FROM INDIVIDUALS TO POPULATIONS

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1. MODEL TYPES
2. DISEASE TYPES
3. EPIDEMIOLOGICAL QUESTIONS
4. MATHEMATICAL TECHNIQUES FOR ANALYSIS
5. DISCUSSION ISSUES

Models are inherently stochastic, *appropriate* deterministic models may approximate population-level properties.

Focus is on models that are amenable to mathematical analysis.

MODEL TYPES

- LOCALLY LARGE — Classical compartmental/ deterministic models
- SPATIAL — Lattice and non-lattice
- NETWORK/RANDOM GRAPH
- META POPULATION — Households
- COMPLEX SIMULATION

  (MULTI TYPE VERSIONS)

DISEASE TYPES

- S/R
- ENDEMIC, NO DEMOGRAPHIC EFFECTS

  SIS/SIRS
- ENDEMIC WITH DEMOGRAPHIC EFFECTS

  SIR with vital dynamics

  .

  .

  .
- Host vector
- STDs
- Multi strain

  .

  .

  .

IMPORTANT EPIDEMIOLOGICAL QUESTIONS

SIR models

- INVASION THRESHOLDS
  R_0, R_*, λ_c
- FINAL OUTCOME (LOCAL/GLOBAL)

SIS/SIRS models

- INVASION/PERSISTENCE THRESHOLDS
- ENDEMIC LEVELS (LOCAL/GLOBAL)
- TIME TO EXTINCTION

SIR with vital dynamics

- INVASION/PERSISTENCE THRESHOLDS
- ENDEMIC BEHAVIOUR (CYCLIC?)
- FADE OUT / TIME TO EXTINCTION

COMPLEX SIMULATION MODELS

- Realistic, so easy to sell.
- Often only approach for giving quantitative answers to key questions.
- Computationally expensive so can be difficult to
  - interpret (e.g. effects of parameters),
  - attach confidence intervals to predictions,
  - perform sensitivity analyses.

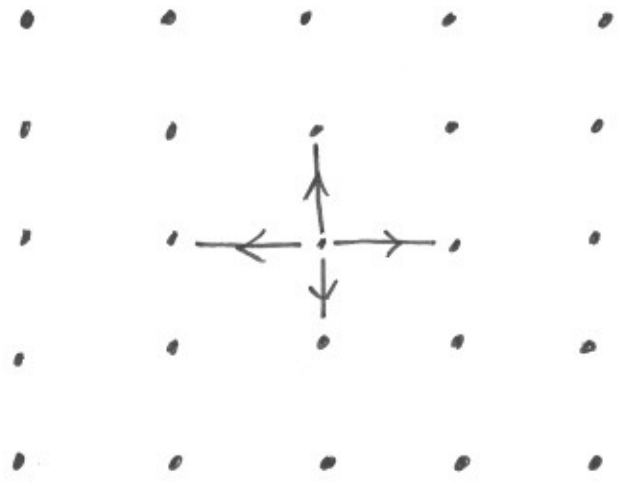
LOCALLY LARGE MODELS

If population is split into groups, e.g. by age, sex, geographical location, then *each* of these groups (and not just the *total* population) is large.

- Classical compartmental models
- Implicitly assumed in
  - deterministic models
  - many stochastic threshold theorems

  } R_0
- Considerable theoretical/analytical progress possible but models do not reflect finite local structure of human populations
- Viewing stochastic locally large models at an individual level has greatly facilitated their analysis

SPATIAL MODELS (LATTICE)



