Whither disease ecology?
Old problems and new solutions in a complex world.

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With valuable comments from Pete Hudson, Monique Ambrose, Michael Buhnerkempe & Miran Park, and many helpful chats with many others...
Outline and themes

Models of zoonoses – lessons and gaps

‘Reservoir’ dynamics – persistence in a multi-host world

Pathogen interactions in multi-host systems

Epidemiological dark matter

Why subcritical and non-maintenance populations can’t be ignored.
Lessons from zoonotic pathogens

Aim: Survey the epidemic modeling literature on transmission dynamics of zoonotic microparasites.

→ Reviewed 442 modeling papers on 85 zoonotic pathogens (“everything” up till 2008)

Co-authors: Dylan George, Kim Pepin, Ginny Pitzer, Juliet Pulliam, Andy Dobson, Peter Hudson, Bryan Grenfell

Lloyd-Smith et al, Science 2009
Lessons from zoonotic pathogens

Circulation in reservoir  Cross-species spillover  Stuttering chains ($R_0<1$, subcritical)  Epidemics and persistence ($R_0>1$, supercritical)

Directly transmitted zoonoses

- Epidemics
- Stuttering
- Spillover
- Reservoir

Number of phases included in each model

Lloyd-Smith et al, Science 2009
Spillover and stuttering chains: the problem

Key challenge: To disentangle contributions of zoonotic spillover versus human-to-human transmission.

Essential in order to:
- estimate transmissibility (≈pandemic risk) of emerging pathogens
- quantify spillover in order to study and control
Spillover and stuttering chains: the problem

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Progress on subcritical transmission...

New methods to infer parameters from subcritical outbreak data, based on branching processes, and building on results from post-elimination surveillance of childhood infections.  
(e.g. Farrington et al. Biostat. 2003)

• Outbreak size distributions  
  (Blumberg & Lloyd-Smith, PLoS CB 2013, Epidemics 2013)
  • Allows estimation of $R_0$ and possibly transmission heterogeneity even if infection sources aren’t known,  
    BUT struggles if case detection rate is too low (or is unknown, or biased).

• Proportion of cases infected by reservoir  
  (Cauchemez et al. PLoS Med 2013)
  • Allows estimation of $R_0$ and possibly case detection rate, even if case detection rate is very low, 
    BUT requires that infection sources (and heterogeneity) are known.
Progress on subcritical transmission...
... but still major challenges

For many diseases with spillover and subcritical transmission,
(e.g. non-emergency zoonoses,
wildlife-livestock systems,
wildlife-wildlife systems)
infection sources and case detection rates are unknown,
and difficult to estimate!
‘Epidemiological dark matter’

What is the influence of unobserved, unsampled entities in disease transmission systems?

Modelling challenges:
Can we infer the presence of ‘dark matter’?
Can we predict its impact, and correct for it?

Orton et al, Phil Trans RSB (2013)
Reservoir dynamics  (aka ‘All of disease ecology’)

Identifying Reservoirs of Infection: A Conceptual and Practical Challenge

Daniel T. Haydon,* Sarah Cleaveland,*Louise H. Taylor,* and M. Karen Laurenson*

“We propose that a reservoir be defined as one or more epidemiologically connected populations or environments in which the pathogen can be permanently maintained and from which infection is transmitted to the defined target population.”

Conceptually clear, but hard to implement in a multi-host world!

Studying multi-host reservoirs

1. Identify all infected species
Studying multi-host reservoirs

1. Identify all infected species

Epidemiological dark matter
**Studying multi-host reservoirs**

1. Identify all infected species.
2. Assign each species as **maintenance** or **non-maintenance**.

   *Can the pathogen be maintained permanently in that host species alone?*

   *Is its size above the Critical Community Size (CCS)?*
Studying multi-host reservoirs

1. Identify all infected species.
2. Assign each species as maintenance or non-maintenance.
3. Estimate cross-species transmission rates.
Identifying maintenance populations

CCS is a classic problem, and a hard one. Even harder for wildlife populations.

Maintenance ≠ supercritical. $R_0 > 1$ is necessary but not sufficient.

‘Threshold’ for persistence is not abrupt, and is not a simple function of population size.
- relative timescales of disease and demographic turnover are crucial.

