AN ABSTRACT OF THE DISSERTATION OF

Yang Xie for the degree of Doctor of Philosophy in Zoology presented on December 5, 2014.

Title: Complexity in Host-Pathogen Dynamics: Dispersal Uncertainties, Metapopulation Persistence and the Role of a Changing Climate

Abstract approved:

_____

Andrew R. Blaustein

Emerging infectious diseases impact both human and wildlife populations. Infectious agents, in particular the aquatic fungus *Batrachochytrium dendrobatidis* (chytrid), have an influential role in driving global amphibian population declines. The emergence of the chytrid fungus has aspects of both geographic spread as well as climate shifts altering environmental conditions and host-pathogen interactions. My dissertation examines the spatial spread of chytrid by host dispersal at the metapopulation level, as well as how spatial risk from chytrid is associated with the climate.

In Chapter 2 of my thesis, I examine preexisting conclusions in the wildlife disease literature on the relationship between disease spread mediated by host dispersal and metapopulation persistence. I show how explicit inclusion of local dynamics and dispersal-induced synchronization alters conclusions derived by previous metapopulation disease models. Contrary to existing models that do not include explicit local dynamics, I find that synchronization increases metapopulation extinction risks and regional persistence is optimized at intermediate dispersal levels when disease transmission rate from external sources are low. However, at high rates of external infections, I come to the similar conclusion that increased dispersal monotonically increases metapopulation persistence.

In Chapter 3, I use a spatially explicit, individual-based model to simulation disease spread dynamics in a set of connected mountain yellow-legged frog population. I compare the simulated disease forecasts to field data, and test for the sensitivity of these results to assumptions of host dispersal potential. I find that chytrid is able to spread across the majority of the metapopulation even with assumptions of low host dispersal potential and that metapopulation extinction rate increases with increased host dispersal.

In Chapter 4, I examine how chytrid distribution is influenced by climatic variables based on the most comprehensive and up-to-date set of global chytrid surveillance data. Using a machine learning algorithm, I generate predictions showing how chytrid distributions might be expected to change according to IPCC projected scenarios of future climate change. I conclude that chytrid distribution is likely to shift to higher altitudes and latitudes with overall increases in environmental suitability in the high latitudes of the Northern Hemisphere. The chosen input climatic variables yields excellent performance when predicting chytrid occurrence at a site, but no single variable has dominant predictive power.

My dissertation provides insight into the applicability of conclusions derived from existing metapopulation disease models to specific conservation contexts. Much research has been invested in the chytrid-amphibian system at the individual and population level, yet how disease management might integrate into conservation planning targeted at the metapopulation level remains largely unknown. My research will form an important part in addressing amphibian conservation in spatially-fragmented, pathogen-ridden landscapes, which is especially important in today's changing climate.

Complexity in Host-Pathogen Dynamics: Dispersal Uncertainties, Metapopulation
Persistence and the Role of a Changing Climate

by
Yang Xie

A Dissertation

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of

Doctor of Philosophy

Presented December 5, 2014
Commencement June 2015

Doctor of Philosophy dissertation of Yang Xie presented on December 5, 2014

APPROVED:

_____

Major Professor, representing Zoology

_____

Chair of the Department of Integrative Biology

_____

Dean of the Graduate School

I understand that my thesis will become part of the permanent collection of Oregon State University libraries. My signature below authorizes release of my thesis to any reader upon request.

_____

Yang Xie, Author

ACKNOWLEDGEMENTS

I would like first and foremost to thank Andy, my advisor who has supported me in so many ways with his kindness, patience, and the occasional wake-up call and pep talk distributed as needed. You have been a great mentor, advocate and friend to me. I have learned so much about science and myself during my studentship with you. I remember the day I told you I had passed the comprehensive exams for my concurrent masters in statistics – you were proud and excited, as well as exasperated that I would so be surprised that I had passed. That exasperation was a great indicator of your tireless vote of confidence for me. Thank you for encouraging me to take on new challenges, and to trust myself with my own abilities – I imagine it takes a bit of faith some times, on both of our sides. You're truly amazing, and it is an honor to be your student and friend.

A loving thanks to my family in China, most of all my parents, Shaohua Xie and Ying Huang. Mom and dad, thank you for supporting me in the ways only the greatest parents could support a child. You've driven me to conferences, field sites, sampled frogs with me and have been endlessly patient and forgiving when I went through the ritualistic up and downs of the grad school life. I could not be here without you.

I would also like to thank my collaborators for generously sharing data and experience with me, and my lab mates for their input which has made my research all the more rigorous. In particular, Nathan Schumaker, you have single-handedly educated me on the many intricacies of HexSim and crafted much machinery in HexSim for me. You have been a great friend and advisor. It was working with you that first inspired my interest in modeling and programming.

CONTRIBUTION OF AUTHORS

Andrew R. Blaustein contributed to experimental design and editing of all chapters.

Chapter 3: Nathan H. Schumaker and Allen Brookes helped design the chytrid model. Roland A. Knapp, Cheryl J. Briggs shared field data and insights on how to devise an appropriate spatial model for chytrid. Kathleen R. Matthews and Karen L. Pope shared telemetry data on dispersal patterns of Mountain Yellow-legged frogs.

Chapter 4: Deanna Olsen managed the data inventory and collection.

TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

LIST OF FIGURES

LIST OF FIGURES (Continued)

LIST OF TABLES

CHAPTER 1

INTRODUCTION

Biodiversity loss is one of the most important and pressing environmental issues of our time. The global rate of species extinctions so dwarfs the estimated background extinction rates that the current biodiversity crises has been dubbed the sixth major extinction (Chivian and Berstein 2008, Wake and Vredenburg 2008). The leading cause of this crisis is habitat destruction and fragmentation (Pimm and Raven 2000, Sih et al. 2000, Becker et al. 2007). A major paradigm for studying the effect of habitat loss and fragmentation on species persistence is the metapopulation concept (Levin 1970, Hanski 1999). The term "metapopulation" has received many evolving definitions since it was first coined by Andrewartha and Birch (1954). The classic metapopulation concept was defined by Levin (1969, 1970) as "a population of populations which go extinct locally and recolonize", and was first mathematically described with the equation:

$$p' = mp(1-p) - ep$$

where p is the proportion of occupied habitat patches and p' its first derivative, m is the colonization or migration rate, and e is the local extinction rate. From this formulation, it is evident that a higher m will lead to a higher proportion of occupied patches. Levin's model posits that metapopulation persistence depends on the balance between extinction of occupied patches and recolonization of empty patches (Sih et al. 2000) and implicitly assumes that

colonization and local extinctions occur at independent rates. More restrictive definitions of the metapopulation concept require that populations also have independent (uncorrelated) fluctuations (Hanski and Gilpin 1991).

These restrictive metapopulation definitions have been criticized for making major oversimplifications to facilitate formulation of mathematical models, which in turn undermine their utility to conservation (Sih et al. 2000, Baguette and Mennechez 2004). Stochastic patch occupancy models (SPOM) are derived directly from these oversimplifications and receive the same criticisms (Baguette and Mennechez 2004). These models treat patches as either occupied or unoccupied, and ignore within-population dynamics (Sih et al 2000, Baguette and Mennechez 2004). More complex models have shown that assumptions of local dynamics drastically influence estimates of metapopulation persistence (Baguette and Schtickzelle 2003, Yaari et al. 2012). SPOMs also ignore spatial context and assume that all occupied patches are equally likely to supply colonists to all empty patches, while in reality most successful dispersal and recolonization comes from nearby patches (Sih et al 2000). The lack of spatial context in these models precludes estimation of regional extinction rates, a desirable quantity for management and conservation objectives (Durrett and Levin 1994, Earn et al. 2000). Once spatial context is taken into consideration, the issue of local synchrony and its effect on regional extinction rates also arises. Dispersal, the process by which colonists are supplied, may synchronize population fluctuations, making assumptions of locally independent dynamics unrealistic. Nicholson (1933) first lighted on the importance of independent local dynamics, noting that the persistence of otherwise unstable parasitoid–host interactions on a regional scale is promoted when there are ''large numbers of independent local systems of oscillations, all

phases of oscillations being represented in the environment at any given time''. In essence, the power of the metapopulation paradigm to conservation is to put eggs in multiple independent baskets since the probability of simultaneous extinction of all populations is exponentially smaller than the extinction rate of one population. Subsequently, a number of models have shown repeatedly that independence in local dynamics is pivotal to metapopulation persistence (reviewed in Briggs and Hoppes 2004).

In both Levin's model and SPOMs, this independence is presumed and no consideration is given to the effects of spatial synchrony and how it might undermine metapopulation persistence (reviewed in Sih et al. 2000, Baguette and Mennechez 2004). In view of these criticisms, the current consensual metapopulation concept relaxes assumptions to refer to a set of local populations within some large area, where migration from one local population to at least some other patches is possible (Hanski and Simberloff 1997) and employs more complex and realistic modelling approaches (Sih et al. 2000, Baguette and Mennechez 2004). The evolution of the metapopulation concept reflects metapopulation research trending away from abstract models toward real-world applications in conservation (Akçakaya et al. 2007), in which the metapopulation is increasingly the unit of management (e.g. Lindborg and Eriksson 2004, Whitesel et al. 2004, Donald and Evans 2006, Wright 2010, Artzy-Randrup & Stone 2010, Sandeep et al. 2013). Conservation options for species that exist in metapopulations include those that aim to facilitate local persistence, and those aimed to promote metapopulation by managing migration rates (e.g., by the use corridors etc.). The latter of which has been the focus of much metapopulation research (reviewed in Yaari et al. 2012).

Wherever wildlife conservation concerns the movement of individuals across structured habitat, its scale of operations will encompass metapopulation dynamics (Akçakaya et al. 2007). The relationship between dispersal (colonization rate) and metapopulation persistence has received vigorous and continuous research and is a central component to metapopulation theory. Metapopulation persistence is typically predicted to be optimized at intermediate levels of dispersal; i.e. dispersal events may be infrequent, but must occur frequently enough to compensate for local extinctions. (Gyllenberg et al. 1993, Hastings 1993, Casagrandi & Gatto 2006, Yaari et al. 2012). At extremely low levels of dispersal, recolonizations ("rescue effects") are not sufficient to compensate for extinctions. At high levels of dispersal, population dynamics may be regionally synchronized and no longer independent, so that there is no risk spreading from conserving spatial segregate populations (Yaari et al. 2012). Synchrony also alters the probability of recolonization of a patch after a local extinction (Heino et al. 1997). When dynamics of neighbor patches are correlated, patches in which populations are extinct or nearly so will tend to be neighbored by others in similar states and cannot output many colonizers. Thus, regional synchrony precludes the rescue effect and increases the risk of extinction (Heino et al. 1997, Sih et al. 2000). The general consensus is that an intermediate rate of dispersal allows the rescue effect without inducing regional synchrony, thus optimizing metapopulation persistence (Allen 1975, Comins et al. 1992, Hastings 1993, Hanski and Gilpin 1997, Molofsky and Ferdy 2005, Abta et al. 2007, Yaari et al. 2012).

The metapopulation approach has been employed to yield insights into management of emerging infectious diseases (EIDs) in spatially structured landscapes in both human (e.g. bubonic plague, Keeling and Gilligan 2000; SARS, Colizza et al. 2006; AIDS, Coffee et al.

2007; measles, Bjørnstad and Grenfell 2008) and wildlife systems (e.g. White plague II, Sokolow et al. 2009, canine distemper virus, Almberg et al. 2010, non-system specific: Hess 1996, Gog 2002, McCallum and Dobson 2002, Park 2012). EIDs are those infectious diseases that have increased in incidence, virulence, host or geographic range and play an important role in the dynamics of human and animal populations (Daszak et al. 2003). EIDs can have serious consequences for wildlife populations, ecosystem structure and biodiversity (Scott 1988, Harwood and Hall 1990, Dazsak et al. 2000, Lyons et al. 2004, Lips et a. 2006, Wyatt et al. 2009). For example, the rinderpest panzootic was introduced into Africa in 1889, extirpated more than 90% of Kenya's buffalo population, and caused secondary effects on predator populations and local extinctions of the tsetse fly (Plowright 1982).

EIDs may interact with a naturally or artificially fragmented landscape to influence the disease risks experienced at the local and metapopulation levels (McCallum and Dobson 2002, Allan et al. 2003, Jousimo et al. 2013). Theoretical research has examined this interaction, with an emphasis on host migration rates inherited from the general metapopulation paradigm (Hess 1996, Gog 2002, McCallum & Dobson 2002, Sokolow et al. 2009, Park 2012). Hess (1996) suggested that dispersal of the host species aids the spread of infectious agents, and increases the probability of metapopulation extinction as an "anti-rescue effect" (Harding and McNamara 2002). Increased contact among populations almost universally increases the prevalence, incidence, and epidemic duration at the metapopulation level (Andreasen and Christiansen 1989, Sattenspiel & Castillo-Chavez 1990, Jesse et al. 2008). Due to these deleterious effects and a non-monotonically increasing relationship between patch occupancy and dispersal rate, Hess (1996) suggested that while some dispersal is necessary to maintain a metapopulation, too much

host dispersal could increase disease hazard. Follow-up work contends that Hess (1996) unrealistically assumes extremely low rates of disease transmission from sources outside the focal host species (Gog 2002, McCallum and Dobson 2002, Park et al. 2013). Diseases with serious impacts on endangered wildlife populations frequently occur as spillovers from species other than the focal host that harbor the pathogen; i.e. "reservoir hosts" (Woodroffe 1999, Power and Mitchell 2004, Daniels et al. 2007). These subsequent models demonstrate that if the rate of disease transmission from reservoir hosts to the focal host is sufficiently high, patch occupancy monotonically increases with dispersal rate (Gog et al. 2002, McCallum & Dobson 2002, Park 2012). Thus, the higher the rate of disease spillover, the more readily the benefits of increased dispersal will outweigh the costs (Gog et al 2002.).

These models (e.g. Gog et al. 2002, McCallum & Dobson 2002, Sokolow et al. 2009, Park 2012) suggest that increasing host dispersal will rarely have negative effects on metapopulation persistence (McCallum & Dobson 2002, Gog et al. 2002, Park 2011). This is contrary to metapopulation persistence optimized at intermediate dispersal rates as is predicted by the general body of metapopulation literature. However, these models are in general derived directly from Levin's classic definition of metapopulations and reduce patches to two states only – occupied and extinct. In fact, should disease be removed during their formulation, many of these models reduce exactly to Levin's model (e.g. Hess 1996, Gog 2002, McCallum and Dobson 2002, Sokolow et al. 2009, Park 2012). Consequently, they also inherit the suite of assumptions that limits Levin's model. Therefore, it is little surprise that they conclude a higher host migration rate is better. Indeed, using a model that incorporates explicit local dynamics, Hess (1996) showed that extinction probabilities are the lowest at intermediate dispersal but did

not determine why conclusions differed from the patch occupancy models. Indeed, formulation without explicit population dynamics or spatial context limits the insight and applicability of the conclusions derived from these models to conservation management. **In Chapter 2 of my thesis, I examine how explicit inclusion of local dynamics and dispersal-induced synchronization alters conclusions derived by previous metapopulation disease models on the relationship between host migration and metapopulation persistence.**

Amphibians are a group that could potentially receive much conservation benefit from research on metapopulation disease dynamics. Amphibian declines and extinctions on a global scale are one of the most dramatic examples of the biodiversity crisis. Most amphibian extinctions after 1500 have occurred since 1980, and the estimated amphibian extinction rate is 25,000-45,000 times the expected background rate (McCallum 2007). These widespread declines cannot be attributed to a single cause. Habitat destruction and degradation, invasive species, chemical pollution, overexploitation, environmental and climate change and infectious disease are the contributing causes to global amphibian population declines and extinctions (reviewed in Alford and Richards 1999, Daszak et al. 1999, Blaustein and Kiesecker 2002, Collins and Storfer 2003, Stuart et al. 2004, Lannoo 2005, Hays 2010, Blaustein et al. 2011). The relative importance of these factors and their interactions are highly context-dependent; therefore the extent and intensity of amphibian declines exhibit strong spatial-temporal heterogeneity (Alford and Richards 1999, Blaustein and Kiesecker 2002, Blaustein et al. 2011). In the past decade, much research has been directed towards to the role of EID as a proximal cause for amphibian population declines and extinctions (Berger et al. 1998, Lips 1998, Kiesecker et al. 2001, Daszak et al. 2003, Kiesecker et al. 2004, Rachowicz et al. 2006, Kilpatrick et al 2010,

Blaustein et al. 2011). Amphibians encounter a broad spectrum of parasites in their natural habitat that include viral, bacterial, trematode, and fungal pathogens associated with varying levels of individual mortality and population decline (reviewed in Whitaker & Wright 2001, Blaustein et al. 2012, e.g. ranavirus, Chinchar 2002; red-legged disease caused by the bacterium *Aeromonas hydrophila*, Bradford 1991; the trematode *Ribeiroia ondatrae,* Johnson et al. 1999; the fungi Saprolegnia spp. and *Batrachochytrium dendrobatidis*, Blaustein et al. 1994, Berger et al. 1998, Carey et al. 1993). Among these, the pathogenic fungus *Batrachochytrium dendrobatidis* (hereafter **chytrid**) has been suggested as having induced "the most spectacular loss of vertebrate biodiversity due to disease in recorded history" (Skerratt et al. 2007), and is associated with population declines and extinctions of amphibian species around the globe (Laurance et al. 1996, Berger et al. 1998, Bosch et al. 2001, Fellers et al. 2001, Young et al. 2001, Bosch et al. 2006; Lips 1998, Lips 2006, McCallum 2007, Crawford et al. 2010, Olson et al. 2013)).

Chytrid belongs to the phylum *Chytridiomycota* (Longcore et al. 1999). It is one of the only two species in its genus that has been associated with dramatic declines in vertebrate hosts (Berger et al. 1998). The other species is *Batrachochytrium salamandrivorans,* a recently discovered pathogen that has caused mass mortality in fire salamander populations in the Netherlands (Martel et al. 2013). The chytrid lifecycle involves a motile environmental zoospore stage for transmission and a non-motile reproductive zoosporangium stage on the host (Longcore et al. 1999, Berger et al. 2005). Zoospores can survive for up to 7 weeks in lake water, 3-4 weeks in deionized water (Johnson and Speare 2003), and up to 12 weeks in sterile moist river sand without nutrients (Johnson and Speare 2005). As a group, fungi are generally non-parasitic

saprobes and capable of self-sustaining in the environment without the presence of a host. Therefore, it has been suggested that chytrid may be capable of persisting in a "resting" stage or a saprobic form within the abiotic environment (Longcore et al. 1999; Di Rosa et al. 2007). Motile chytrid zoospores encyst onto amphibian dermis, develop into zoosporangia with keratin as its substrate and in turn release more zoospores into the environment (Longcore et al 1999, Berger et al. 2005). Chytrid is apparently not host-specific amongst amphibians, and currently over 500 amphibian species have been tested positive for chytrid infection (Olson et al. 2013).

Infection by the chytrid fungus causes the disease chytridiomycosis, and pathogenesis is both stage and species dependent. In tadpoles, keratinization and correspondingly infection is limited to the mouthparts (Berger et al. 1998), which may lead to mouthparts damages (Rachowicz and Vredenburg 2004, Parris and Cornelius 2004). This has the potential to decrease foraging efficiency, reduce growth and developmental rates, but seldom induces mortality (Parris and Cornelius 2004, Rachowicz and Vredenburg 2004, Blaustein et al. 2005, Garner et al. 2009, Venesky et al. 2010, Gervasi et al. 2013). For juveniles and adults, however, a large proportion of the dermis is keratinized and fungal infection is extensive (Rachowicz and Vredenburg 2004). Pathogenesis may be associated with chytrid secreted toxins (Berger et al. 2005, Blaustein et al. 2005). Following exposure to proteolytic factors secreted from chytrid zoospores, Brutyn and colleagues (2012) observed disruption of intercellular junctions and death of amphibian epidermal cells, which is hypothesized to contribute substantially to initial pathogen-induced mortality (Rohr et al. 2010). Development of chytridiomycosis induces changes in host osmotic function, which in the extreme case leads to death by cardiac arrest from electrolyte imbalance (Voyles et al. 2009). Species variation in thickness of adult and juvenile dermis may affect how

severe the outcome of infection is (Bancroft et al. 2010, Gahl et al. 2011, Searle et al. 2011, Greenspan et al. 2012). For susceptible species, pathenogenesis is rapid and mortality may occur within weeks of initial exposure to chytrid zoospores (Carey et al. 2006, Voyles et al. 2009, Searle et al. 2011, Murray and Skerratt 2012, Gervasi et al. 2013). In at least some species, disease outcomes may be strongly dependent on the number of zoospores on the host (Vredenburg et al. 2010, Cheng et al. 2011).

Chytrid is currently found on every continent where amphibians exist (Olson et al. 2013). A recent whole genome analysis indicates that while chytrid is an invasive species in many parts of the world, it is also likely endemic in some parts of its range (Rosenblum et al. 2013). Therefore, the emergence of chytrid has aspects of both spatial spread and climatic shifts inducing changes in host-microbe interactions. Examples of recent introduction and spread of chytrid in many regions are well documented (e.g., Australia: Laurance et al. 1996; Central America: Berger et al. 1998, Lips et al. 2006; South America: Lips et al. 2008, North America: Vredenburg et al. 2010). Infected amphibians which could serve as vectors for pathogen transmission have been found in both the wild (e.g. Garner et al. 2006, Walker et al. 2008) and in global commercial trade (e.g., Daszak et al. 2004, Fisher and Garner 2007, Schloegel et al. 2009, 2012). However, as a result of continuing spread of chytrid, its distribution appears far from uniform (Olson et al. 2013).

Chytrid seems to be endemic in other parts of its range, where it can be present for up to decades before noticeable declines in hosts occur (Weldon et al. 2004, Ouellet et al. 2005, Goka et al. 2009). It has been hypothesized that the emergence of chytrid in these regions may be due to increased virulence as a result of environmental changes (Pounds et al. 2006). Chytrid and

chytridiomycosis distribution are frequently associated with climatic variables, with temperature and precipitation metrics in particular (Ron 2005, Pounds et al. 2006, Bosch et al. 2007, Laurance 2008, Walker et al. 2010). In addition, on the hosts' side, climate change may lead to decreased survival and fitness, thus mediating higher susceptibility to chytrid and promoting its emergence (Reading 2007).

Current research efforts focus on processes operating within individuals and populations, and there is little preexisting work that addresses the spatial spread of chytrid and its epidemic consequences at the metapopulation level. Many amphibians exist as metapopulations in habitat that may be naturally or artificially fragmented (reviewed in Alford and Richards 1999, Becker et al. 2007). Local populations of amphibians tend to fluctuate and display non-equilibrium dynamics with periodic extinctions, and migration is pivotal for colonization and regional persistence (e.g. Duellman and Trueb 1986, Gill 1978, Corn and Fogleman 1984, Berven 1990, Sjogren 1991, Petranka et al. 2004, Petranka and Holbrook 2006, Heard et al. 2012, reviewed in Alford and Richards 1999). For example, Hels and Nachman (2002) found that source–sink dynamics were pivotal to regional persistence of a spadefoot toad. Thus, Semlitsch (2008) proposed that the importance of facilitating dispersal for metapopulation species persistence is far greater than maintaining any single local population in terms of conservation efficiency, especially in fragmented and disturbed landscapes (Marsh and Trenham 2001). Given that much existing amphibian conservation planning is couched in the metapopulation paradigm and its focus on dispersal, it is necessary to consider how disease management may integrate into this framework.

There is substantial argument regarding the appropriate spatial scale that defines amphibian metapopulations. While it was previously assumed that between patch migration rates are limited by poor dispersal abilities of amphibians (reviewed in Blaustein et al. 1994b), substantial rates of dispersal among local populations have been documented in some species (e.g. Breckenridge and Tester 1961, Berven and Grudzien 1990, Buckley et al. 1996, reviewed in Alford and Richards 1999). In fact, Smith and Green (2005) suggested that for anurans at least, population differentiation is most likely to occur at scales upward of 2-10 km. Fine-scale genetic analyses for spotted salamanders also indicate that nonrandom genetic structure, a proxy for population differentiation, occurs at a scale of approximately 4.8 km (Zamudio and Wieczorek 2006). Based on these findings, Semlitsch (2008) suggested that metapopulation or landscape level management be focused on movements among populations at spatial scales between 1.0–10.0 km. Dispersal is thought to be frequent between populations separated by distances lesser than these thresholds, in which case synchrony is induced and the condition of independent population dynamics violated. In this case, instead of a metapopulation organization, regional dynamics instead resemble that of a single panmictic population (Petranka et al. 2004). In specific application the term "metapopulation" may simply refer to sets of spatially structured populations and the minimal distances that separates one population from another may be relatively small (e.g. < 1km, Conroy and Brook 2003. Hels and Nashman 2001; >400m, Petranka et al. 2004; 100m, Bauer et al. 2010; 100-1000m, Fortuna et al. 2006; 50-1500m, Gamble et al. 2006; 200-800 m, Griffiths et al. 2010). It would seem that the delineation of a minimal demographic unit that defines the structure of a metapopulation is specific to amphibian species dispersal capabilities.

For many species, reliable information of dispersal patterns are scant or absent, which may be why in some cases metapopulations are simply designated based on geographic unit. For example, sets of Mountain Yellow-legged frog population (*Rana muscoa/sierrae*) within individual watersheds in the Sierra Nevada are referred to as metapopulations without reference to inter-population distances at all (USFWS 2006, Knapp et al. 2007, Vredenburg et al. 2010). In such cases, the lack of dispersal information raises two concerns when attempting to extrapolate previously derived conclusions on dispersal-metapopulation persistence relationships to the amphibian system. First, it is difficult to determine whether model assumptions of independent dynamics are violated. Second, even if the populations in effect did behave as a metapopulation, it is hard to determine what are low, intermediate and high rates of dispersal between populations and manage connectivity accordingly. Indeed, amphibians account for only 0.8% of dispersal-related studies, which may be because amphibian research tend to be focused at breeding ponds (Smith and Green 2005, Driscoll et al. 2014). This lack of dispersal information would also undermine the utility of metapopulation disease models to forecast of disease spread dynamics and epidemic consequences at the metapopulation level. **In Chapter 3, I use a spatially explicit, individual-based model to simulate disease spread dynamics in a set of connected Mountain Yellow-legged frog population. I compare the simulated disease forecasts to field data, and test for the sensitivity of these results to assumptions of host dispersal capabilities.**

With disease introduction often having devastating effects on local population densities, and uncertainty in our ability to forecast disease reliably due to the lack of dispersal information, it becomes necessary to pre-identify regions that would be environmental suitable for chytrid

establishment. The climate dependence of the amphibian-chytrid interactions has been demonstrated in all continents where it occurs (Woodhams and Alford 2005, Rachowicz et al. 2006, Pounds et al. 2006, Alford et al. 2007, Bosch et al. 2007, Kriger et al, 2007, Andre et al. 2008, Berger et al. 2008, Laurance 2008, Lips et al. 2008, Rohr et al. 2008). Previous analysis has repeatedly pointed to temperature metrics as the most important predictor of environmental suitability to chytrid presence (Ron 2005, Puschendorf et al. 2009, Rödder et al. 2009, Kilpatrick et al. 2010, Rohr and Raffel 2010, Murray et al. 2011, Olson et al. 2013). Longcore et al. (1999) found that chytrid could grow in cultures at temperatures between 6 and 28 °C. While cultures at 29 °C failed to achieve substantial growth. The growth rate of the chytrid fungus has been shown to be highly sensitive to environmental temperature, with maximum growth between 17-25 °C (Piotrowski et al. 2004). Temperatures less than 17°C slow growth rates and prolong time to zoospores production (Johnson et al. 2003, Piotrowski et al. 2004). The fungus seems to favor cooler temperatures, as temperatures exceeding 30 °C can kill cultures (Longcore et al. 1999, Johnson et al. 2003, Piotrowski et al. 2004). In the laboratory, fluctuating temperatures can retard the pathogen's growth (Woodhams et al. 2003). Species distribution modeling has repeatedly identified climatic variables, in particular temperature metrics as the most influential when predicting chytrid occurrence (Ron 2005, Murray et al. 2011, Olson et al. 2013). High temperatures, which are often associated with high temperature variability, have been shown to decrease chytrid occurrence probability at a site (Murray et al. 2011).

Given this temperature dependency, any consideration of environmentally suitable regions receptive to chytrid invasion should include climate change into consideration. Since chytrid is sensitive to high temperatures (Piotrowski et al. 2004), it has been hypothesized that climate

change might curtail the emergence of chytrid (Harvell et al. 2002). However, despite these generalities on chytrid-temperature relationships derived *in vitro*, it remains ambiguous how climate change might alter future chytrid distributions (Venesky et al. 2013). Pounds et al. (2006) argued for climate change promoting the emergence of chytrid, noting that Harlequin frog declines in Central America were highly correlated with rising air temperature in high-elevation sites. In this case, it was hypothesized that the warming climate enhanced cloud cover at high elevations, leading to cooler days and warmer nights, modulating daily temperature range to converge around a "thermal optimum" for chytrid (Pounds et al. 2006). However, Rohr et al. (2008) argue that the correlation was spurious and could not find a causal link between climate change and chytrid emergence in the same frogs. Based on limited data, Rödder (2009) constructed a species distribution model that suggests that anthropogenic climate change may reduce the geographic range of chytrid. However, chytrid outbreaks in the Neotropics were found to be more common following high temperature years (Rohr and Raffel 2010), suggesting that climate change and the associated increased temperatures might actually promote chytrid emergence (Venesky et al. 2013). These apparently contradictory results describing the chytrid-temperature relationship may arise from complex interactions of climatic variables in the field and highlight the uncertainties in how chytrid distribution might be expected to change when global climates shift. **In Chapter 4, I examine how chytrid distribution is influenced by climatic variables based on the most comprehensive and up-to-date set of global chytrid surveillance data. Using a machine learning algorithm, I generate predictions as to how chytrid distributions might be expected to change according to IPCC projected scenarios of future climate change.**

My dissertation provides new information on disease ecology in a spatially differentiated landscape, with applications specific to the amphibian-chytrid system. Understanding the effect of dispersal on regional species persistence and how the lack of dispersal-related information necessary to formulate realistic models will help us explain how disease management could be integrated into conservation management planning targeted at the metapopulation level. I also model possible future ranges shifts/expansions of the amphibian chytrid fungus in response to climate change, the result of which will shed light on how emergence patterns of wildlife diseases will change corresponding to climate shifts and help mitigate further losses of biodiversity.

References

Abta R, Schiffer M and NM Shnerb. 2007. Amplitude-dependent frequency, desynchronization, and stabilization in noisy metapopulation dynamics. Physical Review Letters 98:098104.

Akçakaya HR, G Mills and CP Doncaster. 2007. The role of metapopulations in conservation. Pages 64-84 in Key Topics in Conservation Biology. D.W. Macdonald and K. Service, editors. Blackwell Publishing.

Alford RA, Bradfield KS and SJ Richards. 2007. Ecology: global warming and amphibian losses. Nature 447:E3–E4

Alford RA and SJ Richards. 1999. Global amphibian declines: A problem in applied ecology. Annual Review of Ecology and Systematics 30: 133-165.

Allan BF, Keesing F and RS Ostfeld. 2003. Effect of Forest Fragmentation on Lyme Disease Risk. Conservation Biology 17: 267–272.

Allen JC. 1975. Mathematical models of species interactions in time and space. American Naturalist. 109:319–342.

Almberg ES, Cross PC and DW Smith. 2010. Persistence of canine distemper virus in the Greater Yellowstone Ecosystem's carnivore community. Ecological Application 20:2058–2074.

Andre SE, Parker J and CJ Briggs. 2008. Effect of temperature on host response to *Batrachochytrium dendrobatidis* infection in the mountain yellow-legged frog (Rana muscosa). Journal of Wildlide Diseases 44:716–720.

Andreasen V and FB Christiansen. 1989. Persistence of an infectious disease in a subdivided population. Mathematical Biosciences 96:239-253.

Andrewartha HG and LC Birch. 1954. The Distribution and Abundance of Animals. The University of Chicago Press, Chicago, Illinois.

Artzy-Randrup Y and L Stone. 2010. Connectivity, Cycles, and Persistence Thresholds in Metapopulation Networks. PLoS Computational Biology 6(8): e1000876.

Baguette M and N Schtickzelle. 2003. Local population dynamics are important to the conservation of metapopulations in highly fragmented landscapes. Journal of Applied Ecology 40: 404–412.

Baguette M and Mennechez, G. 2004. Resource and habitat patches, landscape ecology and metapopulation biology: a consensual viewpoint. Oikos 106: 399–403.

Bancroft B, Han BA, Searle CL, Biga LM, Olson DH, Kats LB, Lawler JJ and AR Blaustein. 2011. Species-level correlates of susceptibility to the pathogenic amphibian fungus *Batrachochytrium dendrobatidis* in the United States. Biodiversity and Conservation 20: 1911-1920.

Bauer DM, PWC Paton and KS Stephen. 2010. Are Wetland Regulations Cost Effective for Species Protection? A Case Study of Amphibian Metapopulations. Ecological Applications 20: 798-815.

Becker CG, Fonseca CB, Haddad CFB, Batista RF and Prado PI. 2007. Habitat split and the global decline of amphibians. Science 318:1775–1777.

Berger L, R Speare, HB Hines, G Marantelli, AD Hyatt, KR McDonald, LF Skerratt, V Volsen, JM Clarke, G Gillespie, M Mahony, N Sheppard, C Williams and MJ Tyler. 2008. Effect of season and temperature on mortality in amphibians due to chytridiomycosis. Australian Veterinary Journal 82: 434-439.

Berger L, R Speare, P Daszak, DE Green, AA Cunningham, CL Goggin, R Slocombe, MA Ragan, AD Hyatt, KR McDonald, HB Hines, KR Lips, G Marantelli and H Parkes. 1998. Chytridiomycosis causes amphibian mortality associated with population declines in the rain forests of Australia and Central America. Proceedings of the National Academy of Sciences of the United States of America 95: 9031-9036.

Berger L, Hyatt AD, Speare R and JE Longcore. 2005. Life cycle stages of the amphibian chytrid *Batrachochytrium dendrobatidis*. Diseases of Aquatic Organisms 68: 51-63.

Berven KA and TA Grudzien. 1990. Dispersal in the wood frog (Rana sylvatica): implications for genetic population structure. Evolution 44:2047-56

Bjørnstad ON and BT Grenfell. 2008. Hazards, spatial transmission and timing of outbreaks in epidemic metapopulations. Environmental and Ecological Statistics 15:265–277.

Blaustein AR, Romansic JM, Scheessele EA, Han BA, Pessier AP, and JE Longcore. 2005. Interspecific variation in susceptibility of frog tadpoles to the pathogenic fungus *Batrachochytrium dendrobatidis*. Conservation Biology 19:1460–1468.

Blaustein AR and JM Kiesecker. 2002. Complexity in conservation: lessons from the global decline of amphibian populations. Ecology Letters 5: 597-608.

Blaustein, AR, BA Han, RA Relyea, PTJ Johnson, JC Buck, SS Gervasi and LB Kats. 2011. The complexity of amphibian population declines: understanding the role of cofactors in driving amphibian losses. Annals of the New York Academy of Sciences 1223: 108-119.

Blaustein AR, DB Wake and WP Sousa. 1994b. Amphibian declines: judging stability, persistence, and susceptibility of populations to local and global extinctions. Conservation Biology 8:60-71.

Blaustein AR, Hokit DG, O'Hara RK, and RA Holt. 1994a. Pathogenic fungus contributes to amphibian losses in the Pacific Northwest. Biological Conservation 67: 251-254.

Bosch J and I Martinez-Solano. 2006. Chytrid fungus infection related to unusual mortalities of Salamandra salamandra and Bufo bufo in the Penalara Natural Park, Spain. Oryx 40: 84-89.

Bosch J, Carrascal LM, Duran L, Walker S and MC Fisher. 2007. Climate change and outbreaks of amphibian chytridiomycosis in a montane area of Central Spain; is there a link? Proceedings of the Royal Society London B 274:253–260.

Bosch J, Martinez-Solano I and M Garcia-Paris. 2001. Evidence of a chytrid fungus infection involved in the decline of the common midwife toad (*Alytes obstetricans*) in protected areas of central Spain. Biological Conservation 97: 331-337.

Bradford DF. 1989. Allotopic distributions of native frogs and introduced fishes in high Sierra Nevada lakes of California: implications of the negative effect of fish introductions. Copeia 1989:775-78

Bradford DF. 1991. Mass mortality and extinction in a high elevation population of Rana muscosa. Journal of Herpetology 25: 369-377.

Breckenridge WJ and JR Tester. 1961. Growth, local movements and hibernation of the Manitoba toad, Bufo hemiophyrys. Ecology 42: 637-46.

Briggs CJ and M Hoppes. 2004. Stabilizing effects in spatial parasitoid–host and predator–prey models: a review. Theoretical Population Biology 65: 299–315.

Buckley D, Arano B, Herrero P and G Lorente. 1996. Population structure of Moroccan water frogs: genetic cohesion despite a fragmented distribution. Journal of Zoological Systematics and Evolutionary Research 34: 173-79.

Carey C, Bruzgul JE, Livo LJ, Walling ML, Kuehl KA, Dixon BF, Pessier AP, Alford RA and KB Rogers. 2006. Experimental Exposures of Boreal Toads (Bufo Boreas) to a Pathogenic Chytrid Fungus (*Batrachochytrium Dendrobatidis*). EcoHealth 3: 5–21.

Carey C. 1993. A Hypothesis concerning the causes of the disappearance of boreal toads from the mountains of Colorado. Conservation Biology 7: 355-362.

Casagrandi R and MJ Gatto. 2006. The intermediate dispersal principle in spatially explicit metapopulations. Theoretical Biology 239(1): 22-32.

Cheng TL, Rovito SM, Wake DB and VT Vredenburg. 2011. Coincident mass extirpation of neotropical amphibians with the emergence of the infectious fungal pathogen *Batrachochytrium dendrobatidis*. Proceedings of the National Academy of Sciences USA 108(23):9502-7.

Chinchar VG. 2002. Ranaviruses (family Iridoviridae): emerging cold-blooded killers. Archeological Virology. 147: 447-470.

Chivian E and A Bernstein (eds.) 2008. Sustaining life: How human health depends on biodiversity. Center for Health and the Global Environment. Oxford University Press, New York.

Coffee M, Lurie MN and GP Garnett. 2007. Epidemiology and Social Modelling the impact of migration on the HIV epidemic in South Africa. AIDS 21: 343–350.

Colizza V, Barrat A, Barthélemy M and A Vespignani. 2006. The role of the airline transportation network in the prediction and predictability of global epidemics. Proceedings of the National Academy of Science USA 103: 2015–2020.

Collins JP and A Storfer. 2003. Global amphibian declines: Sorting the hypotheses. Diversity and Distributions 9: 89-98.

Comins JN, Hassell MP and RM May. 1992. The spatial dynamics of host–parasitoid systems. Journal of Animal Ecology 61: 735–748.

Conroy SDS and BW Brook. 2003. Demographic sensitivity and persistence of the threatened white- and orange-bellied frogs of Western Australia. Population Ecology 45:105–114.

Corn PS and JC Fogleman. 1984. Extinction of montane populations of the Northern Leopard Frog (*Rana pipiens*) in Colorado. Journal of Herpetolology 18:147-52.

Corn PS and RB Bury. 1989. Logging in western Oregon: responses of headwater habitats and stream amphibians. Forest Ecology Management 29:39-57.

Crawford AJ, KR Lips and E Bermingham. 2010. Epidemic disease decimates amphibian abundance, species diversity, and evolutionary history in the highlands of central Panama. Proceedings of the National Academy of Science USA 107: 13777-13782.

Daniels PW, Halpin K, Hyatt A and D Middleton. 2007. Infection and disease in reservoir and spillover hosts: determinants of pathogen emergence. Current Topics in Microbiological Immunology 315:113-31.

Daszak P, Cunningham AA and AD Hyatt. 2000. Emerging infectious diseases of wildlife--threats to biodiversity and human health. Science 287(5452):443-9.

Daszak P, Cunningham AA and AD Hyatt. 2003. Infectious disease and amphibian population declines. Diversity and Distributions 9: 141-150.

Daszak P, Berger L, Cunningham AA, Hyatt AD, Green E and R Speare. 1999. Emerging infectious diseases and amphibian population declines. Emerging Infectious Diseases 5: 735-748.

Daszak P, Strieby A, Cunningham AA, Longcore JE, Brown CC and D Porter. 2004. Experimental evidence that the bullfrog (Rana catesbeiana) is a potential carrier of chytridiomycosis, an emerging fungal disease of amphibians. Herpetological Journal 14: 201-207.

Di Rosa I, Simoncelli F, Fagotti A and Pascolini R. 2007. Ecology: the proximate cause of frog declines? Nature 447: E4-R5.

Donald PF and AD Evans. 2006, Habitat connectivity and matrix restoration: the wider implications of agri-environment schemes. Journal of Applied Ecology 43(2): 209–218.

Driscoll DA, Banks SC, Barton PS, Ikin K, Lentini P, et al. 2014. The Trajectory of Dispersal Research in Conservation Biology. Systematic Review. PLoS ONE 9(4): e95053.

Duellman WE and Trueb L. 1986. Biology of Amphibians. New York: McGraw-Hill. 670 pp.

Durrett R and SA Levin. 1994. The importance of being discrete (and spatial). Theoretical Population Biology 46:363–394.

Earn DJD, Levin SA and P Rohani. 2000. Coherence and conservation. Science 290:1360–1364.

Fellers GM, DE Green, and JE Longcore. 2001. Oral chytridiomycosis in the mountain yellow-legged frog (Rana muscosa). Copeia 2001: 945-953.

Farrer RA, Weinert LA, Bielby J, Garner TWJ, Balloux F et al. 2011. Multiple emergences of genetically diverse amphibian-infecting chytrids include a globally hypervirulent recombinant lineage. Proceedings of the National Academy of Sciences USA 108: 18732-18736.

Fisher MP and TW Garner. 2007. The relationship between the introduction of Batrachochytrium dendrobatidis, the international trade in amphibians and introduced amphibian species. Fungal Biology Review 21: 2–9.

Fisher MC, Garner TWJ and SF Walker. 2009. Global emergence of *Batrachochytrium dendrobatidis* and amphibian chytridiomycosis in space, time and host. Annual Review of Microbiology 63: 291-310.

Fortuna MA, Gomez-Rodriguez C and J Bascompte. 2006. Spatial network structure and amphibian persistence in stochastic environments. Proceedings of the Royal Society B 206:1429–1434.

Gahl MK, Longcore JE and JE Houlahan. 2011. Varying responses of Northesastern North American amphibians to the chytrid pathogen *Batrachochytrium dendrobatidis*. Conservation Biology 26, 135-141.

Gamble LR, McGarigal K and BW Compton. 2007. Fidelity and dispersal in the pond-breeding amphibian, *Ambystoma opacum*: Implications for spatio-temporal population dynamics and conservation. Biological Conservation 139:247-257.

Garner TWJ, Perkins MW, Govindarajulu P, Seglie D, Walker S, Cunningham AA and MC Fisher. 2006. The emerging amphibian pathogen *Batrachochytrium dendrobatidis* globally infects introduced populations of the North American bullfrog, *Rana catesbeiana*. Biology Letters 2: 455-459.

Garner TWJ, Walker S, Bosch J, Leech S, Rowcliffe JM, Cunningham AA and MC Fisher. 2009. Life history tradeoffs influence mortality associated with the amphibian pathogen *Batrachochytrium dendrobatidis*. OIKOS 118: 783-791.