Nearest-neighbour

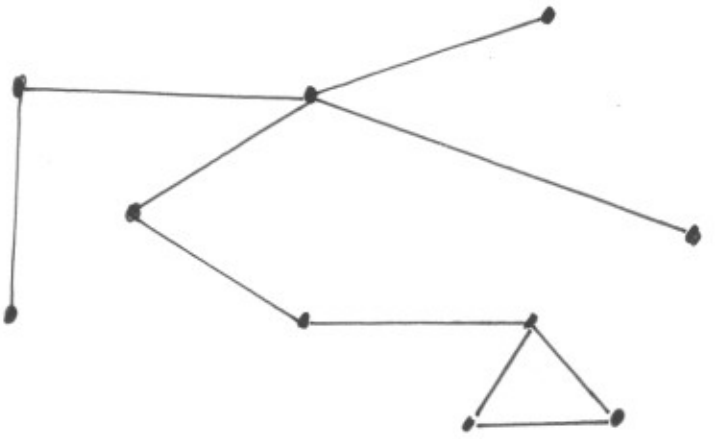
Contact distribution

- *very* hard to analyse rigorously
- theoretical results often "just" prove existence of phenomena; e.g. critical λ_c known for very few models
- lattice structure too rigid for human populations

  suitable for plant and some animal diseases

  (e.g. fox rabies)

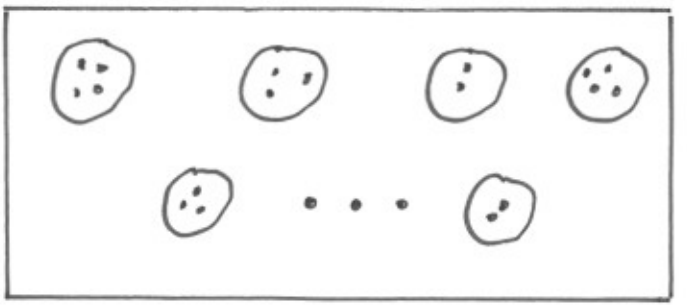
NETWORK/RANDOM GRAPH MODELS



- 'independent' random graph of possible contacts satisfying given degree distribution $P(D = k) = p_k$ $(k = 1, 2, \ldots)$
- spread epidemic on graph
- 'independence' assumption $\Rightarrow$
  - model amenable to analysis (e.g. threshold behaviour and final outcome for SIR)
  - model "close" to homogeneous mixing
  - too few triangles in network
- 'correlated' graphs difficult to analyse rigorously
- dynamic networks

METAPOPULATION MODELS

Households model



m_n households
of size n
$(n = 1, 2, \ldots)$

$N = \sum nm_n$

Individual $\longrightarrow$ individual infection rates local λ_L

global λ_G/N

- treat households as macro-individuals (with internal dynamics) that mix homogenously
- SIR (and SIS?) models well understood

Two levels of mixing

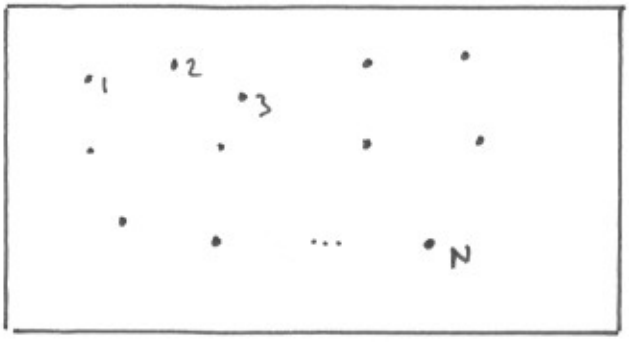
- overlapping subgroups (e.g. household/ workplace), hard to make analytic progress without very restrictive assumptions
- "small world" – great circle model
- network models with global mixing

Extensions

- hierarchical levels of mixing (e.g. towns, households, individuals) spatial scales/asymptotic regimes
- non-SIR; households with vital dynamics

GENERAL SIR EPIDEMIC MODEL WITH TWO LEVELS OF MIXING

(Ball and Neal (2002))



