIMULATION APPROACHES TO REPRESENTING THE TRANSMISSION INFECTION



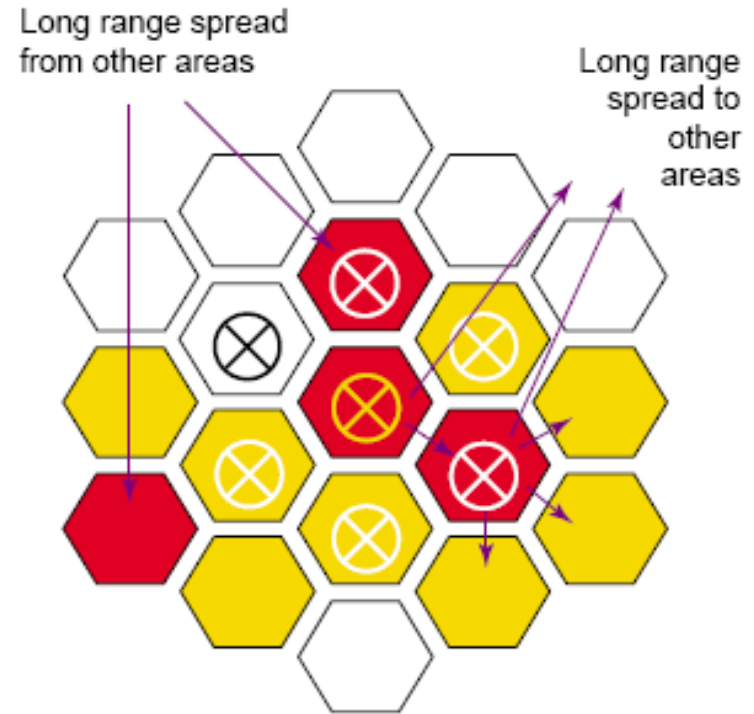
DISCRETE UNIT SIMULATION MODELS

- Also known as individual-based or agent based models
- State-transition approaches
- Can incorporate stochastic elements via Monte-Carlo methods
- Individuals can have different attributes
 - Demographics
 - Spatial attributes
 - Functional connections
- Heterogeneity may lead to more realism
- Longer development times & difficult to verify/validate



PSEUDO-SPATIAL (CELLULAR AUTOMATA) APPROACHES

- Units are organised in a regular lattice
- Spread across lattice boundaries
- Simplistic spatial representation
- Less data requirements but less realistic than spatially explicit approaches



FMD model of Kao 2001
(picture from Kao 2002)



SPATIALLY EXPLICIT APPROACHES

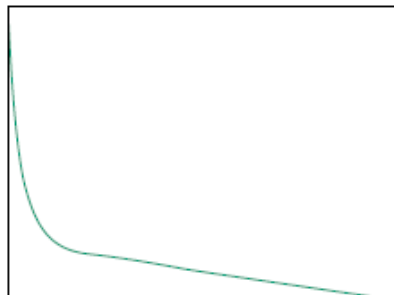
- Table of distances between fixed locations
- Units represented by point coordinates or regions
- These factors incorporated in transmission/control algorithms

	F1	F2	Fn
F1	0	d_{12}	...	d_{1n}
F2	d_{21}	0
...
Fn	d_{n1}	0

Distances between farms

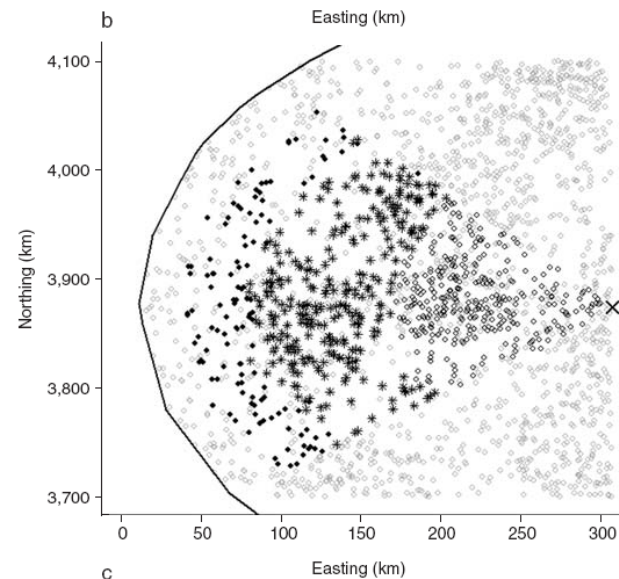


Weighted probability of infection



Distance

Keeling et al. 2001

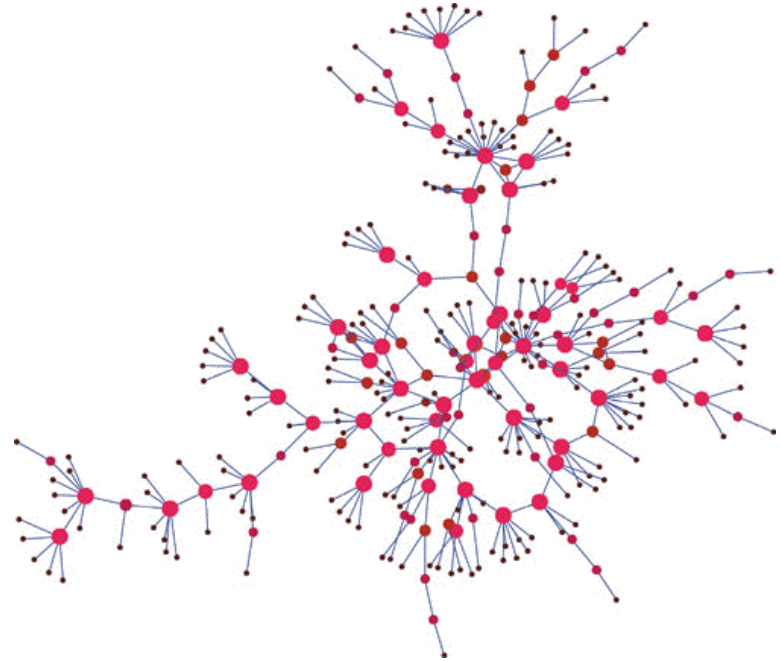


Dubé et al. 2007



NETWORK MODELLING APPROACHES

- Behavioural/operational characteristics may mean contacts not random
- Contacts between individuals can be represented as a network
- Transmission on network governed by probabilities
- Connections may represent movements of animals/fomites between farms for example



Potterat et al. 2002



DISCUSSION AND CONCLUSIONS

- Design of a model should be appropriate for the objectives of the study
- Providing insight into complex problems may require complex approaches
- Mathematical approaches limited by tractability of equations
- Discrete unit simulation models favour more complex representations of the population/disease dynamics
 - Data hungry!
- Complex approaches not necessarily better if there is poor quality data available



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