Gervasi SS, Gondhalekar C, Olson DH and AR Blaustein. 2013. Host identity matters in the amphibian-*Batrachochytrium dendrobatidis* system: fine-scale patterns of variation in responses to a multi-host pathogen. PLoS ONE 8: e54490.

Gill DE. 1978. The metapopulation ecology of the red-spotted newt, *Notophthalmus viridescens* (Rafinesque). Ecological Monograph 48: 145-66.

Gog J, Woodroffe R and J Swinton. 2002. Disease in endangered metapopulations: the importance of alternative hosts. Proceedings of the Royal Society B 269:671–676.

Goka K, Yokoyama J, Une Y, Kuroki T, Suzuki K, Nakahara M, Kobayashi A, Inaba S, Mizutani T, and AD Hyatt. 2009. Amphibian chytridiomycosis in Japan: distribution, haplotypes, and possible route of entry into Japan. Molecular Ecology 18: 4757-4774.

Green DE, KA Converse and AK Schrader. 2006. Epizootiology of Sixty-Four Amphibian Morbidity and Mortality Events in the USA, 1996-2001. Annals of the New York Academy of Sciences 969: 323-339.

Greenspan SE, Longcore JE and AJK Calhoun. 2012. Host invasion by *Batrachochytrium dendrobatidis*: fungal and epidermal ultrastructure in model anurans. Diseases of Aquatic Organisms 100: 201-210.

Griffiths RA, Sewell D and RS McCrea. 2010. Dynamics of a declining amphibian metapopulation: Survival, dispersal and the impact of climate. Biological Conservation 143: 485–491.

Gyllenberg M, Soderbacka G and S Ericsson. 1993. Does migration stabilize local-population dynamics – analysis of a discrete metapopulation model. Mathematical Biosciences 118: 25–49.

Haensch S, Bianucci R, Signoli M, Rajerison M, Schultz M, Kacki S, Vermunt M, Weston DA, Hurst D, Achtman M, Carniel E and B Bramanti. 2010. Distinct Clones of *Yersinia pestis* Caused the Black Death. PLoS Pathogens 6 (10): e1001134.

Hanski I and D Simberloff. 1997. The metapopulation approach, its history, conceptual domain, and application to conservation. pp. 5–26. In I. A. Hanski and M. E. Gilpin (eds.), Metapopulation Biology. Academic Press, San Diego, Californina.

Hanski I. 1999. Metapopulation Ecology, Oxford University Press.

Hanski I and M Gilpin. 1991. Metapopulation dynamics: brief history and conceptual domain. Biological Journal of the Linnean Society 42:3–16.

Harding KC and JM McNamara. 2002. A unifying framework for metapopulation dynamics. American Naturalist 160: 173–185.

Harvell CD, Mitchell CE, Ward JR, Altizer S, Dobson AP, Ostfeld RS and MD Samuel. 2002. Climate warming and disease risks for terrestrial and marine biota. Science 296: 2158–2162.

Harwood J and A Hall. 1990. Mass mortality in marine mammals: its implications for population dynamics and genetics. Trends in Ecology and Evolution 5:254-257.

Hastings A. 1993. Complex interactions between dispersal and dynamics – lessons from coupled logistic equations. Ecology 74: 1362–1372.

Hayes TB 2010. The cause of global amphibian declines: a developmental endocrinologist's perspective. Journal of Experimental Biology 213, 921-933.

Heard GW, Scroggie MP and BS Malone. 2012. Classical metapopulation theory as a useful paradigm for the conservation of an endangered amphibian. Biological Conservation 148: 156-166.

Heino M, Kaitala V, Ranta E and J Lindstrom. 1997. Synchronous dynamics and rates of extinction in spatially structured populations. Proceedings of the Royal Society B: Biological Sciences 264: 481–486.

Hels T and G Nachman. 2002. Simulating viability of a spadefoot toad *Pelobates fuscus* metapopulation in a landscape fragmented by a road. Ecography 25: 730–744.

Hess G. 1996. Disease in metapopulations: implications for conservation. Ecology 77: 1617-1632.

James TY, Litvintseva AP, Vilgalys R, Morgan JAT, Taylor JW, Fisher MC, Berger L, Weldon C, du Preez L and JE Longcore. 2009. Rapid global expansion of the fungal disease chytridiomycosis into declining and healthy amphibian populations. PLoS Pathogens 5(5): e1000458.

Jesse M, Ezanno P, Davis S, and JAP Heesterbeek. 2008. M. A fully coupled, mechanistic model for infectious disease dynamics in a metapopulation: movement and epidemic duration. Journal of Theoretical Biology 254: 331–338.

Johnson ML and R Speare. 2003. Survival of *Batrachochytrium dendrobatidis* in water: quarantine and disease control implications. Emerging Infectious Diseases 9: 922-925.

Johnson ML and R Speare. 2005. Possible modes of dissemination of the amphibian chytrid *Batrachochytrium dendrobatidis* in the environment. Diseases of aquatic organisms 65: 181-186.

Johnson PTJ, Lunde KB, Ritchie EG and AE Launer. 1999. The effect of trematode infection on amphibian limb development and survivorship. Science 284: 802-804.

Jousimo J, AJM Tack, O Ovaskainen, T Mononen, H Susi, C Tollenaere, and AL Laine. 2014. Ecological and evolutionary effects of fragmentation on infectious disease dynamics. Science 344 (6189): 1289-1293.

Kaiser K and J Pollinger. 2012. *Batrachochytrium dendrobatidis* shows high genetic diversity and ecological niche specificity among haplotypes in the Maya mountains of Belize. PLoS ONE 7: e32113.

Keeling MJ and CA Gilligan. 2000. Bubonic plague: a metapopulation model of a zoonosis. Proceedings of the Biological Society 267(1458): 2219–2230.

Kiesecker JM, Blaustein AR and LK Belden. 2001. Complex causes of amphibian population declines. Nature 410: 681-684.

Kiesecker, JM, Belden LK, Shea K, and MJ Rubbo. 2004. Amphibian decline and emerging disease. American Scientist 92: 138-147.

Kilpatrick AM, Briggs CJ and P Daszak. 2010. The ecology and impact of chytridiomycosis: an emerging disease of amphibians. Trends in Ecology & Evolution 25: 109–118.

Knapp RA, DM Boiano and VT Vredenburg. 2007. Removal of nonnative fish results in population expansion of a declining amphibian (mountain yellow-legged frog, Rana muscosa). Biological Conservation 135:11-20.

Kriger KM and JM Hero. 2007. Large-scale seasonal variation in the prevalence and severity of chytridiomycosis. Journal of Zoology 271:352–359.

Lannoo M. 2005. Amphibian Declines: The Conservation Status of United States. University of California Press. Berkeley, CA.

Laurance WF. 2008. Global warming and amphibian extinctions in eastern Australia. Australian Ecology 33:339–408.

Laurance WF, McDonald KR and R Speare. 1996. Epidemic disease and the catastrophic decline of Australian rain forest frogs. Conservation Biology 10, 406-413.

Levins R. 1969. Some demographic and genetic consequences of environmental heterogeneity for biological control. Bulletin of the Entomological Society of America 15:237–240.

Levins R. 1970. Extinction. In Some Mathematical Problems in Biology (Gestenhaber, M., ed.), pp. 77–107, American Mathematics Society.

Lindborg R and O.Eriksson. 2004. Historical Landscape Connectivity Affects Present Plant Species Diversity. Ecology 85:1840–1845.

Lips KR, Diffendorfer J, Mendelson III Jr and MW Sears. 2008. Riding the wave: reconciling the roles of disease and climate change in amphibian declines. PLoS Biol 6:e72.

Lips KR, F Brem, R Brenes, JD Reeve, RA Alford, J Voyles, C Carey, L Livo, AP Pessier and JP Collins. 2006. Emerging infectious disease and the loss of biodiversity in a Neotropical amphibian community. Proceedings of the National Academy of Sciences USA 102: 3165-3170.

Lips KR, Reeve JD and L Witters. 2003. Ecological traits predicting amphibian population declines in Central America. Conservation Biology 17: 1078–1088.

Lips KR. 1998. Decline of a tropical montane fauna. Conservation Biology 12:106-117.

Longcore JE, Pessier AP and DK Nichols. 1999. *Batrachochytrium dendrobatidis* gen. et sp. nov., a chytrid pathogenic to amphibians. Mycologia 91: 219-227.

Lötters S, Kielgast J, Bielby J, Schmidtlein S, Bosch J, Veith M, Walker SF, Fisher MC and D Rödder. 2009. The Link Between Rapid Enigmatic Amphibian Decline and the Globally Emerging Chytrid Fungus. EcoHealth 6: 358–372.

Lyons SK, Smith FA, Wagner PJ, White EP and JH Brown. 2004. Was a 'hyperdisease' responsible for the late Pleistocene megafaunal extinction? Ecology Letters 7: 859–868.

Marsh DM and PC Trenham. 2001. Metapopulation dynamics and amphibian conservation. Conservation Biology 15: 40-49.

Martel A, Spitzen-van der Sluijs A, Blooia M, Bert W, Decatelle R, Fisher MC, Woeltjes A, Bosman W, Chiers K, Bossuyt F and F Pasmans. 2013. *Batrachochytrium salamandrivorans* sp. nov. causes lethal chytridiomycosis in amphibians. Proceedings of the National Academy of Science 110: 15325-15329.

McCallum ML. 2007. Amphibian Decline or Extinction? Current Declines Dwarf Background Extinction Rate. Journal of Herpetology 41: 483-491

McCallum H and A Dobson. 2002. Disease, habitat fragmentation and conservation. Proc. R. Soc. Lond. Ser. B Biol. Sci. 269:2041–2049.

Murray KA, Retallick RWR, Puschendorf R, Skerratt LF, Rosauer D, McCallum HI, Berger L, Speare R and VanDerWal J. 2011. Assessing spatial patterns of disease risk to biodiversity: implications for the management of the amphibian pathogen, *Batrachochytrium dendrobatidis*. Journal of Applied Ecology 48: 163–173.

Murray KA and Skerratt LF. 2012. Predicting wild hosts for amphibian chytridiomycosis: integrating host life-history traits with pathogen environmental requirements. Human Ecology Risk Assessment 18: 200–224.

Nichols DK, Lamirande EW, Pessier AP and JE Longcore, J.E. 2001. Experimental transmission of cutaneous chytridiomycosis in dendrobatid frogs. Journal of Wildlife Diseases 37: 1-11.

Nicholson AJ. 1933. The balance of animal populations. Journal of Animal Ecology 2: 132–178.

Olson DH, Aanensen DM, Ronnenberg KL, Powell CI, Walker SF, Bielby J, Garner TWJ and Weaver G. The BD Mapping Group and MC Fisher. 2013. Mapping the global emergence of *Batrachochytrium dendrobatidis*, the amphibian chytrid fungus. PLoS ONE 8: e56802.

Ouellet M, Mikaelian I, Paul BD, Rodrigue J and DM Green. 2005. Historical evidence of widespread chytrid infection in North American amphibian populations. Conservation Biology 19: 1431-1440.

Park AW. 2012. Infectious disease in animal metapopulations: the importance of environmental transmission. Ecology and Evolution 2(7): 1398–1407. doi: 10.1002/ece3.257

Parris MJ and TO Cornelius. 2004. Fungal pathogen causes competitive and developmental stress in larval amphibian communities. Ecology 85: 3385-3395.

Petranka JW and CT Holbrook. 2006. Wetland restoration for amphibians: Should local sites be designed to support metapopulations or patchy populations? Restoration Ecology 14:404-411.

Petranka JW, Smith CK and AF Scott. 2004. Identifying the minimal demographic unit for monitoring pond-breeding amphibians. Ecological Applications 14:1065-1078.

Picco AM and JP Collins. 2008. Amphibian commerce as a likely source of pathogen pollution. Conservation Biology 22: 1582-1589.

Pimm SL and P Raven. 2000. Extinction by numbers. Nature 403: 843-845.

Piotrowski JS, Annis SL and JE Longcore. 2004. Physiology of *Batrachochytrium dendrobatidis*, a chytrid pathogen of amphibians. Mycologia 96: 9-15.

Plowright W. 1982. The effects of rinderpest and rinderpest control on wildlife in Africa. In: Animal disease in relation to animal conservation. M. A. Edwards and U. Mcdonnell eds. Academic Press, 336 pages.

Pounds JA, Bustamante MR, Coloma LA, Consuegra JA, Fogden MP, Foster PN, La Marca E, Masters KL, Merino-Viteri A, Puschendorf R, Ron SR, Sánchez-Azofeifa GA, Still CJ, and BE Young. 2006. Widespread amphibian extinctions from epidemic disease driven by global warming. Nature 439(7073):161-7.

Power AG and CE Mitchell. 2004. Pathogen spillover in disease epidemics. The American Naturalist 164 Suppl 5:S79-89.

Puschendorf R, Carnaval AC, VanDerWal J, Zumbado-Ulate H, Chaves G, Bolanos F, et al. 2009. Distribution models for the amphibian chytrid *Batrachochytrium dendrobatidis* in

Costa Rica: proposing climatic refuges as a conservation tool. Diversity and Distributions 15:401–408.

Rachowicz LJ and VT Vredenburg. 2004. Transmission of *Batrachochytrium dendrobatidis* within and between amphibian life stages. Disease of Aquatic Organisms 61:75–83.

Rachowicz LJ, Knapp RA, Morgan JAT, MJ Stice, VT Vredenburg, JM Parker and CJ Briggs. 2006. Emerging infectious disease as a proximate cause of amphibian mass mortality. Ecology 87:1671–1683.

Raffel TR, Romansic JM, Halstead NT, McMahon T, Venesky MD and JR Rohr. 2013. Disease and thermal acclimation in a more variable and unpredictable climate. Nature Climate Change 3: 145–151.

Rödder D, Kielgast J and S Lötters. 2010. Future potential distribution of the emerging amphibian chytrid fungus under anthropogenic climate change. Diseases of Aquatic Organisms 92:201–207.

Rödder D, Kielgast J, Bielby J, Schmidtlein S, Bosch J, Garner TWJ, et al. 2009. Global amphibian extinction risk assessment for the panzootic chytrid fungus. Diversity 1:52–66.

Rohr JR and TR Raffel. 2010. Linking global climate and temperature variability to widespread amphibian declines putatively caused by disease. Proceedingsof the National Academy of Sciences of the United States of America 107, 8269–8274.

Rohr JR, Raffel TR and CA Hall. 2010. Developmental variation in resistance and tolerance in a multi-host—parasite system. Functional Ecology 24: 1110-1121.

Rohr JR, Raffel TR, Romansic JM, McCallum H and PJ Hudson. 2008. Evaluating the links between climate, disease spread, and amphibian declines. Proceedings of the National Academy of Science USA 105:17436–17441.

Rollins-Smith LA, Carey C, Longcore J, Doersam JK, Boutte A, Bruzgal JE and JM Conlon. 2002. Activity of antimicrobial skin peptides from ranid frogs against *Batrachochytrium dendrobatidis*, the chytrid fungus associated with global amphibian declines. Developmental and Comparative Immunology 26, 471-479.

Ron SR. 2005. Predicting the distribution of the amphibian pathogen Batrachytrium dendrobatidis in the New World. Biotropica 37:209–221.

Sandeep S, Dutta T, Maldonado JE, Wood TC, Panwar HS and J Seidensticker. 2013. Forest corridors maintain historical gene flow in a tiger metapopulation in the highlands of central India. Proceedings of the Royal Society B 280: 20131506

Sattenspiel L. 1987. Epidemics in nonrandomly mixing pop-ulations: a simulation. American Journal of Physical Anthropology 73:251-265.

Schloegel LM, Toledo LF, Longcore JE, Greenspan SE, Vieira CA, Lee M, Zhao S, Wangen C, Ferreira CM, Hipolito M, Davies AJ, Cuomo CA, Daszak P and TY James. 2012. Novel, panzootic and hybrid genotypes of amphibian chytridiomycosis associated with the bullfrog trade. Molecular Ecology 21: 5162-5177.

Schloegel LM, Picco AM, Kilpatrick AM, Davies AJ, Hyatt AD and P Daszak. 2009. Magnitude of the US trade in amphibians and presence of *Batrachochytrium dendrobatidis* and ranavirus infection in imported North American bullfrogs (*Rana catesbeiana*). Biological Conservation 142: 1420-1426.

Scott ME. 1988. The impact of infection and disease on animal populations: implications for conservation biology. Conservation Biology 2: 40-56.

Searle CL, Gervasi SS, Hua J, Hammond JI, Relyea RA, Olson DH and AR Blaustein. 2011. Differential host susceptibility to *Batrachochytrium dendrobatidis*, an emerging amphibian pathogen. Conservation Biology 25: 965-974.

Semlitsch RD. 2008. Differentiating Migration and Dispersal Processes for Pond-Breeding Amphibians. Journal of Wildlife Management 72: 260-67.

Shulse CD et al., Influence of Design and Landscape Placement Parameters on Amphibian Abundance in Constructed Wetlands, 30 Wetlands 915-28 (2010).

Sih A, Jonsson BG and Luikart G. 2000. Habitat loss: ecological, evolutionary and genetic consequences. Trends in Ecology and Evolution 15: 132−134

Sjogren-Gulve P. 1994. Distribution and extinction patterns within a northern metapopulation of the pool frog, *Rana lessonae*. Ecology 75: 1357-1367

Sjogren P. 1991. Extinction and isolation gradient in metapopulations: the case of the pool frog (*Rana lessonne*). Biological Journal of the Linnean Society 42: 135-47.

Skerratt LF, Berger L, Speare R, Cashins S, McDonald KR, Phillott AD, Hines HB and N Kenyon. 2007. Spread of chytridiomycosis has caused the rapid global decline and extinction of frogs. Ecohealth 4: 125-134.

Smith AM and MD Green. 2005. Dispersal and the metapopulation paradigm in amphibian ecology and conservation: are all amphibian populations metapopulations? Ecography 28: 110–128.

Sokolow SH, Foley JE, Hastings A and LJ Richardson. 2009. Editor's choice: disease dynamics in marine metapopulations: modelling infectious diseases on coral reefs. Journal of Applied Ecology 46:621–631.

Soto-Azat C, Clarke BT, Poynton JC and AA Cunningham. 2009. Widespread historical presence of *Batrachochytrium dendrobatidis* in African pipid frogs. Diversity and Distributions 15: 1-6

Stuart SN, Chanson JS, Cox NA, Young BE, Rodrigues ASL, Fischman DL and RW Waller. 2004. Status and Trends of Amphibian Declines and Extinctions Worldwide. Science 306, 1783-1786.

Venesky MD, Parris MJ and A Storfer. 2010. Impacts of *Batrachochytrium dendrobatidis* infection on tadpole foraging performance. Ecohealth DOI: 10.1007/s10393-009-0272-7.

Venesky MD, Raffel TR, McMahon TA and JR Rohr. 2014. Confronting inconsistencies in the amphibian-chytridiomycosis system: implications for disease management. Biological Reviews 89: 477–483.

Voyles J, Young S, Berger L, Campbell C, Voyles WF, Dinudom A, Cook D, Webb R, Alford RA, Skerratt LF and R Speare. 2009. Pathogenesis of chytridiomycosis, a cause of catastrophic amphibian declines. Science 326: 582-585.

Vredenburg VT, Knapp RA, Tunstall TS and CJ Briggs. 2010. Dynamics of an emerging disease drive large-scale amphibian population extinctions. Proceedings of the National Academy of Sciences 107: 9689-9694.

Wake DB and VT Vredenburg. 2008. Are we in the midst of a sixth major extinction? A view from the world of amphibians. Proceedings of the National Academy of Sciences of the United States of America 105: 11466-11473.

Walker SF, Bosch J, Gomez V, Garner TWJ, Cunningham AA, Schmeller DS, Ninyerola M, Henk DA, Ginestet C, Arthur CP and MC Fisher. 2010. Factors driving pathogenicity vs. prevalence of amphibian panzootic chytridiomycosis in Iberia. Ecology Letters 13: 372–382.

Weldon KM, LH Preez, AD Hyatt, R Muller and R Speare. 2004. Origin of the amphibian chytrid fungus. Emerging Infectious Diseases 10: 2100-2105.

Whitaker BR and KN Wright. 2001. Amphibian Medicine and Captive Husbandry. Krieger Publishing Co., Malabar.

Whitesel TA and 7 coauthors. 2004. Bull Trout Recovery Planning: A review of the science associated with population structure and size. Science Team Report # 2004-01, U.S. Fish and Wildlife Service, Regional Office, Portland, Oregon, USA.

Woodhams DC and RA Alford. 2005. Ecology of Chytridiomycosis in Rainforest Stream Frog Assemblages of Tropical Queensland. Conservation Biology, 19: 1449–1459.

Woodhams DC, Alford RA and G Marantelli. 2003. Emerging disease of amphibians cured by elevated body temperature. Diseases of Aquatic Organisms 55: 65-67.

Woodhams DC, Alford RA, Briggs CJ, Johnson M and LA Rollins-Smith. 2008. Life-history trade-offs influence disease in changing climates: strategies of an amphibian pathogen. Ecology 89, 1627-1639.

Woodroffe R. 1999. Managing threats to wild mammals. Animal Conservation 2: 185-193.

Wright C. 2010. Spatiotemporal dynamics of prairie wetland networks: power-law scaling and implications for conservation planning. Ecology 91(7): 1924–1930.

Wyatt KB, Campos PF, Gilbert MTP, Kolokotronis S-O, Hynes WH, et al. 2009. Historical Mammal Extinction on Christmas Island (Indian Ocean) Correlates with Introduced Infectious Disease. PLoS ONE 4(1):10.1371

Yaari G, Ben-Zion Y, Shnerb NM, and Vasseur DA. 2012. Consistent scaling of persistence time in metapopulations. Ecology 93:1214–1227.

Young BE, Lips KR, Reaser JK, Ibanez R, Salas AW, Cedeno JR, Coloma LA, Ron S, La Marca E, Meyer JR, Munoz A, Bolanos F, Chaves G and D Romo. 2001. Population declines and priorities for amphibian conservation in Latin America. Conservation Biology 15: 1213-1223.

Zamudio KR and AM Wieczorek. 2007. Fine-scale spatial genetic structure and dispersal among spotted salamander (*Ambystoma maculatum*) breeding populations. Molecular Ecology 16: 257–274.

Chapter 2

Complexity in Host-Pathogen Dynamics: Dispersal, Population Synchrony, and Metapopulation Persistence in the Presence of Reservoir Hosts

Yang Xie and Andrew R. Blaustein

Abstract

The role of infectious diseases has been much discussed in the context of wildlife conservation at the metapopulation level, emphasizing the relationship between host dispersal and metapopulation persistence. Previous models have demonstrated that this relationship is sensitive to the rate infections spill over from reservoir hosts, and generally suggests that high dispersal rates will rarely be detrimental to metapopulation persistence. These models are often patch-based, without the explicit local dynamics that allow examination of risks posed by regional synchrony via enhanced dispersal. We formulate a stochastic model with population-level dynamics, and show that external sources of infection may lead to cyclic dynamics in a stochastic setting when its deterministic counterpart predicts extinction. This cyclicity increases temporal variance locally. Synchrony via host dispersal amplifies this temporal variance at the metapopulation level. We find that the relationship between metapopulation persistence and dispersal qualitatively differs from conclusions in previous work at low to intermediate rates of external infections, with persistence time optimized at intermediate dispersal rates. This indicates that benefits from dispersal do not always outweigh its risks of regional synchrony. The sensitivity of the dispersal-synchrony curve to the rate of external infections determines that at sufficiently high rates of external infections, our results remain consistent with previous literature.

Introduction

Global biodiversity is declining at a rate that dwarfs background extinction (Chivian and Berstein 2008, Vredenburg and Wake 2008). Habitat loss and fragmentation is the primary cause of species extinctions (Pimm and Raven 2000, Sih et al. 2000, Becker et al. 2007). With increased habitat loss and fragmentation, spatially segregated populations will take on characteristics typically ascribed to metapopulations (Ovaskainen and Hanski 2003) and conservation efforts have been increasingly targeted at the metapopulation level, with much research focusing on connectivity (e.g. Lindborg and Eriksson 2004, Donald and Evans 2006, Wright 2010, Artzy-Randrup and Stone 2010, Sandeep et al. 2013). Emerging infectious diseases (EIDs) are also gaining attention as potent threats to wildlife populations (Dazsak et al. 2000, Jones et al. 2008). For example, the severe negative impact of EIDs on population viability are found in birds (e.g. avian malaria in Hawaiian honey creepers, Smith et al. 2006), mammals (e.g. canine distemper in black-footed ferrets, Williams et al. 1988) and amphibians (Skerratt et al. 2007). The interrelationships among biodiversity and disease have received increasing empirical and theoretical attention. EIDs may interact with a fragmented landscape to influence the disease risks experienced at the local and metapopulation level (McCallum and Dobson 2002, Allan et al. 2003). Recent theoretical research has examined this interaction in the context of wildlife conservation, with an emphasis on connectivity inherited from the general metapopulation paradigm (Hess 1996, Gog et al. 2002, McCallum and Dobson 2002, Park 2012).

Hess (1996) suggested that dispersal of the host species between populations (i.e. connectivity) may aid the spread of infectious agents, and thereby increase the probability of metapopulation

extinction. Indeed, increased contact among populations almost universally increases the prevalence, incidence, and the duration of disease in metapopulations (Andreasen and Christiansen 1989, Sattenspiel and Castillo-Chavez 1990, Jesse et al. 2008). Hess's (1996) model shows that patch occupancy first increases with dispersal rate as recolonization takes place quicker than extinction of both susceptible and infected patches. Past a certain dispersal threshold, though, patch occupancy decreases sharply as most patches become infected and experience a higher extinction rate. Once disease becomes pandemic, higher rates of dispersal can have little further negative impacts through enhanced rates of disease spread, and occupancy again increases due to accelerated recolonizations. Due to these deleterious effects and the non-monotonically increasing relationship between patch occupancy and dispersal rate, Hess (1996) suggested that, while some dispersal is necessary to maintain a metapopulation, too much host dispersal could create a potentially critical disease hazard.

Follow-up work argues that Hess's (1996) conclusion is based on unrealistic assumptions of extremely low rates of disease transmission from sources outside the focal host species (Gog et al. 2002, McCallum and Dobson 2003, Park 2012). Indeed, diseases with serious impacts on endangered wildlife populations often occur as spillovers from reservoir hosts (Woodroffe 1999, Power and Mitchell 2004, Daniels et al. 2007). Subsequent models that incorporate background sources of infection demonstrate that if the rate of infection from a background source is sufficiently high (compared to the extinction rate of a healthy host population), patch occupancy monotonically increases with host dispersal (Gog et al. 2002, McCallum and Dobson 2002, Park 2012). The higher the rate of disease spillover, the more readily the benefits of increased dispersal will outweigh the costs (Gog et al 2002.). These models suggest that if the background

rate of infection is sufficiently high, increasing host dispersal will always be favorable for metapopulation persistence (McCallum and Dobson 2002, Gog et al. 2002, Park 2011).

This conclusion is somewhat surprising when viewed in the context of general metapopulation research without reference to disease. Metapopulation persistence is typically predicted to be optimized at intermediate levels of dispersal (Gyllenberg et al. 1993, Hastings 1993, Casagrandi and Gatto 2006, Yaari et al. 2012). At extremely low levels of dispersal between populations, patch recolonizations cannot catch up with extinctions; while at high levels of dispersal, population dynamics may be regionally synchronized so that there is no risk spreading from conserving spatially segregated populations and rescue effects are prevented (Yaari et al. 2012). An intermediate rate of dispersal allows the rescue effect without inducing regional synchrony, and populations are asynchronous enough that "statistical stabilization" occurs (Briggs and Hoppes 2004, otherwise known as the "portfolio effect", Anderson et al 2013), thus optimizing metapopulation persistence (Hanski and Gilpin 1997).

Where infectious agents and reservoir hosts are present, it may be beneficial to consider that connected populations may be prone to synchronization and its associated risks. The extent of dispersal-induced synchronization and its associated risk is contingent on mechanisms of local population regulation (Yaari et al 2012). Both models and empirical evidence suggest that the effects of dispersal on population stability are likely to be stronger in the presence of natural enemies (Ims and Steen 1990, Rohani et al. 1996, Vasseur and Fox 2009, Vogwill et al. 2009). One explanation for this might be that processes such as predation and parasitism are considered key regulators of cyclic host populations (Wearing et al. 2004), and theoretical research indicates that cyclic populations are readily synchronized at even low dispersal rates, including

those induced by the presence of pathogens (Bjornstad et al 1999, Rosenblum et al. 1996, Hagenaars et al. 2004). With an ecological role blurred with that of the predator, pathogens are also capable of producing cyclic population dynamics (e.g. fox rabies, Anderson et al. 1981; nematode in Red Grouse, Hudson et al. 1998; cowpox virus in vole populations, Cavanaugh et al. 2004). If we consider again that many wildlife diseases occur as spillovers (Woodroffe 1999, Power and Mitchell 2004, Daniels et al. 2007), and that diseases with a density-dependent form of transmission are likely to go extinct before its host, it is likely that the presence of reservoir hosts may act to repeatedly reintroduce the disease and contribute to inducing cyclic host dynamics. For example, recurrent bubonic plague in London is thought to arise from reservoir rat hosts (Keeling and Gilligan 2000). Therefore, disease systems with reservoir hosts might be predisposed to synchronization by dispersal if cyclic local dynamics are induced by infectious agents.

These cyclic dynamics increase the temporal variance of local population sizes, which decreases population stability and increases extinction rates (Pimm et al. 1988, Schoener and Spiller 1992). Once sets of cyclic populations are synchronized, this temporal variance (i.e. instability) is amplified at the metapopulation level as is metapopulation extinction risk (Heino et al. 1997). If this is the case, increased host dispersal may not be favorable for metapopulation persistence when the variance-amplifying effect of synchronization is considered. However, this negative aspect to dispersal has received little attention in the context of metapopulation disease dynamics in the presence of reservoir hosts. In the body of literature advocating for high rates of host dispersal in the presence of reservoir hosts, Levins-type models without explicit population dynamics are typically used which precludes the examination of synchrony levels, and patches

are often modelled with state changes only (i.e. categorization into susceptible, infected and recovered patches, e.g. Gog et al. 2002, McCallum and Dobson 2003, Park 2012). Here, we investigated metapopulation persistence time and how changes in synchrony may be influenced by dispersal in the presence of implicit reservoir hosts, using a mechanistic model with explicit population trajectories. We show that an external source of infection may lead to cyclic dynamics in a stochastic setting whereas deterministic models predict extinction, and that these dynamics are prone to synchronization via host dispersal to different degrees at varying rates of external infections.

Modeling methods

Deterministic formulation

Two identically parameterized coupled populations were simulated. A deterministic version of the model for within-population demographic and disease dynamics follows the formulation of an SIRS model (Susceptible-Infected-Recovered-Susceptible) with variable population size (schematic system in fig. 2.1). In this model, susceptible individuals (healthy but without immunity) transition into the infected class through disease transmission, infected individuals may recover from the disease and gain temporary immunity. Once the immunity is lost, a recovered individual once again transitions to the susceptible class. Population growth in the model is governed by the logistic equation as described in Gao and Hethcote (1992) with an additional term gS_i to represent infection from an background source in a density-dependent manner. Here a susceptible in a population becomes infected at a per capita rate of g from a background source. The deterministic representation of model in ordinary differential equations is as follows (parameter values shown in table 2.1):

$$\dot{S}_1 = \lambda S_1 - dS_1 - gS_1 - \mu(N_1)S_1 - \beta S_1 I_1 + \delta R_1 - m_{12}S_1 + m_{21}S_2$$
$$\dot{I}_1 = \beta S_1 I_1 + gS_1 - (\alpha + d + \mu(N_1) + \gamma)I_1 - m_{12}I_1 + m_{21}I_2$$
$$\dot{R}_1 = \gamma I_1 - (d + \mu(N_1) + \delta)R_1 - m_{12}R_1 + m_{21}R_2$$
$$\dot{S}_2 = \lambda S_2 - dS_2 - gS_2 - \mu(N_2)S_2 - \beta S_2 I_2 + \delta R_2 - m_{21}S_2 + m_{12}S_1$$
$$\dot{I}_2 = \beta S_2 I_2 + gS_2 - (\alpha + d + \mu(N_2) + \gamma)I_2 - m_{21}I_2 + m_{12}I_1$$
$$\dot{R}_2 = \gamma I_2 - (d + \mu(N_2) + \delta)R_2 - m_{21}R_2 + m_{12}R_1$$

where $\mu(N_1) = (\lambda - d)\frac{N_1}{K}$ and $\mu(N_2) = (\lambda - d)\frac{N_2}{K}$ are the competition-induced mortality rates

in population 1 and 2. Only susceptible individuals reproduce in the model, therefore in the

absence of disease (including infections from background sources, i.e. $g = 0$), a single

population exhibits logistic growth with annual per capita birth rate λ, natural mortality rate d,

carrying capacity K. The density-dependence term, $(\lambda - d)\frac{N_1}{K}$ is distributed entirely on the

population death rate in this parameterization, but note that any distribution of this term

between birth and death rates is equivalent (Gao and Hethcote 1992, Yaari et al. 2012). The

separation of competition-induced mortality and natural mortality is equivalent to the

formulation of the logistic growth portion of Gao and Hethcote's SEIR model (1992) with a

convex combination coefficient of 1. In the stochastic simulation algorithm, the separation of

these terms prevents the system from exhibiting logistic-map type behaviors instead of the

continuous logistic growth we assumed here. β is the transmission coefficient for an infectious

agent with density-dependent transmission, of which the disease-related death rate is α. Infected

individuals recover with rate γ and gain an temporary immunity, which is lost with rate δ before

the individual returns to the susceptible class. At the metapopulation level, the two populations

are fully connected. Dispersers arrive at population 2 from population 1 at a rate of m_{12}, and

vice versa at a rate of m_{21}. It is assumed that SIR classes are equal in their dispersal rate and that individuals do not change disease status during dispersal.

Stochastic realization

To ensure that extinctions of both the disease and populations are possible in the model, integer-valued population dynamics were simulated with an event-driven continuous time Markov chain. The Gillespie Stochastic Simulation Algorithm (SSA) is used to implement the chain (Gillespie 1976). The state of a population is defined by (S, I, R), the size of the respective classes. The SSA algorithm assigns relative probabilities to all possible events described in the deterministic formulation according to their respective rates. All possible events within a population and their relative rates are described in table 2.2. For example, in the absence of disease, the rate of susceptible individuals being born in population 1 is λS_1, the rate of a susceptible individual dying of natural mortality is dS_1, and the rate of competition-induced mortality is $\mu(S_1)$ since $S_1 = N_1$. The relative probability of an event is calculated as the proportion of its rate in the sum of the rates of all events. Following the previous example, the relative probability of a birth, natural death, and competition-induced death event would be $\frac{\lambda S_1}{\lambda S_1 + dS_1 + \mu(N_1)}$, $\frac{dS_1}{\lambda S_1 + dS_1 + \mu(N_1)}$, and $\frac{\mu(N_1)}{\lambda S_1 + dS_1 + \mu(N_1)}$, respectively. These relative probabilities then define a multinomial distribution of all possible events. One event is then selected at random from this multinomial distribution and the population state is updated. If a birth event is selected, the state of the population is updated from (S_1, I_1, R_1) to $(S_1 + 1, I_1, R_1)$, whereas is a death events was chosen the populations is updated from (S_1, I_1, R_1) to $(S_1 - 1, I_1, R_1)$. After the

event, simulation time is advanced by a randomly generated time interval, and this process is repeated until the end time point is reached.

Simulations

We combined a range of background infection rates g and host dispersal rates m in a factorial design. For each combination we ran 10^3 to 10^4 simulations (numbers adjusted to reduce the variance is simulation metrics for some parameter combinations). In all cases, one population was inoculated at carrying capacity K with 10% infected individuals at the initial time, while all other populations were initialized with a random integer number of susceptibles chosen from a uniform distribution defined on [1, K]. We estimated the mean metapopulation persistence time and level of synchrony between the two populations (determined by the Spearman correlation coefficient (Buonaccorsi et al. 2001)) for each parameter combination. We quantified the degree of temporal variance in population and metapopulation abundances using the temporal coefficient of variation σ/μ, where σ and μ are the standard deviation and mean of the metapopulation size during a simulation, respectively (Secor et al. 2009, Schindler et al. 2010; Carlson and Satterthwaite 2011, Anderson et al. 2013). All simulations were performed in MATLAB.

Results

Comparison of deterministic and stochastic dynamics

The discretization and addition of stochasticity induces qualitatively different behaviors compared to the deterministic formulation (fig. 2.2). While in the deterministic model the SIR classes persist indefinitely at non-integer values less than unity (i.e. effective extinction of the

population), in the stochastic model the alternative outcome to extinction is population recovery after the extinction of the disease. When contact with reservoir sources is possible, cyclic dynamics arise in the system as a population repeatedly experiences disease extinction, recovery and disease reintroduction. As g increases, local population persistence time decreases (i.e. increased extinction rates). This is due both to a decrease in the mean size of the local population as externally acquired infections become more frequent and an increase in σ/μ (fig. 2.3). At the metapopulation level, for two populations originally out of sync when there is no dispersal, relatively small values of m may be sufficient to induce synchrony (fig. 2.2C).

Effect of external infection and dispersal on metapopulation persistence time

Metapopulation persistence time decreases monotonically with the external infection rate g (fig. 2.4), as is consistent with observations on the local level. At smaller to intermediate ranges of g (10^{-4} to 10^{-2}), metapopulation persistence time is optimized at intermediate rates of m (host dispersal) but does not increase again with dispersal past the initial decline. This observation at smaller to intermediate ranges of g departs from some of what the previous literature suggests (Hess 1996, Gog et al. 2002, McCallum and Dobson 2002). This optimal range of host dispersal rate shifts to the higher end of the dispersal spectrum with increases in g since higher recolonization rates are necessary to balance local extinction rate increases. This trend continues in the parameter space investigated until at high ranges of g from 10^{-1} to 10^{0} a monotonically increasing relationship between dispersal and metapopulation persistence time is observed, which is consistent with previous literature (Hess 1996, Gog et al. 2002, McCallum and Dobson 2002). We considered that these behaviors might be a result of insufficient investigation of the parameter space, instead of being truly reflective of the divergence or agreement with previous

research. To determine this, we ran further simulations at $g = 0.0032$ and $g = 1.6384$ on an extended range of dispersal rates (m from $0 - 100$). At $g = 0.0032$, metapopulation persistence time is optimized at intermediate dispersal rates as is typical of low to intermediate g, while at $g = 1.6384$ persistence time monotonically increases with dispersal rates as is typical of high g. These values were therefore chosen to further examine whether the relationship between metapopulation persistence time and dispersal at low to intermediate and high rates of external infections are a result of insufficient exploration of the dispersal range. The results displayed in fig. 2.4 B&C indicates that the observed behaviors in the model persist for a wide range of dispersal rates. At an intermediate g, metapopulation persistence time does not increase again past the initial decline, and at high ranges of g persistence time remains monotonically increasing with the extended range of dispersal rates. This indicates that our results agree with previous literature when rate of external infections are high, but diverge at low to intermediate levels.

Temporal variance and synchrony

Metapopulation persistence time is inversely related to the temporal coefficient of variation $/\mu$, an indicator of the temporal variance relative to the mean of the metapopulation (fig. 5). This result is intuitive: if the metapopulation mean is greater than the standard deviation, metapopulation size is less likely to be sampled at a value below the extinction threshold. For instance, if $\sigma/\mu < 1$ the population is more likely to fluctuate around the mean without going extinct; while if $\sigma/\mu > 1$, temporal variance is large relative to the mean and the population is likely to undergo stochastic extinctions, especially if the mean is small. This inverse relationship between metapopulation persistence time and temporal variance is consistent at all

levels of g, indicating that whenever temporal variance is large relative to the mean, metapopulations are more likely to experience extinction.

This inverse relationship between metapopulation persistence and temporal variance suggests that synchrony is the most likely cause of the patterns observed here. Where local systems are naturally cyclic, the temporal variance at the metapopulation scale increases with synchrony. Also, the ratio of temporal variance relative to the mean is larger at the metapopulation scale than at the local scale when synchrony is present. This suggests that synchrony amplifies that temporal variance at the metapopulation scale when local fluctuations are inherent, thus introducing instability. At all values of g, changes in σ/μ closely track the change in synchrony, which also has an inverse relationship with metapopulation persistence time (fig. 5). Synchrony initially undergoes an interval of decline with increased dispersal, and then increases with dispersal (most evident at intermediate levels of g, fig. 5B). Within both of these intervals, synchrony and metapopulation persistence time remain inversely correlated regardless of how dispersal is associated with synchrony. The range of dispersal in which we observe a decrease in synchrony is narrow at low g, but gets successively extended as g increases. This is consistent with the relationship between dispersal and metapopulation persistence time, in which the peak in metapopulation persistence time is continuously shifted to the higher end of the dispersal spectrum with increasing g. At low to intermediate values of g, the range of low synchrony and maximum metapopulation persistence occurs at intermediate dispersal rates, while at the highest value of g we investigated (1.6384), synchrony monotonically decreases with increased dispersal, and correspondingly, metapopulation persistence time monotonically increases.

Discussion

Using a stochastic model with explicit local dynamics, we have shown that the conclusions derived from patch based Levin-type metapopulation models with an external source of infection are altered when the synchronization effects of dispersal are considered. Our model system allows us to consider the effects of an external source of infection on local population dynamics. Repeated disease introductions from such a source induce fluctuations in the population trajectory. Within the context of our model, these fluctuations are presented as cyclic dynamics that effect the temporal variance relative to the mean of the metapopulation. At the local level, we observe in our model that a higher external infection rate of a severe disease decreases the population mean and increases the temporal variance relative to the mean. This gives rise to the intuitive result when contact and transmission from reservoirs hosts are frequent, local population sizes are small and temporal fluctuations are relatively larger, resulting in high patch extinction rates.

The presence and degree of local population fluctuations are amplified at the metapopulation level by synchronization via host dispersal. Accordingly, we find that metapopulation persistence time is always inversely correlated with synchrony where there is at least some dispersal (when there is no dispersal, synchrony is low but metapopulation persistence time is also low as there is no recolonization of extinct patches). Both measures are model outcomes and therefore it might be argued that such correlation does not imply causality. However, there is ample literature that has shown that synchrony does indeed reduce metapopulation persistence time. Synchronous fluctuations at the local level increase the extinction risk of the metapopulation by hampering the rescue effect and generating temporally correlated extinctions (Hanski 1991; Heino et al. 1997; Earn et al. 2000, Yaari et al. 2012). From a statistical

perspective, the relationship between the amplified temporal variance induced by synchrony at the metapopulation and population extinction rate is intuitive. Suppose that the number of individuals in two connected populations at time t are defined by the random variables (X_t, Y_t) with metapopulation size $N_t = X_t + Y_t$. The local population sizes are unaffected by synchrony. While at the expected size (i.e. the mean) of the metapopulation at time t (described by the random variable N_t) is the linear combination $E(N_t) = E(X_t) + E(Y_t)$, the variance at the metapopulation level is $Var(N_t) = Var(X_t) + Var(Y_t) + 2Cov(X_t, Y_t)$. The last covariance term is proportional to the correlation between the two population sizes. Therefore, the more synchronized two populations are, the larger the metapopulation variance will be relative to metapopulation mean at time t. In this case, if the expected metapopulation size $E(N_t)$ is close to 0 to start with, then an inflated variance term relative to the mean implies there is a larger probability that the sampled N_t will fall below the extinction threshold. Therefore, if the presence of reservoir hosts could induce temporal fluctuation in the host population by the stochastic nature of encounters and recurrent disease reintroductions, the system might be synchronized at low dispersal rates, thereby increasing metapopulation extinction rates.