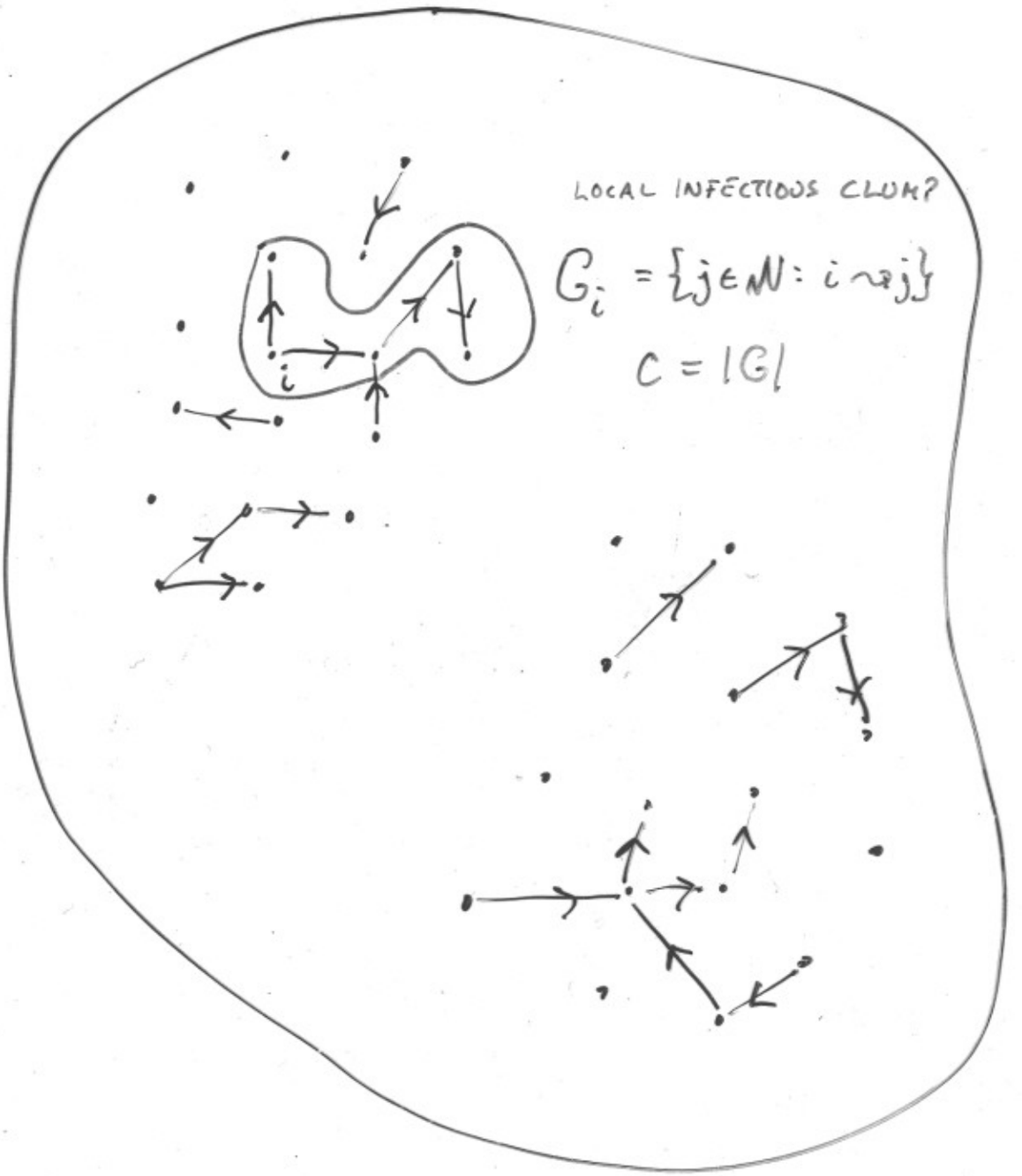
Population $\mathcal{N} = \{1, 2, \ldots, N\}$

- Infectious individuals have iid infectious periods, distributed according to a random variable T_I.
- If infected, individual i makes

  LOCAL CONTACTS with j ($\in \mathcal{N} \backslash \{i\}$) at the points of a Poisson process with rate λ_{ij}^L

  GLOBAL CONTACTS with individuals chosen independently and uniformly from $\mathcal{N}$, at the points of a Poisson process with rate λ_G.
- If a contacted individual is susceptible then it becomes infected, otherwise nothing happens.
- Epidemic ceases as soon as there is no infective present.

