

Space: The final frontier of predator evolution?

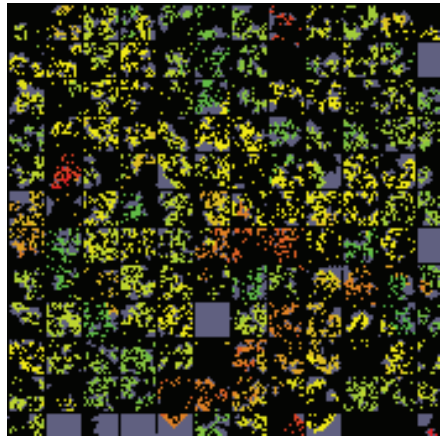
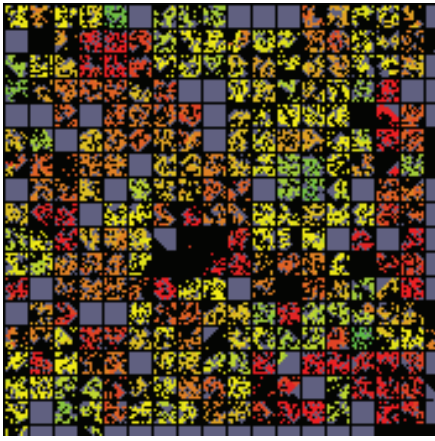
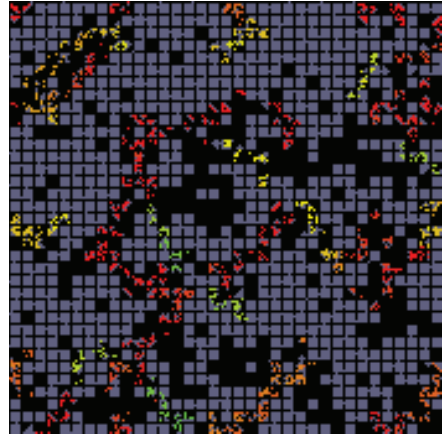
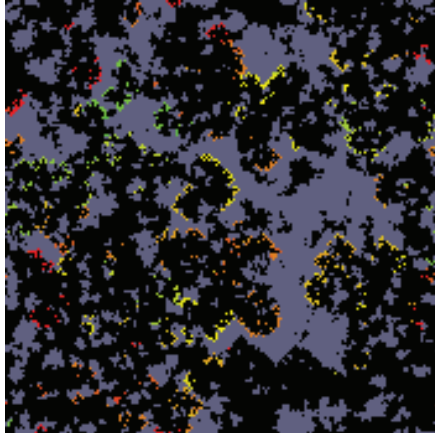
by

Susanna M. Messinger

A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
(Ecology and Evolutionary Biology)
in The University of Michigan
2012

Doctoral Committee:

Associate Professor Annette Ostling, Chair
Professor Mark D. Hunter
Professor Aaron A. King
Associate Professor Johannes Foufopoulos



© Susanna M. Messinger 2012

All Rights Reserved

For Alex.

ACKNOWLEDGEMENTS

I would like to thank my advisor, Dr. Annette Ostling, for her patience and understanding throughout my six years at the University of Michigan. I learned a lot from her, not the least of which is that it is possible to have a family and achieve at a high level in a competitive research environment. There are so many other things I am grateful to her for. I am grateful to her for her composure in meetings which began with the words "Remember that thing I showed you last week? Well, it was a coding error." I am grateful that she took an active role in guiding my research even though she had as much to learn about the topic as I did. I am grateful that she took the time to find opportunities that she thought would be educational or improve my professional development.

I would also like to thank the rest of my committee: Dr. Mark Hunter, Dr. Aaron King, and Dr. Johannes Foufopoulos. I may have only seen them once a year, but they were incredibly helpful in developing the ideas I present here. Aside from his help with my research, I thank Dr. Mark Hunter for writing letter of recommendation after letter of recommendation for me.

I would like to thank my partner in everything, Alex Mettler. When I take a step back from my research, I am astonished at how much of my success I have to contribute to Alex. From the beginning his decisions and attitude have nothing but ensured that I would succeed. He came with me to Michigan without a job or a plan, simply because it was what I wanted. He got a job that was well beneath his potential so that we could survive, followed by several other jobs of equal caliber. He kept his jobs while attending school at EMU to get his teaching certificate. After our family grew, he gave up the possibility of a full time teaching position and committed to staying at home so that I could continue to work toward finishing. His unfailing support, amazing culinary skills, and positive attitude have all been key to my perseverance.

Last, but certainly not least, is a long list of incredible friends and family. Thank you to my sister, for wanting to hear about my research, reading a million drafts of every application or proposal I have ever written, and for commiserating when the going got rough. Thank you to my mom, for believing that I am one of the most

intelligent people in the world and for her invaluable moral support. Thank you to my dad, who planted the seed of a love of math and programming. Thank you to Heather for daily stress relief runs and encouraging me to have goals outside of school. Thank you to Rachel for invaluable advice, therapeutic bike rides and runs, and for being a good example. Thank you to Tory for listening to my daily complaints, accepting me when I was happy and sad alike, and supporting my caffeine addiction. Thank you to Brian for being at work on weekends when the halls are otherwise lonely and empty and for always being up for a beer. Thank you to Dave, for sharing Rachel and providing stimulating conversations about beer and biking for Alex. Last, but not least, thank you to Mike, for being a research rock-star and still hanging out with me.