In summary, the presence of an external source of infection increases temporal variance relative to the mean as well as the patch extinction rate at the local level, and synchronization by host dispersal amplifies this variability and extinction probability at the metapopulation level. Considering that populations with cyclic dynamics can be readily synchronized at relatively low dispersal rates (Rosenblum 1996), the coupling of these two observations leads us to conclude that metapopulation persistence time may be optimized at intermediate ranges of host dispersal at least for low to intermediate ranges of external infection rates. This conclusion

differs qualitatively from some of the previous literature, where it was found that when disease becomes pandemic, further increases in dispersal can only serve to benefit metapopulation persistence (Hess 1996, Gog et al. 2002, McCallum and Dobson 2002). Our results demonstrate that such further increases in host dispersal also carry the risk of regional synchrony. This implies that for diseased wildlife populations, where reservoirs hosts are present, it is necessary to encourage dispersal to some extent such that the metapopulation is functional and recolonizations outrace local extinctions, but further increases in dispersal may increase extinction risks for the metapopulation as a whole when temporal variances at the local level is large.

The form of the relationship between synchrony and dispersal rates observed in this simulation is that of an initial decrease in synchrony with increased dispersal rate, followed by a positive association upon further increase in dispersal rate. Jasen (2001) also observed this relationship in a predator-prey metapopulation model: when coupling (i.e. dispersal) is too strong or too weak, the oscillations phase lock and synchronous oscillations result, whereas at intermediate dispersal rates asynchrony may arise. This asynchrony may arise as one patch produces enough prey to sustain enough predators, and the larger outflow of predator may result in prey extinction at the destination patch. This pattern has also been shown on coupled lattice models of host-parasitoid dynamics (Hassell et al. 1991, Comins et al. 1992). Here this decrease in synchrony at intermediate dispersal rates could arise from similar reasons – as population becomes abundant enough to produce a density of susceptibles high enough to encounter reservoir hosts, the overflow of infected individuals into the other patch could result in extinctions by disease at the destination patch. As the rate of disease transmission from

reservoir hosts increase, populations fluctuate around lower levels, and higher dispersal rates may be necessary to obtain the same number of dispersal events that will disrupt the synchronous oscillations. This could be why the region of initial synchrony that declines with dispersal is extended to higher dispersal rates as g increases.

The definition of this optimal range of "intermediate" host dispersal that maximizes metapopulation persistence time therefore depends on the rate of external infections. It is observed that this optimal range shifts continuously to the higher end of the dispersal spectrum as the rate of external infections increases, which is consistent with the pattern we observe between synchrony and dispersal. This shift is due to successively higher recolonization rates necessary to balance the accompanying increase in local extinction rate and the change in the range of low synchrony. The contingency of this optimal range of host dispersal on the rate of external infections allows consistency with previous models. At high rates of external infections, metapopulation persistence time might appear monotonically increasing with host dispersal within the dispersal ability of the host. In this respect, our results are apparently consistent with previous literature. Gog et al. (2002) attributes this monotonicity at high background infection rates to the observation that dispersal can only serve to increase occupancy when the disease becomes pandemic. Here we show that this monotonicity can also arise because synchrony decreases over a large range of dispersal rates when background infection sources are high. In this case, our analysis also indicates that dispersal should be facilitated as much as possible when transmission from reservoir hosts if frequent.

The applicability of our findings to conservation of endangered wildlife populations will depend on the role of disease in the host population and the rate at which infections are acquired from

reservoir hosts. When contact rate with reservoir hosts is high, corridor building to encourage host dispersal is always beneficial, as the risk of regional synchrony is low. However, natural dispersal abilities of hosts may not be sufficient to overcome increased local extinction rate, and local populations may be so suppressed that there are few dispersers. In this case, there might be little that connectivity enhancement can achieve, and management should prioritize regulation of reservoir host density instead. When contact rate with reservoir hosts are low, the relationship between dispersal rate and metapopulation persistence will be less straightforward. Again, the extent to which connectivity enhancement will benefit metapopulation persistence is dependent on the natural dispersal capabilities of the host. If inherent host dispersal ability is not enough to induce regional synchrony, dispersal should always be encouraged. However, if inherent host dispersal ability is strong enough to induce regional synchrony, coupled with a small number of populations and relatively homogeneous conservation area, corridors could pose an added risk (Hilty et al. 2006), especially when cyclic disease dynamics are present at the local level. In this case, conservation managers should aim to remove cycles at the local level to enhance population stability, and conserve a large number of populations in a spatially heterogeneous landscape to prevent regional synchrony or alternatively, isolate populations enough that synchrony caused by dispersal can be reduced (Hilty et al. 2006).

The results presented here are based on several simplifying assumptions. One such simplification is the implicit formation of the transmission process from the reservoir host. Indeed, the presence and density of reservoirs hosts may not be uniform in all patches at all times, and this spatial heterogeneity may disrupt the process of synchronization by dispersal. The addition of spatial heterogeneity may therefore alter these conclusions on the relationship

between metapopulation persistence time and host dispersal rates substantially, warranting further research.

References

Abbott KC. 2011. A dispersal-induced paradox: synchrony and stability in stochastic metapopulations. Ecology Letters 14: 1158–1169.

Allan BF, F Keesing and RS Ostfeld. 2003. Effect of Forest Fragmentation on Lyme Disease Risk. Conservation Biology 17: 267–272.

Anderson RM, HC Jackson, RM May and AM Smith. 1981. Population dynamics of fox rabies in Europe. Nature 289: 765 – 771.

Anderson SC, AB Cooper and NK Dulvy. 2013. Ecological prophets: quantifying metapopulation portfolio effects. Methods in Ecology and Evolution 4(10): 971–981.

Andreasen V and FB Christiansen. 1989. Persistence of an infectious disease in a subdivided population. Mathematical Biosciences 96:239-253.

Artzy-Randrup Y and L Stone. 2010. Connectivity, Cycles, and Persistence Thresholds in Metapopulation Networks. PLoS Computational Biology 6(8): e1000876.

Becker CG, CB Fonseca, CFB Haddad, RF Batista and PI Prado. 2007. Habitat split and the global decline of amphibians. Science 318:1775–1777.

Bjornstad ON, RA Ims and X Lambin. 1999. Spatial population dynamics: analyzing patterns and processes of population synchrony. Trends in Ecology and Evolution 14: 427–432.

Briggs CJ and M Hoppes. 2004. Stabilizing effects in spatial parasitoid–host and predator–prey models: a review. Theoretical Population Biology 65: 299–315.

Buonaccorsi JP, JS Elkinton, SR Evans and A Liebhold. 2001. Measuring and testing for spatial synchrony. Ecology 82:1668–1679.

Carlson SM and WH Satterthwaite. (2011) Weakened portfolio effect in a collapsed salmon population complex. Canadian Journal of Fisheries and Aquatic Sciences, 68, 1579{1589.

Casagrandi R and MJ Gatto. 2006. The intermediate dispersal principle in spatially explicit metapopulations. Theoretical Biology 239(1): 22-32.

Cavanagh RD, X Lambin, T Ergon, M Bennett, IM Graham, D van Soolingen and M Begon. 2004. Disease dynamics in cyclic populations of field voles (*Microtus agrestis*): cowpox virus and vole tuberculosis (*Mycobacterium microti)*. Proceedings of the Royal Society of London, Series B, Biological Sciences 271:859–867.

Chivian E and A Bernstein. (Eds.) 2008. Sustaining Life: How Our Health Depends on Biodiversity. New York, NY: Oxford University Press, USA.

Comins HN, MP Hassell and RM May. 1992. The spatial dynamics of host-parasitoid systems, Journal of Animal Ecology 61: 735-748.

Daniels PW, K Halpin, A Hyatt and D Middleton. 2007. Infection and disease in reservoir and spillover hosts: determinants of pathogen emergence. Current Topics in Microbiological Immunology 315:113-31.

Daszak P, AA Cunningham and D Hyatt. 2000. Emerging infectious diseases of wildlife — threats to biodiversity and human health. Science 287: 443–449.

Donald PF and AD Evans. 2006, Habitat connectivity and matrix restoration: the wider implications of agri-environment schemes. Journal of Applied Ecology 43(2): 209–218.

Earn D, SA Levin and P Rohani. 2000. Coherence and conservation. Science 290: 1360–1364.

Gao LQ and HW. Hethcote. 1992. Disease transmission models with density dependent demographics. Journal of Mathematical Biology 30: 717-731.

Gillespie DT. 1976. A general method for numerically simulating the stochastic time evolution of coupled chemical reactions. Journal of Computational Physics 22:403–434.

Gog J, R Woodroffe and J Swinton. 2002. Disease in endangered metapopulations: the importance of alternative hosts. Proceedings of the Royal Society B 269:671–676.

Yaari G., Ben-Zion Y, Shnerb NM, and Vasseur DA. 2012. Consistent scaling of persistence time in metapopulations. Ecology 93:1214–1227.

Gyllenberg M, G Soderbacka and S Ericsson. 1993. Does migration stabilize local-population dynamics – analysis of a discrete metapopulation model. Mathematical Biosciences 118: 25–49.

Hagenaars TJ, CA Donnelly and NM Ferguson. 2004. Spatial heterogeneity and the persistence of infectious diseases. Journal of Theoretical Biology 229: 349–359.

Hanski I. 1991. Single-species metapopulation dynamics: concepts, models and observations. In: Metapopulation Dynamics: Empirical and Theoretical Investigations. (ed. Gilpin, M. and Hanski, I.). Harcourt Brace Jovanovich, London, pp. 17–38.

Hanski IA and ME Gilpin. 1997. Metapopulation biology: ecology, genetics and evolution. Academic Press; San Diego, California, USA.

Hassell MP, HN Comins and RM May. 1991. Spatial structure and chaos in insect population dynamics, Nature 363: 252-258.

Hastings A. 1993. Complex interactions between dispersal and dynamics – lessons from coupled logistic equations. Ecology 74: 1362–1372.

Heino M, V Kaitala, E Ranta and J Lindstrom. 1997. Synchronous dynamics and rates of extinction in spatially structured populations. Proceedings of the Royal Society B: Biological Sciences 264: 481–486.

Hess G. 1996. Disease in metapopulations: implications for conservation. Ecology 77: 1617-1632.

Hilty J, W Lidicker, A Merenlender and AP Dobson. 2006. Corridor Ecology: The Science and Practice of Linking Landscapes for Biodiversity Conservation. Island Press, San Diego.

Hudson, P. J., A. P. Dobson, and D. Newborn. 1998. Prevention of population cycles by parasite removal. Science 282: 2256–2258.

Ims RA and H. Steen. 1990. Geographical synchrony in microtine population-cycles – a theoretical evaluation of the role of nomadic avian predators. Oikos 57: 381–387.

JansenVAA. 2001. The dynamics of two diffusively coupled predator–prey populations. Theoretical Population Biology 59: 119–131.

Jesse M, P Ezanno, S Davis, and JAP Heesterbeek. 2008. M. A fully coupled, mechanistic model for infectious disease dynamics in a metapopulation: movement and epidemic duration. Journal of Theoretical Biology 254: 331–338.

Jones KE, NG Patel, MA Levy, A Storeygard, D Balk, JL Gittleman and P Daszak. 2008. Global trends in emerging infectious diseases. Nature 451: 990–993.

Keeling MJ and CA Gilligan. 2000. Metapopulation dynamics of bubonic plague. Nature 407: 903-5.

Koelle K and J Vandermeer. 2005. Dispersal-induced desynchronization: from metapopulations to metacommunities. Ecology Letters 8: 167–175.

Lindborg R and O Eriksson. 2004. Historical Landscape Connectivity Affects Present Plant Species Diversity. Ecology 85:1840–1845.

Lourenço J and M Recker. 2013. Natural, Persistent Oscillations in a Spatial Multi-Strain Disease System with Application to Dengue. PLoS Computational Biology 9(10): e1003308. doi:10.1371/journal.pcbi.1003308

McCallum H and A Dobson. 2002. Disease, habitat fragmentation and conservation. Proc. R. Soc. Lond. Ser. B Biol. Sci. 269:2041–2049.

Ovaskainen O and I Hanski. 2003. How much does an individual habitat fragment contribute to metapopulation dynamics and persistence? Theoretical Population Biology 64: 481–495.

Pimm SL, HL Jones, and J Diamond. 1988. On the risk of extinction. The American Naturalist. 132:757-785.

Power AG, and CE Mitchell. 2004. Pathogen spillover in disease epidemics. The American Naturalist 164 Suppl 5:S79-89.

Rohani P, RM May and MP Hassell. 1996. Metapopulations and equilibrium stability: the effects of spatial structure. Journal of Theoretical Biology 181: 97–109.

Rosenblum, M. G., A. S. Pikovsky, and J. Kurths. 1996. Phase Synchronization of Chaotic Oscillators. Physical Review Letters 76:1804–1807.

Sandeep S, T Dutta, JE Maldonado, TC Wood, HS Panwar and J Seidensticker. 2013. Forest corridors maintain historical gene flow in a tiger metapopulation in the highlands of central India. Proceedings of the Royal Society B 280: 20131506

Sattenspiel L. 1987. Epidemics in nonrandomly mixing pop-ulations: a simulation. American Journal of Physical Anthropology 73:251-265.

Schindler DE, R Hilborn, B Chasco, CP Boatright, TP Quinn, LA Rogers and M. S. Webster. 2010. Population diversity and the portfolio effect in an exploited species. Nature 465: 609-612.

Schoener TW and DA Spiller. 1992. Is Extinction Rate Related to Temporal Variability in Population Size? An Empirical Answer for Orb Spiders. The American Naturalist 139(6): 1176-1207.

Secor DH, Kerr LA and SX Cadrin. 2009. Connectivity effects on productivity, stability, and persistence in a herring metapopulation model. ICES Journal of Marine Science 66: 1726-1732.

Sih A, BG Johnson and G Luikart. 2000. Habitat loss: ecological, evolutionary and genetic consequences. Trends in Ecology and Evolution 15: 132–134.

Skerratt LF, L Berger, R Speare, S Cashins, KR McDonald, AD Phillott, HB Hines and N Kenyon. 2007. Spread of chytridiomycosis has caused the rapid global decline and extinction of frogs. EcoHealth 4: 125-134.

Smith KF, DF Sax and KD Lafferty. 2006. Evidence for the role of infectious disease in species extinction and endangerment. Conservation Biology 20(5): 1349-1357.

Stuart LP and P Raven. 2000. Biodiversity: Extinction by numbers. Nature 403: 843-845.

Vasseur DA and JW Fox. 2009. Phase-locking and environmental fluctuations generate synchrony in a predator-prey community. Nature 460(7258):1007-10.

Vogwill T, A Fenton and MA Brockhurst. 2009. Dispersal and natural enemies interact to drive spatial synchrony and decrease stability in patchy populations. Ecology Letters 12(11):1194-200.

Wake DB and VT Vredenburg. 2008. Are we in the midst of the sixth mass extinction? A view from the world of amphibians. Proceedings of the National Academy of Science USA 105:11466–11473.

Wearing HJ, SM Sait, TC Cameron, and P Rohani. 2004. Stage-structured competition and the cyclic dynamics of host–parasitoid populations. Journal of Animal Ecology 73:706–722.

Williams ES, ET Thorne, MJ Appel, and DW Belitsky. 1988. Canine distemper in black-footed ferrets (*Mustela nigripes*) from Wyoming. Journal of Wildlife Diseases 24(3): 385–398.

Woodroffe R. 1999. Managing threats to wild mammals. Animal Conservation 2: 185-193.

Wright C. 2010. Spatiotemporal dynamics of prairie wetland networks: power-law scaling and implications for conservation planning. Ecology 91(7): 1924–1930.

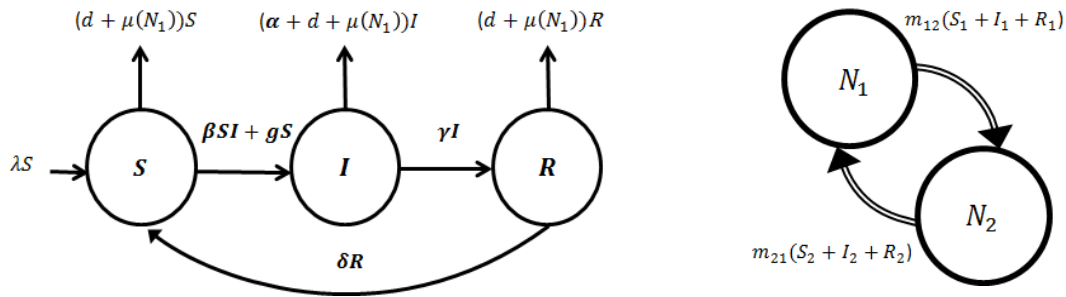**Figure 2.1** Left, demographic and disease (in bold) processes within a single population. Susceptible individuals may become infected from contact with members of the population, or from an external source at a rate of *g*. Right, metapopulation scheme with dispersal of individuals between populations from susceptible, infected and recovered classes. Here we assume that dispersal rates do not depend on disease status.

Table 2.1 Description of parameters used in simulations. Specific values were chosen to be on the same magnitude as those described in Jesse et al. (2008).

Parameters	Description	Value
λ	Birth rate	0.5
d	Death rate	0.1
K	Carrying capacity	50
β	Disease transmission rate between focal hosts	4
α	Disease-induced mortality	0.7
γ	Recovery rate	0.3
δ	Loss of immunity rate	0.3
g	External infection rate	0.0001-1.6384 in power of 2
m	Host dispersal rate	0-0.04 by increments of 0.001, 0.05-0.1, by 0.01, 0.11-0.29 by 0.02, 0.3-1 by 0.1, 1.1-4.9 by 0.2

Table 2.2 Possible events and their corresponding rates in the model. Only events at population 1 population are shown. Since populations are identical, events in population 2 would differ only in subscripts.

| Event	State change	Rate
A susceptible is born	$(S_1, I_1, R_1) \rightarrow (S_1 + 1, I_1, R_1)$	λS_1
A susceptible dies of natural mortality	$(S_1, I_1, R_1) \rightarrow (S_1 - 1, I_1, R_1)$	dS_1
A susceptible dies of competition	$(S_1, I_1, R_1) \rightarrow (S_1 - 1, I_1, R_1)$	$\mu(N_1)S_1$
A susceptible is infected	$(S_1, I_1, R_1) \rightarrow (S_1 - 1, I_1 + 1, R_1)$	$\beta S_1 I_1$
A susceptible is infected from an external source	$(S_1, I_1, R_1) \rightarrow (S_1 - 1, I_1 + 1, R_1)$	gS_1
A susceptible migrates to the patch	$(S_1, I_1, R_1) \rightarrow (S_1 + 1, I_1, R_1)$	$m_{21}S_2$
A susceptible migrates away	$(S_1, I_1, R_1) \rightarrow (S_1 - 1, I_1, R_1)$	$m_{12}S_1$
An infected dies of natural mortality	$(S_1, I_1, R_1) \rightarrow (S_1, I_1 - 1, R_1)$	dI_1
An infected dies of competition	$(S_1, I_1, R_1) \rightarrow (S_1, I_1 - 1, R_1)$	$\mu(N_1)I_1$
An infected dies of disease	$(S_1, I_1, R_1) \rightarrow (S_1, I_1 - 1, R_1)$	αI_1
A infected recovers	$(S_1, I_1, R_1) \rightarrow (S_1, I_1 - 1, R_1 + 1)$	γI_1
An infected migrates to the patch	$(S_1, I_1, R_1) \rightarrow (S_1, I_1 + 1, R_1)$	$m_{21}I_2$
An infected migrates away	$(S_1, I_1, R_1) \rightarrow (S_1, I_1 - 1, R_1)$	$m_{12}I_1$
A recovered dies of natural mortality	$(S_1, I_1, R_1) \rightarrow (S_1, I_1, R_1 - 1)$	dR_1
A recovered dies of competition	$(S_1, I_1, R_1) \rightarrow (S_1, I_1, R_1 - 1)$	$\mu(N_1)R_1$
A recovered loses immunity	$(S_1, I_1, R_1) \rightarrow (S_1 + 1, I_1, R_1 - 1)$	δR_1
A recovered migrates to the patch	$(S_1, I_1, R_1) \rightarrow (S_1, I_1, R_1 + 1)$	$m_{21}R_2$
A recovered migrates away	$(S_1, I_1, R_1) \rightarrow (S_1, I_1, R_1 - 1)$	$m_{12}R_1$
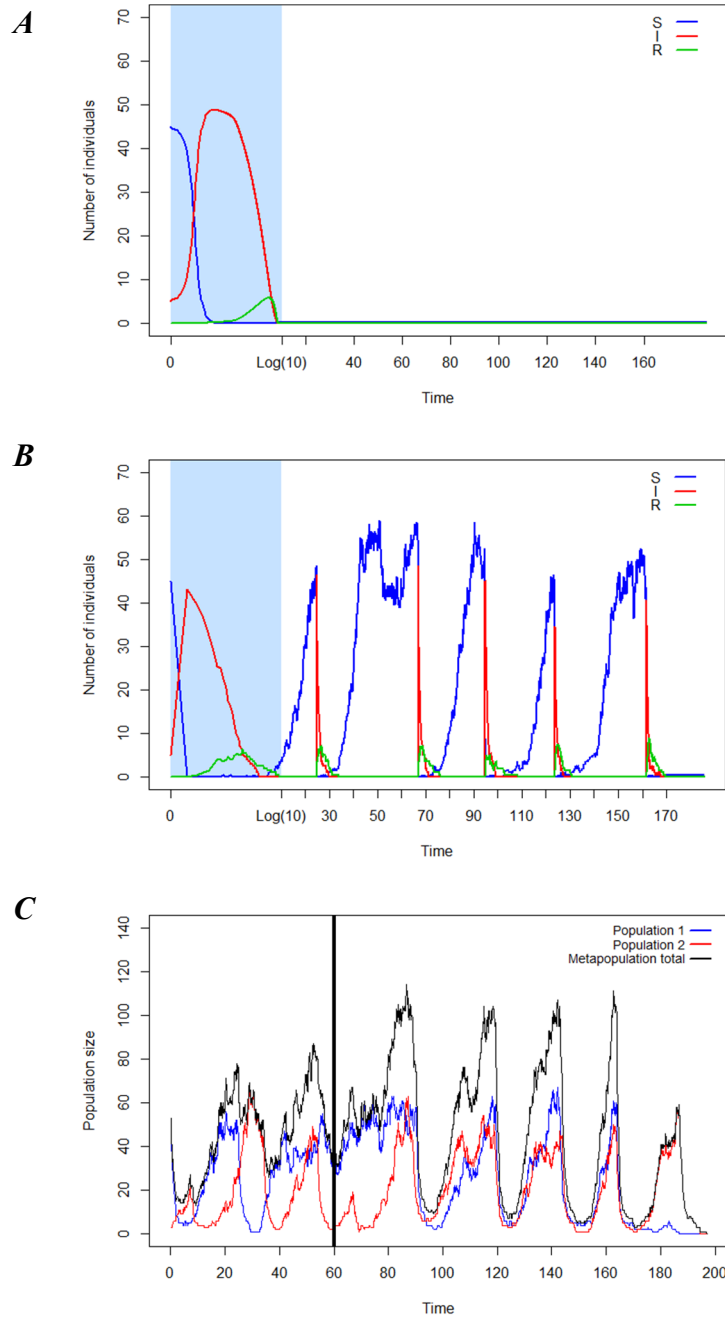
Figure 2.2 A) Deterministic trajectory ($g = 0.0004$), first 10 time steps plotted on log scale (shaded) to give more detail and enable comparison with stochastic dynamics. In the deterministic setting, the population quickly goes extinct. B) In a stochastic realization, the populations may exhibit cyclic dynamics. Extinction of the population and disease is also possible. C) two populations with no initial coupling. The metapopulation size is relatively stable as local populations fluctuate independently. Host dispersal ($m = 0.01$) is introduced at time 60 (vertical line). The system transitions to synchronized dynamics with larger fluctuations at the metapopulation level. Eventually, the metapopulation goes extinct.
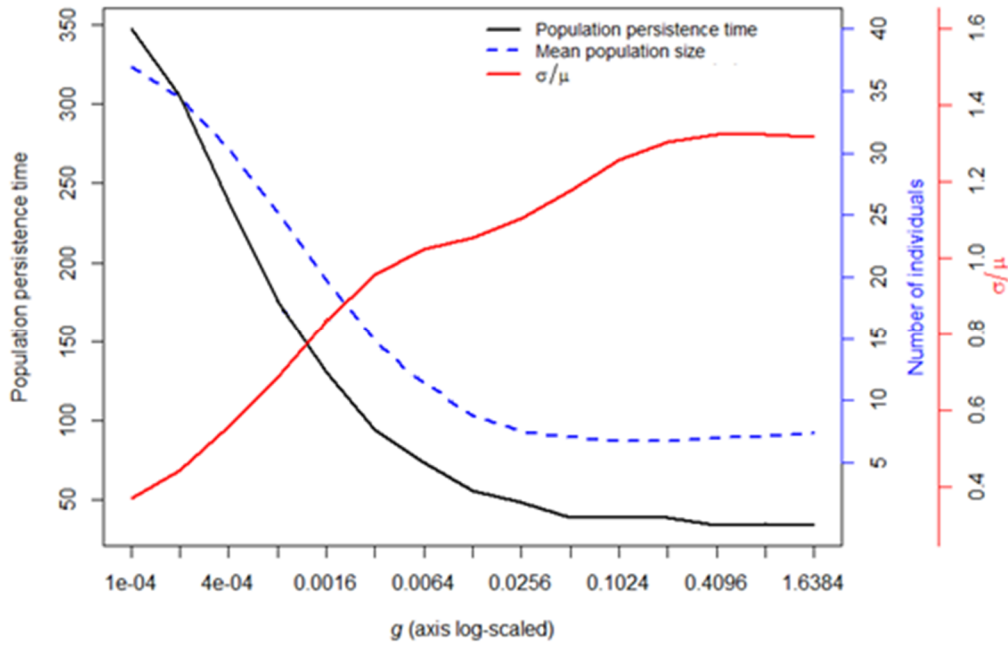
Figure 2.3 The effect of the per capita external rate of infection g on local dynamics. As g increases, population persistence time decreases monotonically. This is consistent with the decrease in the mean size of the local population. The metapopulation variance relative to the mean, as indicated by the quantity $\frac{\sigma}{\mu}$, increase monotonically with g and is inversely correlated with metapopulation persistence time.
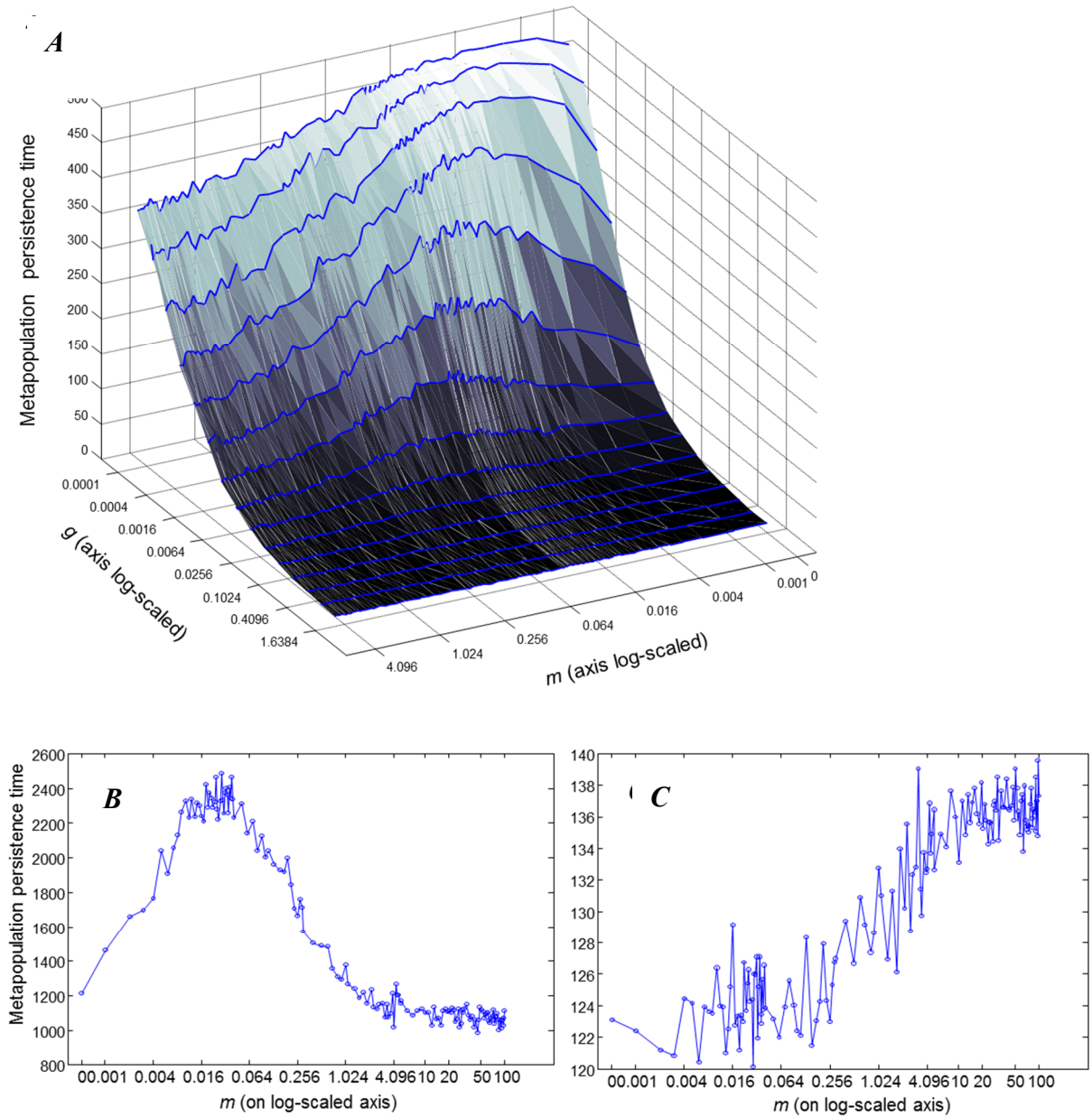
Figure 2.4 A. Metapopulation persistence time changes with host dispersal rate m and external infection rate g. Shading indicates the duration of metapopulation persistence; transition from light to dark shading indicates that persistence time decreases monotonically with increase in g, consistent with observations at the local level. For a fixed g at low to intermediate levels, the hump-shaped curve indicates that persistence is optimized at intermediate dispersal rates. B & C show the relationship of persistence time with extended ranges of dispersal rates ($m = 0\text{-}100$) for for B) $g = 0.0032$ and C) $g = 1.6384$. For g at low to intermediate levels, the pattern in B indicates that persistence optimization at intermediate levels of dispersal is true for a wide range of dispersal rates. While the pattern in C indicates that at high g, persistence increase monotonically with dispersal.
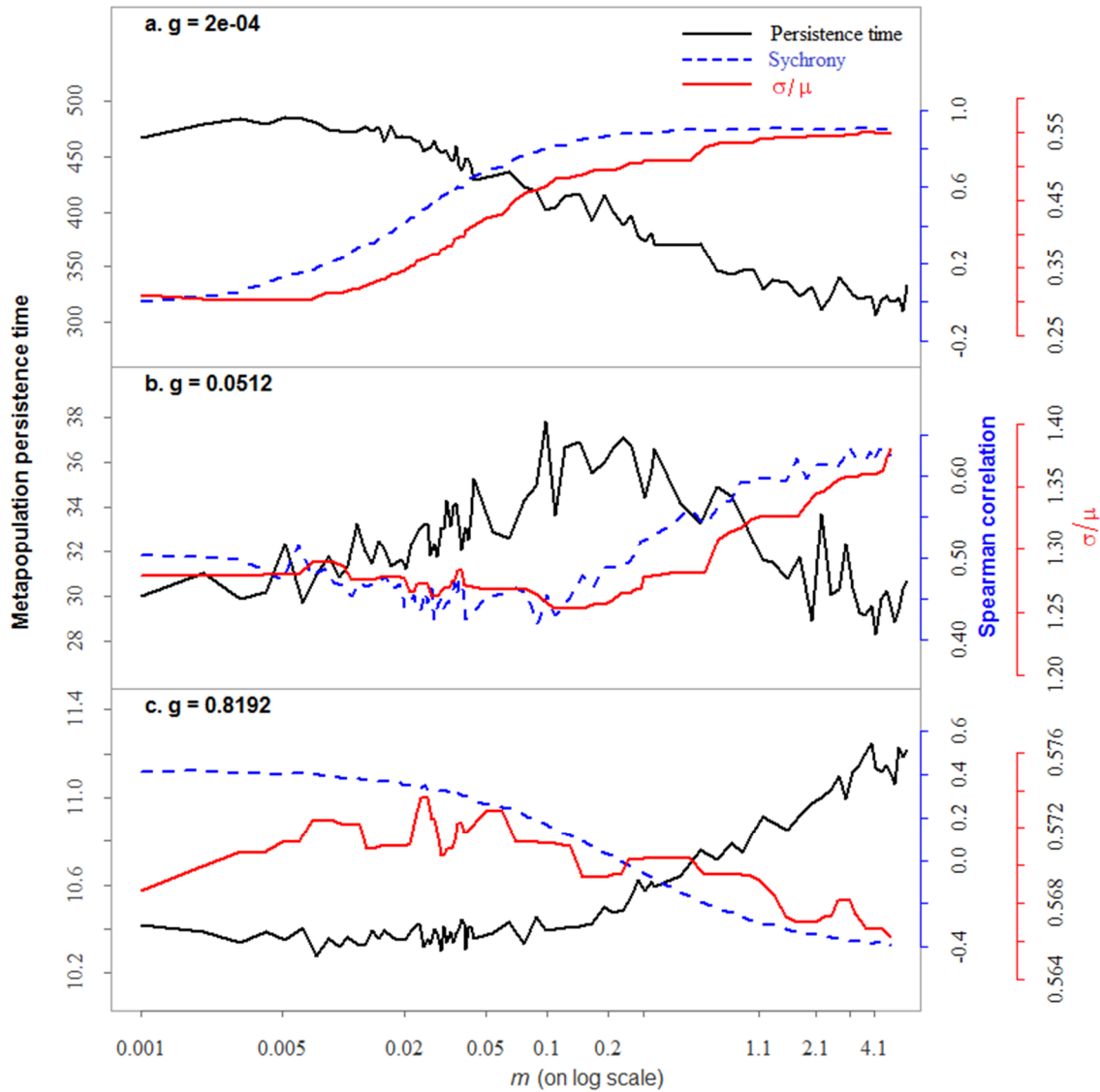
Figure 2.5 Relationship of synchrony, metapopulation persistence time, and the temporal coefficient of variation (σ/μ) at different rates of background infection. A) $g = 0.0002$, B) $g = 0.0512$, C) $g = 0.8192$. At different levels of g the synchrony exhibits different relationships with dispersal rate m. At low to intermediate rates of g, synchrony generally increases with dispersal, while at high g (infections are predominantly coming from outside of the focal host population) synchrony is negatively correlated with dispersal. σ/μ is positively associated with synchrony and negatively associated with metapopulation persistence time, indicating that synchrony increases metapopulation variance and extinction risks. This is consistent across all levels of external infection rates.

Chapter 3

Simulating the Spread of the Chytrid Fungus in an Amphibian Metapopulation and the Effect of Dispersal Distance Upper Limits Assumptions

Yang Xie, Nathan H. Schumaker, Allen Brookes, Roland A. Knapp, Cheryl J. Briggs, Karen L. Pope, Kathleen R. Matthews, Andrew R. Blaustein

Abstract

Emerging infectious diseases have been recognized as a major threat to global biodiversity. When habitat destruction and fragmentation remains the primary drivers of biodiversity loss, it is necessary to consider these two factors in concert. Metapopulation models are often employed as a conservation tool, and previous research has shed light on how they might be employed for disease management in a fragmented landscape. However, lack of dispersal information in these models limits their applicability. We simulate spread of the amphibian chytrid fungus in a set of spatially fragmented mountain yellow-legged frog populations under various assumptions of host dispersal potential. We find that disease forecasts are sensitive to the extremes of dispersal distribution and that disease arrival time decreases exponentially with linear increases in the upper limits of the dispersal distribution. Upon disease introduction, host populations rapidly incur local extinctions and metapopulation extinction risk increases with the upper limits of host dispersal. We suggest that the utility of the metapopulation paradigm may be limited as applied to this system, and that management should be targeted at improving local survival.

Introduction

Emerging infectious diseases (EIDs) are a potent driver of global biodiversity decline (Dazsak et al. 2000, Chivian and Berstein 2008, Vredenburg and Wake 2008). With conservation management efforts increasingly targeted at the landscape level and ongoing habitat fragmentation, a growing body of literature has emerged that examines disease dynamics within spatially segregated populations (Hess 1996, Gog et al. 2002, McCallum and Dobson 2002, Park 2012, Manica et al. 2013). These studies focus on the relationship between regional species persistence and host dispersal. The simulation models formulated in these studies may be applied towards preventative disease management in human and wildlife populations. For example, the analysis of SARS spread on the global airport network shows that models that take full account of the complexity of connectivity between populations can provide reliable forecast of disease spread (Colizza et al. 2006). Analogously, using radio-tracking data to model cane toad (*Rhinella marina*) invasions in Australia, Tingley et al. (2014) estimated that the toads could be excluded from 268,000 km^2 of their potential range by selectively removing artificial water bodies. Such models could be used to forecast disease spread into naïve populations and advise preventatively conservation measures such as immunization, evacuation and quarantine.

Amphibians as a taxon would stand to benefit from simulation models that allows forecast of epidemic spread in spatially-segregated habitats. Amphibians often exist in naturally or artificially fragmented habitats, and habitat destruction and fragmentation is a primary cause of amphibian declines (Cushman 2005). In the absence of disease, amphibian metapopulation dynamics is heavily dependent on individual dispersal among breeding sites (e.g. Marsh and Trenham 2001, Smith and Green 2005, Fortuna et al. 2006). EIDs, in particular the pathogenic

chytrid fungus *Batrachochytrium dendrobatidis* (chytrid), also act as an important threat to global amphibian population viability (Blaustein and Kiesecker 2002, Stuart et al. 2004, Cushman 2006, Skerratt et al. 2007). Chytrid is associated with the decline of more than 200 amphibian species and (McCallum 2007, Skerrat et al. 2007). More than 500 amphibians species have tested positive for chytrid globally (Olson et al. 2013), though pathogenesis is highly species and context dependent (Blaustein et al. 2005; Searle et al. 2011, Gervasi et al. 2013). Chytrid produces motile zoospores that infect hosts through environmental transmission and uses keratin in the amphibian dermis as substrate to produce more zoospores (Berger et al. 2005). A major driver of chytrid's emergence is its invasion as a novel pathogen into new geographic areas (Laurance et al. 1996, Berger et al. 1999, Daszak et al. 1999, Weldon et al. 2004). Chytrid is now present in all amphibian-occupied continents, but its distribution is far from uniform (Olson et al. 2013). This spatial heterogeneity is partially due to the rapid and continuing spread of chytrid into naïve regions (Olsen et al. 2013). Under these circumstances, metapopulation disease models could be used to forecast the spatial spread of chytrid in amphibian metapopulations and facilitate preventative conservation planning.

For application to specific conservation settings, simulation models will need to be species-focused and tend to be parameter rich. Species life history and interactions with landscape components need to be well-understood to allow full parameterization of these models. To model disease spread in a spatially segregated landscape, one essential piece of information is that of host dispersal patterns. In comparison to human systems where transportation networks are relatively well described, detailed dispersal information for wildlife populations is generally not readily available and of standardized quality (Driscoll et al. 2010, Wilson et al. 2011,

Edwards et al. 2010). Furthermore, dispersal-related literature is strongly biased in terms of numbers of studies towards mammals and birds (Holyoak et al. 2008, Clark and May 2002). Amphibians account for only 0.8% of dispersal-related studies (Driscoll et al. 2014), which may be because amphibian research in general tends to be focused at breeding ponds (Smith and Green 2005).

Predictions generated by simulation models can be heavily influenced by assumptions of dispersal (Naujokaitis-Lewis et al. 2009). Our assumptions about the upper limits of amphibian dispersal potential may be one aspect that influences the forecast of epidemic spread. Amphibians are often assumed to have limited dispersal (Duellman and Trueb 1986, Blaustein et al. 1994), but recent literature has indicated that such a generalization may be inappropriate for many species (Funk et al. 2005, Smith and Green 2006, Semlitsch 2008). The distributions of amphibian dispersal distances are highly skewed for many species: while most individuals move short distances, there is also a strong likelihood that some individuals will disperse long distances (Smith and Green 2005). Since vertebrate dispersal studies are typically associated with limited number of samples (Gamble et al. 2007), the upper limits of dispersal distances are less likely to be captured and described. In contrast, the lower limit of a dispersal distance distribution is naturally bounded by 0 and would be relatively unaffected. These stochastic long-distance dispersal events play an important role in influencing the forecast the spread of invasive species (Nichols 1989, With 2002, Tingley et al. 2013). Models that do not account for these long-distance dispersal events can severely underestimate the rate and extent of species invasions (Kot et al. 1996). Similarly, unaccounted for long-distance dispersal events may have disproportion impacts for forecasting disease spread in amphibian metapopulations.

We use the mountain yellow-legged frog (*Rana muscosa*/*Rana sierra*) and chytrid system to consider the sensitivity of disease spread forecasts to assumptions of the upper limits of host dispersal distance distributions. Yellow-legged frogs occupy high-elevation lakes in the Sierra Nevada of California, and it is assumed that populations within individual watersheds form metapopulations (USFWS 2003). Chytrid has been present in yellow-legged frog populations in the Sierra Nevada of California since 1970s and is thought to have induced major declines in the 1990s (Bradford 1991, Ouellet et al. 2005, Vredenburg et al. 2010). Recent work has documented its spread into river basins containing naïve frog populations (Vredenburg et al. 2010). As a result, mountain yellow-legged frogs have undergone precipitous decline (Vredenburg et al. 2010). Many study have explained how chytrid affects yellow-legged frogs individually and at the population level (Knapp and Morgan 2006, Wake and Vredenburg 2006, Briggs et al. 2010, Vredenburg et al. 2010), but metapopulation dynamics have received less attention. Vredenburg et al. (2010) suggests that the rate of chytrid spread is consistent with dispersal patterns of yellow-legged frogs. Due to the extreme environment in their high elevation habitat (long winters, sustained freezing), frogs are often only active for a few months during the summer after snowmelt and before the winter freeze (Matthews and Pope 1999, Vredenburg 2010). Frogs emerge from overwintering habitats, breed in deeper overwintering lakes, spread into other habitats during the summer, and retreat back to the overwintering habitats in the fall (Matthews and Pope 1999). While host life history and disease dynamics are well described, dispersal information of the mountain yellow-legged frogs remains relatively limited. Sample sizes of dispersal distances are low and indicate strong seasonality in movement

patterns (12, 9, and 3 frogs tagged in each month surveyed from August to October by Matthews and Pope 1999).