DIRECTED GRAPH OF LOCAL CONTACTS

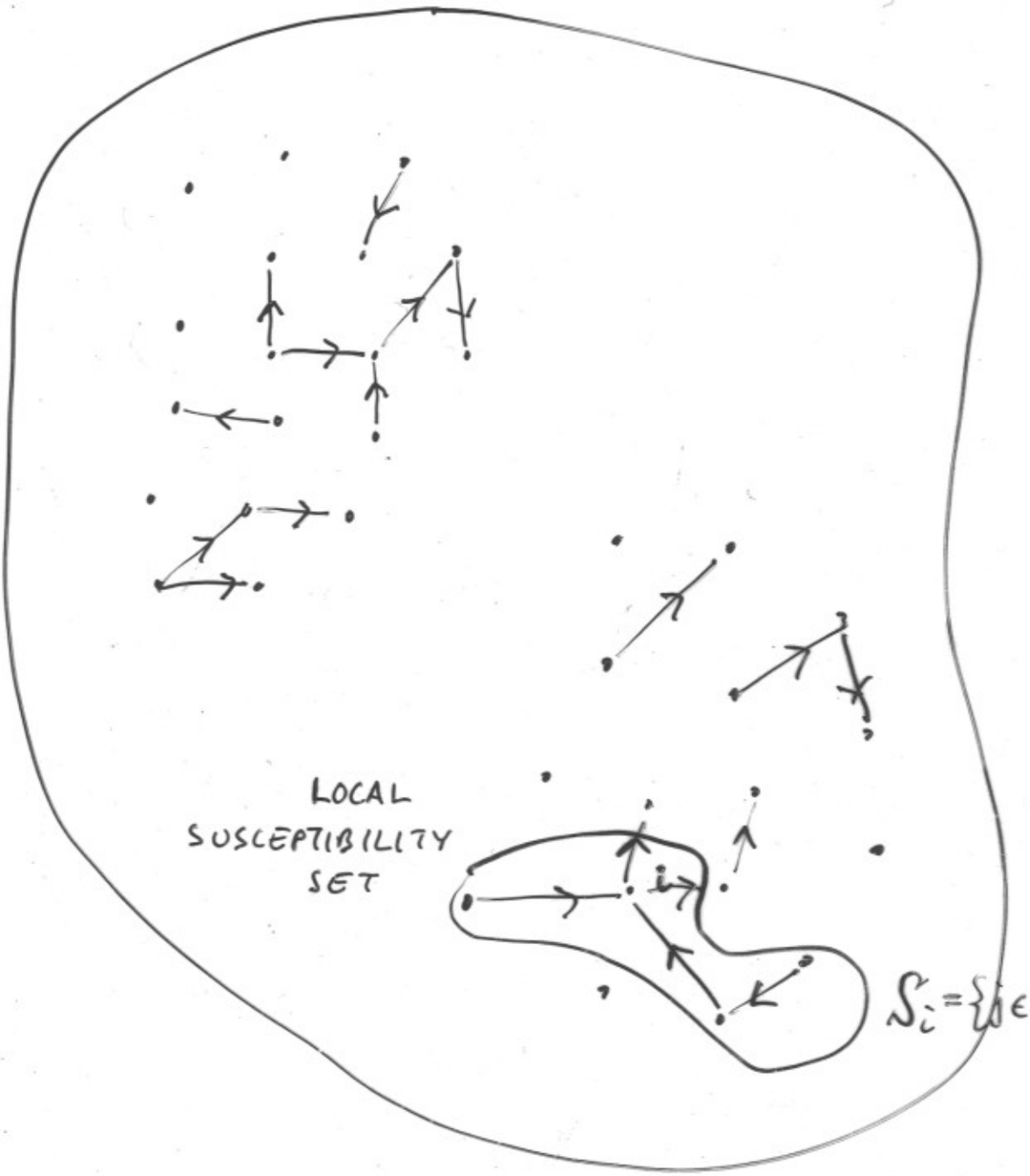


$i \to j \Leftrightarrow$ i contacts j locally

$i \rightsquigarrow j \Leftrightarrow$ there exists chain of directed arcs from i to j

