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Eight challenges in modelling disease ecology in multi-host, multi-agent systems

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ABSTRACT

Many disease systems exhibit complexities not captured by current theoretical and empirical work. In particular, systems with multiple host species and multiple infectious agents (i.e., multi-host, multi-agent systems) require novel methods to extend the wealth of knowledge acquired studying primarily single-host, single-agent systems. We outline eight challenges in multi-host, multi-agent systems that could substantively increase our knowledge of the drivers and broader ecosystem effects of infectious disease dynamics.

Introduction

Over the past 20 years, a combination of theoretical, observational, and experimental approaches has advanced our understanding of the ecology of infectious diseases. This work has often focused on dynamics in single-host, single-agent systems with acute and symptomatic infections, which are the most theoretically and empirically tractable. As a consequence, patterns have been explored using foundational theoretical concepts, such as the basic reproduction number, R_0. Yet the predominance of R_0 in disease ecology has sometimes overshadowed complexities that can influence dynamics, such as feedbacks between diseases and ecosystem structure and function. Inclusion of these complexities will require re-interpretation and extension of these foundational concepts, as well as novel modelling tools, data, and thinking. This problem is exemplified by disease systems involving interactions among multiple host species and/or multiple infectious agents. In these systems, we can hope to borrow principles from community ecology and build on the strong link between disease dynamics and population ecology. Here, we outline eight challenges that will be important to understanding disease dynamics in multi-host, multi-agent systems, at scales from within-host dynamics to ecosystem-level processes.

1. What defines a maintenance population?

Classically, conditions required for maintenance of infections in populations of single host species have been defined through host population thresholds. In particular, population size or density thresholds are often used to specify the host abundance that is sufficient to maintain uninterrupted transmission of the infectious agent without subsequent imports. However, maintenance of infectious agents depends as much on demographic rates as on population size especially when epidemic intensity fluctuates far from equilibrium. This raises particular challenges in systems where

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density-dependent or strongly seasonal recruitment causes host abundance and relevant demographic rates to fluctuate (Lloyd-Smith et al., 2005). Reliance on population abundance thresholds is further complicated when disease risk is influenced by factors like age- or sex-structure, territoriality, or herding behaviour, making the definition and quantification of host abundance as it relates to disease maintenance difficult.

Consequently, analyses of single population maintenance must be refined to recognize mechanisms beyond simple population thresholds. Spatial effects such as percolation (Davis et al., 2008) or metapopulation structure (George et al., 2013) may be important drivers of agent persistence. In addition, modelling and empirical studies are needed to understand how maintenance is influenced by diverse host/agent interactions, including phenomena such as chronic infections, intermittent shedding, or waning immunity. Data requirements to study infectious agent maintenance are always demanding, and appropriate measures of local extinction can be difficult to define (Conlan et al., 2010). This problem is exacerbated due to frequent difficulties in surveillance of both the disease process and host population size and distribution, highlighting the importance of long-term, high-resolution, time series.

2. What defines a maintenance community?

In many systems multiple host species can be infected, suggesting that an infectious agent may be maintained by several host species in a maintenance community (Haydon et al., 2002). Here, it is crucial to assess whether each infected species is infected via a dead-end process (i.e., spillover and subcritical transmission) or is contributing to maintenance by on-going transmission. Strong inferences can be made using manipulations or disturbances, such as culls or fencing, that clarify the contributions of individual species to maintenance in the broader host community. Without such perturbations, models will play a key role integrating available evidence and identifying the manipulations that could confirm species' contribution to maintenance (Viana et al., 2014).

Of the current models, type reproduction number methods (Roberts and Heesterbeek, 2003) have been used to explore multi-host maintenance at human-animal interfaces (Funk et al., 2013) and to identify species-specific contributions to transmission (Nishiura et al., 2009). These approaches typically assume a system at endemic equilibrium, although new methods have relaxed this assumption (Streicker et al., 2013). As outlined in Challenge 1, these non-equilibrium dynamics can be crucial to persistence, especially in systems with seasonality or temporally varying outbreaks. Cross-sectional data in these cases are often not at a resolution to address such variation. This problem is particularly pronounced when infection can only be determined post-mortem, highlighting the importance of assessing disease status longitudinally through non-destructive sampling. Models analyzing these data must address transient dynamics in host abundances and infection patterns, potentially building on methods for transient analysis used in conservation biology (e.g., Buhnerkempe et al., 2011).

3. What mechanisms underlie the dilution effect, and when do they apply?

Some observational data from vector-borne diseases support a 'dilution effect' whereby increasing host diversity decreases infection risk in a focal species, such that (in contrast to Challenge 2) greater host diversity can diminish maintenance of the infection (Keesing et al., 2010). To test this properly, experimental perturbations of the host community are needed to reveal the mechanisms driving such a relationship and to test the underlying assumption that host competence is generally associated with species resilience. Experimental work has begun to explore such mechanisms (Johnson et al., 2013; Venesky et al., 2013), but further work is needed, especially in systems that are not conducive to laboratory manipulations. At the same time, better theory is needed to identify key experiments in these systems and to integrate resulting mechanistic insights, thus strengthening inferences about existing data.

A broader understanding of how non-host species might contribute to the dilution effect is also needed. Competitive and trophic interactions between host and non-host species can influence host abundance and community structure and hence, indirectly, the dilution effect. Network approaches may prove useful in exploring these types of interactions (see Challenge 7). Because species assemblages vary in space and time, models should also address feedbacks between larger-scale species richness and community assembly and succession processes in addition to local community composition.

4. How to estimate cross-species transmission in field settings?

Empirical estimates of cross-species transmission are crucial to understanding multi-host systems, but obtaining such estimates is a long-standing and unsolved problem. New data types are bringing new opportunities from both bottom-up and top-down perspectives, but these also raise new challenges. Once again focused experiments to quantify cross-species transmission would be helpful. In bottom-up approaches, contact is measured directly (e.g., by shared space use or spatial proximity loggers), but defining an epidemiologically relevant contact remains difficult. Even for well-defined contacts, estimating the probability of transmission per contact is a struggle. Alternatively, when transmission experiments measure the probability of infection given a contact (e.g., Bouwknegt et al., 2008), it is difficult to relate forced contact in the lab to natural systems. These problems typically limit inference from bottom-up approaches to relative transmission hazards among regions or groups of animals. In top-down approaches, data from multiple host species can be integrated with mechanistic or time-series models to infer cross-species transmission rates (e.g., Begon et al., 1999). However, these approaches are data-hungry, and their sensitivity and accuracy are basically unknown; similarly the relation between sampling resolution and infectious agent life history (e.g., acute vs. chronic, transmission mode) will determine the power of this approach.

Genetic studies offer increasingly powerful tools to study cross-species transmission (e.g., Streicker et al., 2010). However, unresolved issues remain regarding the translation of genetic patterns into estimates of transmission rates, particularly given incomplete sampling of hosts. Also, current genetic methods for inferring cross-species transmission assume all cases in a 'recipient' species come directly from cross-species spillover. This assumption ignores the potential for onward, subcritical transmission in the recipient species, which will boost the number of cases biasing estimates. If transmissibility in the recipient species is known, this effect could be accounted for, but transmission data in these species are often lacking. At a minimum, future genetic models will need to characterize this potential bias or relax the spillover assumption to infer within- and between-species transmission jointly.

5. How do complex multi-host life cycles affect maintenance?

Parasites with heteroxenous life-cycles, where there is a sequence of hosts necessary to complete the parasite's life-cycle