Given the importance of chytrid in these populations, we investigate how this lack of dispersal information may impact our capabilities for preventative disease management in this system. Here, we are specifically interested in how underestimating host dispersal potential would influence disease forecasts, and focus on the assumptions of the upper limits of dispersal distances. It should be noted that dispersal distance is but one aspect of dispersal behavior, which may be moderated by complex interactions between the abiotic and biotic environment, as well as physiological and behavioral states of the disperser (Bonte et al. 2012, Schick et al. 2008, Nathan et al. 2008). An individual's translocation on the landscape is the result of its probability of dispersal, dispersal distance, directionality, and perception of the surrounding environment quality, etc. (Driscoll et al. 2013). However, dispersal distance is often the easiest to define and quantify amongst these characteristics. Therefore, while dispersal distance is only one of the many characteristics that describe dispersal behavior, it is often the metric in which metapopulation models of amphibians are directly based on (e.g. Hels and Nachman 2001, Fortuna et al. 2006, Bauer et al. 2010, Griffith et al. 2010, Heard et al. 2011, Tingley et al. 2013). Dispersal rate between two habitats is often inferred as a function of the distance separating these habitats and the maximum or average dispersal distance of the focal species (e.g. Hels and Nachman 2001, Fortuna et al. 2006, Bauer et al. 2010, Griffith et al. 2010, Wright 2010, Heard et al. 2011, Tingley et al. 2013). Alternatively, dispersal rates may be inferred from distances between habitats alone (e.g. Conroy and Brooks 2003). Using HexSim, we build a

spatially explicit individual-based model framework to explore the sensitivity of metapopulation disease spread rates to changes in the upper limits of dispersal distances.

Methods

Spatial data

This study focuses on the chytrid spread dynamics at Barrett Lakes Basin in the Kings Canyon National Park located in the southern Sierra Nevada. The basin measures approximately 10.1 km^2 in area, and contains 42 populations in 56 water bodies. A map of ponds and streams in the basin was generated based on GIS shapefiles of the basin and discretized into a grid of 587,454 hexagons 10m in width (86.6m^2) for simulation using HexSim. From this initial map we created two input maps describing habitat quality and dispersal mortality rates. Yellow-legged frogs are highly aquatic, therefore we scored habitat quality for each hexagon based on vicinity to water bodies. Pond perimeters were initially assigned a relative habitat quality score of 20. We estimated the number of adults in each pond in 2004 (totally to 1780 adults), the year immediately prior to chytrid discovery in the basin (data provided by R. Knapp). If a pond has n adults, we randomly assigned n/5 hexagons from the pond perimeter as suitable overwintering habitat. This was based on an estimate of 1 frog per 2 meters of shoreline and the 10m hexagon width. Each overwintering hexagon may contain 5 adults as group members, and were given a relative habitat quality score of 30 (fig. 3.1). The number of overwintering hexagons restricts local carrying capacity in the simulation through overwintering survival (details in life history section). This process is repeated for each pond to create a map such that the number of adults in overwintering hexagons across all ponds equals to the total number of adults observed in 2004.

All other water body features (streams) received a relative habitat quality score of 10, and all other hexagons in the landscape (terrestrial habitat) received a relative habitat quality score of 0. The map was then smoothed to create a continuous gradient so that hexagons near the pond received increasingly higher scores. Hexagons with a score of 30 were ignored in the smoothing process, therefore their numbers and correspondingly the number of adults in each population remains unchanged. We also created a map for dispersal mortality by assigning a mortality rate of 0 to hexagons that represent streams or ponds, and a mortality rate of 0.0001 to features that were not streams or ponds to reflect the assumption that dispersers experience some low rate of dispersal mortality.

Model description

Our model replicates the amphibian life history and disease dynamics described in Briggs et al. (2010) within individual hexagons. This discretization of the landscape into hexagons introduces spatial heterogeneity in the distribution of zoospores and thus the encounter rate between hosts and zoospores in the landscape. In Briggs et al. (2010), zoospore encounter rates were a major factor determining whether populations were able to persist with chytrid or suffer eventual extinction. Lower encounter rates were found to allow a higher probability of host populations persisting with the disease at an endemic state, and culling to create lower host densities at the onset of the epidemic was suggested as a means to facilitate local persistence (Briggs et al. 2010). However, in the formulation of the Briggs et al. (2010) model, encounter rates are uncoupled to local host densities. In contrast, the zoospore encounter rates in our model emerge from the interaction between host densities and movement. The active period of frogs in the Briggs et al. (2010) model was 100 days. Similarly, our model repeats a yearly

cycle of a 90 day active period, since frog movement was observed to occur predominantly within a 3 month period (Matthews and Pope 1999). All life stages including tadpoles, juveniles, and adults are modeled. All parameters relating to host life history and chytrid disease dynamics are described in table 3.1. Movement parameters are described in table 3.2.

Life history. Reproduction occurs at day 20 of the active period, and all adults occupying an overwintering hexagon reproduce. In the Briggs et al. (2010) model, each adult has a 0.25 probability of reproduction, and those that do produce 100 tadpoles. Since the question of interest lies in disease spread and simulations were slow when modeling all tadpoles explicitly, we chose instead to use 1 "meta-tadpole" to represent 100 actual tadpoles. Each adult occupying a suitable habitat (an overwintering hexagon) produces 1 meta-tadpole. Meta-tadpoles spend two years in the ponds and experiences two winters, and they have a 70% chance of surviving each winter (Briggs et al. 2010). In the beginning of the meta-tadpole's 3rd year, it is replaced with 25 juveniles. Juvenile transition into the adult stage if they find an overwintering hexagon that contains less than 5 adults (i.e. under the carrying capacity). Those that fail to do so by the end of the year are removed from the simulation. Likewise, all adults that do not occupy an overwintering hexagon by the end of the year are removed. For adults within an overwintering hexagon, a mortality rate of 0.1 is imposed each winter (Briggs et al. 2010). Figure 3.2 shows a schematic representation of this life cycle.

Zoospore dynamics. Since pathogenesis of the chytrid fungus exhibits load-dependency, it is necessary to explicitly model zoospore load on the host and landscape (i.e. each hexagon) as well as their exchange. Our simulated zoospores experience mortality both on frogs and when in the environment, but they are only produced on frogs. Frogs shed and take up zoospores from

their local environment (the hexagons they reside in). Every day of the active period, each host loses 20% of its zoospores, and each sporangium on the host outputs 17.5 zoospores into the hexagon (Briggs et al. 2010). Zoospores are lost from the environment at a rate of 50% per day (Briggs et al. 2010). Recent evidence supports the hypothesis that chytrid may persist in the environment (Chestnut et al. 2014). Here, we assumed environmental persistence of zoospores by specifying that once a hexagon was infected, it would always contain a minimum of 10 zoospores. Subsequently, adults and juveniles take up 10% of environmental zoospores, while meta-tadpoles take up all zoospores in their hexagon (since they represent 100 tadpoles). Zoospore loads are cleared when tadpoles transitions to juveniles, since zoospore loads are typically lost during metamorphosis (Briggs et al. 2010). Transitions from juveniles to adults preserve zoospore loads. Disease-induced mortality is stratified by zoospore load. Meta-tadpoles do not experience zoospore-induced mortality as in tadpoles infection is restricted to the mouthparts only. Meta-tadpole zoospore load have an upper limit of 1,000,000, which is 100 times the highest upper limit for tadpoles (10,000 zoospores) in the Briggs et al. 2010 model (1 meta-tadpole represents 100 tadpoles). Juveniles die when zoospore loads reach 1000, while adults die when loads reach 10,000 (Vredenburg et al. 2010). Zoospores on both hosts and in hexagons incur an additional 50% mortality during each winter (Briggs et al. 2010). Figure 3.3 shows a schematic representation of zoospore dynamics in the environment and on the host.

Movement. Movement was not affected by disease status. Meta-tadpoles move 10m per day and are restricted to the perimeters of pond. Daily movement of adults and juveniles was based on data gathered by Matthews and Pope (1999) in the immediately neighboring Dusy Basin. Since no data exist on life-stage specific movement rates for this species and previous literature has

shown that dispersal is not stage-dependent for other species (Smith and Green 2006), we chose to parameterize juvenile and adult movement identically. Each tracked frog was observed over several sampling periods (Matthews and Pope 1999). We calculated average daily dispersal distances over each sampling period for each frog. A one-way random effects model found no significant variation in daily dispersal distances between sampled individuals in each month (p = 0.36 for sampled individuals as the random effect term). Therefore we combined observations from all frogs, treating each sampling period as an independent. We calculated the average daily dispersal distances for each month the frogs were active (August-October in Matthews and Pope 1999 data). We used a log-normal distribution to parameterize movement in HexSim, and adjusted the distribution means and variances so that the average daily dispersal distances from the model were approximately equal to those observed in the field (±10m, see table 3.2).

Simulation. We truncated the upper limit of dispersal distance distributions at 6-15 hexagons to create 10 scenarios, each replicated 100 times. Since the maximum observed daily distance is 66m, we define truncation at 6 hexagons as our "best estimate". Simulations were initialized with 2000 adults and for 7 years, at which time a single infected adult with a zoospore load of 1000 was introduced into the population where chytrid was first observed in 2005 at Barret Basin. Each simulation lasted 1350 time steps (15 years with a 90 day active period per year). We evaluate disease spread in terms of two parameters, the level of concordance between the order in which disease spreads through populations, and mean disease arrival times at each population (Gautreau et al. 2008). Disease arrival order is the sequence by which populations become infected. It is quantified by ordering populations by their disease arrival time, and estimating Kendall's τ-b for a pair of randomly chosen simulations. τ-b is scaled on [-1,1] with

1 indicating that disease spreads through the populations in exactly the same order and -1 vice versa. Disease arrival times are defined as the first day in which an infected individual appears in a population. We also compare simulated dynamics in scenarios with the "best estimates" for host movement to those observed in the field.

Results

Local and metapopulation disease dynamics

Upon introduction of disease, disease prevalence levels (the density of infected individuals) at infected sites rapidly increases towards 100% (fig. 3.4). This is consistent with field observations (Vredenburg et al. 2010). The 10% quantile of prevalence levels is almost identical to the mean prevalence levels, indicating that regardless of population identity or upper limits of the dispersal distance distribution, there is little variability in this trend of rapid prevalence increase. Local extinction in 2-3 years is the dominant trend for infected populations (fig. 3.4b). New metamorphs and adults alike quickly reach their respective zoospore threshold and succumb to infection. Subsequently, the population may persist due to the presence of the multi-year tadpole stage and by receiving immigrants from other populations (fig. 3.5 a&b). However, colonists and new metamorphs likewise quickly incur disease induced mortality. We observed the type of endemic dynamics described in Briggs et al. (2010) in which post-metamorphic individuals may persist while maintaining a sublethal zoospore level in some populations (fig. 3.5 c&d). These populations with rank in the lowest 10% in carrying capacity (number of overwintering hexagons per total population area) and consequently have the lowest density of frogs. It is likely that reduced contact rate is the mechanism for persistence here. Due to their low carrying capacities, often these population do not persist unless by immigration from

neighbors with higher carrying capacity. Once those neighboring populations succumb to disease, these low-densities populations tend to follow suit.

In the absence of disease, the majority of sites are occupied for both scenarios (fig. 3.6). When disease is introduced, the proportion of infected populations quickly increases and the proportion of occupied patches decreases. Sharp increases in both global prevalence and the proportion of infected patches coincide with the timing of metamorphosis, indicating the importance of the juvenile stage in disease spread. Since juvenile and adult movement parameterizations are identical, the sharp increase in the number of mobile individuals upon metamorphosis should account for these trends. In both cases, hosts may persist for many years after chytrid introduction at the landscape level. However, all populations that persist to the end of the simulation are uninfected, suggesting that metapopulation disease outcome is predominantly determined by whether disease was able to reach a population instead of variability in local dynamics.

Comparison of simulated and field disease spread patterns

We compared disease spread patterns in the field to those in the scenario with the "best estimate" for movement (daily dispersal distances truncated at 6 hexagons). We regressed the distance of infected populations to the location of initial disease introduction on disease arrival times at each population, and interpreted the coefficient of time as disease spread rate. The regression line was forced through the origin, and all data points from the simulations were used. The rate of disease spread is 11.10 m per day (1 s.e. = 0.38), adjusting for the 90 day yearly cycle in the simulation this value becomes 999.13 m per year. We used data from Barrett Lakes Basin from

2005-2008 to derive a field estimate for disease spread with the same method. It is estimated that chytrid spread at a rate of 758.14 m per year (1 s.e. = 64.31) within Barrett Basin.

The order in which disease arrives at each population is highly similar between replicate simulations as indicated by a τ-b of 0.83 (1 s.d. = 0.04) for 1,000 pairs of randomly chosen simulations. For comparisons with real data, it is necessary to adjust for how sampling was conducted in the field. For example, some populations were sampled on the same day of the month, creating multiple ties in disease spread order; or populations found infected in one month have not been sampled with other populations earlier on in the year, making it hard to determine whether these populations were infected later or simply sampled later. To account for this, we attributed tied ranks to populations infected within the same year for the empirical data. For the simulated data, we ranked only those populations that were represented in the field sampling and likewise gave tied ranks to populations infected in the same year. A τ-b of 0.73 (1 s.d. = 0.01) was estimated in comparing simulations with the empirical disease spread order.

Sensitivity to upper limits of dispersal distances

Varying the upper limits of dispersal distances has little effect on disease arrival order when disease is introduced in the same initial population (fig. 3.7a). We ran another set of simulations that introduces infected individuals at random locations. In this case, we found that if disease were introduced at different sites, the degree of similarity in subsequent spread through populations is substantially lower (fig. 3.7b). Therefore, the initial location of disease introduction almost completely determines disease arrival orders.

We constructed a multiple linear regression model to assess the relationship of log-transformed mean arrival times with the upper limits of host dispersal distances. Population ID was included in the model as a factor. In our analysis, we excluded arrival times at the initial location of disease introduction since it is always 1. It is estimated that mean arrival time of disease decreases exponentially with the upper limits of dispersal distances by a factor of -0.47 (1 s.e. = 0.029, fig. 3.8a). We compared this model to a more complex model containing interactions between dispersal upper limits and population ID. The Aikaike Information Criterion of the two models are 838.2 and 865.0, respectively. However, we chose the simpler model for ease of interpretation. In constructing separate regression models for each population, the mean coefficient for dispersal upper limits was -0.48, which is quantitatively similar to estimates from the simpler model. As a result, metapopulation extinction risks correspondingly increases rapidly with upper limits of dispersal distances (fig. 3.8b).

Discussion

We show that chytrid introduction not only has immediate effect on local population viability, but may have long term impacts on metapopulation viability. In the model, all remaining populations at the end of the simulation reside in spatial refuges uncontaminated by chytrid presence. Immigrants to previously infected sites quickly suffer disease-induced mortality due to environmentally persistent zoospores. This is consistent with field observation in which frogs reintroduced to sites that previously contained infected populations also quickly succumb to chytridiomycosis (Knapp, personal communication). Our simulations here show that even if we assume conservative estimations of the upper limits of yellow-legged frog dispersal distances, chytrid is able to rapidly spread through the landscape. Local extinctions are the dominant trend

and dispersers are unable to reestablish extirpated populations due to the zoospore persistence, thus accompanying disease spread with what is effectively habitat loss.

In the absence of disease, pond-breeding amphibians are subject to a high degree of local stochasticity in population size (Marsh 2008). Therefore, management focus typically emphasizes population viability at larger landscape scales, with dispersal as a key process to maintaining regional persistence (Fortuna et al. 2006, Marsh 2008). As a result, most conservation planning for the protection of amphibian species tend to be targeted at the metapopulation level (Marsh 2008). To facilitate dispersal between populations, restoring or enhancing habitat connectivity is often treated as a high priority for amphibian conservation (Funk et al. 2005). In the presence of chytrid, however, facilitated dispersal may exacerbate disease spread and increase regional extinction rates of amphibians. Therefore, for amphibian species that are stressed both by habitat fragmentation and chytrid introduction, there might be difficulty in reconciling conservation management measures. In addition, since sites that had once contained infected yellow-legged frog populations effectively become uninhabitable, the utility of the metapopulation paradigm becomes less obvious since colonization rates will not increases proportionally with host dispersal rates.

For amphibian populations where chytrid is a primary threat to local population viability, instead of framing conservation planning in the metapopulation paradigm, management effort might benefit from a more local perspective before scaling to the metapopulation level. For example, before chytrid arrival, predation of non-native trout on tadpole and juvenile stages were the predominant threat to yellow-legged frog population persistence (Knapp and Matthews 2000, Knapp et al. 2003, Vredenburg 2004). In the presence of trout, extirpated ponds were

unable to be recolonized; after trout removal, ponds were quickly recolonized without further intervention (Knapp et al. 2007). In this case, the benefits of local interventions were extended to the recovery of metapopulation structure by natural recolonization. It has been suggested in Briggs et al. (2010) that zoospore encounter rates drive the difference between populations that persist or decline to extinction, and culling to create lower local densities may allow populations to persist. In our simulations, populations with low densities are able to persist with some individuals carrying a sublethal zoospore load. However, we find that the densities of these populations are too low to be self-sustaining in the long run without recolonization from neighboring populations. Conversely, if these neighbors are able to self-sustain, their high host densities will typically result in local extinctions. This suggests that local densities may have to be extremely low to avoid rapid buildup of zoospore loads on individual hosts. An alternative means for management is to boost host resistance to chytrid infection by actively interfering with pathogenesis at the individual level. Microbial bioaugmentation can be effective for amphibians as an extension of the hosts' innate immune system (Harris et al. 2009, Vredenburg et al. 2011, Myers et al. 2012, Rollins-Smith & Woodhams 2012, reviewed in Bletz et al 2013). Both infection and mortality rate of amphibian hosts may be reduced by anti-fungal peptides secreted by skin microbes (Harris et al. 2009, Becker et al. 2011, Muletz et al. 2012). Furthermore, field bioaugmentation of an anti-Bd species, *Janthinobacterium lividum*, on Yellow-legged frogs reduced zoospore loads compared to untreated controls (Vredenburg et al. 2011). If this measure were to be successful and allow individuals to persist in the presence of an environmental source of chytrid, the benefits may extend beyond the local level since Yellow-legged frogs readily recolonize empty sites. Similarly, metapopulation structure of the

yellow-legged frogs might be restored by natural colonization if local populations are more resistant to extinctions by disease.

Ideally, though, preventative management should be informed by models forecasts of disease *a priori*. We show here that the utility of simulations models in forecasting the spread of the chytrid fungus depends on our assumptions of host dispersal potential and stochastic factors. The order in which disease spreads between populations is a function of host dispersal, landscape topology and the identity of the 'seed' population. That the initial location of disease introduction has considerable influence on subsequent spread has been shown for graph-type models of human transportation networks (Colizza et al. 2006, Gautreau et al 2007). We reach the same conclusions using a spatially explicit model in which movement on a continuous landscape does not conform to a pre-identified path. Superficially, the order of disease spread between populations seems highly predictable and varies little to assumptions of host dispersal potential. However, this predictability is contingent on information being available on the initial location of disease introduction. To pre-identify possible disease introduction sites, knowledge of potential vectors and their dispersal behaviors are necessary, but may not be easy to come by. In the well-studied yellow-legged frogs and chytrid system, there is little information on vectors of chytrid spread between watersheds. It has been speculated that birds and wind-carried insects may be involved in this inter-basin transmission (Vredenburg et al. 2010). If this were true, pre-identifying possible locations of initial disease introduction to any accuracy would require information on movement patterns of these vectors as well. An alternative means of preventative management is to increase surveillance effort in order to detect the presence of chytrid in the early stages of disease spread.

Disease arrival order is a low-resolution epidemic forecast metric since it does not give any information on the time frame of disease spread. Forecasts of specific arrival times, in contrast, are sensitive to assumptions of upper limits of dispersal distances. While our simulation model predicts a spread rate of chytrid qualitatively similarly to that observed in the field using the best movement estimates, it should be noted that our predicted rates are somewhat higher than the field estimate. Several reasons might account for this disparity. Overestimation of movement is a possible but unlikely cause. Compared to the field data, dispersal distances in the "best estimate" scenario are truncated at a lower value than the maximum in the field. Sampling differences may be driving the disparities in estimates of disease spread rates. For the simulated data, the disease status of all individuals may be determined for any time; therefore disease will be detected as soon as it arrives. The same cannot be accomplished in field sampling, which would lead to overestimation of infection dates in the field data, thus underestimating the actual disease spread rates. This is especially the case with the Barrett Basin, as populations were surveyed only once per summer.

Underestimating the upper limits of host dispersal could significantly underestimate disease arrival times, which could lead to delayed management action. For amphibian chytridiomycosis, the high transmission and mortality rate quickly drive populations extinct locally and untimely management could lead to dire consequences. Therefore, sufficient resources should be allocated on amphibian dispersal patterns at different spatial scales *a priori* in anticipation of chytrid introductions. In our model, although adult and juveniles share the same movement parameterization, juveniles emerge en masse upon metamorphosis and greatly increase the number of mobile individuals and long distance dispersal events. As a result, global prevalence

and proportion of infected patches rapidly surges during a short time frame. This would seem to indicate the importance of the juvenile stage in disease spread. Indeed, amphibian dispersal populations are predominantly connected through juvenile dispersal (Preisser et al. 2001, Guerry and Hunter 2002, Rothermel 2004). Dispersal distance distribution may exhibit apparent juvenile-bias due to juvenile being more abundant in numbers (Smith and Green 2006) and/or juveniles moving relative larger distances than adults (Preisser et al. 2001). Therefore, we emphasize the necessity of information on juvenile dispersal in particular. When host dispersal information becomes available, managers can reliably employ simulation models to forecast disease spread and test management options.

References

Banks SC, Peakall R. 2012. Genetic spatial autocorrelation can readily detect sex-biased dispersal. Molecular Ecology 21: 2092–2105.

Becker MH, Harris RN, Minbiole KPC, Schwantes CR, Rollins-Smith LA, Reinert LK, Brucker RM, Domangue RJ and Gratwicke B. 2011. Towards a better understanding of the use of probiotics for preventing chytridiomycosis in Panamanian golden frogs. EcoHealth 8: 501-506

Berger L, Speare R, Daszak P, Green DE, Cunningham AA and CL Goggin. 1998. Chytridiomycosis causes amphibian mortality associated with population declines in the rain forests of Australia and Central America. Proceedings of the National Academy of Sciences of the United States of America 95: 9031-9036.

Blaustein AR, Romansic JM, Scheessele EA, Han BA, Pessier AP and JE Longcore. 2005. Interspecific variation in susceptibility of frog tadpoles to the pathogenic fungus *Batrachochytrium dendrobatidis*. Conservation Biology 19:1460-1468.

Blaustein AR and JM Kiesecker. 2002. Complexity in conservation: lessons from the global decline of amphibian populations. Ecology Letters 5: 597-608.

Bletz MC, Loudon AH, Becker MH, Bell SC, Woodhams DC, Minbiole KPC and Harris RN. 2013. Mitigating amphibian chytridiomycosis with bioaugmentation: characteristics of effective probiotics and strategies for their selection and use. Ecology Letters 16(6): 807–820.

Bonte D, Van Dyck H, Bullock JM, Coulon A, Delgado M, et al. 2012. Costs of dispersal. Biological Reviews 87: 290–312.

Bowler DE and Benton TG. 2005. Causes and consequences of animal dispersal strategies: relating individual behaviour to spatial dynamics. Biological Reviews 80: 205–225.

Briggs CJ, Knapp RA and VT Vredenburg. 2010. Enzootic and epizootic dynamics of the chytrid fungal pathogen of amphibians. Proceedings of the national academy of science 107: 9695–9700.

Broquet T and Petit EJ. 2009. Molecular Estimation of Dispersal for Ecology and Population Genetics. Annual Review of Ecology, Evolution, and Systematics 40: 193–216.

Ceballos G, Vale MM, Bonacic C, Calvo-Alvarado J, List R, et al. 2009. Conservation Challenges for the Austral and Neotropical America Section. Conservation Biology 23: 811–817.

Chestnut T, Anderson C, Popa R, Blaustein AR, Voytek M, et al. 2014. Heterogeneous Occupancy and Density Estimates of the Pathogenic Fungus *Batrachochytrium dendrobatidis* in Waters of North America. PLoS ONE 9(9): e106790. doi:10.1371/journal.pone.0106790

Chivian E and A Bernstein (eds.) 2008. Sustaining life: How human health depends on biodiversity. Center for Health and the Global Environment. Oxford University Press, New York.

Clark JA and RM May. 2002. Taxonomic bias in conservation research. Science 297: 191–192.

Conroy SDS and BW Brook. 2003. Demographic sensitivity and persistence of the threatened white- and orange-bellied frogs of Western Australia. Population Ecology 45:105–114.

Cushman SA. 2006. Effects of habitat loss and fragmentation on amphibians: A review and prospectus. Biological Conservation 128: 231 – 240.

Daszak P, Cunningham AA and AD Hyatt. 2000. Emerging infectious diseases of wildlife: threats to biodiversity and human health. Science 287: 443-449

Daszak P, Berger L, Cunningham AA, Hyatt AD, Green E and R Speare. 1999. Emerging infectious diseases and amphibian population declines. Emerging Infectious Diseases 5: 735-748.

Driscoll DA, Lindenmayer DB, Bennett AF, Bode M, Bradstock RA, et al. 2010. Resolving conflicts in fire management using decision theory; assetprotection versus biodiversity conservation. Conservation Letters 3: 215–223.

Edwards HJ, Elliott IA, Pressey RL and PJ Mumby. 2010. Incorporating ontogenetic dispersal, ecological processes and conservation zoning into reserve design. Biological Conservation 143: 457–470.

Funk WC, Greene AE, Corn PS and FW Allendorf. 2005. High dispersal in a frog species suggests that it is vulnerable to habitat fragmentation. Biology Letters 1: 13–16.

Gamble LR, McGarigal K and BW Compton. 2007. Fidelity and dispersal in the pond-breeding amphibian, *Ambystoma opacum*: Implications for spatio-temporal population dynamics and conservation. Biological Conservation 139:247-257.

Griffiths RA. 2004. Great crested newts (*Triturus cristatus*) in Europe: effects of metapopulation structure and juvenile dispersal on population persistence. Pages 312–324 in H. R. Akçakaya, M. A. Burgman, O. Kindvall, C. C. Wood, P. Sjögren-Gulve, J. S. Hatfield, and M. A. McCarthy, editors. Species conservation and management: case studies. Oxford University Press, Oxford.

Gog J, Woodroffe R and J Swinton. 2002. Disease in endangered metapopulations: the importance of alternative hosts. Proceedings of the Royal Society B 269:671–676.

Guerry AD and ML Hunter Jr. 2002. Amphibian distributions in a landscape of forests and agriculture: an examination of landscape composition and configuration. Conservation Biology 16: 745–754.

Hadley AS and Betts MG. 2012. The effects of landscape fragmentation on pollination dynamics: absence of evidence not evidence of absence. Biological Reviews 87: 526–544.

Harris RN, Brucker RM, Walke JB, Becker MH, Schwantes CR, Flaherty DC, Lam BA, Woodhams DC, Briggs CJ, Vredenburg VT and KPC Minbiole. 2009. Skin

microbes on frogs prevent morbidity and mortality caused by a lethal skin fungus. The ISME Journal, 3, 818-824

Harris RN, Lauer A, Simon MA, Banning JL and RA Alford. 2009. Addition of antifungal skin bacteria to salamanders ameliorates the effects of chytridiomycosis. Diseases of Aquatic Organisms, 83, 11–16

Hatfield JS, Price AH, Diamond DD and CD True. 2004. Houston toad (*Bufo houstonensis*) in Bastrop County, Texas: the need for protecting multiple subpopulations. Pages 292–297 in H. R. Akçakaya, M. A. Burgman, O. Kindvall, C. C. Wood, P. Sjögren-Gulve, J. S. Hatfield, and M. A. McCarthy, editors. Species conservation and management: case studies. Oxford University Press, Oxford.

Hess G. 1996. Disease in metapopulations: implications for conservation. Ecology 77: 1617-1632.

Hels T and G Nachman. 2002. Simulating viability of a spadefoot toad *Pelobates fuscus* metapopulation in a landscape fragmented by a road. Ecography 25: 730–744.

Holyoak M, Casagrandi R, Nathan R, Revilla E and O Spiegel. 2008. Trends and missing parts in the study of movement ecology. Proceedings of the National Academy of Sciences of the United States of America 105: 19060–19065.

Jaquiery J, Broquet T, Hirzel AH, Yearsley J and N Perrin. 2011. Inferring landscape effects on dispersal from genetic distances: how far can we go? Molecular Ecology 20: 692–705.

Kingsford RT, Watson JEM, Lundquist CJ, Venter O, Hughes L, et al. 2009. Major conservation policy issues for biodiversity in Oceania. Conservation Biology 23: 834–840.

Knapp RA and KR Matthews. 2000. Non-native fish introductions and the decline of the mountain yellow-legged frog from within protected areas. Conservation Biology 14:428–438.

Knapp RA, Matthews KR, Preisler HK and R Jellison. 2003. Developing probabilistic models to predict amphibian site occupancy in a patchy landscape. Ecological Applications 13:1069–1082.

Knapp RA. 1996. Non-native trout in natural lakes of the Sierra Nevada: an analysis of their distribution and impacts on native aquatic biota. Pages 363-407 in Sierra Nevada Ecosystem Project: Final Report to Congress. Volume III: Assessments, Commissioned Reports, and Background Information. Davis: University of California, Centers for Water and Wildland Resources.

Knapp RA and KR Matthews. 2000. Non-native fish introductions and the decline of the mountain yellow-legged frog from within protected areas. Conservation Biology 14:428-438.

Knapp RA, DM Boiano and VT Vredenburg. 2007. Removal of nonnative fish results in population expansion of a declining amphibian (mountain yellow-legged frog, *Rana muscosa*). Biological Conservation 135:11-20.

Kot M, Lewis MA and P van den Driessche. 1996. Dispersal data and the spread of invading organisms. Ecology 77: 2027–2042.

Lacy RC, Miller PS, Nyhus PJ, Pollak JP, Raboy BE, et al. 2013. Metamodels for Transdisciplinary Analysis of Wildlife Population Dynamics. PLoS ONE 8(12): e84211. doi:10.1371/journal.pone.0084211

Lips KR. 1998. Decline of a tropical montane fauna. Conservation Biology 12: 106-117.

Matthews KR and Pope KL. 1999. A Telemetric Study of the Movement Patterns and Habitat Use of *Rana muscosa*, the Mountain Yellow-legged Frog, in a High-elevation Basin in Kings Canyon National Park, California. Journal of Herpetology 33(4): 615-624.

Morton SR, Hoegh-Guldberg O, Lindenmayer DB, Olson MH, Hughes L, et al. 2009 The big ecological questions inhibiting effective environmental management in Australia. Austral Ecology 34: 1–9.

Muletz CR, Myers JM, Domangue RJ, Herrick JB and RN Harris. 2012. Soil bioaugmentation with amphibian cutaneous bacteria protects amphibian hosts from infection by *Batrachochytrium dendrobatidis*. Biological Conservation, 152, 119–126

Nathan R, Getz WM, Revilla E, Holyoak M, Kadmon R, et al. 2008. A movement ecology paradigm for unifying organismal movement research. Proceedings of the National Academy of Sciences of the United States of America 105: 19052–19059.

Naujokaitis-Lewis IR, Curtis JMR, Arcese P, Rosenfeld J. 2009. Sensitivity Analyses of Spatial Population Viability Analysis Models for Species at Risk and Habitat Conservation Planning. Conservation Biology 23: 225–229.

Nichols RA. 1989. The fragmentation of tension zones in sparsely populated areas. The American Naturalist 134: 969–977.

Noss RF, Fleishman E, Dellasala DA, Fitzgerald JM, Gross MR, et al. 2009. Priorities for Improving the Scientific Foundation of Conservation Policy in North America. Conservation Biology 23: 825–833.

Ouellet M, Mikaelian I, Pauli BD, Rodrigues J and DM Green. 2005. Historical evidence of widespread chytrid infection in North American amphibian populations. Conservation Biology 19: 1431-1440.

Park AW. 2012. Infectious disease in animal metapopulations: the importance of environmental transmission. Ecology and Evolution 2(7): 1398–1407. doi: 10.1002/ece3.257

Preisser EL, Kefer JY and JD Lawrence. 2001. Vernal pool conservation in Connecticut: an assessment and recommendations. Environmental Management 26(5): 503–513.

Pullin AS, Baldi A, Can OE, Dieterich M, Kati V, et al. 2009. Conservation focus on Europe: major conservation policy issues that need to be informed by conservation science. Conservation Biology 23: 818–824.

Risk BB, de Valpine P, Beissinger SR. 2011. A robust-design formulation of the incidence function model of metapopulation dynamics applied to two species of rails. Ecology 92: 462–474.

Rothermel BB. 2004. Migratory success of juveniles: a potential constraint on connectivity for pond-breeding amphibians. Ecological Applications 14(5): 1535–1546.

Rustigian, HL, Santelmann MV and NH Schumaker. 2003. Assessing the potential impacts of alternative landscape designs on amphibian population dynamics. Landscape Ecology 18:65–81.

Schick RS, Loarie SR, Colchero F, Best BD, Boustany A, et al. 2008. Understanding movement data and movement processes: current and emerging directions. Ecology Letters 11: 1338–1350.

Skerratt LF, Berger L, Speare R, Cashins S, McDonald KR, Phillott AD, Hines HB and N Kenyon. 2007. Spread of chytridiomycosis has caused the rapid global decline and extinction of frogs. Ecohealth 4: 125-134.

Smith AM and DM Green. 2006. Sex, Isolation and Fidelity: Unbiased Long-Distance Dispersal in a Terrestrial Amphibian. Ecography 29: 649-658.

Smith AM and DM Green. 2005. Dispersal and the metapopulation paradigm in amphibian ecology and conservation: are all amphibian populations metapopulations? Ecography 28: 110/128.

Stuart SN, Chanson JS, Cox NA, Young BE, Rodrigues ASL, Fischman DL and RW Waller. 2004. Status and Trends of Amphibian Declines and Extinctions Worldwide. Science 306: 1783-1786.

Sutherland WJ, Adams WM, Aronson RB, Aveling R, Blackburn TM, et al. 2009. One Hundred Questions of Importance to the Conservation of Global Biological Diversity. Conservation Biology 23: 557–567.

Sutherland WJ, Armstrong-Brown S, Armsworth PR, Brereton T, Brickland J, et al. 2006. The identification of 100 ecological questions of high policy relevance in the UK. Journal of Applied Ecology 43: 617–627.

Tingley R, Phillips BL, Letnic M, Brown GP, Shine R, et al. 2013. Identifying optimal barriers to halt the invasion of cane toads *Rhinella marina* in arid Australia. Journal of Applied Ecology 50: 129–137.

U. S. Fish and Wildlife Service. 2003. Petition to list the Mountain yellow-legged frog: Finding of Warranted but Precluded. 68 FR 2283.

United States Fish and Wildlife Service. 2006. Designation of critical habitat for the southern California distinct population segment of the Mountain Yellow-Legged Frog (*Rana muscosa*). In: Federal Register 71(178):54344-54386. Washington D.C.: United States Fish and Wildlife Service.

Vredenburg VT. 2004. Reversing introduced species effects: Experimental removal of introduced fish leads to rapid recovery of a declining frog. Proceedings of the National Academy of Sciences USA 101:7646–7650.

Vredenburg VT, Knapp RA, Tunstall TS and CJ Briggs. 2010. Dynamics of an emerging disease drive large-scale amphibian population extinctions. Proceedings of the National Academy of Sciences 107: 9689-9694.

Wake DB and VT Vredenburg. 2008. Are we in the midst of the sixth mass extinction? A view from the world of amphibians. Proceedings of the National Academy of Science USA 105:11466–11473.

Wilson KA, Lulow M, Burger J, Fang Y-C, Andersen C, et al. 2011. Optimal restoration: accounting for space, time and uncertainty. Journal of Applied Ecology 48: 715–725.

With KA. 2002. The landscape ecology of invasive spread. Conservation Biology 16: 1192–1203.

Woodhams DC, Geiger CC, Reinert LK, Rollins-Smith LA, Lam B, Harris RN, Briggs CJ, Vredenburg VT and J Voyles. 2012. Treatment of amphibians infected with chytrid fungus: learning from failed treatments with itraconazole, antimicrobial peptides, bacteria, and heat therapy. Diseases of Aquatic Organisms 98: 11-25.
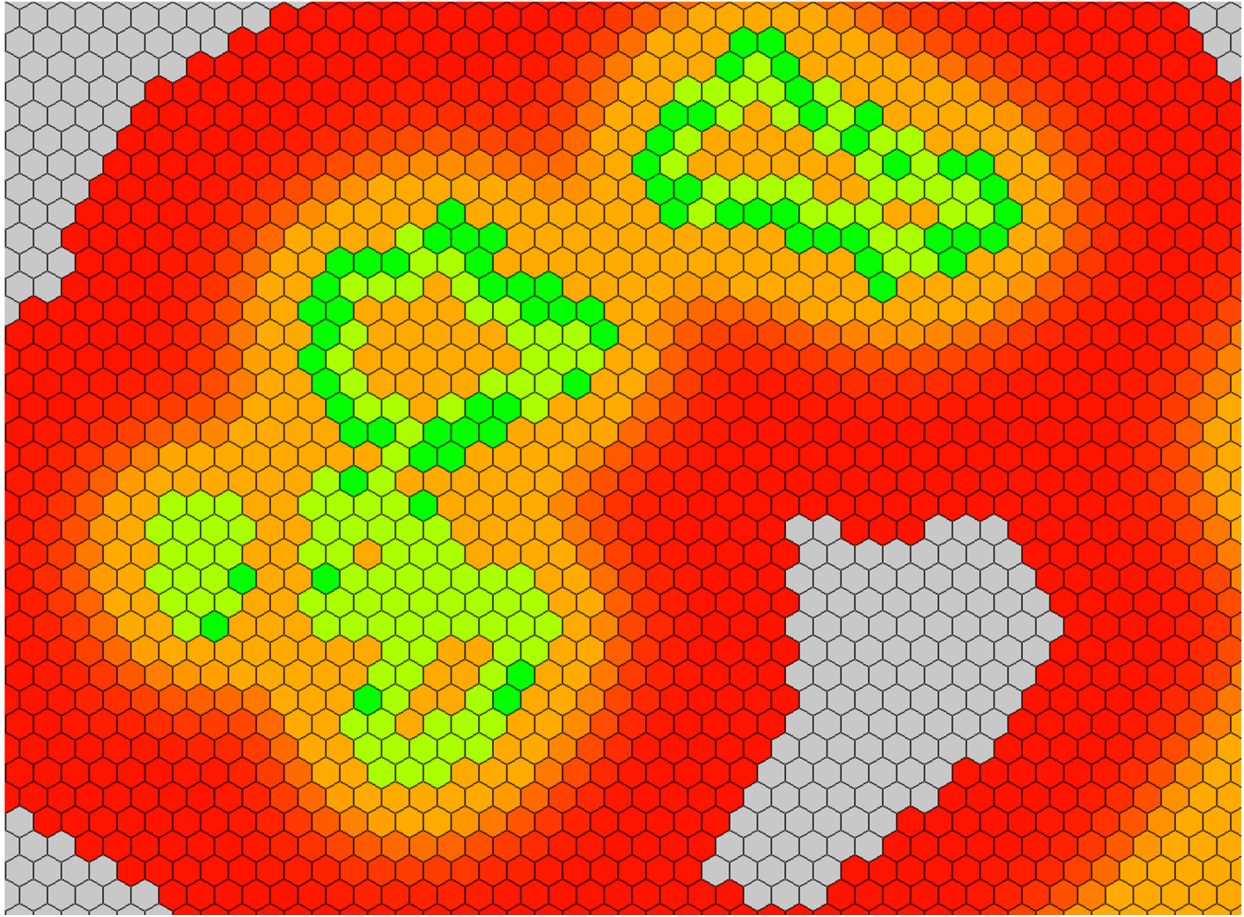
Figure 3.1 Representation of aquatic and terrestrial habitats within HexSim. Green/Yellow hexagons designate pond habitat. Green hexagons identified overwintering hexagons of relative habitat quality 30. Each overwintering hexagon may contain a maximum of 5 individuals. Adults occupying these hexagons at day 20 of each year in the simulation may reproduce. Juveniles occupying these hexagons are transitioned into adults. During winter, all adult and juvenile individual not occupying these hexagons are removed from the simulation to mimic overwintering mortality and observe carrying capacity of the ponds in the field data.

Table 3.1 Description of model parameters. With the aim of replicating the model described by Briggs et al. (2010), we used identical parameter values where possible for host life history and chytrid disease dynamics.

| Parameters	HexSim model	Briggs et al. (2010)
Length of active period	90 days	100 days
Adult reproduction probability	1 for those occupying an overwintering hexagon; 0 otherwise.	0.25
Birth rate	1 meta-tadpole per reproductive adult	100 tadpoles per reproductive adult
Juvenile production	1 meta-tadpole = 25 juveniles	1 tadpole = 1 juveniles
Overwintering mortality	adult 0.1; juveniles 1; meta-tadpoles 0.3	adult 0.1, juveniles 0.3; tadpoles 0.3
Production rate of zoospores from sporangium	17.5 zoospores day^{-1}	17.5 zoospores day^{-1}
Loss rate of sporangia on the host	0.2 day^{-1}	0.1-0.3 day^{-1}
Loss rate of sporangia in the environment	0.5 day^{-1}	1/60 - 1 day^{-1}
Environmental persistence	10 zoospores per hexagon	Poisson distribution with mean $\varepsilon_Z=1000$
Max number of sporangia an adult/juvenile can tolerate before death due to chytridiomycosis	adults 10,000; juveniles 1,000	adults 10,000; juveniles 1,000 – 10,000
Maximum number of sporangia that a tadpole can host	1,000,000 per meta-tadpole (1,000,000 = 10,000 x 100).	1,000 – 10,000 per tadpole.
Zoospore uptake rate	adult and juveniles 0.1 day^{-1}; meta-tadpoles 1 day^{-1}	
Zoospore winter mortality (host and environment)	0.5 per winter	0.5 per winter
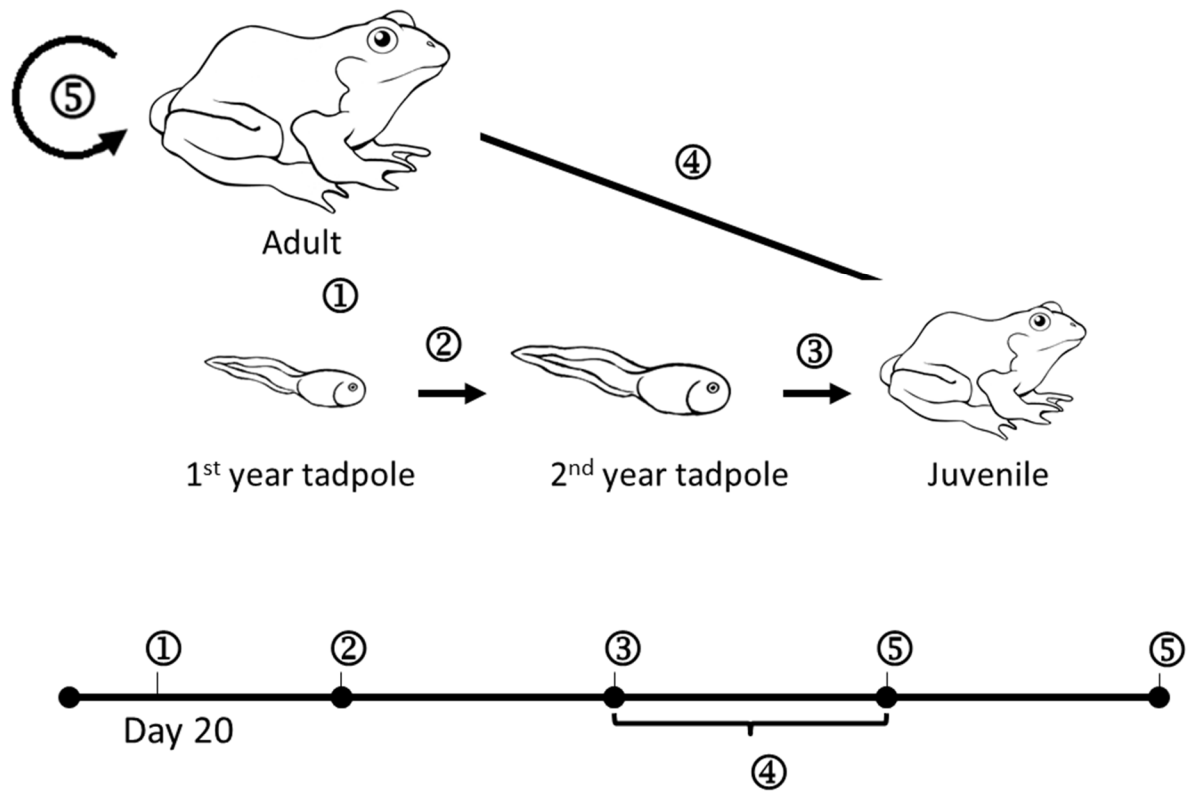
Figure 3.2 Life history of hosts as shown by the development of a tadpole from birth to reproductive adult status. Main events in the life history include:

① Each adult gives birth to a meta-tadpole.