$(i \rightsquigarrow i)$

DIRECTED GRAPH OF LOCAL CONTACTS



$i \to j \Leftrightarrow$ i contacts j locally

$i \rightsquigarrow j \Leftrightarrow$ there exists chain of directed arcs from i to j $\quad (i \rightsquigarrow i)$

THRESHOLD THEOREM

Let $R_* = \lambda_G E[T_I]E[C]$ $(= \lambda_G E[T_I]E[S])$. Then in the limit as $N \to \infty$, if the epidemic is initiated by a fixed finite set I_0 of initial infectives,

(a) a global epidemic occurs with non-zero probability if and only if $R_* > 1$;

(b) the probability of a global epidemic is $1 - \psi_{I_0}(\lambda_G(1-p))$, where p is the smallest root of $\psi(\lambda_G(1-s)) = s$ in $[0,1]$;

$[\psi(\theta) = E[\exp(-\theta A)]$, where A is the *severity* (i.e. sum of infectious periods) of typical local infectious clump

$\psi_{I_0}(\theta) = E[\exp(-\theta A_{I_0})]$, where A_{I_0} is the severity of the local infectious clump $\mathcal{C}_{I_0} = \{j \in \mathcal{N} : i \rightsquigarrow j \text{ for some } i \in I_0\}]$

(c) if $R_* > 1$, then (i) the proportion of initial susceptibles ultimately infected by a global epidemic, $\hat{z}$ say, is given by the unique root in $(0,1]$ of $1 - z = f_S(e^{-\lambda_G z E[T_I]})$; (ii), if H is a fixed finite set of initial susceptibles and X_H denotes the set of individuals in H that ultimately avoid infection, then in the event of a global epidemic

$$P(X_H = F) = \sum_{F \subseteq G \subseteq H} (-1)^{|G|-|F|} f_{S_G}(\hat{\pi}) \quad (F \subseteq H),$$

where $\hat{\pi} = \exp(-\lambda_G \hat{z} E[T_I])$;

$[f_{S_G}(s) = E[s^{S_G}]$, where $S_G = |\{j \in \mathcal{N} : j \rightsquigarrow i \text{ for some } i \in G\}|$ is the size of G's local susceptibility set]

and (iii) central limit theorem can be derived for the final outcome of a global epidemic.

TECHNIQUES FOR ANALYSIS

	Method	Model-type	Model features
1	Percolation	spatial SIR	Invasion
2	Interacting particle systems	spatial SIS	"Long-term" behaviour
3	Mean-field, deterministic	LL, MP, (N)	"Long-term"
4	Moment closure	LL	behaviour
5	Density dependent processes	LL, MP	
6	Coupling	All	Most
7	Branching process approx.	LL, MP, N	Invasion
8	Embedding	LL, MP, (N)	Final outcome (SIR only)
9	Quasi-stationary dsns	LL (non-SIR)	endemic levels and time to extinction
10	Pair approximations	N, S	"Long-term" behaviour