Lloyd-Smith et al, TREE (2005)
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Modelling/theory challenges:
- Generalized CCS that accounts for N and demographic rates.
- Account for population fluctuations and density-dependent host demography. → Implications for control by culling?
- Extend theory to include mechanisms aiding persistence: chronic carriers, environmental reservoirs, heterogeneities and structure.
- Account for alternative hosts.

Lloyd-Smith et al, TREE (2005)
Gold standard: Experimental perturbation

Reduce or eliminate infection in certain host species, and observe whether infection persists in other species.

*Brucella in Spain*

Gold standard: Experimental perturbation

Reduce or eliminate infection in one host species, and observe whether infection persists in another species.

*Brucella in Spain*

Brucellosis controlled in cattle, sheep and goats by test & removal.

Brucellosis prevalence drops to (near) zero in neighboring red deer population, despite rising density.

Red deer are not a maintenance population in this system.

Typical situation: probing mechanisms in a focal species

Often have good data on one host species, and little or no information about other possible hosts.

Typical approach:
1. Study natural history of host-pathogen interaction.
2. Build model and estimate parameters.
3. Can model explain observed patterns? e.g. can proposed reservoir host maintain the pathogen?

Challenges:
- Circular logic? Need independent data to estimate parameters.
- What is the power to detect unobserved factors?
Detecting dark matter: lions of the Serengeti

**Epidemiological dark matter**
(other species affected, but no good data)

Observed data in lions could not be explained with a single species model.

Tested models including jackals and/or hyenas.
→ Could match intensity and spatial correlations, and put bounds on cross-species transmission.  


Can we strengthen and formalize this kind of inference?
Detecting dark matter: cryptic but crucial processes

What if key processes are inapparent in available data?

**Example:** host-pathogen interaction where a small fraction of hosts become asymptomatic chronic carriers.

→ undetectable effect on outbreak trajectories, but huge effect on long-term persistence.

Buhnerkempe et al, in prep.

Can we devise methods to detect such cryptic processes? Possibly by integrating genetic or immunological data? Could such processes be detectable by SMC approaches? (cf. detection of inapparent cholera cases by King et al. *(Nature 2008)*)
Estimating cross-species transmission

**Bottom-up approach**

Cross-species FOI = Prevalence in source host population \( \times \) Contact rate between host species \( \times \) Probability of infection given contact

- Measurable
- Perhaps measurable
  - Contact loggers
  - GIS telemetry
  - Behavioural data
  - etc
- Very hard, for most wildlife systems.

Only describes *opportunities* for transmission

**Top-down approach**

Study spatiotemporal correlations in incidence in two species.

→ Viable in principle, but only for simple systems with good data and strong coupling.

Estimating cross-species transmission: genetic approaches

Very promising approach, but...

• Estimation of transmission rates based on strong assumptions.
• Sampling issues – species bias, and bias from subcritical transmission.
• How to generalize for slower timescales of genetic change?
Why can’t we ignore subcritical and non-maintenance hosts?

1. They could act as bridges to the target host. (‘zoonotic tunnelling’?)

2. They may bias inferences about cross-species transmission.

3. They may contribute rare but influential events that alter large-scale dynamics.

4. They could emerge as supercritical or maintenance hosts.
Genetic tools may also reveal hidden complexity.

Challenge: What are appropriate levels of aggregation? Are there important ecological interactions between presently undifferentiated types?
The next frontier: Multi-host, multi-pathogen systems

Very challenging...

Possible to tackle by studying emergence or elimination events, when pathogen community has been perturbed?

Case study: competitive release of monkeypox after eradication of smallpox.

Implications for other eradication campaigns?

Rimoin et al, PNAS (2010)
Lloyd-Smith, Phil Trans RSB (2013)
Abundant dark matter is the norm in disease ecology.

- Need methods to detect its presence and understand its impacts.

Spillover and subcritical transmission are important throughout multi-host systems.

- Need new methods, particularly for linking to (imperfect) data.

Basic concepts of CCS and persistence ‘thresholds’ still need development for natural host populations, non-acute pathogens.

- Need theoretical work and pragmatic tools (and more empirical study!).
- Further challenges for multi-host systems.