② Meta-tadpole survives its 1st winter with 0.7 probability.

③ Meta-tadpole survives its 2nd winter with 0.7 probability. Each surviving 2nd year meta-tadpole metamorphoses into 25 juveniles at the beginning of the next year.

④ Juvenile move daily. Those that find occupancy in an overwintering hexagon by the end of the year may transition to adults.
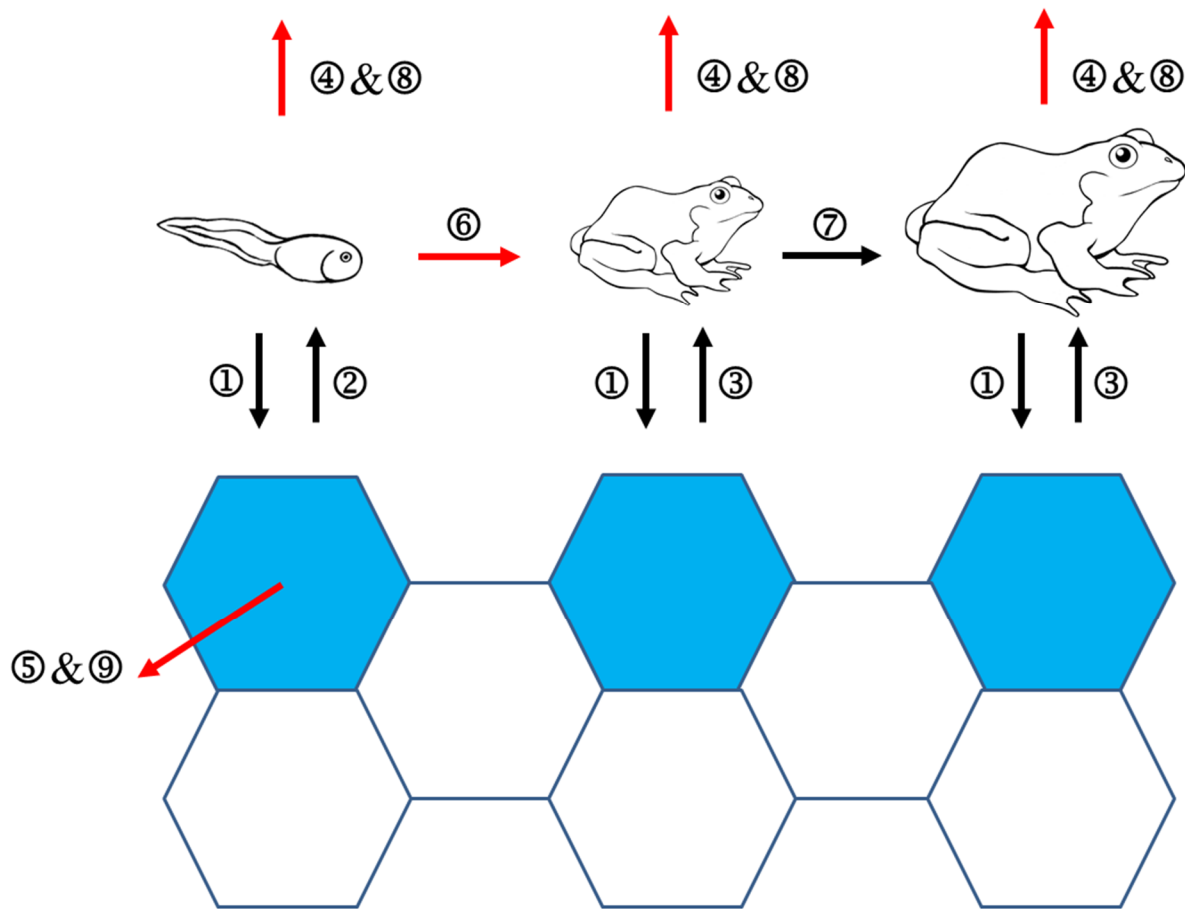
⑤ Adults survive winters with 0.9 probability.

Figure 3.3 Process of zoospore load change in hosts and in the environment. Processes by which zoospores are lost from the system are indicated in red. Processes describing change in zoospore numbers include:

① Each sporangia on the individual output 17.5 zoospores per day into the environment.
② Meta-tadpole takes up 100% of all environmental zoospores per day. Meta-tadpoles may carry as many as 1,000,000 zoospores.
③ Juveniles and adults take up 10% of environmental zoospores per day.
④ 20% of sporangia on each host is lost per day.
⑤ 50% of zoospores is lost from the environment per day.
⑥ Zoospore loads are cleared when transitioning from tadpole to juveniles.
⑦ Zoospore loads are retained when transitioning from juveniles to adults.
⑧ 50% of zoospore loads on the hosts are lost during winter.
⑨ 50% of zoospore loads in the environment is lost during winter.

Table 3.1 Comparison of observed field and simulation daily displacement distances (mean and one standard deviation in parenthesis). Movement in the simulation was parameterized with log-normal distributions. The distributions were truncated at an upper limit of 6 hexagons and run with 5000 individuals for the construction this table.

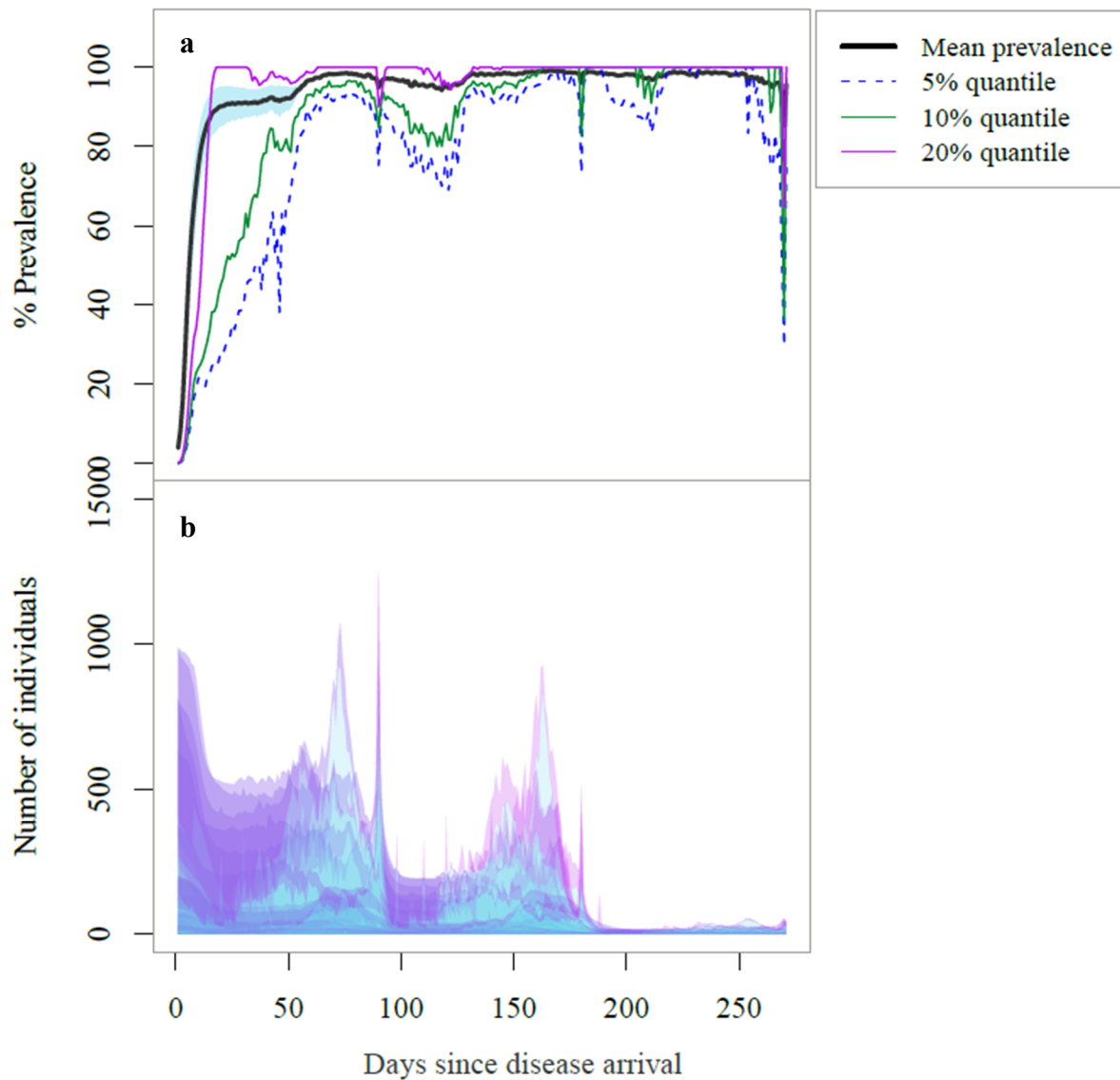| Month	Daily displacement distances (m)	
	Field	Model
August	20.61 (17.61)	27.15 (21.19)
September	26.82 (19.22)	35.78 (31.20)
October	7.35 (7.57)	16.01 (14.67)

Figure 3.4 (a) Trajectory of disease prevalence in a population upon arrival of the chytrid fungus (all populations from all scenarios are pooled together). Local prevalence increases quickly to 100% upon disease arrival. Quantile curves of prevalence indicate that this trend of rapid increase in prevalence varies little according to population identity. (b) Mean population size (in blue) plus one standard deviation (purple) for all population plotted together. Again, there is little variation in local trends upon disease arrival: population size quickly decreases and eventually the population decline to extinction.
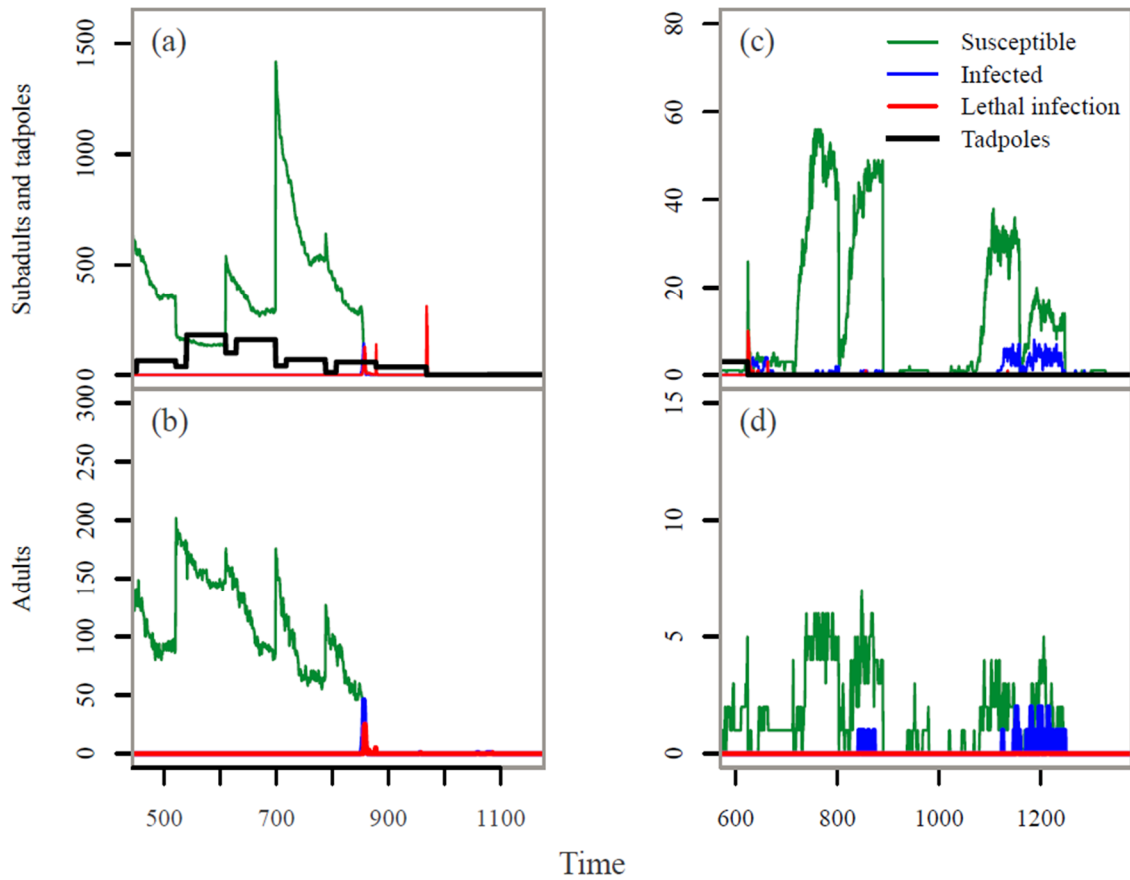
Figure 3.5 a&b: Change in adult and juvenile disease status upon disease arrival for an example population, in which the populations undergo rapid extinctions. Most populations exhibit these types of dynamics in which all individuals quickly become infected, accumulate lethal zoospores loads and succumb to infection. c&d: Persistent dynamics in which individuals may persist with sublethal loads of zoospores. Populations that exhibit these dynamics belong to the lowest 10% in carrying capacity (number of overwintering hexagons per population area). However, these populations undergo stochastic extinctions due to low number of individuals and the lack of colonists from nearby populations.
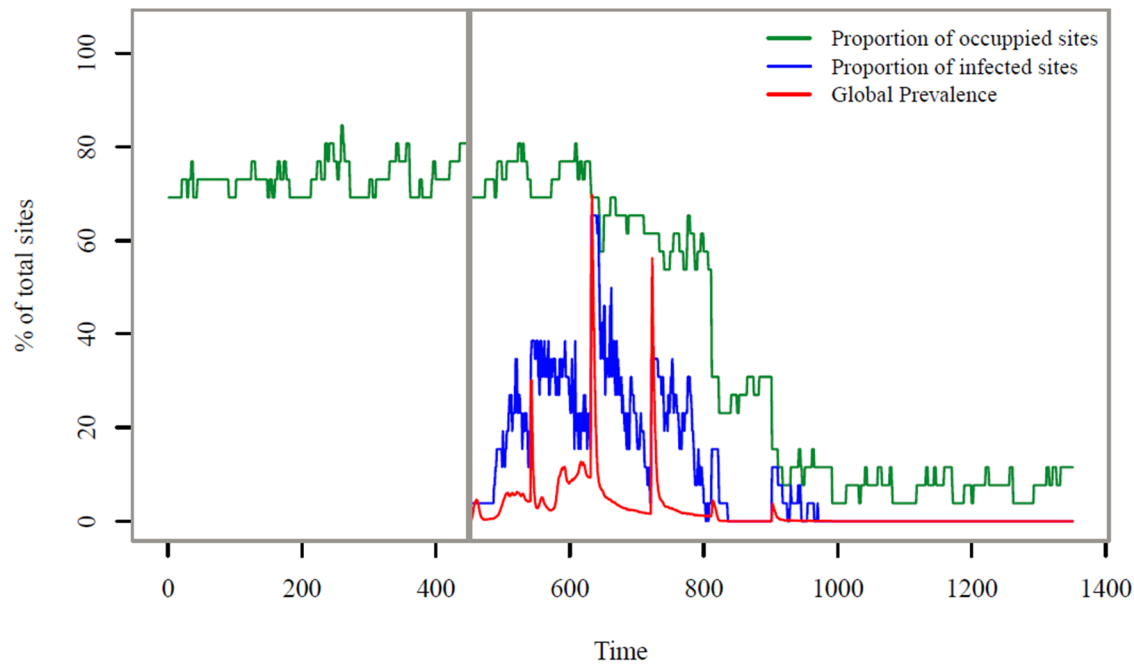
Figure 3.6 A sample trajectory of occupancy, proportion of infected populations and global prevalence from the scenario with the "best estimate" for yellow-legged frog movement. Proportion of occupied patches decreases quickly upon disease arrival. The proportion of infection populations spikes on the days that juveniles emerge onto terrestrial habitats. Juvenile emergence increases the number of mobile individuals and contributes substantially to the spread of disease. All population surviving to the end of the simulation are uninfected. Remaining individuals do not manage to colonize and reestablish populations at extirpated sites due to the environmental persistence of zoospores.
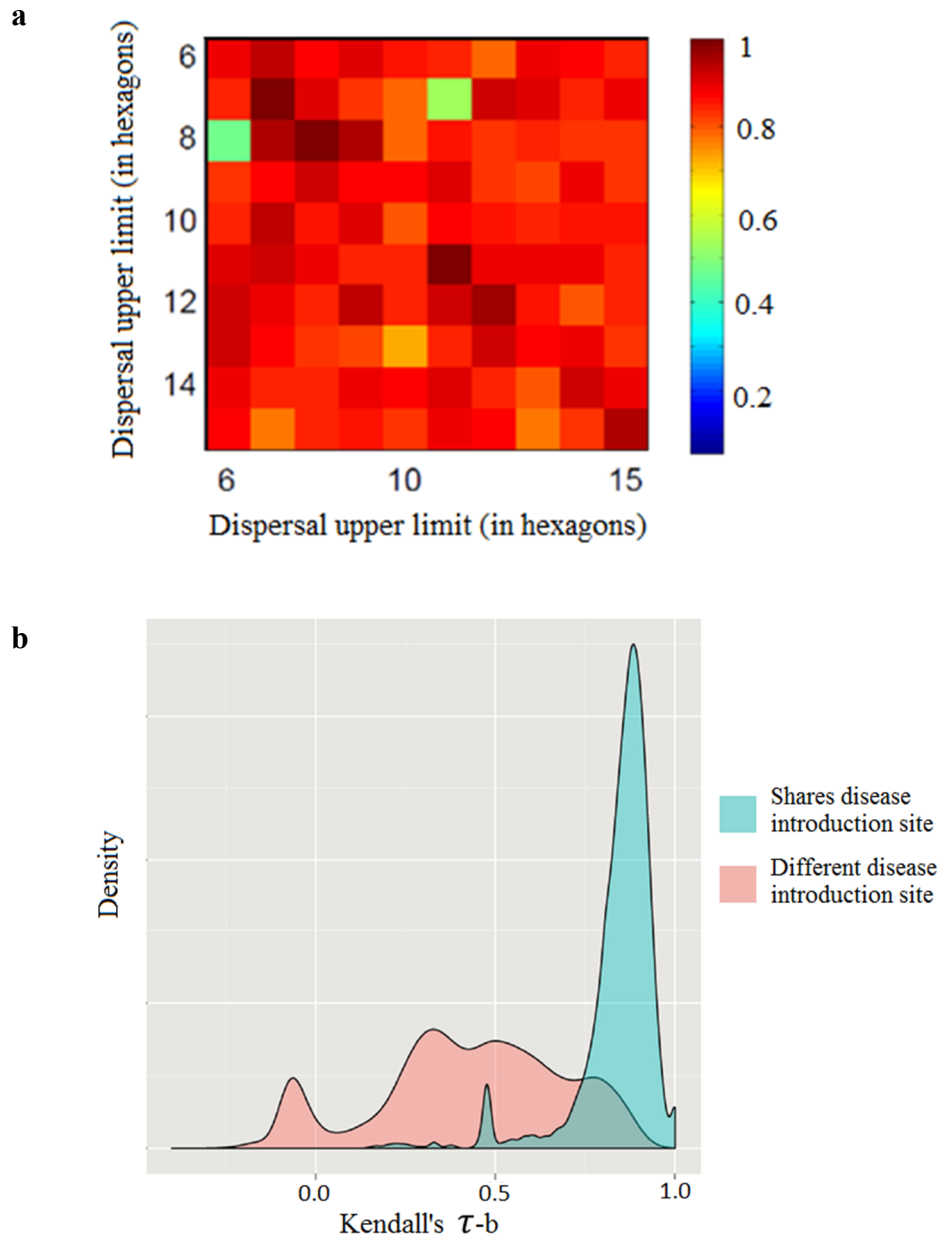
a

b

Figure 3.7 a. Similarity in chytrid arrival orders as indicated by Kendall's tau-b is high even between simulations with different dispersal upper limits (in hexagons), once controlling for the initial site of chytrid introduction. This indicates the assumptions about the dispersal upper limits have little effect on forecasting the sequence in which chytrid spreads through the populations. b. Disease arrival order subsequent to introductions at different sites substantially lowers the predictability of disease spread. These two observations coupled indicate that the initial site of chytrid introduction almost completely determines subsequent disease arrival order.
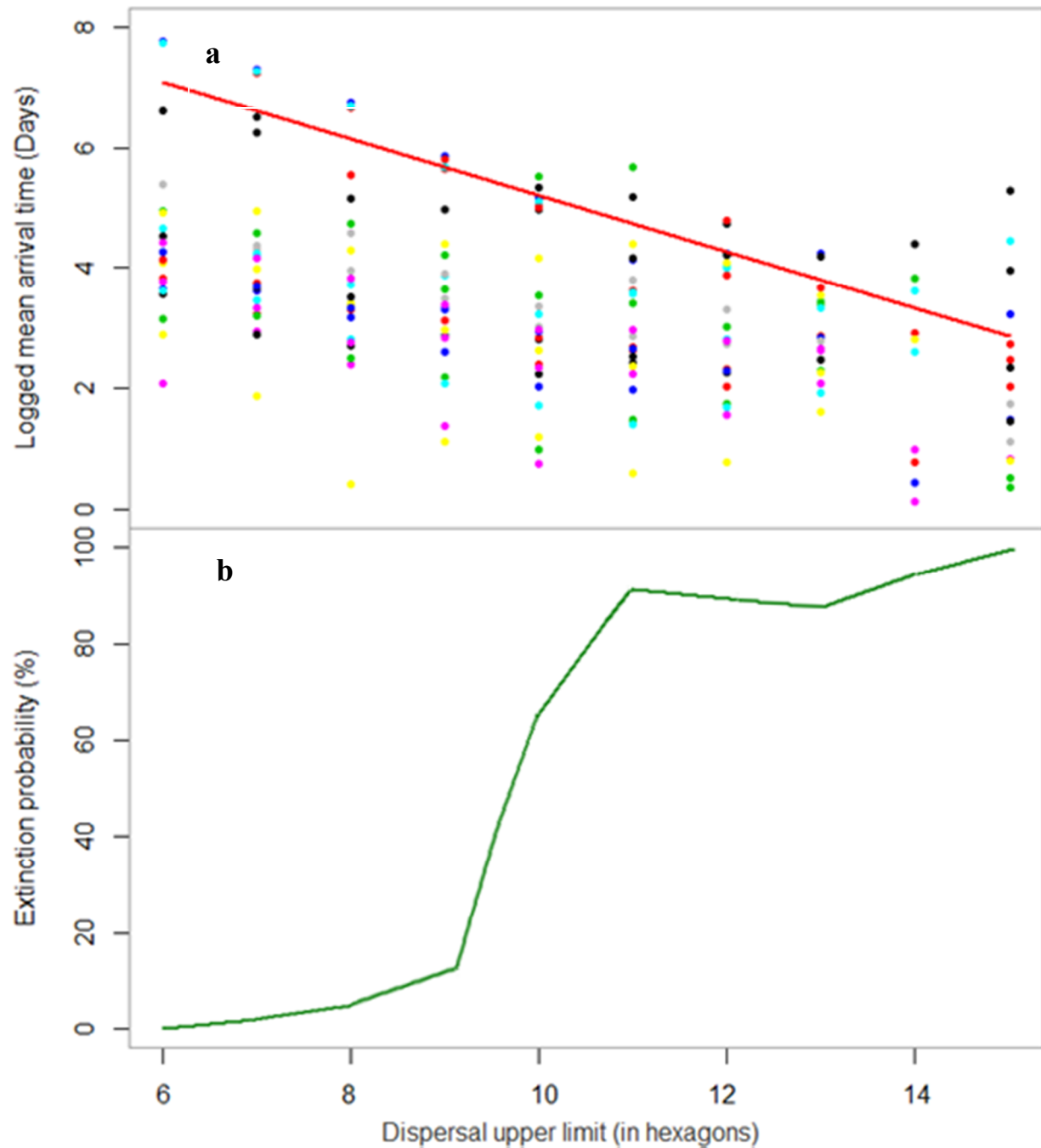
Figure 3.8 a. Logged mean disease arrival times decreases exponentially with a factor of -0.47 with increases in the dispersal distance upper limit (in hexagons). Logged mean disease arrival time of each population is shown in a different color. b. Metapopulation extinction rate increases with assumed dispersal distance upper limit.

Chapter 4

Projecting Global Amphibian Chytrid Fungus Distribution Based on IPCC Climate Futures

Yang Xie, Deanna Olson, Andrew R. Blaustein

Abstract

Climate change represents one of the greatest challenges to biodiversity conservation of this century. As a response to climatic change modifying environmental suitability, species from various taxa have experienced mortality events and range shifts. Pathogens are likewise limited by climate thresholds and therefore their emergence and equilibrium distribution are expected to be impacted by climate change. We consider how future climate change may influence the global distribution of the amphibian chytrid fungus, *Batrachochytrium dendrobatidis*. Previous research has shown the presence and prevalence of the chytrid fungus to be strongly dependent on climatic variables, in particular temperature metrics. We trained ensemble-learning algorithm based on the most comprehensive compilation of world chytrid sampling records to date (~5,000 site records) with various climatic variables as input features. The learning model was trained both with all the worldwide data combined (non-region specific), and trained separately for each region. Differences in these models indicate that the climate-chytrid relationship might differ between geographic regions. In general, using projected climate change scenarios to model the potential future distribution of the chytrid fungus, we predict that its range would shift into higher latitudes and altitudes. In particular, our model predicts a broad expansion of areas environmentally suitable for chytrid establishment on amphibian hosts in the temperate zones of the Northern Hemisphere.

Introduction

Climate change represents one of the greatest challenges to biodiversity conservation in its power to compromise the integrity and services of ecosystems worldwide. One area necessitating consideration is its influence on the emergence of infectious diseases in both wildlife and human populations (Daszak et al. 2000). During the last decades, several emergent infectious diseases (*e.g.*, AIDS, Ebola) have affected humans, domestic animals, and/or wildlife species (Daszak et al. 2000). As a general trend, the incidence of emerging infectious disease (EIDs) has increased due to a suite of anthropogenic factors that favor the propagation, dispersal and transmission of pathogens (Daszak et al 2000, Jones et al. 2008). Global climate change is considered an important driver behind these changes.

One of the most serious wildlife diseases impacting vertebrate biodiversity at this time is chytridiomycosis. This disease is caused by infection of amphibian hosts by the fungal pathogen *Batrachochytrium dendrobatidis* (hereafter chytrid) (described by Longcore et al. 1999). Overall, amphibians have displayed disproportionate declines relative to other taxa and are now threatened worldwide. Although there are multiple causes for amphibian declines, much research and conservation effort has focused on chytridiomycosis as an emerging infectious disease in amphibians. Chytrid has been implicated in many rapid and recent amphibian declines (Skerratt et al. 2007, Wake and Vredenburg 2008). In just the past 30 years, chytrid has caused catastrophic population declines or even extinctions (in many cases within a single year) of at least 200 species (Skerratt et al. 2007). Currently, chytrid is currently found in association with >500 amphibian species and on all continents where amphibians occur (Olson et al. 2013).

Given its apparent host non-specificity, many more amphibian species are likely to become suitable hosts when chytrid becomes present in their habitats (Murray et al. 2011). While chytrid is endemic to some parts of its range, a large part of present distribution is derived from its relatively recent introductions in many parts of the world (Lips et al. 2008, Rosenblum et al. 2013). However, it is hypothesized that its emergence has aspects of both spatial spread and climatic shift, the latter of which may induce change in host-pathogen interactions by decreasing host fitness or increasing pathogen virulence (Pounds et al. 2006, Alford et al. 2007).

Currently the spatial distribution of chytrid is highly heterogeneous due to its continuing spread into naïve regions (Olson et al. 2013). To inform preventative management and resource prioritization, correlative species distribution models (SDMs) have been used to characterize environmental suitability (ES) and the potential range for chytrid (Gascon et al. 2007, Murray et al. 2011). In general, SDMs are only appropriate where the range of the target species is expected to be mainly regulated by environmental variables (e.g. climate, biome, habitat type) (Murray et al. 2011). For many pathogens, this may be inappropriate if internal environments within hosts are highly regulated and the pathogen lifecycle is insulated from external environmental conditions, which is especially true for internal, directly transmitted pathogens of endothermic hosts (Murray et al. 2011). For chytrid, amphibian hosts are ectothermic and there is an environmental zoospore stage for transmission (Johnson and Speare 2003, Berger et al. 2004, Piotrowski et al. 2004). As a result, chytrid is directly subject to the effects of environmental variables, in particular temperature and moisture (Johnson and Speare 2003, Piotrowski et al. 2004, Woodhams et al. 2008, Murray et al. 2011). Indeed, recent field research has revealed that chytrid occupancy in the environment does not depend on the presence of

amphibian hosts in the same locale (Chestnut et al. 2014). Therefore, SDMs may be an appropriate and valuable tool to evaluate ES for chytrid and allow managers to identify areas suitable to the establishment of chytrid (Murray et al. 2011). Nevertheless, it should be noted that as long as sampling of chytrid is predominantly conducted by swabbing amphibian hosts, the resultant data should in the strict sense be interpreted as chytrid presence or absence on amphibians at a site. Thus, while it might be tempting to interpreting SDM outputs directly as chytrid occurrence probability or ES, the sampling process dictates that these outputs should really be treated as occurrence probability of chytrid on amphibians at a site.

The sensitivity of the growth and development of chytrid to climatic variables, in particular temperature and moisture regimes, has been demonstrated repeatedly in laboratory and experimental settings. Field observations of seasonal and altitudinal differences in chytrid outbreak patterns has long suggested the climatic dependency of chytrid (Woodhams et al. 2005, Pounds et al. 2006, Kriger and Hero 2007, Berger et al. 2008, Conradie et al 2011). These observations have been repeatedly supported by laboratory experiments both *in vitro* and *in vivo* (Johnson and Speare 2003, Piotrowski et al. 2004, Woodhams et al. 2008). Indeed, previous SDMs have also shown that both chytridiomycosis and chytrid distribution is strongly associated with climatic variables (Ron 2005, Pounds et al. 2006, Bosch et al. 2007, Laurance 2008, Murray et al. 2010, Walker et al. 2010, Rödder 2010, Olson et al. 2013).

Given this climate-dependency, it is beneficial to consider the influence of climate change when mapping environmental suitability for chytrid during long-term management planning. Climatic change may alter environmental suitability for chytrid and ultimately affect the potential range it may expand into. In culture, chytrid exhibits optimal growth between 17 and 25 °C and may be

killed when incubated at 30 °C and higher (Piotrowski et al. 2004, Woodhams et al. 2008).
However, although naturally warm conditions may inhibit disease (Woodhams et al. 2003,
Berger et al. 2008), the fungus appears to maintain pathogenicity over a broad range of lower
temperatures. Accordingly, previous SDM's predict an extensive range of suitable pathogen
habitat (Ron 2005, Laurance et al. 2008, Lötters et al. 2009, Puschendorf et al. 2009, Rödder et
al. 2009). As a result, it was suggested that the emergence of chytrid may be curbed by a
general warming trend of the climate (Harvell et al. 2002) and a previous SDM indeed suggests
that anthropogenic climate change may reduce the geographic range of chytrid (Rödder 2009).

Nonetheless, this prediction is inconsistent with some field observations (Vensky et al. 2013).
Initially, climate change was thought to be promoting chytrid emergence based on observation
of Harlequin frogs declining in sync with temperature increases in high-elevation regions of
Central America (Pounds et al. 2006). At these high altitudes, increasing cloud cover may be
modulating daily minimum and daily maximum temperatures to converge around a ''chytrid
thermal optimum'' (Pounds et al. 2006). This hypothesis is consistent with the laboratory
observation and that fluctuating temperatures retards chytrid growth (Woodhams et al. 2003).
Furthermore, chytrid outbreaks in the Neotropics were found to be more common following
high temperature years (Rohr and Raffel 2010), suggesting that climate change and the
associated increased temperatures might actually promote chytrid emergence (Venesky et al.
2013). These apparently contradictory results describing the chytrid-climate relationship may
arise from complex interactions of climatic variables in the field and highlight the uncertainties
in how environmental suitability to chytrid and its potential distribution might be affected by
climate change. In this paper, we formulate a predictive model based on high-resolution gridded

climate datasets with the most current and extensive global chytrid detection dataset and attempt to project future chytrid distributions under projected climate change scenarios. We construct SDMs for chytrid using random forest models, which is one of the most accurate learning algorithms (Li and Wang 2013). Random forest is ideal for datasets with many explanatory variables and complex higher order interaction, and has been consistently shown to yield high prediction performance in comparison to other methods (Breiman 2001, Pearson et al. 2006, Cutler et al. 2007, Iverson et al. 2008, Kampichler et al. 2010, Li and Wang 2013).

Methods

Chytrid occurrence data. Chytrid presence/absence data were downloaded from spatialepidemiology.net (compiled from published literature and unpublished studies). All of the available entries in the database (up to October 2014) were used. This consisted of 5166 observations at sites with specific coordinate information. In possessing the data, we found duplicated observations taken at sites with the same coordinates. In total, duplicated observations were taken at 129 sites. These duplicated observations were often inconsistent in recording chytrid presence; therefore we scored a site as chytrid-positive as long as one observation out of all the duplicates at that site showed chytrid presence. All other duplicates were removed in subsequent analysis. Since our explanatory variables data were extracted from a grid with a resolution of 0.5 degrees latitude and longitude, 56 sites had the same explanatory information since they were clustered within the same boxes on the grid, essentially duplicating each other. We averaged the coordinates for these sites and similarly attributed the site as chytrid-positive as long as one record demonstrated chytrid presence. We believe that these procedures have the effects of clarifying the relationship between response and explanatory

variables by removing inconsistent classification at the same sites and also reduce clustering. A final number of 4967 sites entered into the analysis (fig. 4.1). It should be noted that samples taken at these sites may be from animals with various representations of chytrid infection, i.e. they could be symptomatic or not.

Model formulation. We examined the associations between chytrid occurrence at a site with both climatic and ecological variables. Here, we focus on climatic variables and included 13 temperature and precipitation metrics (table 4.1), which have been shown to perform well in previous chytrid environmental suitability analysis (Ron 2005, Lötters et al. 2009, Puschendorf et al. 2009, Rödder et al. 2009, Murray et al. 2011). Additionally, we include elevation, biome and amphibian species richness at the site in the initial model since they have been shown to correlation with chytrid occurrence (Olson et al. 2013). Climate variables were extracted per coordinate from grids with a resolution of 0.5 degrees latitude and longitude available from the Climatic Research Unit at University of East Anglia (Norwich, UK; www.cru.uea.ac.uk) for the years 2000-2010 and averaged over the period. While samples at a site may be gathered outside of this time span, we believe that these averaged climate metrics would be able to represent "typical" climate at a site and reflect the immediate climate impacts on chytrid occurrence. The correlative nature of SDMs is highlighted here: if a site was sampled prior to 2000-2010, we cannot make the inference there is a causal link between chytrid occurrence at that site and the climate during 2000-2010. While climate conditions might still be helpful in predicting chytrid occurrence on the basis of correlations alone, caution must be exercised in using performance of these SDMs as evidence supporting the causal link between climate and chytrid occurrence at a

site. It is possible that chytrid occurrence may in fact be determined by some unmeasured variables highly correlated by climate.

Binary observations (chytrid presence/absence) were positively spatially correlated (fig. 4.2a). We fitted a full model using all variables using both a logistic regression model and a general additive logistic regression model with a smoothed interaction term between longitude and latitude of the observations to see if model variables are capable of accounting for the spatial autocorrelation. However, residuals from both models remain spatially correlated. As a result, we opted for a nonparametric random forest classifier model instead to allow for implicit modeling of complex non-linear interactions. A random forest is an ensemble of random decision tree classifiers that makes predictions by averaging the predictions of the individual trees. Versions of the procedure differ in how randomness is introduced in the tree building process. Here we implement the procedure through sci-kit learn in the Python environment (Pedregosa et al. 2011), in which bootstrap samples of the original training data is used to train individual decision trees. A decision tree learner is constructed recursively. At each step of the construction of the tree, a random set of variables are selected with equal probability from the suite of training variables. The learner then estimates how to optimally split the training examples based on these selected variables so as to minimize the number of misclassified training points. The procedure is repeated until every cell is pure or if some minimum number of observations for each node is reached.

Here, we trained two sets of random forest mode. First, we trained a forest on all the available data as latitude is the most important control of climate and samples are well-distributed along the latitudinal gradient. Nonetheless, sampling effort was unequally distributed between

geographic regions (table 4.2). To prevent an overall model from being overfitted to regions with larger sample sizes, we then trained separate forests for each region with more than 100 samples. Each forest contained 1000 trees with a maximum depth of 12, a minimum node size of 2 and specifies that a maximum of 30% of all features may be used to split a node. These restrictions are imposed to prevent over-fitting of the trees to the training data. We randomly withheld 50% of the data as test data for cross-validation, and used the rest as training data for the forest (a.k.a. 2-fold or 'holdout' cross-validation). This procedure is repeated 100 times, with the evaluation metrics mean accuracy and AUC (area under the receiver-operator curve) calculated to provide an estimate of prediction performance. Accuracy is defined as the percentage of trees in the forest that correctly classifies an observation as chytrid present or absent, and mean accuracy is the average accuracy over all observations in the test set. While each tree classifies an observation as 0/1 (absence/presence), the forest as a whole outputs the probability of chytrid being present for each observation by averaging over all trees. To evaluate the performance of the forests, we need to select a probability cutoff point above which an observation is classified as chytrid-present. The true positive rate (the percentage a chytrid presence is correctly classified as present) and the false positive rate (the percentage of chytrid absences incorrectly classified as present) thus depends on the selection of the cutoff point. The receiver-operator curve is derived from evaluating the true positive rate and false positive rate at variable cutoff points, and plotting the true positive rate against the false positive rate. The area under the curve (AUC) is maximized at 1 and will be large if at any cutoff point there is a desired large true positive rate and small false positive rate. A higher AUC indicates increased classification precision. The relative importance of a feature importance is evaluated by the

decrease in classification accuracy when the values of that feature are permutated (Cutler et al. 2007).

Predictions. Using the fitted random forest models (trained with all data and trained separately for each region), we generated two sets of predictions of chytrid occurrence probabilities based on climatic current condition, as well as those predicted for the year 2100 by the Hadley Global Environment Model 2 – Atmosphere Ocean (HADGEM2 - AO) with the IPCC's CMIP5 project. We predict global chytrid occurrence probabilities used the model trained with all data, and for regions with more than 100 sample sizes using models trained specifically with data from those regions). We project chytrid occurrence probabilities based future climatic conditions predicted by the Representative Concentration Pathway (RCP) family of experiments. RCPs are four greenhouse gas concentration trajectories adopted by the IPCC for its fifth Assessment Report, and describe four possible climate futures encompassing a wide range of possible future changes in anthropogenic greenhouse gas emissions (Moss et al. 2008). There are four RCPs: RCP2.6, RCP4.5, RCP6, and RCP8.5. The postfixes are so chosen according to the increase in radiative forcing (i.e. the difference between solar energy absorbed by the Earth and that radiated back to space) in the year 2100 relative to pre-industrial values each scenario describes (2.6, 4.5, 6.0, and 8.5 W/m^2, respectively, fig. 3).

Results

Model validation and feature importance

For the random forest model fitted with all data, spatial autocorrelation remained in the 50% sampled training data and showed a similar trend to the full data set (fig. 4.2 a&b). Predictions

generated from the random forest models preserved the spatial autocorrelation structure, but residuals were not spatially correlated (fig. 4.2 c&d). These observations remain true for models fitted per region, and suggest that variables in the model and their interactions were able to capture the spatial patterns in chytrid distribution. Mean accuracy was 0.9071 (s.d. = 0.0046), and mean AUC was 0.9642 (s.d. = 0.0019) for the model trained with all data (table 4.2). AUC was uniformly high for all regions, but mean accuracy was lower in Australasia, Europe and North America. Although these 3 regions have the largest sample sizes, the model does not seem to be biased towards those regions with fewer samples. However, region-specific models further improved performances both in terms of mean accuracy and AUC (table 4.3). Model-based uncertainties in terms of the variation in predicted chytrid occurrence probability per grid cell were low, per cell standard deviation ranges from 0.0024 – 0.087 for all models considered. In the model trained with all data, temperature range was the most important feature for classification. Temperature maximums were also important predictors, with the lowest, average and maximum monthly average maximum temperature ranked after temperature range. However, in general the input features do not differ substantially in terms of their relative importance (fig. 4.4). Regions specific models do not preserve this ordering if variable importance. Nonetheless, the importance of temperature and precipitation variables seem to far outweigh whether a site has experienced enigmatic amphibian declines or amphibian species richness (but see Asia as an exception where species richness seems to be at least as important as climate metrics (fig. 4.5-10).

Spatial patterns

Based on the non-region specific model, similar to previous studies (Ron 2005, Lötters et al. 2009, Puschendorf et al. 2009, Rödder et al. 2010), the areas of highest predicted chytrid occurrence probabilities are expected to be patchily distributed (fig. 4.11). These 'hotspots' occur on all continents occupied by amphibians, but are more restricted in range in Eurasia, Oceania and Africa in contrast to the Americas. Around the equator, predicted chytrid occurrence probabilities are generally low. In the southern hemisphere, past the equatorial region, chytrid occurrence probability generally increases, and hotspots are associated with coastal regions (e.g. Australia, Africa) and mountainous terrain of higher elevation (e.g. Andes in South America, Ethiopian highlands and the highlands along the Great Rift Valley in Africa). In the Northern hemisphere, where contiguous land masses extend further towards to polar region, the higher latitudes in Asia and North America exhibit low predicted chytrid occurrence probability. Hotspots are again associated with areas of high elevation (e.g. the Kunlun, Qinling, Taihang, and Nanling mountains in China, Hida and Ou mountains in Japan, the Rockies, Appalachians and Interior Highlands in North America). In Europe, these hotspots coincide with the Alps, Kjolen, Ural Mountains Areas but overall predicted chytrid occurrence probability is high.