Key S spatial, LL locally large, MP metapopulation, N network

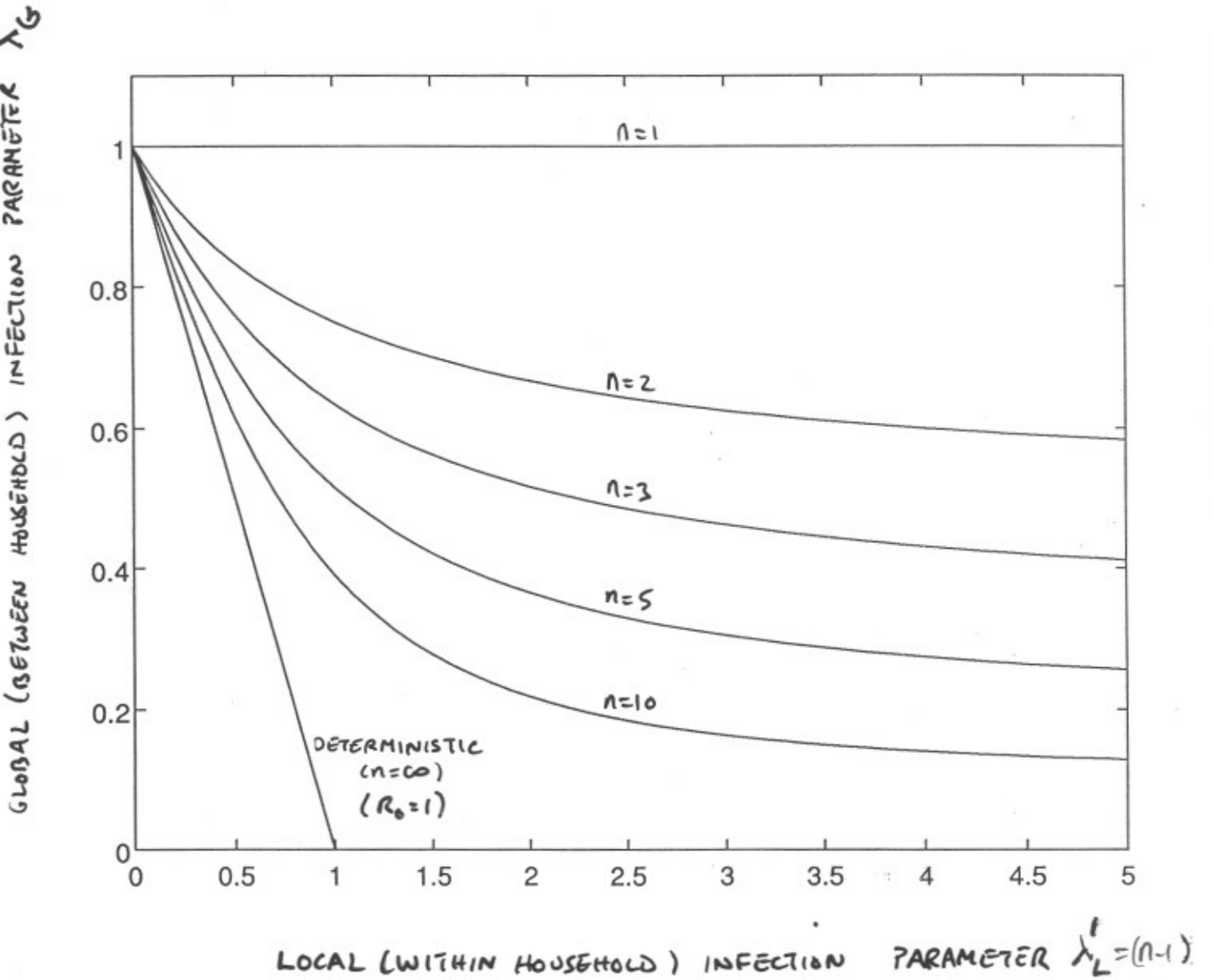
Methods 4, 10 and (3?) are approximate; rest are fully rigorous, e.g. justified by limit theorems.

COMPARISON/CROSS-FERTILISATION OF METHODOLOGIES

- Which methods are most suited for different types of model structure, disease, model properties ...
- Other important techniques
  - previously used in epidemic modelling
  - not previously used in epidemic modelling.
- Techniques have evolved in different disciplines (e.g. probability, applied maths, mathematical physics ...) – considerable scope for cross-fertilisation.