Based on regions specific models, the distribution of areas with higher chytrid occurrence probability largely coincides with those predicted by the model non-region specific model (fig. 4.12). However, there is a decrease in overall predicted chytrid occurrence probabilities, and this trend is especially true for Asia and Australasia. We notice that the areas representing low to intermediate (blue to green) chytrid occurrence probability do not fully agree with that predicted by the non-region specific model. In North America, the region-specific model

predicts no apparent 'hotspots' in the mid-latitudes. In the higher latitudes the same model predicts that the region of intermediate chytrid occurrence probabilities would extend further towards the North Pole than non-region specific model. In contrast, in Asia and Australasia, region-specific models predict that the areas of low chytrid occurrence probability (predominantly in the higher latitudes) would extend further into the mid-latitudes in comparison to the non-region specific model. In South America, the most disagreement occurs in the northern regions. The region-specific model predicts that the Northern Andes are not predicted to contain noticeable hotspots, and that the Amazon basin will have intermediate chytrid occurrence probabilities. In contrast, the non-region specific model predicts an area of low chytrid occurrence here in the basin and hotspots in the northern Andes. In Africa, we notice that the regions of low chytrid occurrence probabilities (dark blue) are shifted more towards the equator as predicted by the region-specific model. These observations indicate that while maps may be used to identify chytrid hotspots (which are largely in agreement), caution needs to be applied in interpreting spatial risk from chytrid where models predict low to intermediate occurrence probability.

The relative changes in predicted chytrid occurrence probability in the year 2100 as predicted by the non-region specific model are shown in fig. 4.13-15. The area and extent of relative change are progressively larger with projected increases in radiative forcing. This change is most notable in the higher latitudes of the northern hemisphere, where large areas in North America and Asia that was previously unsuitable for chytrid exhibit the largest increases in chytrid predicted occurrence probability. This area of increase shifts progressively north with increase in radiative forcing. Other areas of increase include forested areas around the equator

such as the Malaysian and Indonesian islands, northeastern Brazil, and lowland regions around the equatorial belt in Africa. The high elevation regions that were previously associated with predicted chytrid occurrence hotspots generally exhibit shrinkages, which is particularly apparent in the Andes Mountains of South America. Due to the sensitivity of the chytrid fungus to temperature and the apparent importance of temperature as a predictor variable, it may be that climate change shifts these high altitude regions out of the optimum thermal envelop for chytrid (Beniston and Fox, 1996).

This trend of more drastic change associated increased radiative forcing remains true for predictions generated by the region-specific models (fig. 4.16-18). Under climate change projected by RCP 2.6, the regions of relative increase and decrease approximately agree for most geographic regions with the notable exception of Australasia. In this case, the region-specific model predicts that continental Australia will undergo a decrease in overall chytrid occurrence probability in the coastal regions and an increase in the inlands. The non-region specific model, however, predicts the opposite. Under RCP 6.0, a major inconsistency lies in predictions close to the equatorial regions. The non-region specific model predicts an increase in chytrid occurrence probability in the Amazon basin and other forested regions near the equator in Africa and the Indonesian and Malaysian islands. This increase is much less prominent according to the region-specific models. Again, Australasia stands out in that while the region-specific models predict overall no change or a decrease in chytrid occurrence probability, the non-region specific models predicts an increase in coastal regions. The differences in predicted chytrid occurrence probabilities under RCP 8.5 between region-specific and non-region specific models are similar to those observed under RCP 6.0. Despite these

differences, all models and climate scenarios are consistent in predicting an increase in chytrid occurrence probabilities in the higher latitudes, with the zones of highest increase shifting towards the North Pole progressively with increases in radiative forcing.

Discussion

Using the most comprehensive set of chytrid surveillance data up to date, we implement a machine learning ensemble model that uses both presence and absence data to predict current and future distributions of chytrid under progressively severe future climate change scenarios. We build random forest models combining data gathered from all regions in the world, and also separate forests for relatively well-sampled geographic regions using region-specific data. Random forests have been shown to perform well in predicting the distribution of invasive species (Cutler et al. 2007). We find here that using climate variables, we are able to capture the spatial correlation patterns in present chytrid distribution. This observation may be argued as supporting climate as a important controlling factor of the present distribution of chytrid.

As with free-living species, pathogens likewise have optimum climatic envelopes, which make them susceptible to potential distribution shifts in the presence of climate change (Lafferty 2009). It has been argued that since chytrid prefers cool, moist conditions, its emergence might be curbed by climate warming (Harvell et al. 2002). Indeed, as is consistent with observed responses to ongoing climate change in other species (Parmesan and Yohe 2003, Sekercioglu et al. 2008), our models consistently forecast that chytrid occurrence probabilities will experience the most increase in the higher latitudinal regions of the Northern Hemisphere, which may correspond to a range shift. This increase in chytrid occurrence probability in the temperate zones due to climate change has been previously lighted on by Bosch et al. (2007), who

show that the occurrence of chytrid-related disease was linked to rising temperatures that moderated the severe winters. In addition, precipitation is expected to increase in higher latitudes, which may further enhance the environmental suitability of the temperate zones to chytrid. It is unclear whether this range shift will represent a shrinkage or expansion in chytrid distribution since the larger landmass in the higher latitudes in the Northern Hemisphere may compensate for lost range in the lower latitudes.

Our region-specific models possess higher predictive performance than the non-region specific model, and generated predictions are consistent with previous SDMs (Ron 2005, Lötters et al. 2008, Puschendorf et al. 2009, Rödder et al. 2009, Rödder et al 2010, Murray et al. 2011). Both our region-specific and non-specific models predict that the extent and magnitude of change in chytrid occurrence probabilities increases with projected changes in radiative forcing relative to preindustrial levels. In general, more extensive areas of larger increases in predicted chytrid occurrence probability are expected with increasing radiative forcing. However, inconsistencies exist in the predictions generated by the region-specific and non-region specific models. Under all climate scenarios, the non-region specific model predicts a higher overall chytrid occurrence probability. These mismatches are especially noticeable in regions of the Southern Hemisphere, with disagreement between models most severe in equatorial regions and in continental Australia. This may indicate that the chytrid-climate relationship differs between regions, which may be due to variation in chytrid strain between regions (Rosenblum et al. 2010) or other unmeasured variables causing these differences. Specific to the Malaysian and Indonesian islands, northeastern Brazil, and lowland regions around the equatorial belt in Africa, we find the predictions from the non-region specific model to also be inconsistent with Rödder et al.

(2010). Both region-specific and non-specific models agree with Rödder et al. (2010) in that based on present conditions, chytrid occurrence probability should generally be low in these regions. This is in line with the empirical observation that under laboratory settings, the growth of chytrid is inhibited by higher temperatures and in the extreme case induces mortality (Piotrowski et al. 2004). However, our non-region specific model predicts a general increase in chytrid occurrence probabilities in these regions while Rödder et al. (2010) forecasts little change or decrease. We suspect that these model uncertainties in the tropics zone are due to extrapolations outside of the climate data range in the available chytrid records. Currently, the tropics already experience the highest temperature and precipitations regimes. Even if aggressive measures were taken to reducing greenhouse gas emissions, the annual mean temperature in an average location would be shifted out of its previous normal range due to climate change by 2069 (Mora et al. 2013). Therefore, predictions generated for this region beyond this time frame will likely be based on extrapolating outside the range of climatic variables present in the training data. As a result, while the tropics are affected by climate change to a lesser degree than temperate zones (Mora et al. 2013), model uncertainties in these regions warrants further investigation and monitoring of chytrid presence. In addition to these model uncertainties, our prediction maps generated here are point estimates only and do not reflect seasonal or annual variations in climate, therefore at finer spatial and temporal scales they may not be fully reflective of the relative spatial risk of chytrid presence.

Despite an accruing amount of knowledge in chytrid physiology in laboratory settings, our study illustrates that it might be too simplistic to assume that global warming will curtail the spread of the chytrid fungus. Indeed, how climate change will affect chytrid and

chytridiomycosis outbreaks has been the subject of much debate and controversy. Much focus of the discussion has been on the role of temperature, one of the most important environmental factors that influences chytrid growth and development of chytridiomycosis (Kilpatrick et al. 2010). Intuitively, it would seem that increasing temperatures might be expected to decrease chytrid occurrence probabilities due to its intolerance to high temperatures *in vitro* (Piotrowski et al. 2004). However, chytrid-associated amphibian declines in the Neotropics were found to be more likely to occur after high temperature years (Rohr and Raffel 2010), suggesting that climate change might actually increase chytrid occurrence probabilities (Venesky et al. 2013). Our analysis here provides support to the hypothesis that climate change might further promote the emergence of the chytrid fungus, especially in the temperate zones. While this further highlights the controversy and the need for research on climate-chytrid relationships outside of laboratory settings, we note that in contrast to previous chytrid distribution models studies that rely on additive regression models in MaxEnt, out model identify no single climatic variable as wholly determining in chytrid occurrence probabilities. Therefore, we strongly advocate that research attention on climate-chytrid relationships should not be limited to temperature regimes alone, but would benefit from considering complex interactions of climatic variables. Moreover, since sampling of chytrid is predominantly conducted by swabbing amphibians and chytrid may be found outside of amphibian hosts (Chestnut et al. 2014), it is possible that a site deemed chytrid absent may in fact be so due to insufficiently sampling of the environment. While this can only be remedied by more environmental sampling for chytrid, here we caution that SDMs based on these data may be systematically under-predicting chytrid occurrence probabilities.

Despite the higher performances of our models presented here, we again emphasize the correlative nature of SDMs in general. The model we presented here is a non-parametric random forest learning procedure, while is capable of implicitly including complex higher-order interactions. It is possible that the climate variables we have chosen to include here and their interactions yield excellent predictive performance simply because they're highly correlated with other unmeasured variables at each site, which may in fact be the driver of chytrid presence. While temperature and moisture are certainly important variables that determine the propagation of chytrid on the host and in the environment, we should exercise caution in inferring causation from correlative models based on predictive performance.

References

Alford RA, Bradfield KS and SJ Richards. 2007. Ecology: global warming and amphibian losses. Nature 447:E3–E4.

Beniston M and DG Fox. 1996. Chapter 5. Impacts of climate change on mountain regions. pp. 191-213. IPCC.

Berger L, Speare R, Hines HB, Marantelli G, Hyatt AD, McDonald KR, Skerratt LF, Volsen V, Clarke JM, Gillespie G, Mahony M, Sheppard N, Williams C and MJ Tyler. 2008. Effect of season and temperature on mortality in amphibians due to chytridiomycosis. Australian Veterinary Journal 82: 434-439.

Bosch J, Carrascal LM, Duran L, Walker S and MC Fisher. 2007. Climate change and outbreaks of amphibian chytridiomycosis in a montane area of Central Spain; is there a link? Proceedings of the Royal Society London B 274:253–260.

Camilo M, Frazier AG, Longman RJ, Dacks RS, Walton MM, Tong EJ, Sanchez JJ, Kaiser LR, Stender YO, Anderson JM, Ambrosino CM, Fernandez-Silva I, Giuseffi LM and TW Giambelluca. 2013. The projected timing of climate departure from recent variability. Nature 502, 183–187.

Conradie W, Weldon C, Smith KG and Du Preez HH. 2011. Seasonal pattern of chytridiomycosis in common river frog (*Amietia angolensis*) tadpoles in the South African Grassland Biome. African Zoology 46(1):95-102.

Daszak P, Cunningham AA and AD Hyatt. 2000. Emerging infectious diseases of wildlife--threats to biodiversity and human health. Science 287(5452):443-9.

Gascon C, Collins JP, Moore RD, Church DR, McKay JE and JR Mendelson III (eds). 2007. Amphibian conservation action plan: Proceedings: IUCN/SSC Amphibian conservation summit 2005. The World Conservation Union (IUCN), Gland, Switzerland.

Harvell CD, Mitchell CE, Ward JR, Altizer S, Dobson AP, Ostfeld RS and MD Samuel. 2002. Climate warming and disease risks for terrestrial and marine biota. Science 296: 2158–2162.

Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL and P Daszak. 2008. Global trends in emerging infectious diseases. Nature 451: 990-993.

Kilpatrick AM, Briggs CJ and P Daszak. 2010. The ecology and impact of chytridiomycosis: an emerging disease of amphibians. Trends in Ecology and Evolution 25, 109–118.

Lafferty KD. 2009. The ecology of climate change and infectious diseases. Ecology 90:888–900

Laurance WF. 2008. Global warming and amphibian extinctions in eastern Australia. Australian Ecology 33:339–408.

Longcore JE, Pessier AP and DK Nichols. 1999. *Batrachochytrium dendrobatidis* gen. et sp. nov., a chytrid pathogenic to amphibians. Mycologia 91: 219-227.

Lötters S, Kielgast J, Bielby J, Schmidtlein S, Bosch J, Veith M, Walker SF, Fisher MC and D Rödder. 2009. The link between rapid enigmatic amphibian decline and the globally emerging chytrid fungus. EcoHealth 6: 358–372.

Moss R, Babiker M, Brinkman S, Calvo E, Carter T et al. 2008. Towards new scenarios for analysis of emissions, climate change, impacts, and response strategies. Geneva: Intergovernmental Panel on Climate Change. p. 132.

Murray KA, Retallick RWR, Puschendorf R, Skerratt LF, Rosauer D, McCallum HI, Berger L, Speare R and VanDerWal J. 2011. Assessing spatial patterns of disease risk to biodiversity: implications for the management of the amphibian pathogen, *Batrachochytrium dendrobatidis*. Journal of Applied Ecology 48: 163–173.

Olson DH, DM Aanensen, KL Ronnenberg, CI Powell, SF Walker, J Bielby, TWJ Garner, G Weaver, The BD Mapping Group, and MC Fisher. 2013. Mapping the global emergence of *Batrachochytrium dendrobatidis*, the amphibian chytrid fungus. PLoS ONE 8: e56802.

Parmesan C and G Yohe. 2003. A globally coherent fingerprint of climate change impacts across natural systems. Nature 421: 37-42.

Pedregosa et al. 2011. Scikit-learn: Machine Learning in Python JMLR 12: 2825-2830.

Piotrowski JS, Annis SL and JE Longcore. 2004. Physiology of *Batrachochytrium dendrobatidis*, a chytrid pathogen of amphibians. Mycologia 96: 9-15.

Pounds JA, Bustamante MR, Coloma LA, Consuegra JA, Fogden MP, Foster PN, La Marca E, Masters KL, Merino-Viteri A, Puschendorf R, Ron SR, Sánchez-Azofeifa GA, Still CJ and BE Young. 2006. Widespread amphibian extinctions from epidemic disease driven by global warming. Nature 439(7073): 161-7.

Puschendorf R, Carnaval AC, VanDerWal J, Zumbado-Ulate H, Chaves G, Bolanos F, et al. 2009. Distribution models for the amphibian chytrid *Batrachochytrium dendrobatidis* in Costa Rica: proposing climatic refuges as a conservation tool. Diversity and Distributions 15:4 01–408.

Renner IW and DI Warton. 2013. Equivalence of MAXENT and poisson point process models for species distribution modeling in ecology. Biometrics 69: 274–281.

Rödder D, Kielgast J and S Lötters. 2010. Future potential distribution of the emerging amphibian chytrid fungus under anthropogenic climate change. Disease of Aquatic Organisms 92(2-3): 201-7.

Rödder D, Kielgast J, Bielby J, Schmidtlein S, Bosch J, Garner TWJ, et al. 2009. Global amphibian extinction risk assessment for the panzootic chytrid fungus. Diversity 1:52–66.

Rödder D, Veith M and S Lötters. 2008. Environmental gradients explaining prevalence and intensity of infection with the amphibian chytrid fungus: the host's perspective. Animal Conservation 11:513–517.

Rohr JR, Raffel TR, Romansic JM, McCallum H and P Hudson. 2008. Evaluating the links between climate, disease spread, and amphibian declines. Proceedings of the National Academy of Sciences of the United States of America 105:17436–17441.

Rohr JR and TR Raffel. 2010. Linking global climate and temperature variability to widespread amphibian declines putatively caused by disease. Proceedings of the National Academy of Sciences of the United States of America 107: 8269–8274.

Ron SR. 2005. Predicting the distribution of the amphibian pathogen *Batrachochytrium dendrobatidis* in the new world. Biotropica 37:209–221.

Rosenblum EB, James TY, Zamudio KR, Poorten TJ, Ilut D, et al. 2013. Complex history of the amphibian-killing chytrid fungus revealed with genome resequencing data. Proceedings of the National Academy of Sciences of the United States of America 110: 9385–9390.

Royle JA, Chandler RB, Yackulic C and JD Nichols. 2012. Likelihood analysis of species occurrence probability from presence-only data for modelling species distributions. Methods in Ecology and Evolution, 3: 545–554.

Sekercioglu CH, Schneider SH, Fay JP and SR Loarie. 2008. Climate change, elevational range shifts, and bird extinctions. Conservation Biology 22(1):140-50.

Skerratt LF, Berger L, Speare R, Cashins S, McDonald KR, Phillott AD, Hines HB and N Kenyon. 2007. Spread of chytridiomycosis has caused the rapid global decline and extinction of frogs. Ecohealth 4: 125-134.

Stuart SN, Chanson JS, Cox NA, Young BE, Rodrigues ASL, Fischman DL and RW Waller. 2004. Status and trends of amphibian declines and extinctions worldwide. Science 306: 1783-1786.

VanDerWal J, Shoo LP, Johnson CN and SE Williams. 2009. Abundance and the environmental niche: environmental suitability estimated from niche models predicts the upper limit of local abundance. American Naturalist 174: 282–291.

van Vuuren DP, Edmonds J, Kainuma M, Riahi K, Thomson A, Hibbard K et al. 2011. The representative concentration pathways: an overview. Climatic Change 109(1-2): 5-31.

Venesky MD, Raffel TR, McMahon TA and JR Rohr. 2013. Confronting inconsistencies in the amphibian-chytridiomycosis system: implications for disease management. Biological Review of the Cambridge Philosophical Society 89(2):477-83.

Wake DB and VT Vredenburg. 2008. Are we in the midst of a sixth major extinction? A view from the world of amphibians. Proceedings of the National Academy of Sciences of the United States of America 105: 11466-11473.

Woodhams DC, Alford RA and G Marantelli. 2003. Emerging disease of amphibians cured by elevated body temperature. Diseases of Aquatic Organisms 55: 65-67.

Woodhams DC, Alford RA, Briggs CJ, Johnson M and LA Rollins-Smith. 2008. Life-history trade-offs influence disease in changing climates: strategies of an amphibian pathogen. Ecology 89: 1627-1639.

Li X and Y Wang. 2013. Applying various algorithms for species distribution modelling. Integrative Zoology 8: 124–135.

Cutler DR, Edwards TC, Beard KH, Cutler A, Hess KT, Gibson J and JJ Lawler. 2007. Random forests for classification in ecology. Ecology 88(11): 2783–2792.

Breiman L. 2001. Statistical modelling: the two cultures. Statistical Science 16: 199–215.

Kampichler C, Wieland R, Calmé S, Weissenberger H and S Arriaga-Weiss. 2010. Classification in conservation biology: a comparison of five machine-learning methods. Ecological Informatics 5: 441–50.

Pearson RG, Thuiller W, Araujo MB et al. 2006. Model-based uncertainty in species range prediction. Journal of Biogeography 33: 1704–11.

Iverson LR, Prasad AM, Matthews SN and M Peters. 2008. Estimating potential habitat for 134 eastern US tree species under six climate scenarios. Forest Ecology and Management 254, 390–406.

Elith J and CH Graham. 2009. Do they? How do they? Why do they differ? On finding reasons for differing performances of species distribution models. Ecography 32: 66–77.
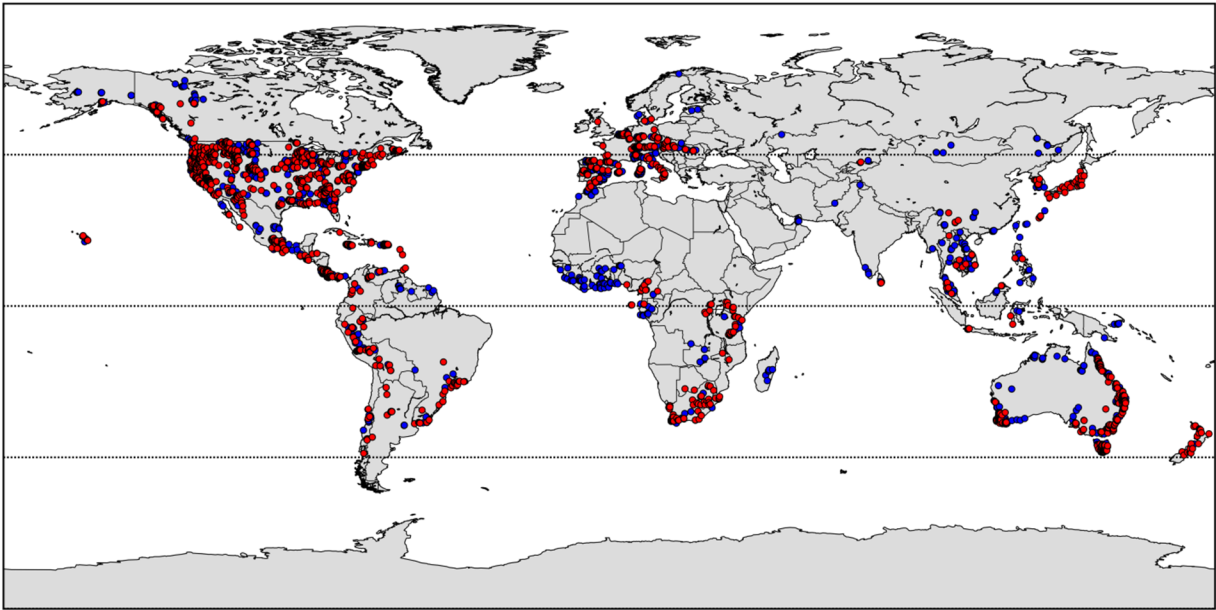
Figure 4.1 Existing sampling points for chytrid survey (red = site tests positive for chytrid, blue = sites tests negative for chytrid).

Table 4.1 List of input features in the random forest model and their definitions. These values were extracted per coordinate for each year during 2000 – 2010, then averaged over the period.

| Variables names	Definition	Units
mean_temp	mean annual temperature	°C
high_mean	highest monthly average temperature in a year	
low_mean	lowest monthly average temperature in a year	
mean_max	annual mean of mean monthly maximum daily temperature	
high_max	annual maximum of mean monthly maximum daily temperature	
low_max	annual minimum of mean monthly maximum daily temperature	
mean_min	annual mean of mean monthly minimum daily temperature	
high_min	annual maximum of mean monthly minimum daily temperature	
low_min	annual minimum of mean monthly minimum daily temperature	
t_range	high_max – low_min	
mean_pre	annual mean of monthly precipitation	mm
high_pre	annual maximum of monthly precipitation	
low_pre	annual minimum of monthly precipitation	
elevation	the altitude of a site	m
eng_dec_in	whether the site has documented enigmatic amphibian declines	
sp_rich	estimated number of amphibian species at the site	
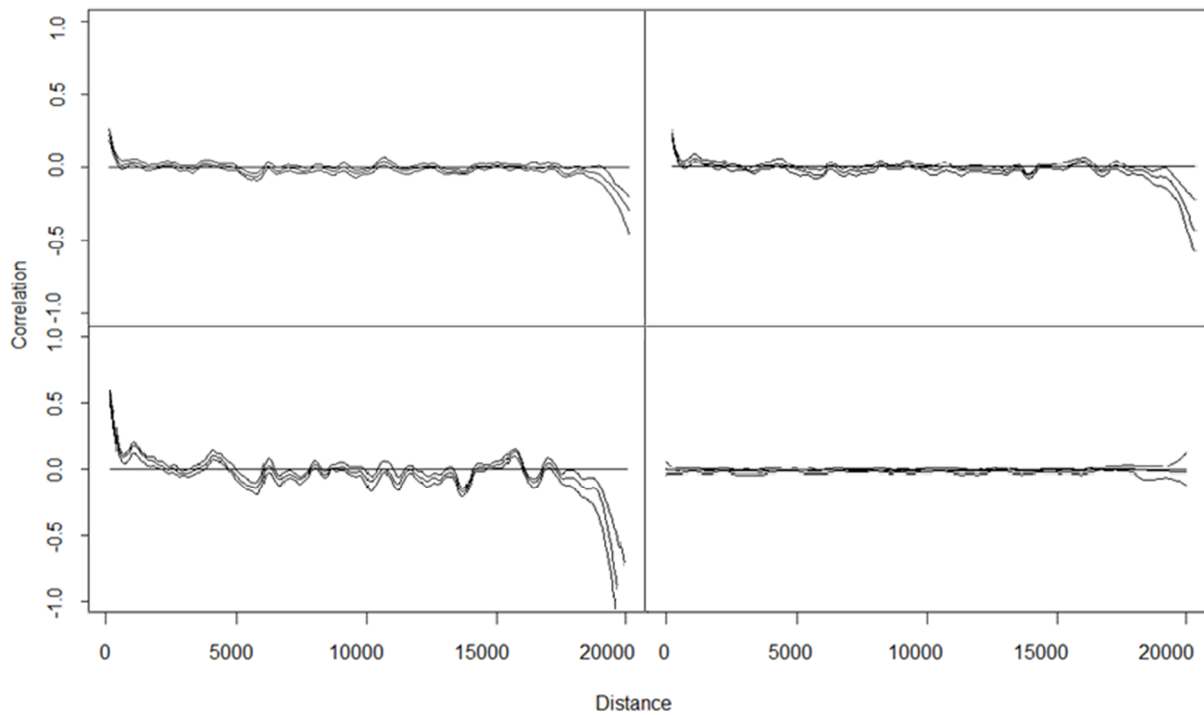
Figure 4.2 a) Correlogram indicates positive spatial autocorrelation in chytrid presence between sampled sites (distance in km); b) spatial autocorrelation remains both in 50% sampled training data and c) predictions generated by the model. However, it is absent in residuals from the random forest model in d).
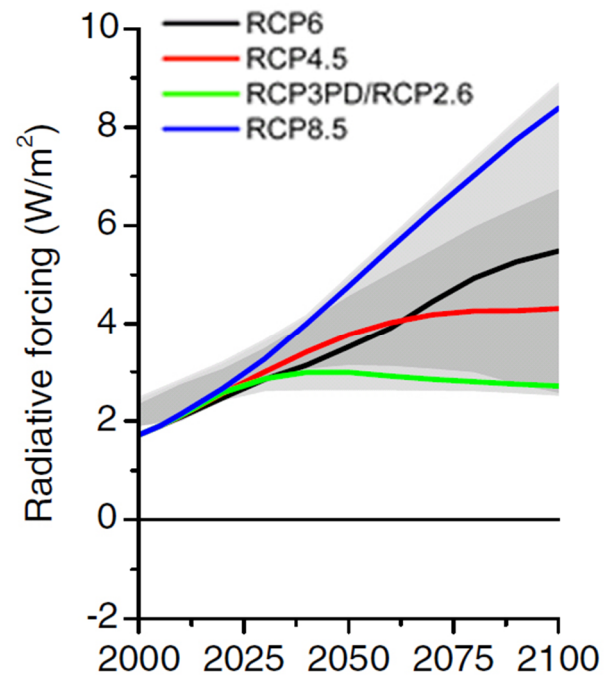
Figure 4.3 Radiative Forcing of the Representative Concentration Pathways. From van Vuuren et al (2011). The light grey area captures 98% of the range in previous Integrative Assessment Model scenarios, and dark grey represents 90% of the range.

Table 4.2 Distribution of samples sizes and chytrid occurrence probabilities in each region. Validation results for each continent based on random forest model trained on combined worldwide data.

Region	Sample size	% of chytrid-present sites	Mean accuracy	AUC
Africa	333	0.3544	0.9550	0.9886
Asia	419	0.1718	0.9761	0.9981
Australasia	847	0.4451	0.8737	0.9488
Caribbean	28	0.6429	1.0000	1.0000
Central America	27	0.6296	0.9630	1.0000
Europe	770	0.3039	0.8623	0.9458
North America	2333	0.4483	0.8933	0.9635
South America	210	0.5429	0.9429	0.9938

Table 4.3 Mean accuracy and area under the ROC curve for each continent based on separate random forest model trained on data from each region.

Region	Mean accuracy	s.d. (Mean accuracy)	AUC	s.d. (AUC)
Africa	0.998126	0.001111	0.976451	0.009383
Asia	0.999541	0.000468	0.983954	0.007389
Australasia	0.99115	0.002234	0.950904	0.008226
Europe	0.997332	0.001014	0.965998	0.006929
North America	0.977234	0.002675	0.914089	0.006598
South America	0.99725	0.001883	0.97518	0.012991
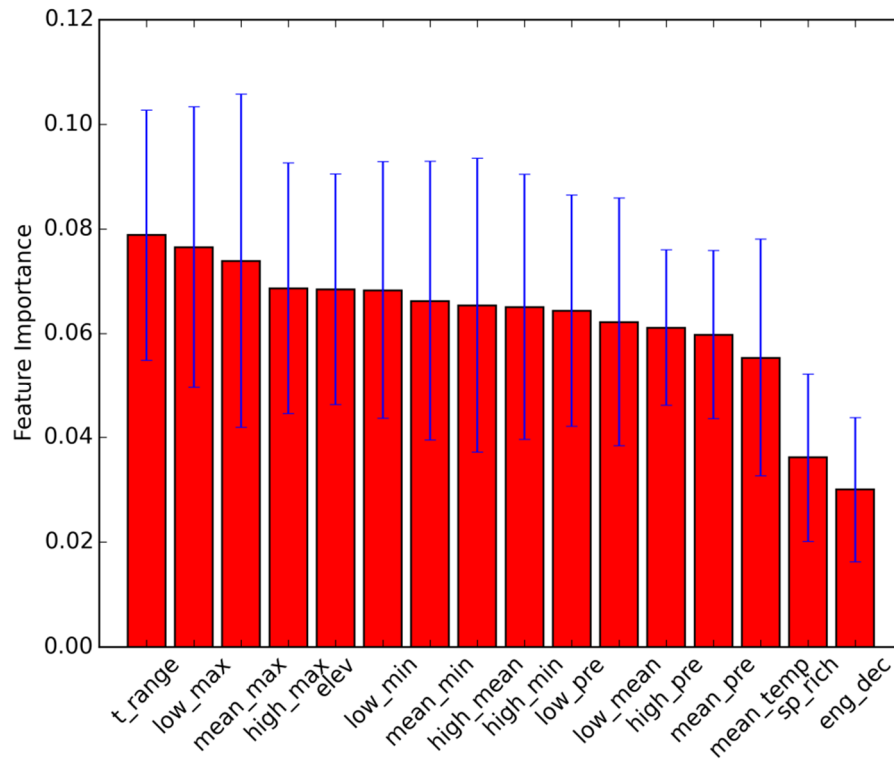
Figure 4.4 Relative importance of input features based on non-region specific model estimated as increase in out-of-bag error if training values for that feature were permutated. Feature importance is plotted with one standard deviation to show variation between trees in the random forest.
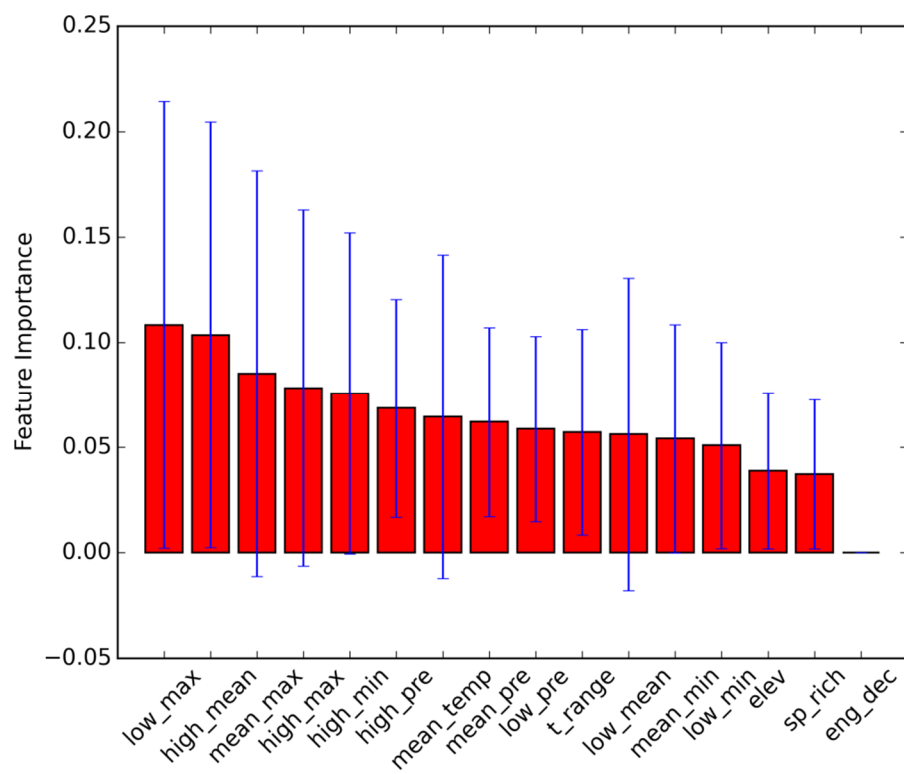
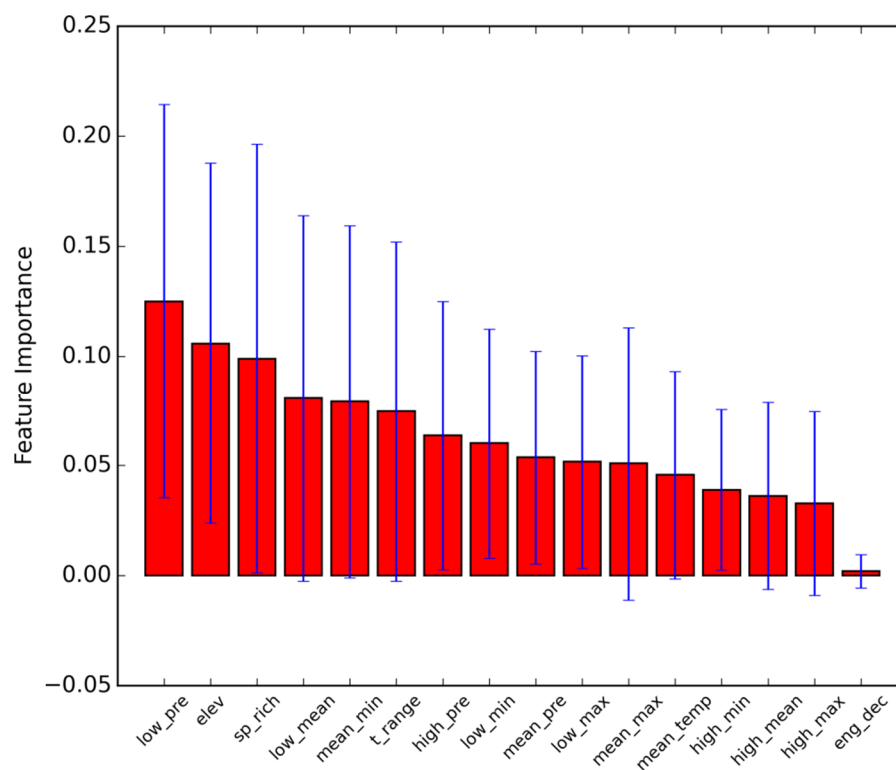**Figure 4.5** Relative importance of input features based on region specific model in Africa.

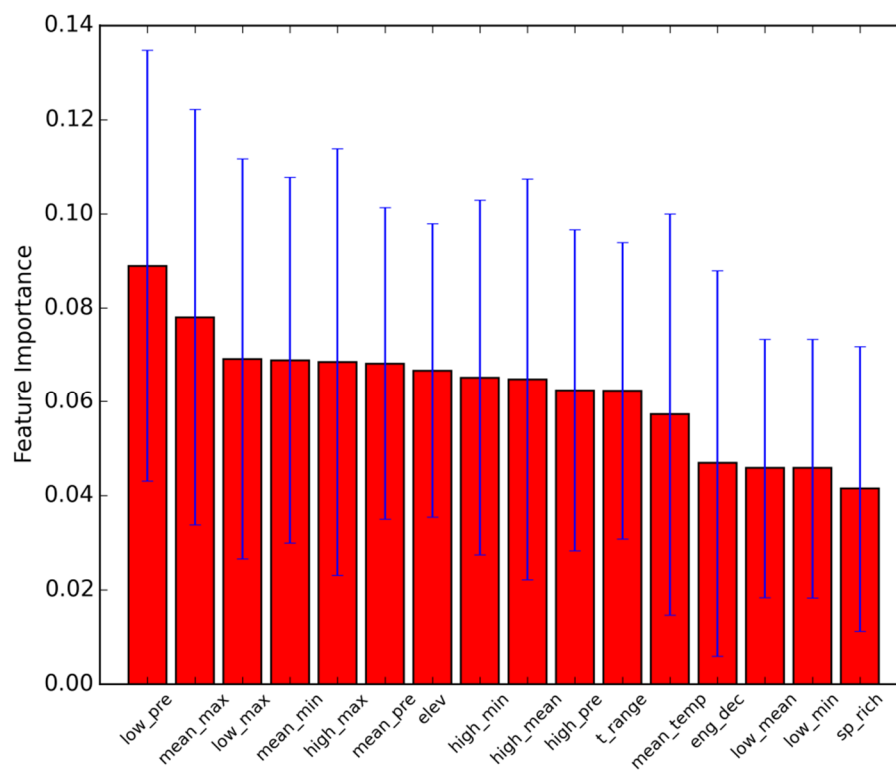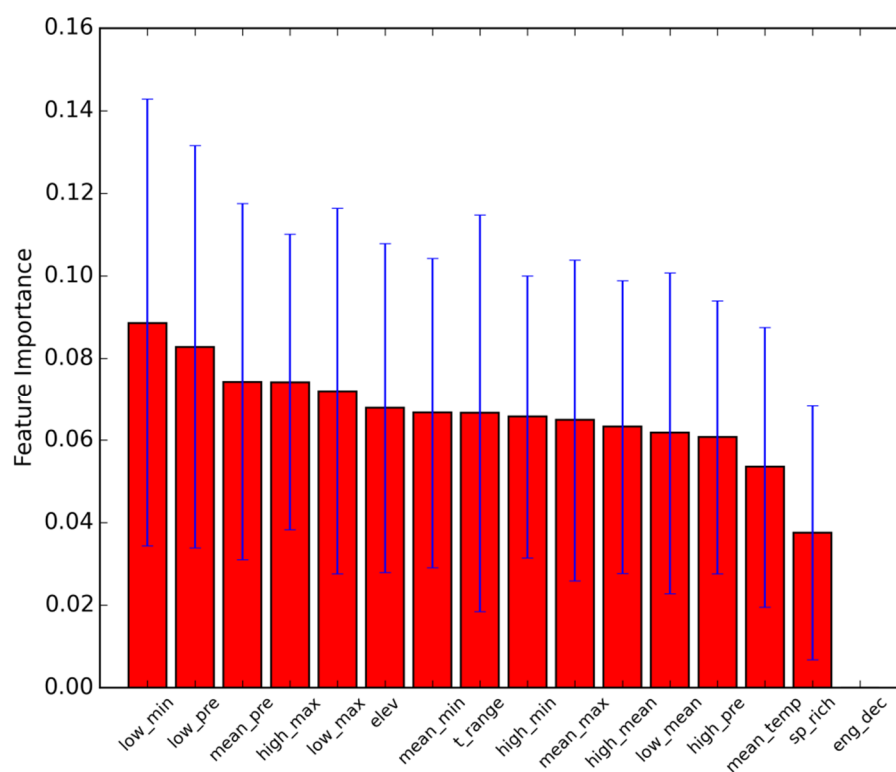**Figure 4.6** Relative importance of input features based on region specific model in Asia.

Figure 4.7 Relative importance of input features based on region specific model in Australasia.

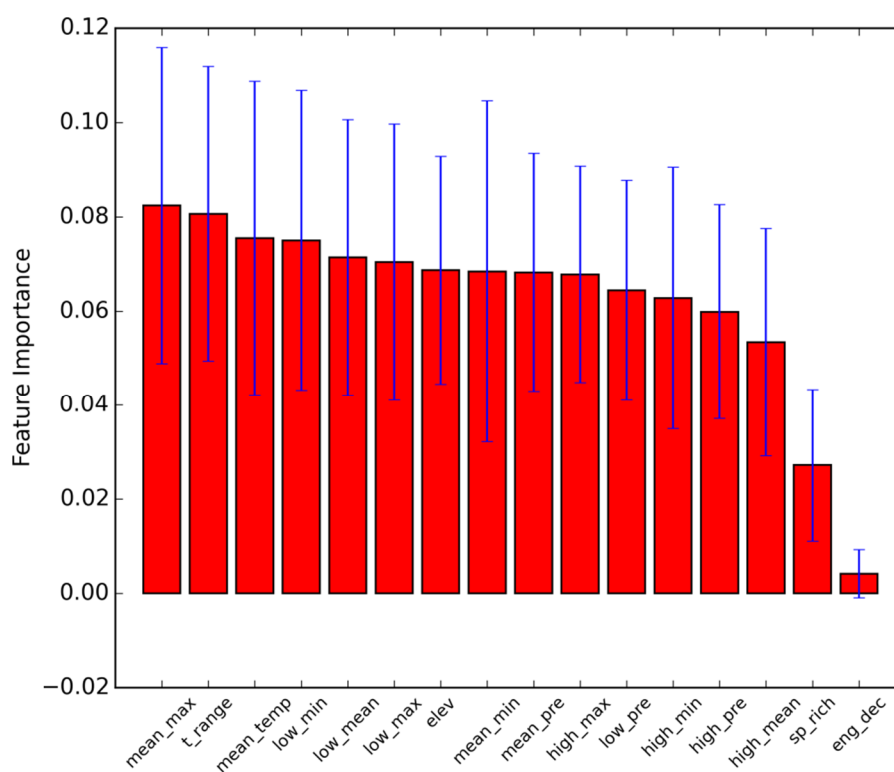**Figure 4.8** Relative importance of input features based on region specific model in Europe.

Figure 4.9 Relative importance of input features based on region specific model in North America.
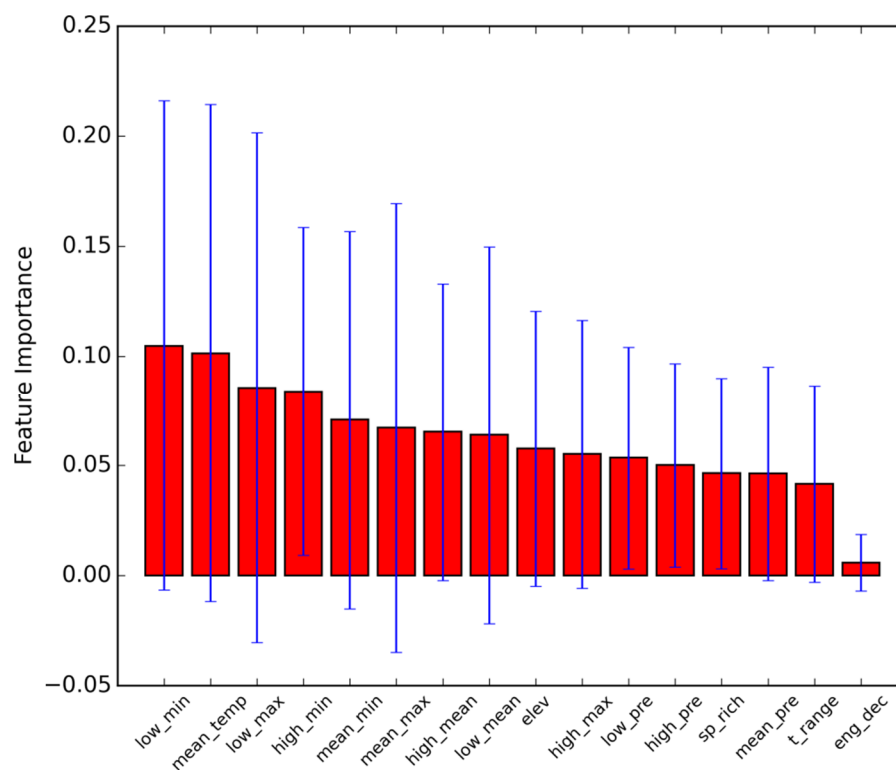
Figure 4.10 Relative importance of input features based on region specific model in South America.
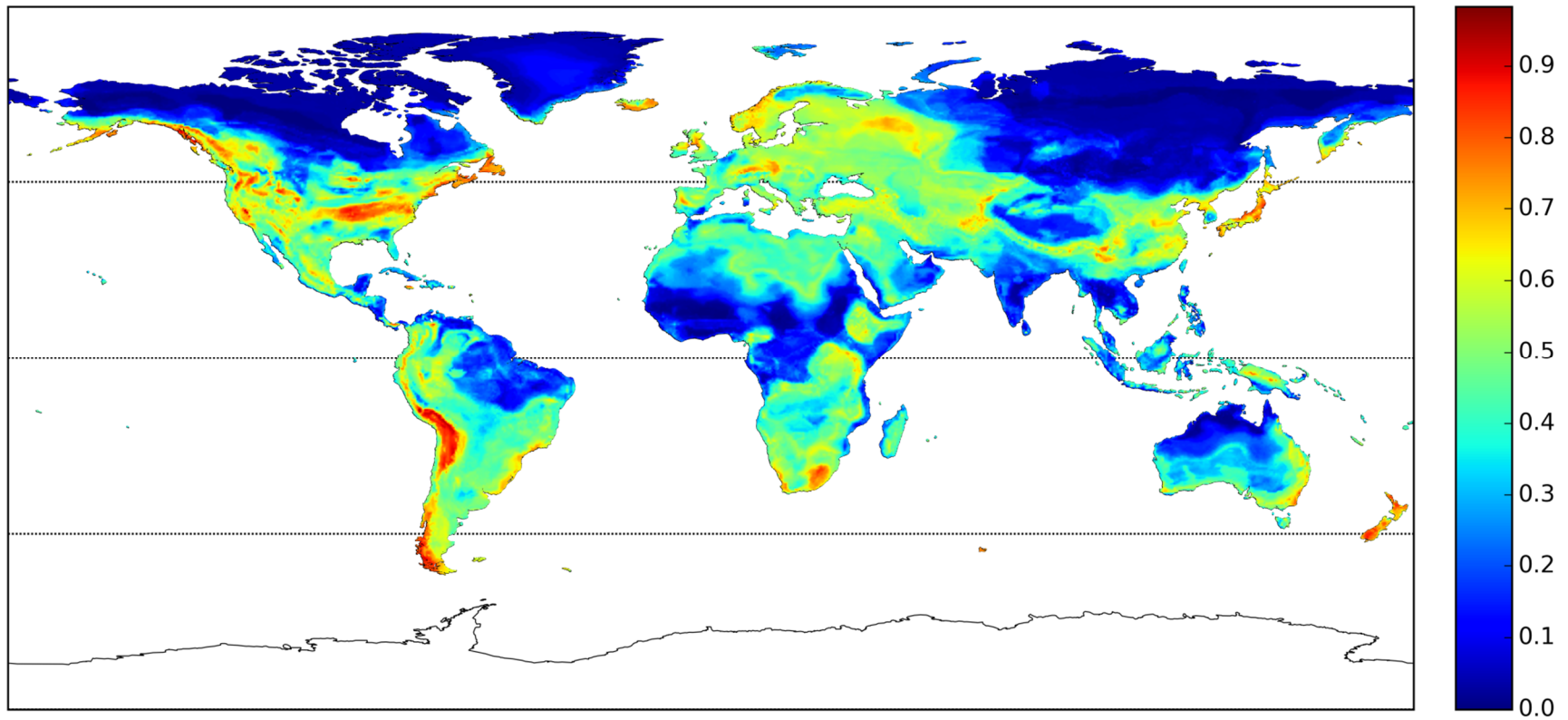
Figure 4.11 Predicted occurrence probability of chytrid based on current climatic conditions based on non-region specific model.
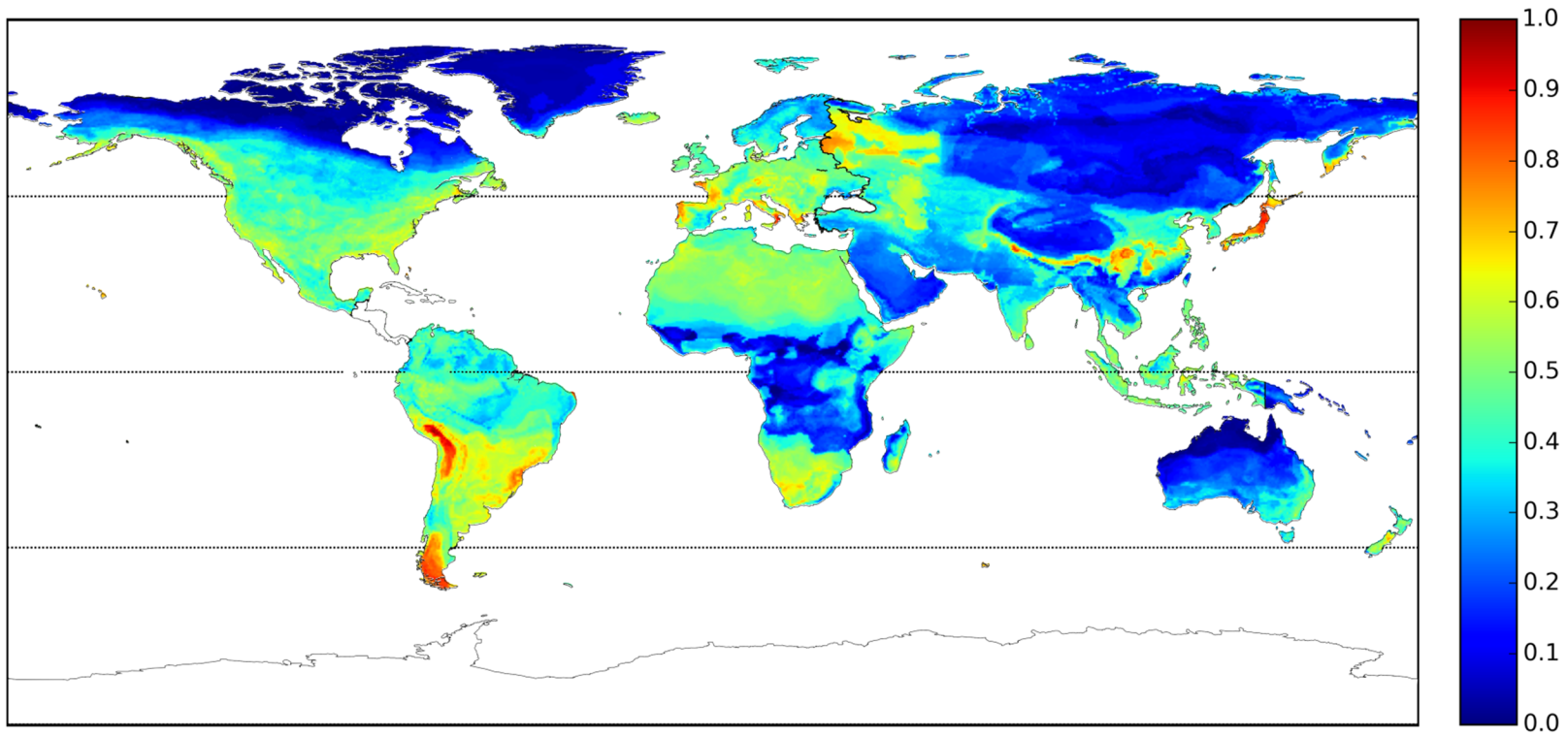
Figure 4.12 Predicted occurrence probability of chytrid based on current climatic conditions. Map combined from region-specific model predictions.
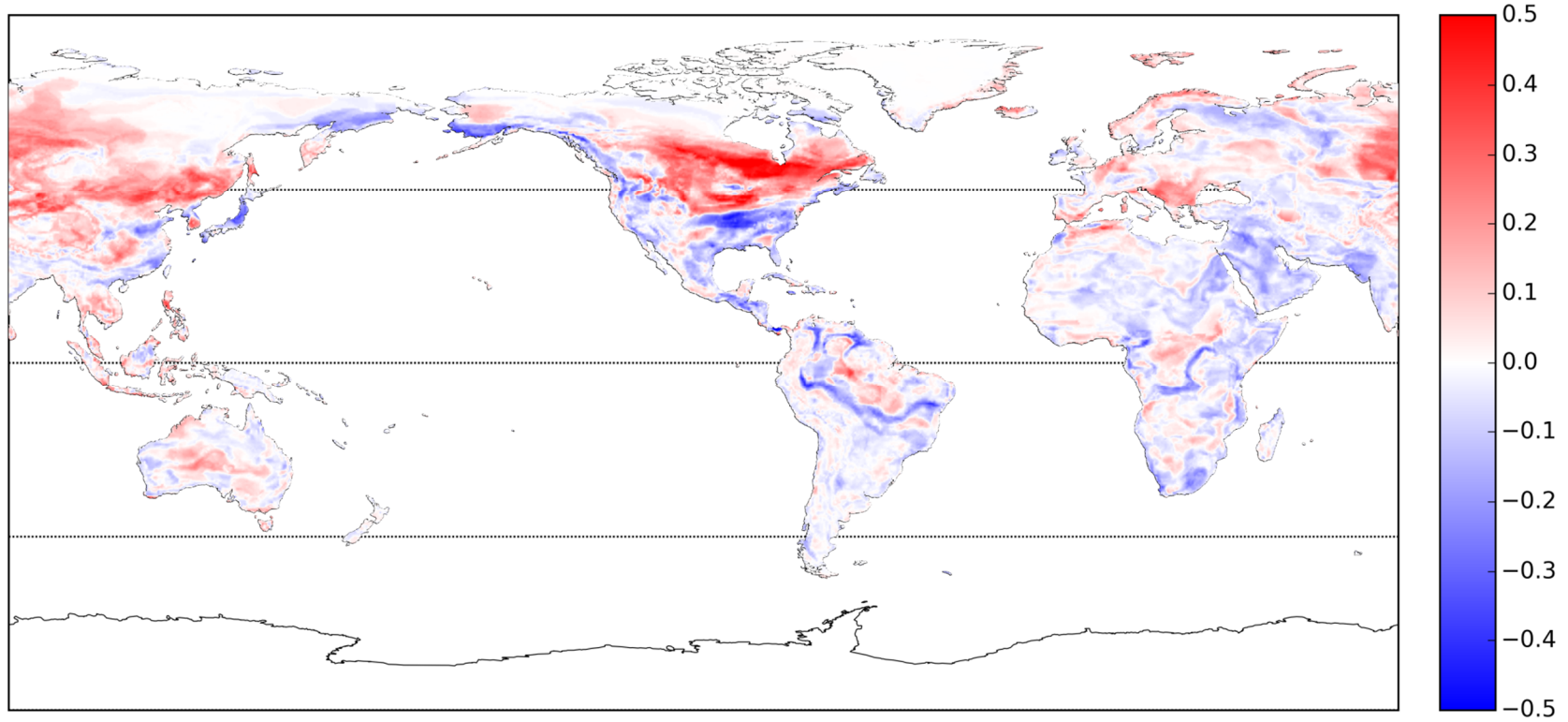
Figure 4.13 Predicted change in occurrence probability of chytrid based on conditions forecasted for 2100 in the RCP 2.6 scenario.

Map based on non-region specific model.

Figure 4.14 Predicted change in occurrence probability of chytrid based on conditions forecasted for 2100 in the RCP 6.0 scenario. Map based on non-region specific model.
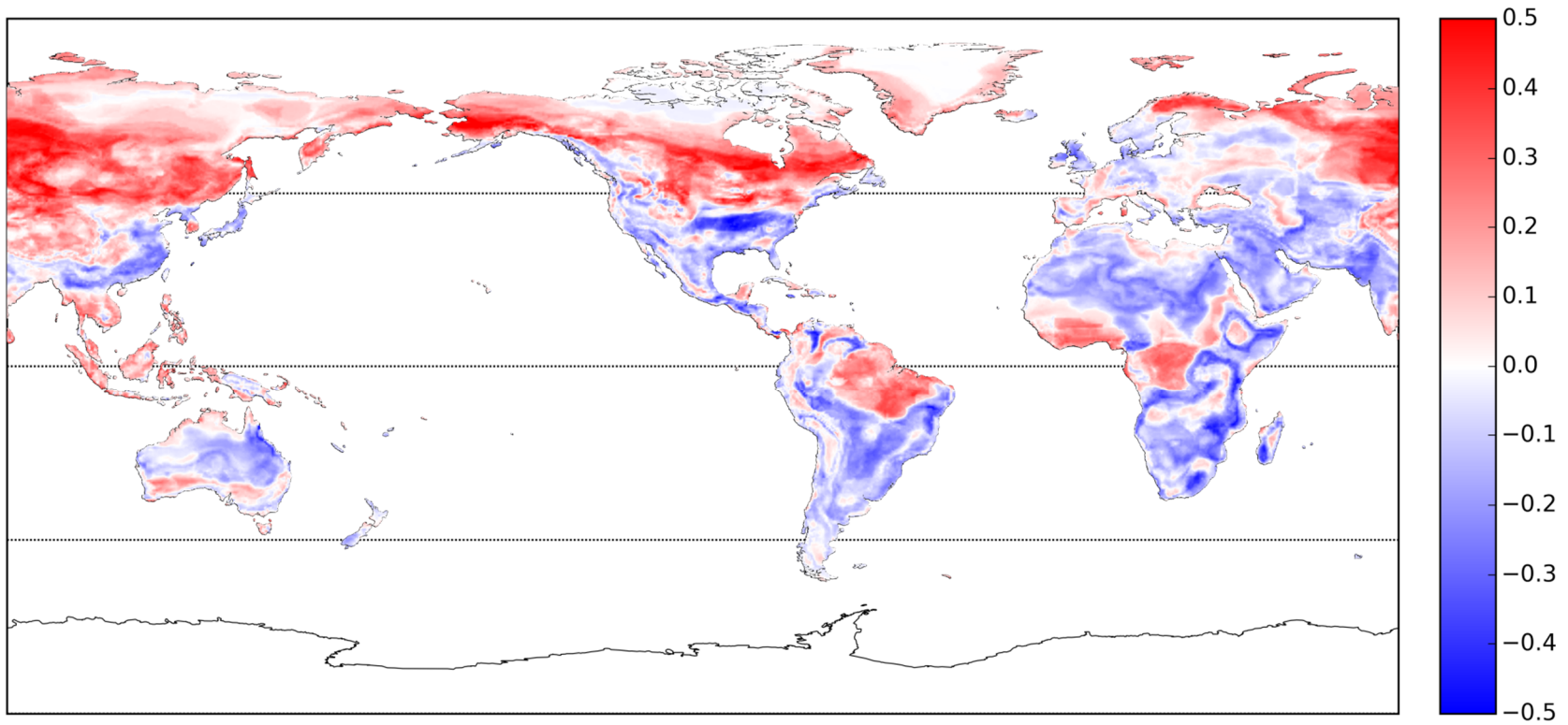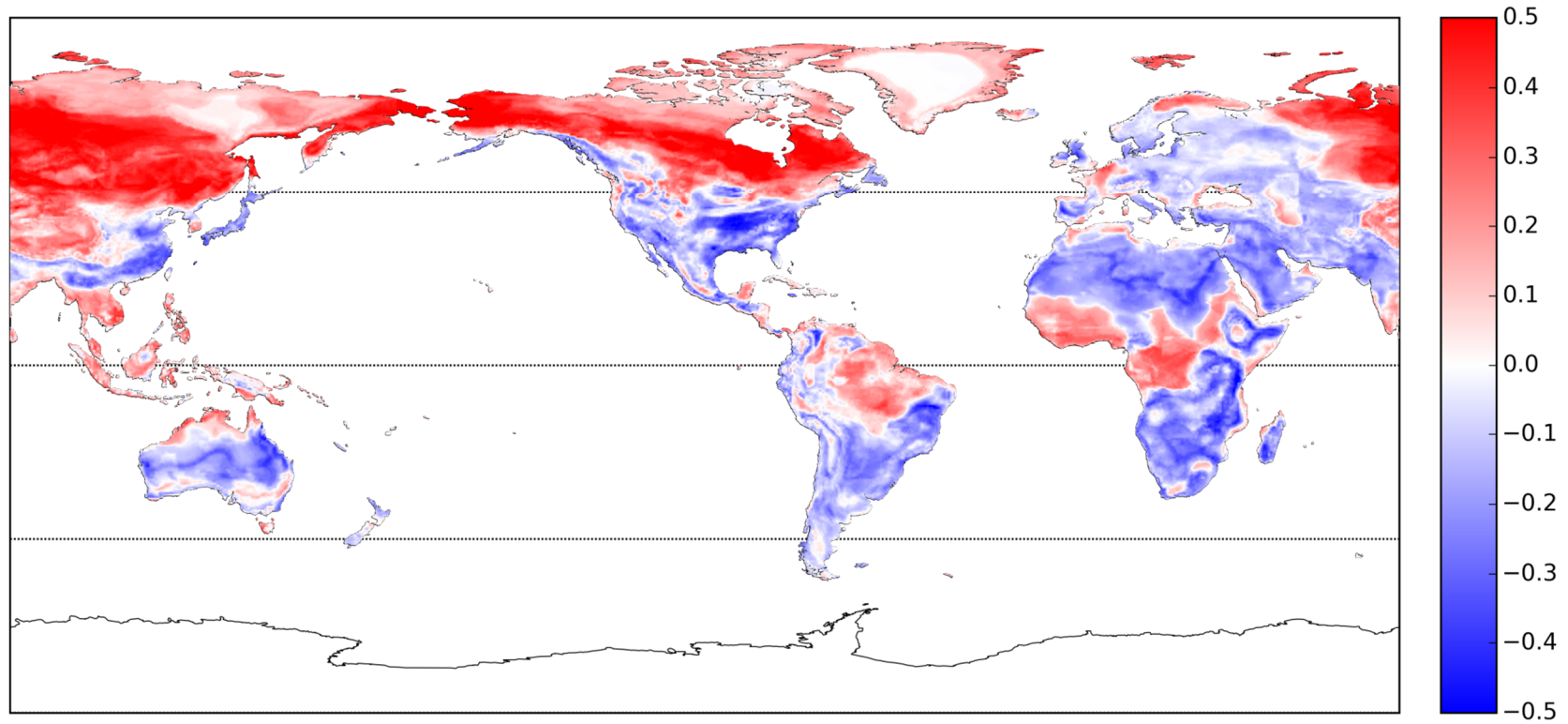
Figure 4.15 Predicted change in occurrence probability of chytrid based on conditions forecasted for 2100 in the RCP 8.5 scenario. Map based on non-region specific model.

Figure 4.16 Predicted change in occurrence probability of chytrid based on conditions forecasted for 2100 in the RCP 2.6 scenario. Map generated by region-specific model.

Figure 4.17 Predicted change in occurrence probability of chytrid based on conditions forecasted for 2100 in the RCP 6.0 scenario. Map generated by region-specific model.
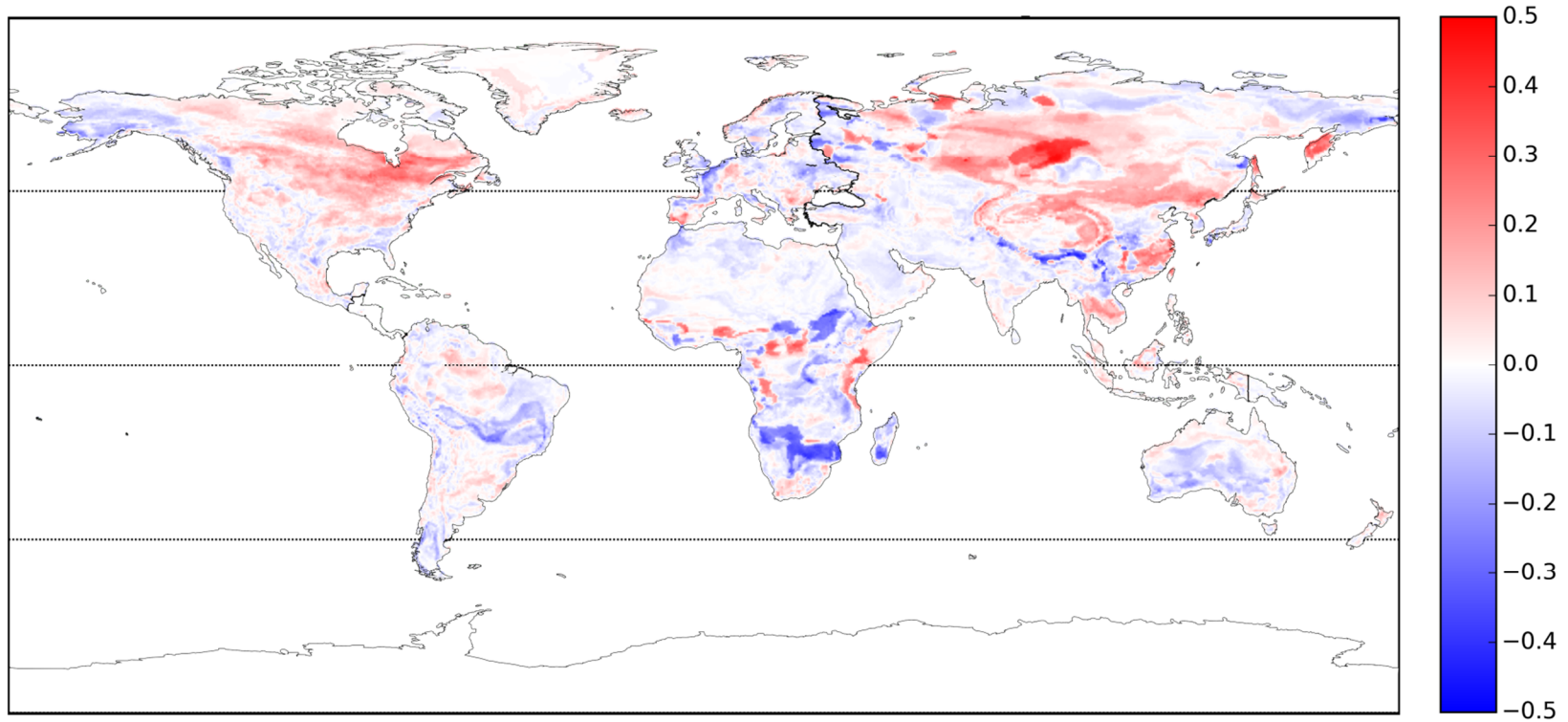
Figure 4.18 Predicted change in occurrence probability of chytrid based on conditions forecasted for 2100 in the RCP 8.5 scenario. Map generated by region-specific model.
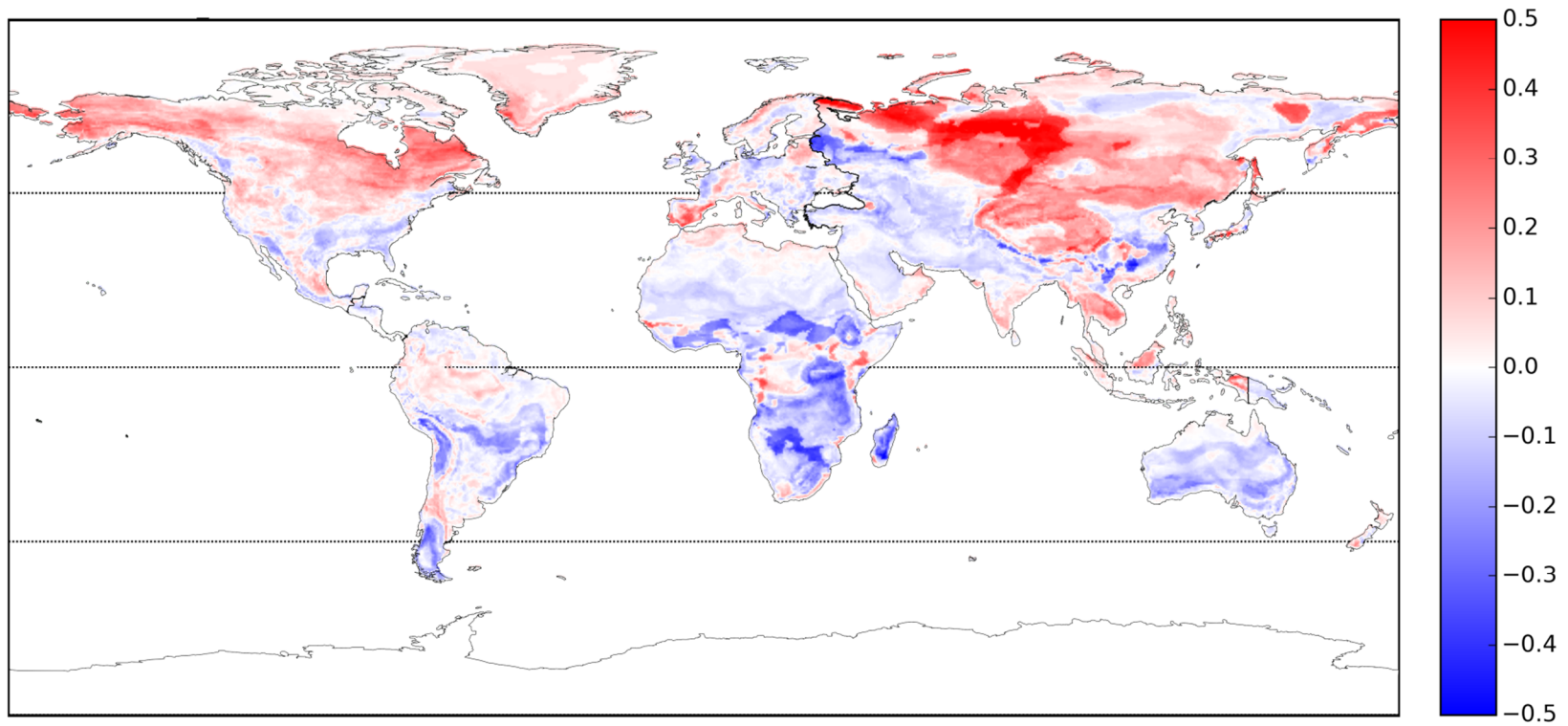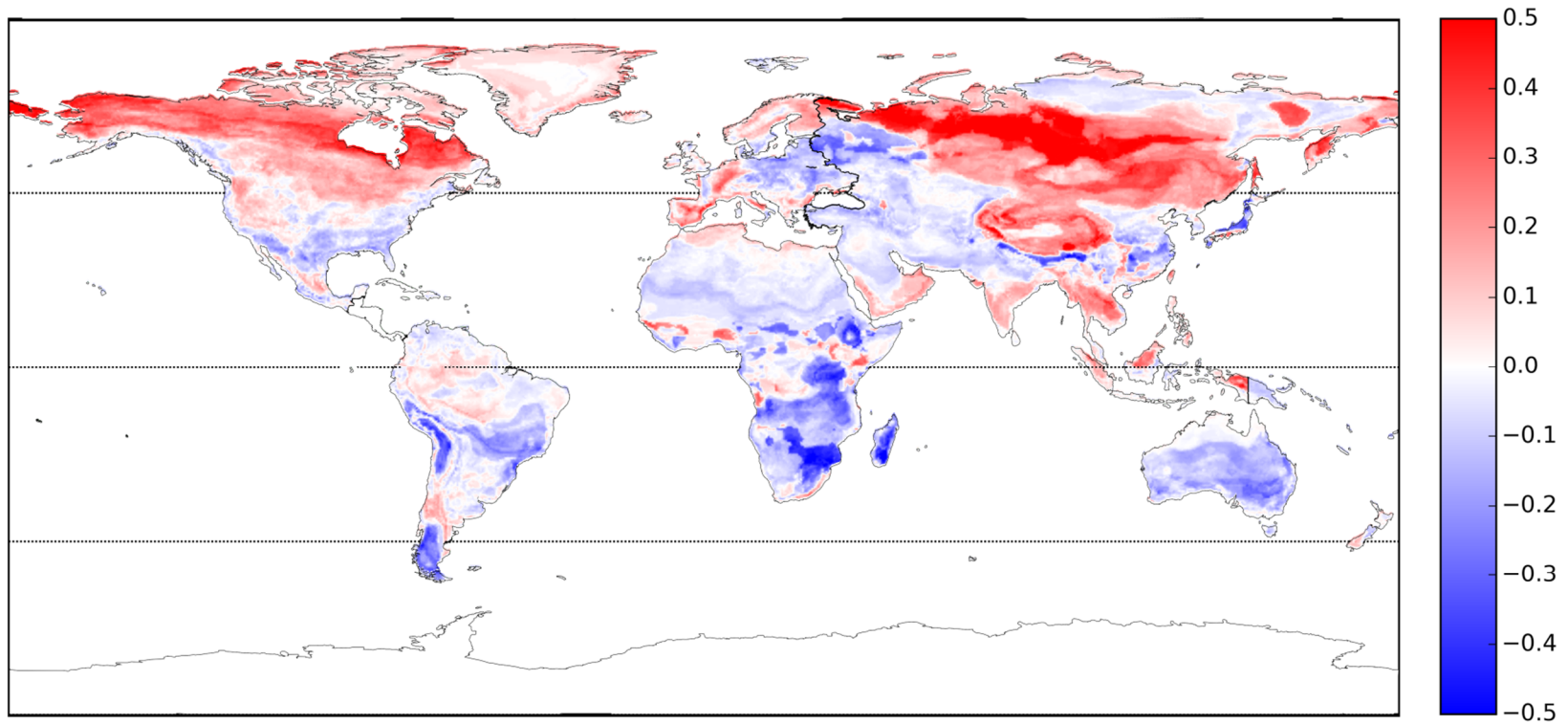
Chapter 5

Conclusions

Chytrid has been associated with amphibian population declines around the world (Skerratt et al. 2007, Olson et al. 2013). This emergence is likely both the result of spread into naïve host populations and environmental changes that alter host-microbe interactions (Rosenblum et al. 2013). My dissertation explores two aspects of the emergence of the chytrid fungus *Batrachochytrium dendrobatidis*: spatial spread at the metapopulation level and climate induction.

Amphibians are frequently found in naturally or artificially fragmented habitats, with many species displaying non-equilibrium local dynamics (Alford and Richards 1999, Becker et al. 2007). As a result, field conservation is often designed within metapopulation paradigm and emphasizes dispersal processes (Semlitsch et al. 2008). To integrate disease management into existing conservation frameworks, it is necessary to consider how disease spreads in a fragmented landscape, as well as how its presence affects the relationship between metapopulation and host dispersal. In the 2nd chapter of my dissertation, I review the existing literature on dispersal-metapopulation persistence relationships and question the overly simplifying assumptions of some existing models. These works yield the general conclusion that increased dispersal is seldom detrimental to metapopulation persistence. I find this to be in disagreement with the general metapopulation literature, which indicate high rates of dispersal would synchronize populations and increase extinction risk. I use a stochastic model with cyclic local dynamics induced by a source of external infections to show that synchrony via host dispersal does indeed increase metapopulation extinction risk. Only when external infection rates are high enough do we observe a monotonically increasing relationship between metapopulation persistence and dispersal. However, under such high external infection rates, population sizes are small and metapopulation persistence time is low. Therefore, in the case of high background infection rates, it might be more efficient to target conservation actions at the local level rather than the metapopulation level. This indicates that benefits from dispersal do not always outweigh its risks of regional synchrony. My 2nd chapter demonstrates the importance of local dynamics and need for more complex models even in theoretical generalizations.

For application of simulation models to realistic conversation contexts, parameter-rich models tailored to individual species must be employed. Any metapopulation disease model would necessitate some implicit or explicit representation of dispersal between populations. However, in many systems species dispersal data is lacking or missing. This is especially the case for amphibians, which are often assumed to have limited dispersal capabilities. In the 3rd chapter of my dissertation, I use a spatially-explicit individual-based model to explore the effects of disease spread in an amphibian metapopulation and the sensitivity of disease forecasts to dispersal information. My results demonstrate that disease forecasts, in particular disease arrival times, are sensitive to dispersal assumptions. This suggests the need for more investment in rigorous dispersal-related research. Similarly to my 2nd chapter, I include an external source of infection in the model in the form of environmentally persistent chytrid zoospores. Again, I find that increasing the upper bounds of dispersal distances does not promote metapopulation persistence. In this case, as zoospores are persistent in the environment, spread of disease into a population acts similar to "pollution" of the habitat, making it unsuitable for recolonization. Local extinction rates are sufficiently high that only population in disease refuges may persist, and disease does not reach an endemic state within the metapopulation. My results suggest that the utility of the metapopulation paradigm may be limited as applied to the amphibian-chytrid system. More importantly, present management schemes that typically target facilitating dispersal may need to adopt a more local perspective if chytrid spread into the region is anticipated.

Given the severe consequences of chytrid introductions into susceptible amphibian populations and paucity in amphibian dispersal information paucity creating uncertainties in forecasting disease spread, it is necessary to pre-identify environmentally-suitable areas receptive to chytrid invasion and establishment. Chytrid exhibits strong dependencies on temperature and moisture variables in both laboratory and field settings. Therefore, pre-identification of regions with high environmental suitability to chytrid must consider climate effects. For long-term planning, this also requires consideration of possible climate change. The impact of climate change has already been felt by many species, as evidenced by species from various taxa experiencing latitudinal and altitudinal shifts (Parmesan and Yohe 2003). *In vitro,* chytrid prefers cool, moist conditions (Piotrowski et al. 2004). However, debates exist on how environmental suitability to

chytrid is expected to change as a response to climate change. Based on the most comprehensive chytrid sampling records up-to-date, we train machine learning algorithm based on combined worldwide data and data specific to particular geographic regions. Our models indicate that the range of the chytrid fungus is expected to shift north and onto higher elevations, which is a prediction similar to that of other species preferring cool temperatures. While our model prediction performance in our model is excellent based on current sampling sites, we find differences in region-specific and non-specific models. This indicates that chytrid-climate relationships may differ depending on location. However, consistent between all models is an overall increase in chytrid occurrence probabilities in the higher latitudes of the Northern Hemisphere. Due to the correlative nature of species distribution models in general, we caution against interpreting the predictive performance of our model presented here and species distribution models in general as a causal link between climate and chytrid presence at a location. We also suggest that since sampling of chytrid is predominantly conducted on amphibian hosts, models built on such data may in fact be under-predicting chytrid presence.

Global biodiversity faces unprecedented challenges today, with habitat fragmentation and emerging infectious diseases as prominent threat factors. My dissertation illustrates that the complexity of the relationship between host dispersal, disease spread and metapopulation persistence. It also underscores the need for more rigorous research on dispersal patterns and pathogen-climate relationships outside of the laboratory setting in order to forecast disease emergence and plan conservation measures preventatively.

Bibliography

Abbott KC. 2011. A dispersal-induced paradox: synchrony and stability in stochastic metapopulations. Ecology Letters 14: 1158–1169.

Abta R, M Schiffer and NM Shnerb. 2007. Amplitude-dependent frequency, desynchronization, and stabilization in noisy metapopulation dynamics. Physical Review Letters 98:098104.

Akçakaya HR, Mills G and CP Doncaster. 2007. The role of metapopulations in conservation. Pages 64-84 in Key Topics in Conservation Biology. D.W. Macdonald and K. Service, editors. Blackwell Publishing.

Alford RA, Bradfield KS and SJ Richards. 2007. Ecology: global warming and amphibian losses. Nature 447:E3–E4.

Alford RA and SJ Richards. 1999. Global amphibian declines: A problem in applied ecology. Annual Review of Ecology and Systematics 30: 133-165.

Allan BF, Keesing F and RS Ostfeld. 2003. Effect of Forest Fragmentation on Lyme Disease Risk. Conservation Biology 17: 267–272.

Allen JC. 1975. Mathematical models of species interactions in time and space. American Naturalist. 109:319–342.

Almberg ES, Cross PC and DW Smith. 2010. Persistence of canine distemper virus in the Greater Yellowstone Ecosystem's carnivore community. Ecological Application 20:2058–2074.

Anderson RM, Jackson HC, May RM and AM Smith. 1981. Population dynamics of fox rabies in Europe. Nature 289: 765 – 771.

Anderson SC, Cooper AB and NK Dulvy. 2013. Ecological prophets: quantifying metapopulation portfolio effects. Methods in Ecology and Evolution 4(10): 971–981.

Andre SE, Parker J, and CJ Briggs. 2008. Effect of temperature on host response to *Batrachochytrium dendrobatidis* infection in the mountain yellow-legged frog (*Rana muscosa*). Journal of Wildlide Diseases 44: 716–720.

Andreasen V and FB Christiansen. 1989. Persistence of an infectious disease in a subdivided population. Mathematical Biosciences 96: 239-253.

Andrewartha HG and LC Birch. 1954. The Distribution and Abundance of Animals. The University of Chicago Press, Chicago, Illinois.

Artzy-Randrup Y and L Stone. 2010. Connectivity, Cycles, and Persistence Thresholds in Metapopulation Networks. PLoS Computational Biology 6(8): e1000876.

Baguette M and N Schtickzelle. 2003. Local population dynamics are important to the conservation of metapopulations in highly fragmented landscapes. Journal of Applied Ecology 40: 404–412.

Baguette M and G Mennechez. 2004. Resource and habitat patches, landscape ecology and metapopulation biology: a consensual viewpoint. Oikos 106: 399–403.

Bancroft B, Han BA, Searle CL, Biga LM, Olson DH, Kats LB, Lawler JJ and AR Blaustein. 2011. Species-level correlates of susceptibility to the pathogenic amphibian fungus *Batrachochytrium dendrobatidis* in the United States. Biodiversity and Conservation 20: 1911-1920.

Banks SC and R Peakall. 2012. Genetic spatial autocorrelation can readily detect sex-biased dispersal. Molecular Ecology 21: 2092–2105.

Bauer DM, Paton PWC and KS Stephen. 2010. Are Wetland Regulations Cost Effective for Species Protection? A Case Study of Amphibian Metapopulations. Ecological Applications 20: 798-815.

Becker CG, Fonseca CB, Haddad CFB, Batista RF and Prado PI. 2007. Habitat split and the global decline of amphibians. Science 318:1775–1777.

Becker MH, Harris RN, Minbiole KPC, Schwantes CR, Rollins-Smith LA, Reinert LK, Brucker RM, Domangue RJ and B Gratwicke. 2011. Towards a better understanding of the use of probiotics for preventing chytridiomycosis in Panamanian golden frogs. EcoHealth, 8, 501-506

Beniston M and DG Fox. 1996. Chapter 5. Impacts of Climate Change on Mountain Regions, pp. 191-213. IPCC.

Berger L, Speare R, Hines HB, Marantelli G, Hyatt AD, McDonald KR, Skerratt LF, Volsen V, JM Clarke, G Gillespie, M Mahony, N Sheppard, C Williams and MJ Tyler. 2008. Effect of season and temperature on mortality in amphibians due to chytridiomycosis. Australian Veterinary Journal 82: 434-439.

Berger L, Hyatt AD, Speare R and JE Longcore. 2005. Life cycle stages of the amphibian chytrid *Batrachochytrium dendrobatidis*. Diseases of Aquatic Organisms 68: 51-63.

Berger L, Speare R, Daszak P, Green DE, Cunningham AA and CL Goggin. 1998. Chytridiomycosis causes amphibian mortality associated with population declines in the rain forests of Australia and Central America. Proceedings of the National Academy of Sciences of the United States of America 95: 9031-9036.

Berven KA and TA Grudzien. 1990. Dispersal in the wood frog (*Rana sylvatica*): implications for genetic population structure. Evolution 44:2047-56

Bjørnstad ON and BT Grenfell. 2008. Hazards, spatial transmission and timing of outbreaks in epidemic metapopulations. Environmental and Ecological Statistics 15:265–277.

Bjornstad ON, Ims RA and X Lambin. 1999. Spatial population dynamics: analyzing patterns and processes of population synchrony. Trends in Ecology and Evolution 14: 427–432.

Blaustein AR, Romansic JM, Scheessele EA, Han BA, Pessier AP and JE Longcore. 2005. Interspecific variation in susceptibility of frog tadpoles to the pathogenic fungus *Batrachochytrium dendrobatidis*. Conservation Biology 19:1460–1468.

Blaustein AR and JM Kiesecker. 2002. Complexity in conservation: lessons from the global decline of amphibian populations. Ecology Letters 5: 597-608.

Blaustein AR, Han BA, Relyea RA, Johnson PTJ, Buck JC, Gervasi SS and LB Kats. 2011. The complexity of amphibian population declines: understanding the role of cofactors in driving amphibian losses. Annals of the New York Academy of Sciences 1223: 108-119.

Blaustein AR, Wake DB and WP Sousa. 1994. Amphibian declines: judging stability, persistence, and susceptibility of populations to local and global extinctions. Conservation Biology 8:60-71.

Blaustein AR, Hokit DG, O'Hara RK and RA Holt. 1994. Pathogenic fungus contributes to amphibian losses in the Pacific Northwest. Biological Conservation 67: 251-254.

Bletz MC, Loudon AH, Becker MH, Bell SC, Woodhams DC, Minbiole KPC and Harris RN. 2013. Mitigating amphibian chytridiomycosis with bioaugmentation: characteristics of effective probiotics and strategies for their selection and use. Ecology Letters 16(6): 807–820.

Bonte D, Van Dyck H, Bullock JM, Coulon A, Delgado M, et al. 2012. Costs of dispersal. Biological Reviews 87: 290–312.

Bosch J and I Martinez-Solano. 2006. Chytrid fungus infection related to unusual mortalities of *Salamandra salamandra* and *Bufo bufo* in the Penalara Natural Park, Spain. Oryx 40: 84-89.

Bosch J, Carrascal LM, Duran L, Walker S and MC Fisher. 2007. Climate change and outbreaks of amphibian chytridiomycosis in a montane area of Central Spain; is there a link? Proceedings of the Royal Society London B 274: 253–260.

Bosch J, I Martinez-Solano and M Garcia-Paris. 2001. Evidence of a chytrid fungus infection involved in the decline of the common midwife toad (*Alytes obstetricans*) in protected areas of central Spain. Biological Conservation 97: 331-337.

Bowler DE and TG Benton. 2005. Causes and consequences of animal dispersal strategies: relating individual behaviour to spatial dynamics. Biological Reviews 80: 205–225.

Bradford DF. 1989. Allotopic distributions of native frogs and introduced fishes in high Sierra Nevada lakes of California: implications of the negative effect of fish introductions. Copeia 1989: 775-78

Bradford DF. 1991. Mass mortality and extinction in a high elevation population of *Rana muscosa*. Journal of Herpetology 25: 369-377.

Breckenridge WJ and JR Tester. 1961. Growth, local movements and hibernation of the Manitoba toad, *Bufo hemiophyrys*. Ecology 42: 637-46.

Briggs CJ and M Hoppes. 2004. Stabilizing effects in spatial parasitoid–host and predator–prey models: a review. Theoretical Population Biology 65: 299–315.

Briggs CJ, Knapp RA and VT Vredenburg. 2010. Enzootic and epizootic dynamics of the chytrid fungal pathogen of amphibians. Proceedings of the national academy of science 107: 9695–9700.

Broquet T and EJ Petit. 2009. Molecular Estimation of Dispersal for Ecology and Population Genetics. Annual Review of Ecology, Evolution, and Systematics 40: 193–216.

Buckley D, Arano B, Herrero P and G Lorente. 1996. Population structure of Moroccan water frogs: genetic cohesion despite a fragmented distribution. Journal of Zoological Systematics and Evolutionary Research 34: 173-79.

Buonaccorsi JP, Elkinton JS, Evans SR and A Liebhold. 2001. Measuring and testing for spatial synchrony. Ecology 82:1668–1679.