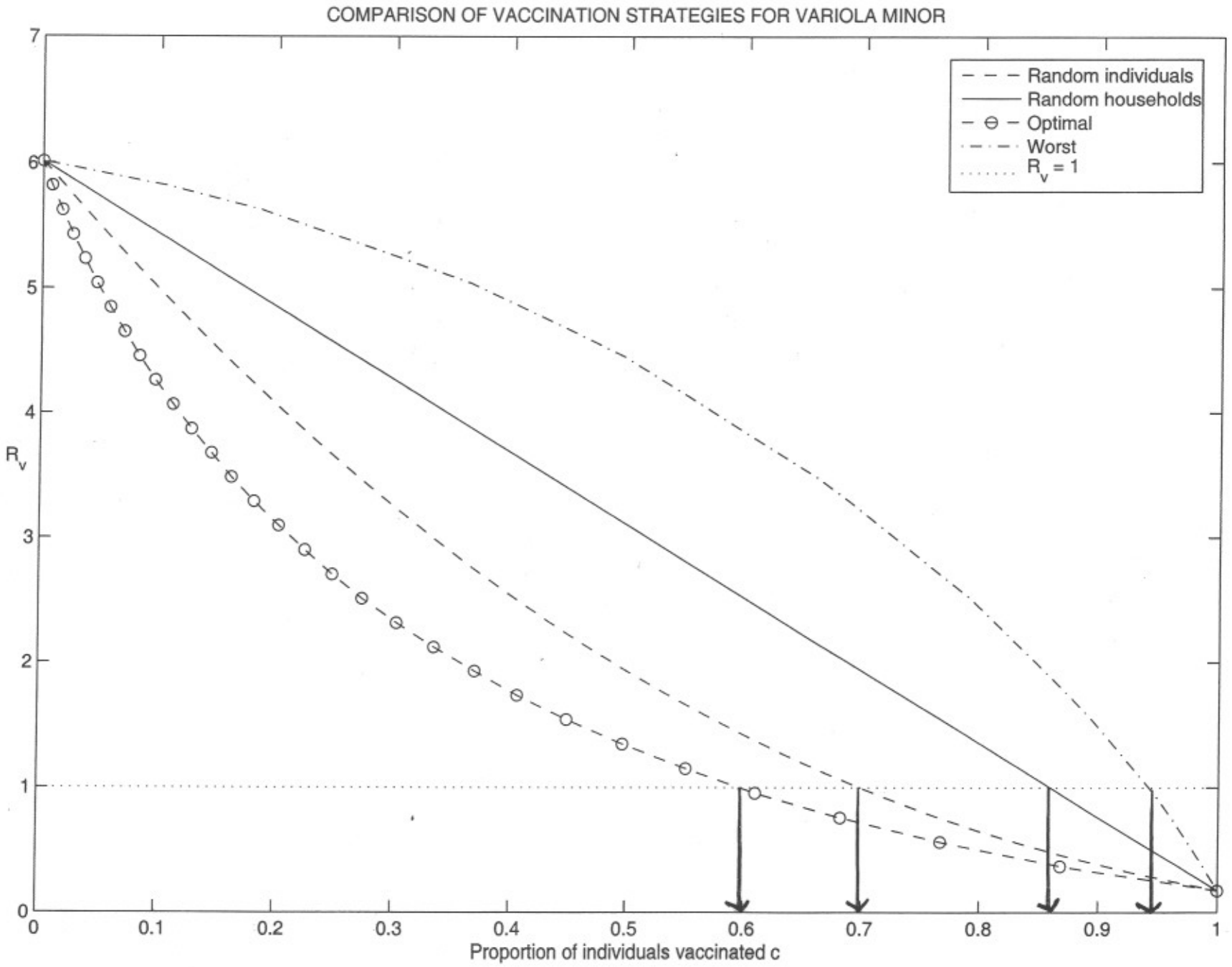
COMPARISON OF MODELS

- Extent to which qualitative/quantitative behaviour of models differ from each other, and from that of simpler, e.g. homogeneously mixing models.
- Global properties qualitatively broadly similar but there can be significant quantitative differences.
- Relationship between local structure and global properties.
- What local structures are important/essential?
- Purpose of model.



CRITICAL PARAMETER VALUES ($R_* = 1$) FOR SIR HOUSEHOLD EPIDEMIC MODEL WHEN $T_I \sim NE(1)$ AND COMMON HOUSEHOLD SIZE n (cf Ball and Lyne (2006))

From Ball and Lyne (2006)



PRACTICAL APPLICABILITY OF MODELS

- Models are over simplified so that they are susceptible to analysis.
- Results are often limit theorems as population size n tends to infinity (in an appropriate fashion).
- Important for understanding disease dynamics

  BUT
- How do (quantitative) predictions carry over to
  - more realistic population/disease structures
  - finite n?
- How can models be made more realistic whilst maintaining tractability?

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