Camilo M, Frazier AG, Longman RJ, Dacks RS, Walton MM, Tong EJ, Sanchez JJ, Kaiser LR, Stender YO, Anderson JM, Ambrosino CM, Fernandez-Silva I, Giuseffi LM and TW Giambelluca. 2013. The projected timing of climate departure from recent variability. Nature 502: 183–187.

Carey C, Bruzgul JE, Livo LJ, Walling ML, Kuehl KA, Dixon BF, Pessier AP, Alford RA and KB Rogers. 2006. Experimental Exposures of Boreal Toads (*Bufo Boreas*) to a Pathogenic Chytrid Fungus (*Batrachochytrium dendrobatidis*). EcoHealth 3: 5–21.

Carey C. 1993. A Hypothesis concerning the causes of the disappearance of boreal toads from the mountains of Colorado. Conservation Biology 7: 355-362.

Carlson SM and WH Satterthwaite. 2011. Weakened portfolio effect in a collapsed salmon population complex. Canadian Journal of Fisheries and Aquatic Sciences 68: 1579-1589.

Casagrandi R and MJ Gatto. 2006. The intermediate dispersal principle in spatially explicit metapopulations. Theoretical Biology 239(1): 22-32.

Cavanagh RD, Lambin X, Ergon T, Bennett M, Graham IM, van Soolingen D and M Begon. 2004. Disease dynamics in cyclic populations of field voles (*Microtus agrestis*): cowpox virus and vole tuberculosis (*Mycobacterium microti)*. Proceedings of the Royal Society of London B 271:859–867.

Ceballos G, Vale MM, Bonacic C, Calvo-Alvarado J, List R, et al. 2009. Conservation Challenges for the Austral and Neotropical America Section. Conservation Biology 23: 811–817.

Cheng TL, Rovito SM, Wake DB and VT Vredenburg. 2011. Coincident mass extirpation of neotropical amphibians with the emergence of the infectious fungal pathogen *Batrachochytrium dendrobatidis*. Proceedings of the National Academy of Sciences USA 108(23):9502-7.

Chestnut T, Anderson C, Popa R, Blaustein AR, Voytek M, et al. 2014. Heterogeneous Occupancy and Density Estimates of the Pathogenic Fungus *Batrachochytrium dendrobatidis* in Waters of North America. PLoS ONE 9(9): e106790. doi:10.1371/journal.pone.0106790

Chinchar VG. 2002. *Ranaviruses* (family Iridoviridae): emerging cold-blooded killers. Archeological Virology. 147: 447-470.

Chivian E. and A Bernstein (eds.) 2008. Sustaining life: How human health depends on biodiversity. Center for Health and the Global Environment. Oxford University Press, New York.

Clark JA and RM May. 2002. Taxonomic bias in conservation research. Science 297: 191–192.

Coffee M, Lurie MN and GP Garnett. 2007. Epidemiology and Social Modelling the impact of migration on the HIV epidemic in South Africa. AIDS 21: 343–350.

Colizza V, Barrat A, Barthélemy M and A Vespignani. 2006. The role of the airline transportation network in the prediction and predictability of global epidemics. Proceedings of the National Academy of Science USA 103: 2015–2020.

Collins JP and A Storfer. 2003. Global amphibian declines: Sorting the hypotheses. Diversity and Distributions 9: 89-98.

Comins JN, Hassell MP and RM May. 1992. The spatial dynamics of host–parasitoid systems. Journal of Animal Ecology 61: 735–748.

Conradie W, Weldon C, Smith KG and HH Du Preez. 2011. Seasonal pattern of chytridiomycosis in common river frog (*Amietia angolensis*) tadpoles in the South African Grassland Biome. African Zoology 46(1): 95-102.

Conroy SDS and BW Brook. 2003. Demographic sensitivity and persistence of the threatened white- and orange-bellied frogs of Western Australia. Population Ecology 45: 105–114.

Corn PS and JC Fogleman. 1984. Extinction of montane populations of the Northern Leopard Frog (*Rana pipiens*) in Colorado. Journal of Herpetolology 18:147-52.

Corn PS and RB Bury. 1989. Logging in western Oregon: responses of headwater habitats and stream amphibians. Forest Ecology Management 29:39-57.

Crawford AJ, Lips KR and E Bermingham. 2010. Epidemic disease decimates amphibian abundance, species diversity, and evolutionary history in the highlands of central Panama. Proceedings of the National Academy of Science USA 107: 13777-13782.

Daniels PW, Halpin K, Hyatt A and D Middleton. 2007. Infection and disease in reservoir and spillover hosts: determinants of pathogen emergence. Current Topics in Microbiological Immunology 315:113-31.

Daszak P, Cunningham AA and AD Hyatt. 2003. Infectious disease and amphibian population declines. Diversity and Distributions 9: 141-150.

Daszak P, Strieby A, Cunningham AA, Longcore JE, Brown CC and D Porter. 2004. Experimental evidence that the bullfrog (*Rana catesbeiana*) is a potential carrier of chytridiomycosis, an emerging fungal disease of amphibians. Herpetological Journal 14: 201-207.

Daszak P, Cunningham AA and AD Hyatt. 2000. Emerging infectious diseases of wildlife: threats to biodiversity and human health. Science 287: 443-449

Daszak P, Berger L, Cunningham AA, Hyatt AD, Green E and R Speare. 1999. Emerging infectious diseases and amphibian population declines. Emerging Infectious Diseases 5: 735-748.

Di Rosa I, Simoncelli F, Fagotti A and R Pascolini. 2007. Ecology: the proximate cause of frog declines? Nature 447: E4-R5.

Donald PF and AD Evans. 2006, Habitat connectivity and matrix restoration: the wider implications of agri-environment schemes. Journal of Applied Ecology 43(2): 209–218.

Driscoll DA, Banks SC, Barton PS, Ikin K, Lentini P, et al. 2014. The Trajectory of Dispersal Research in Conservation Biology. Systematic Review. PLoS ONE 9(4): e95053.

Driscoll DA, Lindenmayer DB, Bennett AF, Bode M, Bradstock RA, et al. 2010. Resolving conflicts in fire management using decision theory: asset protection versus biodiversity conservation. Conservation Letters 3: 215–223.

Duellman WE, Trueb L. 1986. Biology of Amphibians. New York: McGraw-Hill. 670 pp.

Durrett R and SA Levin. 1994. The importance of being discrete (and spatial). Theoretical Population Biology 46:363–394.

Earn D, Levin SA and P Rohani. 2000. Coherence and conservation. Science 290: 1360–1364.

Edwards HJ, Elliott IA, Pressey RL and PJ Mumby. 2010. Incorporating ontogenetic dispersal, ecological processes and conservation zoning into reserve design. Biological Conservation 143: 457–470.

Farrer RA, Weinert LA, Bielby J, Garner TWJ, Balloux F, Clare F, Bosch J, Cunningham AA, Welcon C, duPreez LH, Anderson L, Kosakovsky SL, Shahar-Golan R, Henk D and MC Fisher. 2011. Multiple emergences of genetically diverse amphibian-infecting chytrids include a globally hypervirulent recombinant lineage. Proceedings of the National Academy of Sciences USA 108: 18732-18736.

Fellers GM, Green DE and JE Longcore. 2001. Oral chytridiomycosis in the mountain yellow-legged frog (*Rana muscosa*). Copeia 2001: 945-953.

Fisher MP and TW Garner. 2007. The relationship between the introduction of *Batrachochytrium dendrobatidis*, the international trade in amphibians and introduced amphibian species. Fungal Biology Review 21: 2–9.

Fisher MC, Garner TWJ and SF Walker. 2009. Global emergence of *Batrachochytrium dendrobatidis* and amphibian chytridiomycosis in space, time and host. Annual Review of Microbiology 63: 291-310.

Fortuna MA, Gomez-Rodriguez C and J Bascompte. 2006. Spatial network structure and amphibian persistence in stochastic environments. Proceedings of the Royal Society B 206:1429–1434.

Gahl MK, Longcore JE and JE Houlahan. 2011. Varying responses of Northeastern North American amphibians to the chytrid pathogen *Batrachochytrium dendrobatidis*. Conservation Biology 26, 135-141.

Gamble LR, McGarigal K and BW Compton. 2007. Fidelity and dispersal in the pond-breeding amphibian, *Ambystoma opacum*: Implications for spatio-temporal population dynamics and conservation. Biological Conservation 139:247-257.

Gao LQ and HW Hethcote. 1992. Disease transmission models with density dependent demographics. Journal of Mathematical Biology 30: 717-731.

Garner TWJ, MW Perkins, P Govindarajulu, D Seglie, S Walker, AA Cunningham and MC Fisher. 2006. The emerging amphibian pathogen *Batrachochytrium dendrobatidis* globally infects introduced populations of the North American bullfrog, Rana catesbeiana. Biology Letters 2: 455-459.

Garner TWJ, Walker S, Bosch J, Leech S, Rowcliffe JM, Cunningham AA and MC Fisher. 2009. Life history tradeoffs influence mortality associated with the amphibian pathogen *Batrachochytrium dendrobatidis*. OIKOS 118: 783-791.

Gervasi SS, Gondhalekar C, Olson DH and AR Blaustein. 2013. Host identity matters in the amphibian-*Batrachochytrium dendrobatidis* system: fine-scale patterns of variation in responses to a multi-host pathogen. PLoS ONE 8: e54490.

Gill DE. 1978. The metapopulation ecology of the red-spotted newt, *Notophthalmus viridescens (Rafinesque)*. Ecological Monograph 48: 145-66.

Gillespie DT. 1976. A general method for numerically simulating the stochastic time evolution of coupled chemical reactions. Journal of Computational Physics 22:403–434.

Gog J, Woodroffe R and J Swinton. 2002. Disease in endangered metapopulations: the importance of alternative hosts. Proceedings of the Royal Society B 269:671–676.

Goka K, Yokoyama J, Une Y, Kuroki T, Suzuki K, Nakahara M, Kobayashi A, Inaba S, Mizutani T, and AD Hyatt. 2009. Amphibian chytridiomycosis in Japan: distribution, haplotypes, and possible route of entry into Japan. Molecular Ecology 18: 4757-4774.

Green DE, KA Converse and AK Schrader. 2006. Epizootiology of sixty-four amphibian morbidity and mortality events in the USA, 1996-2001. Annals of the New York Academy of Sciences 969: 323-339.

Greenspan SE, JE Longcore and AJK Calhoun. 2012. Host invasion by *Batrachochytrium dencrobatidis*: fungal and epidermal ultrastructure in model anurans. Diseases of Aquatic Organisms 100: 201-210.

Griffiths RA, Sewell D and RS McCrea. 2010. Dynamics of a declining amphibian metapopulation: Survival, dispersal and the impact of climate. Biological Conservation 143: 485–491.

Griffiths RA. 2004. Great crested newts (*Triturus cristatus*) in Europe: effects of metapopulation structure and juvenile dispersal on population persistence. Pages 312–324 in H. R. Akçakaya, M. A. Burgman, O. Kindvall, C. C. Wood, P. Sjögren-Gulve, J. S. Hatfield, and M. A. McCarthy, editors. Species conservation and management: case studies. Oxford University Press, Oxford.

Gyllenberg M, Soderbacka G and S Ericsson. 1993. Does migration stabilize local-population dynamics – analysis of a discrete metapopulation model. Mathematical Biosciences 118: 25–49.

Hadley AS and MG Betts. 2012. The effects of landscape fragmentation on pollination dynamics: absence of evidence not evidence of absence. Biological Reviews 87: 526–544.

Haensch S, Bianucci R, Signoli M, Rajerison M, Schultz M, Kacki S, Vermunt M, Weston DA, Hurst D, Achtman M, Carniel E and B Bramanti. 2010. Distinct Clones of Yersinia pestis Caused the Black Death. PLoS Pathogens 6 (10): e1001134.

Hagenaars TJ, Donnelly CA and NM Ferguson. 2004. Spatial heterogeneity and the persistence of infectious diseases. Journal of Theoretical Biology 229: 349–359.

Hanski I and M Gilpin. 1991. Metapopulation dynamics: brief history and conceptual domain. Biological Journal of the Linnean Society 42:3–16.

Hanski I. 1999. Metapopulation Ecology, Oxford University Press.

Hanski I and ME Gilpin. 1997. Metapopulation biology: ecology, genetics and evolution. Academic Press; San Diego, California, USA.

Hanski I and D Simberloff. 1997. The metapopulation approach, its history, conceptual domain, and application to conservation. pp. 5–26. In IA Hanski and ME Gilpin (eds.), Metapopulation Biology. Academic Press, San Diego, Californina.

Hanski I. 1991. Single-species metapopulation dynamics: concepts, models and observations. In: Metapopulation Dynamics: Empirical and Theoretical Investigations. (ed. Gilpin, M. and Hanski, I.). Harcourt Brace Jovanovich, London, pp. 17–38.

Harding KC and JM McNamara. 2002. A unifying framework for metapopulation dynamics. American Naturalist 160: 173–185.

Harris RN, Brucker RM, Walke JB, Becker MH, Schwantes CR, Flaherty DC, Lam BA, Woodhams DC, Briggs CJ, Vredenburg VT and KPC Minbiole. 2009. Skin microbes on frogs prevent morbidity and mortality caused by a lethal skin fungus. The ISME Journal 3: 818-824.

Harris RN, Lauer A, Simon MA, Banning JL and RA Alford. 2009. Addition of antifungal skin bacteria to salamanders ameliorates the effects of chytridiomycosis. Diseases of Aquatic Organisms 83: 11–16.

Harvell CD, Mitchell CE, Ward JR, Altizer S, Dobson AP, Ostfeld RS and MD Samuel. 2002. Climate warming and disease risks for terrestrial and marine biota. Science 296: 2158–2162.

Harwood J and A Hall. 1990. Mass mortality in marine mammals: its implications for population dynamics and genetics. Trends in Ecology and Evolution 5:254-257.

Hassell MP, Comins HN and RM May. 1991. Spatial structure and chaos in insect population dynamics, Nature 363: 252-258.

Hastings A. 1993. Complex interactions between dispersal and dynamics – lessons from coupled logistic equations. Ecology 74: 1362–1372.

Hatfield JS, Price AH, Diamond DD and CD True. 2004. Houston toad (*Bufo houstonensis*) in Bastrop County, Texas: the need for protecting multiple subpopulations. Pages 292–297 in H. R. Akçakaya, M. A. Burgman, O. Kindvall, C. C. Wood, P. Sjögren-Gulve, J. S. Hatfield, and M. A. McCarthy, editors. Species conservation and management: case studies. Oxford University Press, Oxford.

Hayes TB 2010. The cause of global amphibian declines: a developmental endocrinologist's perspective. Journal of Experimental Biology 213, 921-933.

Heard GW, Scroggie MP and BS Malone. 2012. Classical metapopulation theory as a useful paradigm for the conservation of an endangered amphibian. Biological Conservation 148: 156-166.

Heino M, Kaitala V, Ranta E and J Lindstrom. 1997. Synchronous dynamics and rates of extinction in spatially structured populations. Proceedings of the Royal Society B: Biological Sciences 264: 481–486.

Hels T and G Nachman. 2002. Simulating viability of a spadefoot toad *Pelobates fuscus* metapopulation in a landscape fragmented by a road. Ecography 25: 730–744.

Hess G. 1996. Disease in metapopulations: implications for conservation. Ecology 77: 1617-1632.

Hilty J, Lidicker W, Merenlender A and AP Dobson. 2006. Corridor Ecology: The Science and Practice of Linking Landscapes for Biodiversity Conservation. Island Press, San Diego.

Holyoak M, Casagrandi R, Nathan R, Revilla E and O Spiegel. 2008. Trends and missing parts in the study of movement ecology. Proceedings of the National Academy of Sciences of the United States of America 105: 19060–19065.

Hudson PJ, Dobson AP and D Newborn. 1998. Prevention of population cycles by parasite removal. Science 282: 2256–2258.

Ims RA and H Steen. 1990. Geographical synchrony in microtine population-cycles – a theoretical evaluation of the role of nomadic avian predators. Oikos 57: 381–387.

James TY, Litvintseva AP, Vilgalys R, Morgan JAT, Taylor JW, Fisher MC, Berger L, Weldon C, du Preez L and JE Longcore. 2009. Rapid global expansion of the fungal disease chytridiomycosis into declining and healthy amphibian populations. PLoS Pathogens 5(5): e1000458.

Jansen VAA. 2001. The dynamics of two diffusively coupled predator–prey populations. Theoretical Population Biology 59: 119–131.

Jaquiery J, Broquet T, Hirzel AH, Yearsley J and N Perrin. 2011. Inferring landscape effects on dispersal from genetic distances: how far can we go? Molecular Ecology 20: 692–705.

Jesse M, Ezanno P, Davis S, and JAP Heesterbeek. 2008. M. A fully coupled, mechanistic model for infectious disease dynamics in a metapopulation: movement and epidemic duration. Journal of Theoretical Biology 254: 331–338.

Johnson ML and R Speare. 2003. Survival of *Batrachochytrium dendrobatidis* in water: quarantine and disease control implications. Emerging Infectious Diseases 9: 922-925.

Johnson ML and R Speare. 2005. Possible modes of dissemination of the amphibian chytrid *Batrachochytrium dendrobatidis* in the environment. Diseases of aquatic organisms 65: 181-186.

Johnson PTJ, Lunde KB, Ritchie EG and AE Launer. 1999. The effect of trematode infection on amphibian limb development and survivorship. Science 284: 802-804.

Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL and P Daszak. 2008. Global trends in emerging infectious diseases. Nature 451: 990-993.

Jousimo J, AJM Tack, O Ovaskainen, T Mononen, H Susi, C Tollenaere and AL Laine. 2014. Ecological and evolutionary effects of fragmentation on infectious disease dynamics. Science 344 (6189): 1289-1293.

Kaiser K and J Pollinger. 2012. *Batrachochytrium dendrobatidis* shows high genetic diversity and ecological niche specificity among haplotypes in the Maya mountains of Belize. PLoS ONE 7, e32113.

Keeling MJ and CA Gilligan. 2000. Metapopulation dynamics of bubonic plague. Nature 407: 903-5.

Keeling MJ and CA Gilligan. 2000. Bubonic plague: a metapopulation model of a zoonosis. Proceedings of the Biological Society 267(1458): 2219–2230.

Kiesecker JM, Blaustein AR and LK Belden. 2001. Complex causes of amphibian population declines. Nature 410: 681-684.

Kiesecker JM, Belden LK, Shea K and MJ Rubbo. 2004. Amphibian decline and emerging disease. American Scientist 92: 138-147.

Kilpatrick AM, Briggs CJ and P Daszak. 2010. The ecology and impact of chytridiomycosis: an emerging disease of amphibians. Trends in Ecology and Evolution 25, 109–118.

Kingsford RT, Watson JEM, Lundquist CJ, Venter O, Hughes L, et al. 2009. Major conservation policy issues for biodiversity in Oceania. Conservation Biology 23: 834–840.

Knapp RA, Matthews KR, Preisler HK and R Jellison. 2003. Developing probabilistic models to predict amphibian site occupancy in a patchy landscape. Ecological Applications 13:1069–1082.

Knapp RA. 1996. Non-native trout in natural lakes of the Sierra Nevada: an analysis of their distribution and impacts on native aquatic biota. Pages 363-407 in Sierra Nevada Ecosystem Project: Final Report to Congress. Volume III: Assessments, Commissioned Reports, and Background Information. Davis: University of California, Centers for Water and Wildland Resources.

Knapp RA and KR Matthews. 2000. Non-native fish introductions and the decline of the mountain yellow-legged frog from within protected areas. Conservation Biology 14:428-438.

Knapp RA, Boiano DM and VT Vredenburg. 2007. Removal of nonnative fish results in population expansion of a declining amphibian (mountain yellow-legged frog, *Rana muscosa*). Biological Conservation 135:11-20.

Koelle K and J Vandermeer. 2005. Dispersal-induced desynchronization: from metapopulations to metacommunities. Ecology Letters 8: 167–175.

Kriger KM and JM Hero. 2007. Large-scale seasonal variation in the prevalence and severity of chytridiomycosis. Journal of Zoology 271:352–359.

Lacy RC, Miller PS, Nyhus PJ, Pollak JP, Raboy BE, et al. 2013. metamodels for transdisciplinary analysis of wildlife population dynamics. PLoS ONE 8(12): e84211. doi:10.1371/journal.pone.0084211

Lafferty KD. 2009. The ecology of climate change and infectious diseases. Ecology 90:888–900

Lannoo M. 2005. Amphibian declines: the conservation status of United States. University of California Press. Berkeley, CA.

Laurance WF. 2008. Global warming and amphibian extinctions in eastern Australia. Australian Ecology 33:339–408.

Laurance WF, McDonald KR and R Speare. 1996. Epidemic disease and the catastrophic decline of Australian rain forest frogs. Conservation Biology 10, 406-413.

Levins R. 1969. Some demographic and genetic consequences of environmental heterogeneity for biological control. Bulletin of the Entomological Society of America 15:237–240.

Levins R. 1970. Extinction. In Some Mathematical Problems in Biology (Gestenhaber, M., ed.), pp. 77–107, American Mathematics Society.

Lindborg, R, and O.Eriksson. 2004. Historical landscape connectivity affects present plant species diversity. Ecology 85:1840–1845.

Lips KR, Diffendorfer J, Mendelson III Jr and MW Sears. 2008. Riding the wave: reconciling the roles of disease and climate change in amphibian declines. PLoS Biol 6:e72.

Lips KR, Brem F, Brenes R, Reeve JD, Alford RA, Voyles J, Carey C, Livo L, Pessier AP and JP Collins. 2006. Emerging infectious disease and the loss of biodiversity in a Neotropical amphibian community. Proceedings of the National Academy of Sciences USA 102: 3165-3170.

Lips KR, Reeve JD and L Witters. 2003. Ecological traits predicting amphibian population declines in Central America. Conservation Biology 17: 1078–1088.

Lips KR. 1998. Decline of a tropical montane fauna. Conservation Biology 12:106-117.

Longcore JE, Pessier AP and DK Nichols. 1999. *Batrachochytrium dendrobatidis* gen. et sp. nov., a chytrid pathogenic to amphibians. Mycologia 91: 219-227.

Lötters S, Kielgast J, Bielby J, Schmidtlein S, Bosch J, Veith M, Walker SF, Fisher MC and D Rödder. 2009. The link between rapid enigmatic amphibian decline and the globally emerging chytrid fungus. EcoHealth 6: 358–372.

Lourenço J and M Recker. 2013. Natural, persistent oscillations in a spatial multi-strain disease system with application to dengue. PLoS Computational Biology 9(10): e1003308. doi:10.1371/journal.pcbi.1003308

Lyons SK, Smith FA, Wagner PJ, White EP, and JH Brown. 2004. Was a 'hyperdisease' responsible for the late Pleistocene megafaunal extinction? Ecology Letters 7: 859–868.

Marsh DM and PC Trenham. 2001. Metapopulation dynamics and amphibian conservation. Conservation Biology 15: 40-49.

Martel A, Spitzen-van der Sluijs A, Blooia M, Bert W, Decatelle R, Fisher MC, Woeltjes A, Bosman W, Chiers K, Bossuyt F and F Pasmans. 2013. *Batrachochytrium salamandrivorans* sp. nov. causes lethal chytridiomycosis in amphibians. Proceedings of the National Academy of Science 110: 15325-15329.

Matthews KR and KL Pope. 1999. A telemetric study of the movement patterns and habitat use of *rana muscosa*, the mountain yellow-legged frog, in a high-elevation basin in Kings Canyon National Park, California. Journal of Herpetology 33(4): 615-624.

McCallum ML. 2007. Amphibian decline or extinction? Current declines dwarf background extinction rate. Journal of Herpetology 41: 483-491

McCallum H and A. Dobson. 2002. Disease, habitat fragmentation and conservation. Proc. R. Soc. Lond. Ser. B Biol. Sci. 269:2041–2049.

Molofsky J and JB Ferdy. 2005. Extinction dynamics in experimental metapopulations. Proceedings of the National Academy of Science USA 102: 3726–3731.

Morton SR, Hoegh-Guldberg O, Lindenmayer DB, Olson MH, Hughes L, et al. 2009 The big ecological questions inhibiting effective environmental management in Australia. Austral Ecology 34: 1–9.

Moss R, Babiker M, Brinkman S, Calvo E, Carter T et al. 2008. Towards new scenarios for analysis of emissions, climate change, impacts, and response strategies. Geneva: Intergovernmental Panel on Climate Change. p. 132.

Muletz CR, Myers JM, Domangue RJ, Herrick JB and Harris R.N. 2012. Soil bioaugmentation with amphibian cutaneous bacteria protects amphibian hosts from infection by *Batrachochytrium dendrobatidis*. Biological Conservation, 152, 119–126

Murray KA, Retallick RWR, Puschendorf R, Skerratt LF, Rosauer D, McCallum HI, Berger L, Speare R and VanDerWal J. 2011. Assessing spatial patterns of disease risk to biodiversity: implications for the management of the amphibian pathogen, *Batrachochytrium dendrobatidis*. Journal of Applied Ecology 48: 163–173.

Murray KA and LF Skerratt. 2012. Predicting wild hosts for amphibian chytridiomycosis: integrating host life-history traits with pathogen environmental requirements. Human Ecology Risk Assessment 18: 200–224.

Nathan R, Getz WM, Revilla E, Holyoak M, Kadmon R, et al. 2008. A movement ecology paradigm for unifying organismal movement research. Proceedings of the National Academy of Sciences of the United States of America 105: 19052–19059.

Naujokaitis-Lewis IR, Curtis JMR, Arcese P and J Rosenfeld. 2009. Sensitivity analyses of spatial population viability analysis models for species at risk and habitat conservation planning. Conservation Biology 23: 225–229.

Nichols DK, Lamirande EW, Pessier AP and JE Longcore. 2001. Experimental transmission of cutaneous chytridiomycosis in dendrobatid frogs. Journal of Wildlife Diseases 37: 1-11.

Nicholson AJ. 1933. The balance of animal populations. Journal of Animal Ecology 2: 132–178.

Noss RF, Fleishman E, Dellasala DA, Fitzgerald JM, Gross MR, et al. 2009. Priorities for Improving the Scientific Foundation of Conservation Policy in North America. Conservation Biology 23: 825–833.

Olson DH, Aanensen DM, Ronnenberg KL, Powell CI, Walker SF, Bielby J, Garner TWJ and G Weaver, The BD Mapping Group, and MC Fisher. 2013. Mapping the global emergence of *Batrachochytrium dendrobatidis*, the amphibian chytrid fungus. PLoS ONE 8: e56802.

Ouellet M, Mikaelian I, Pauli BD, Rodrigues J and DM Green. 2005. Historical evidence of widespread chytrid infection in North American amphibian populations. Conservation Biology 19: 1431-1440.

Ovaskainen O and I Hanski. 2003. How much does an individual habitat fragment contribute to metapopulation dynamics and persistence? Theoretical Population Biology 64: 481–495.

Park AW. 2012. Infectious disease in animal metapopulations: the importance of environmental transmission. Ecol Evol. 2(7): 1398–1407.

Parmesan C and G Yohe. 2003. A globally coherent fingerprint of climate change impacts across natural systems. Nature 421: 37-42.

Parris MJ and TO Cornelius. 2004. Fungal pathogen causes competitive and developmental stress in larval amphibian communities. Ecology 85: 3385-3395.

Pedregosa et al. 2011. Scikit-learn: Machine Learning in Python JMLR 12: 2825-2830.

Petranka JW and CT Holbrook. 2006. Wetland restoration for amphibians: Should local sites be designed to support metapopulations or patchy populations? Restoration Ecology 14:404-411.

Petranka JW, Smith CK and AF Scott. 2004. Identifying the minimal demographic unit for monitoring pond-breeding amphibians. Ecological Applications 14:1065-1078.

Picco AM and JP Collins. 2008. Amphibian commerce as a likely source of pathogen pollution. Conservation Biology 22: 1582-1589.

Pimm SL and P Raven. 2000. Extinction by numbers. Nature 403: 843-845.

Pimm SL, Jones HL and J Diamond. 1988. On the risk of extinction. The American Naturalist. 132:757-785.

Piotrowski JS, Annis SL and JE Longcore. 2004. Physiology of *Batrachochytrium dendrobatidis*, a chytrid pathogen of amphibians. Mycologia 96: 9-15.

Plowright W. 1982. The effects of rinderpest and rinderpest control on wildlife in Africa. In: Animal disease in relation to animal conservation. MA Edwards and U Mcdonnell eds. Academic Press, 336 pages.

Pounds JA, Bustamante MR, Coloma LA, Consuegra JA, Fogden MP, Foster PN, La Marca E, Masters KL, Merino-Viteri A, Puschendorf R, Ron SR, Sánchez-Azofeifa GA, Still CJ and

BE Young. 2006. Widespread amphibian extinctions from epidemic disease driven by global warming. Nature 439(7073):161-7.

Power AG and CE Mitchell. 2004. Pathogen spillover in disease epidemics. The American Naturalist 164 Suppl 5:S79-89.

Pullin AS, Baldi A, Can OE, Dieterich M, Kati V, et al. 2009. Conservation focus on Europe: major conservation policy issues that need to be informed by conservation science. Conservation Biology 23: 818–824.

Puschendorf R, Carnaval AC, VanDerWal J, Zumbado-Ulate H, Chaves G, Bolanos F, et al. 2009. Distribution models for the amphibian chytrid *Batrachochytrium dendrobatidis* in Costa Rica: proposing climatic refuges as a conservation tool. Diversity and Distributions 15:401–408.

Rachowicz LJ and VT Vredenburg. 2004. Transmission of *Batrachochytrium dendrobatidis* within and between amphibian life stages. Disease of Aquatic Organisms 61:75–83.

Rachowicz LJ, Knapp RA, Morgan JAT, MJ Stice, VT Vredenburg, JM Parker and CJ Briggs. 2006. Emerging infectious disease as a proximate cause of amphibian mass mortality. Ecology 87:1671–1683.

Raffel TR, Romansic JM, Halstead NT, McMahon T, Venesky MD and JR Rohr. 2013. Disease and thermal acclimation in a more variable and unpredictable climate. Nature Climate Change 3: 145–151.

Renner IW and DI Warton. 2013. Equivalence of MAXENT and Poisson Point Process Models for Species Distribution Modeling in Ecology. Biometrics 69: 274–281.

Risk BB, de Valpine P, Beissinger SR. 2011. A robust-design formulation of the incidence function model of metapopulation dynamics applied to two species of rails. Ecology 92: 462–474.

Rödder D, Kielgast J and S Lötters. 2010. Future potential distribution of the emerging amphibian chytrid fungus under anthropogenic climate change. Diseases of Aquatic Organisms 92:201–207.

Rödder D, Kielgast J, Bielby J, Schmidtlein S, Bosch J, Garner TWJ, et al. 2009. Global amphibian extinction risk assessment for the panzootic chytrid fungus. Diversity 1:52–66.

Rödder D, Veith M and S Lötters. 2008. Environmental gradients explaining prevalence and intensity of infection with the amphibian chytrid fungus: the host's perspective. Animal Conservation 11:513–517.

Rohani P, May RM and MP Hassell. 1996. Metapopulations and equilibrium stability: the effects of spatial structure. Journal of Theoretical Biology 181: 97–109..

Rohr JR, Raffel TR and CA Hall. 2010. Developmental variation in resistance and tolerance in a multi-host—parasite system. Functional Ecology 24: 1110-1121.

Rohr JR, Raffel TR, Romansic JM, McCallum H and PJ Hudson. 2008. Evaluating the links between climate, disease spread, and amphibian declines. Proceedings of the National Academy of Science USA 105:17436–17441.

Rohr JR and TR Raffel. 2010. Linking global climate and temperature variability to widespread amphibian declines putatively caused by disease. Proceedings of the National Academy of Sciences of the United States of America 107, 8269–8274.

Rollins-Smith LA, Carey C, Longcore J, Doersam JK, Boutte A, JE Bruzgal and JM Conlon. 2002. Activity of antimicrobial skin peptides from ranid frogs against *Batrachochytrium dendrobatidis*, the chytrid fungus associated with global amphibian declines. Developmental and Comparative Immunology 26, 471-479.

Ron SR. 2005. Predicting the distribution of the amphibian pathogen *Batrachochytrium dendrobatidis* in the new world. Biotropica 37:209–221.

Rosenblum EB, James TY, Zamudio KR, Poorten TJ, Ilut D, et al. 2013. Complex history of the amphibian-killing chytrid fungus revealed with genome resequencing data. Proceedings of the National Academy of Sciences of the United States of America 110: 9385–9390.

Rosenblum MG, AS Pikovsky and J Kurths. 1996. Phase Synchronization of Chaotic Oscillators. Physical Review Letters 76:1804–1807.

Royle JA, Chandler RB, Yackulic C and JD Nichols. 2012. Likelihood analysis of species occurrence probability from presence-only data for modelling species distributions. Methods in Ecology and Evolution, 3: 545–554.

Rustigian HL, MV Santelmann and NH Schumaker. 2003. Assessing the potential impacts of alternative landscape designs on amphibian population dynamics. Landscape Ecology 18:65–81.

Sandeep S, T Dutta, JE Maldonado, TC Wood, HS Panwar, and J Seidensticker. 2013. Forest corridors maintain historical gene flow in a tiger metapopulation in the highlands of central India. Proceedings of the Royal Society B 280: 20131506

Sattenspiel L. 1987. Epidemics in nonrandomly mixing pop-ulations: a simulation. American Journal of Physical Anthropology 73:251-265.

Schick RS, Loarie SR, Colchero F, Best BD, Boustany A, et al. 2008. Understanding movement data and movement processes: current and emerging directions. Ecology Letters 11: 1338–1350.

Schindler DE, R Hilborn, B Chasco, CP Boatright, TP Quinn, LA Rogers, and MS Webster. 2010. Population diversity and the portfolio effect in an exploited species. Nature 465: 609-612.

Schloegel LM, LF Toledo, JE Longcore, SE Greenspan, CA Vieira, M Lee, S Zhao, C Wangen, CM Ferreira, M Hipolito, AJ Davies, CA Cuomo, P Daszak and TY James. 2012. Novel, panzootic and hybrid genotypes of amphibian chytridiomycosis associated with the bullfrog trade. Molecular Ecology 21: 5162-5177.

Schoener TW and DA Spiller. 1992. Is extinction rate related to temporal variability in population size? An empirical answer for orb spiders. American Naturalist 139(6): 1176-1207.

Scott ME. 1988. The impact of infection and disease on animal populations: implications for conservation biology. Conservation Biology 2: 40-56.

Searle CL, Gervasi SS, Hua J, Hammond JI, Relyea RA, Olson DH and AR Blaustein. 2011. Differential host susceptibility to *Batrachochytrium dendrobatidis*, an emerging amphibian pathogen. Conservation Biology 25: 965-974.

Secor DH, Kerr LA and SX Cadrin. 2009. Connectivity effects on productivity, stability, and persistence in a herring metapopulation model. ICES Journal of Marine Science 66: 1726-1732.

Sekercioglu CH, Schneider SH, Fay JP and SR Loarie. 2008. Climate change, elevational range shifts, and bird extinctions. Conservation Biology 22(1):140-50.

Semlitsch RD. 2008. Differentiating migration and dispersal processes for pond-breeding amphibians. Journal of Wildlife Management 72: 260-67.

Shulse CD et al. 2010. Influence of design and landscape placement parameters on amphibian abundance in constructed wetlands. Wetlands 30: 915-28.

Sih A, Johnson BG and G Luikart. 2000. Habitat loss: ecological, evolutionary and genetic consequences. Trends in Ecology and Evolution 15: 132–134.

Sjogren-Gulve P. 1994. Distribution and extinction patterns within a northern metapopulation of the pool frog, *Rana lessonae*. Ecology 75: 1357-1367

Sjogren P. 1991. Extinction and isolation gradient in metapopulations: the case of the pool frog (*Rana lessonne*). Biological Journal of the Linnean Society 42: 135-47.

Skerratt LF, L Berger, R Speare, S Cashins, KR McDonald, AD Phillott, HB Hines and N Kenyon. 2007. Spread of chytridiomycosis has caused the rapid global decline and extinction of frogs. Ecohealth 4: 125-134.

Smith AM and DM Green. 2005. Dispersal and the metapopulation paradigm in amphibian ecology and conservation: are all amphibian populations metapopulations? Ecography 28: 110–128.

Smith AM and DM Green DM. 2006. Sex, isolation and fidelity: unbiased long-distance dispersal in a terrestrial amphibian. Ecography. 29: 649-658.

Smith KF, Sax DF and KD Lafferty. 2006. Evidence for the role of infectious disease in species extinction and endangerment. Conservation Biology 20(5): 1349-1357.

Sokolow SH, Foley P, Foley JE, Hastings A and LJ Richardson. 2009. Editor's choice: disease dynamics in marine metapopulations: modelling infectious diseases on coral reefs. Journal of Applied Ecology 46:621–631.

Soto-Azat C, Clarke BT, Poynton JC and AA Cunningham. 2009. Widespread historical presence of *Batrachochytrium dendrobatidis* in African pipid frogs. Diversity and Distributions 15: 1-6

Stuart LP and P Raven. 2000. Biodiversity: Extinction by numbers. Nature 403: 843-845.

Stuart SN, JS Chanson, NA Cox, BE Young, ASL Rodrigues, DL Fischman and RW Waller. 2004. Status and trends of amphibian declines and extinctions worldwide. Science 306, 1783-1786.

Sutherland WJ, Armstrong-Brown S, Armsworth PR, Brereton T, Brickland J, et al. 2006. The identification of 100 ecological questions of high policy relevance in the UK. Journal of Applied Ecology 43: 617–627.

Tingley R, Phillips BL, Letnic M, Brown GP, Shine R, et al. 2013. Identifying optimal barriers to halt the invasion of cane toads *Rhinella marina* in arid Australia. Journal of Applied Ecology 50: 129–137.

US Fish and Wildlife Service. 2003. Petition to list the Mountain yellow-legged frog: Finding of Warranted but Precluded. 68 FR 2283.

US Fish and Wildlife Service. 2006. Designation of critical habitat for the southern California distinct population segment of the Mountain Yellow-Legged Frog (*Rana muscosa*). In: Federal Register 71(178):54344-54386. Washington D.C.: United States Fish and Wildlife Service.

van Vuuren DP, Edmonds J, Kainuma M, Riahi K, Thomson A, Hibbard K et al. 2011. The representative concentration pathways: an overview. Climatic Change 109 (1-2): 5-31.

Vasseur DA and JW Fox. 2009. Phase-locking and environmental fluctuations generate synchrony in a predator-prey community. Nature 460(7258):1007-10.

Venesky MD, MJ Parris and A Storfer. 2010. Impacts of *Batrachochytrium dendrobatidis* infection on tadpole foraging performance. Ecohealth DOI: 10.1007/s10393-009-0272-7.

Venesky MD, Raffel TR, McMahon TA, and JR Rohr. 2013. Confronting inconsistencies in the amphibian-chytridiomycosis system: implications for disease management. Biological Review of the Cambridge Philosophical Society 89(2):477-83.

Vogwill T, A Fenton and MA Brockhurst. 2009. Dispersal and natural enemies interact to drive spatial synchrony and decrease stability in patchy populations. Ecology Letters 12(11):1194-200.

Voyles JS Young, L Berger, C Campbell, WF Voyles, A Dinudom, D Cook, R Webb, RA Alford, LF Skerratt and R Speare. 2009. Pathogenesis of chytridiomycosis, a cause of catastrophic amphibian declines. Science 326: 582-585.

Vredenburg VT. 2004. Reversing introduced species effects: Experimental removal of introduced fish leads to rapid recovery of a declining frog. Proceedings of the National Academy of Sciences, USA 101:7646–7650.

Vredenburg VT, Knapp RA, Tunstall TS and CJ Briggs. 2010. Dynamics of an emerging disease drive large-scale amphibian population extinctions. Proceedings of the National Academy of Sciences 107: 9689-9694.

Wake DB and VT Vredenburg. 2008. Are we in the midst of a sixth major extinction? A view from the world of amphibians. Proceedings of the National Academy of Sciences of the United States of America 105: 11466-11473.

Walker SF, Bosch J, Gomez V, Garner TWJ, Cunningham AA, Schmeller DS, Ninyerola M, Henk DA, Ginestet C, Arthur CP and MC Fisher. 2010. Factors driving pathogenicity vs. prevalence of amphibian panzootic chytridiomycosis in Iberia. Ecology Letters 13: 372–382.

Wearing HJ, Sait SM, Cameron TC and P Rohani. 2004. Stage-structured competition and the cyclic dynamics of host–parasitoid populations. Journal of Animal Ecology 73:706–722.

Weldon KM, Preez LH, Hyatt AD, Muller R and R Speare. 2004. Origin of the amphibian chytrid fungus. Emerging Infectious Diseases 10: 2100-2105.

Whitaker BR and KN Wright. 2001. Amphibian medicine and captive husbandry. Krieger Publishing Co., Malabar.

Whitesel TA et al. 2004. Bull Trout Recovery Planning: A review of the science associated with population structure and size. Science Team Report #2004-01, U.S. Fish and Wildlife Service, Regional Office, Portland, Oregon, USA.

Williams ES, Thorne ET, Appel MJ and DW Belitsky. 1988. Canine distemper in black-footed ferrets (*Mustela nigripes*) from Wyoming. Journal of Wildlife Diseases 24(3): 385–398.

Wilson KA, Lulow M, Burger J, Fang Y-C, Andersen C, et al. 2011. Optimal restoration: accounting for space, time and uncertainty. Journal of Applied Ecology 48: 715–725.

Woodhams DC, Geiger CC, Reinert LK, Rollins-Smith L A , Lam B , Harris R N , Briggs CJ , Vredenburg V T and J Voyles. 2012. Treatment of amphibians infected with chytrid fungus: learning from failed treatments with itraconazole, antimicrobial peptides, bacteria, and heat therapy. Diseases of Aquatic Organisms 98: 11-25.

Woodhams DC and RA Alford. 2005. Ecology of chytridiomycosis in rainforest stream frog assemblages of tropical Queensland. Conservation Biology, 19: 1449–1459.

Woodhams DC, Alford RA and G Marantelli. 2003. Emerging disease of amphibians cured by elevated body temperature. Diseases of Aquatic Organisms 55: 65-67.

Woodhams DC, RA Alford, CJ Briggs, M Johnson and LA Rollins-Smith. 2008. Life-history trade-offs influence disease in changing climates: strategies of an amphibian pathogen. Ecology 89: 1627-1639.

Woodroffe R. 1999. Managing threats to wild mammals. Animal Conservation 2: 185-193.

Wright, C. 2010. Spatiotemporal dynamics of prairie wetland networks: power-law scaling and implications for conservation planning. Ecology 91(7): 1924–1930.

Wyatt KB, Campos PF, Gilbert MTP, Kolokotronis S-O, Hynes WH, et al. 2009. Historical mammal extinction on christmas island (indian ocean) correlates with introduced infectious disease. PLoS ONE 4(1):10.1371

Yaari, G, Ben-Zion Y, Shnerb NM, and Vasseur DA. 2012. Consistent scaling of persistence time in metapopulations. Ecology 93:1214–1227.

Young BE, Lips KR, Reaser JK, Ibanez R, Salas AW, Cedeno JR, Coloma LA, Ron S, La Marca E, Meyer JR, Munoz A, Bolanos F, Chaves G and D Romo. 2001. Population declines and priorities for amphibian conservation in Latin America. Conservation Biology 15: 1213-1223.

Zamudio KR and AM Wieczorek. 2007. Fine-scale spatial genetic structure and dispersal among spotted salamander (*Ambystoma maculatum*) breeding populations. Molecular Ecology 16: 257–274.