These acknowledgements would not be complete without mentioning the entire University of Michigan EEB department. Beyond my committee, I thank the unfailing EEB staff, who make everything possible and never get angry, no matter how many times I lock myself out of my office. I thank the EEB theory group for listening to my ideas and sharing their own. I thank my office mates, Gyuri and Rafael, for treating me as an equal despite my non-physics background and simulation-based research. And for incalculable relief from the monotony of academia, I thank all the other graduate students for entertaining diversions, from Cinco de Mayo parties to Wednesday's at Ashley's to Halloween parties to apple picking, and later, to kid play dates.

Finally, I would like to acknowledge my sources of funding, without which this research would not have been possible: Elizabeth Caroline Crosby Research Award, EEB Block Grant, Margaret Ayers Host Award, Rackham Graduate Student Research Grant, and the Rackham Faculty Research Grant.

TABLE OF CONTENTS

DEDICATION	ii
ACKNOWLEDGEMENTS	iii
LIST OF FIGURES	viii
LIST OF TABLES	x
LIST OF APPENDICES	xi
ABSTRACT	xii
CHAPTER	
I. Introduction	1
1.1 Background	1
1.2 Research Goals	4
1.3 Broader Implications	6
II. The Consequences of Spatial Structure for the Evolution of Pathogen Transmission Rate and Virulence	7
2.1 Introduction	7
2.2 Background	10
2.2.1 Pathogen-host models	10
2.2.2 Predicting the evolution of pathogen transmission rate and virulence	12
2.3 Spatial models of the evolution of pathogen transmission and virulence	14
2.3.1 The competition-persistence tradeoff	14
2.3.2 Simple models	16
2.3.3 More complex models	21
2.3.4 Selection mechanism	24
2.4 Future Research	25

2.4.1	Quantifying pathogen fitness	25
2.4.2	Modeling Developments	26
2.4.3	Experimental and Observational Validation	28
2.5	Conclusions	28
III.	The influence of host demography, pathogen virulence, and relationships with virulence on the evolution of pathogen transmission in a spatial context	30
3.1	Introduction	30
3.2	Materials and Methods	33
3.2.1	Non-spatial model	33
3.2.2	Spatial model	35
3.2.3	Spatial moment equations and improved pair approximation	36
3.2.4	Data analysis	38
3.3	Results	40
3.4	Discussion	46
3.4.1	Effects of host and pathogen ecology	46
3.4.2	Accuracy of the IPA	53
3.4.3	Explaining the effects of ecology	54
3.4.4	Summary	55
IV.	Novel evolutionary effects of predator ecology in a spatial context	56
4.1	Introduction	56
4.2	Methods	59
4.2.1	Non-spatial Predator Evolution	59
4.2.2	Spatial Predator Evolution	60
4.3	Results	64
4.3.1	Predator Conversion Efficiency	64
4.3.2	Prey reproduction rate	65
4.3.3	Predator death rate	67
4.3.4	Predator movement	69
4.4	Discussion	72
V.	Evolutionary stability of food webs arising from spatial structure	76
5.1	Introduction	76
5.2	Methods	78
5.2.1	Deterministic, logistic growth model	79
5.2.2	Deterministic, exponential growth model	80
5.2.3	Stochastic, exponential growth model	80

5.2.4	Food web construction	80
5.2.5	Evolutionary dynamics	81
5.3	Results	82
5.3.1	Two species	82
5.3.2	Three species	86
5.3.3	Five species	89
5.4	Discussion	89
VI.	Conclusion	94
6.1	Introduction	94
6.2	Summary of Findings	95
6.3	Conclusions	97
6.4	Future Directions	97
APPENDICES	99
BIBLIOGRAPHY	116

LIST OF FIGURES

Figure

1.1	Spatial variation in land cover of North America in 2005.	3
3.1	Evolutionary stable transmission rates across transmission-virulence relationship shapes.	39
3.2	Effect of host reproduction rate on the evolutionary stable transmission rate for no transmission-virulence relationship.	42
3.3	Effect of host death rate and virulence on the evolutionary stable transmission rate for no transmission-virulence relationship.	43
3.4	Effect of host reproduction rate on the evolutionary stable transmission rate for linear transmission-virulence relationships.	45
3.5	Effect of host reproduction rate on the evolutionary stable transmission rate for concave-down transmission-virulence tradeoffs.	48
3.6	Effect of host death rate on the evolutionary stable transmission rate for transmission-virulence relationships.	49
3.7	Relative difference between evolutionary stable transmission rate predicted by simulation and improved pair approximation for transmission-virulence relationships.	50
3.8	Population structure for lowest and highest host reproduction rates.	51
4.1	Effect of predator conversion efficiency on the evolutionary stable attack rate.	64
4.2	The evolutionary stable attack rate relative to extinction thresholds.	65
4.3	Effect of prey reproduction rate on the evolutionary stable attack rate.	66

4.4	Effect of prey reproduction rate on the spatial distribution and dynamics of the prey population.	67
4.5	Effect of predator death rate on the evolutionary stable attack rate.	68
4.6	Effect of predator death rate on the spatial distribution of the prey population.	69
4.7	Effect of predator movement on the evolutionary stable attack rate.	70
4.8	Effect of predator movement rate on global prey density and predator type distribution.	71
4.9	Effect of predator movement rate on the relationship between prey reproduction rate and the evolutionary stable attack rate.	72
5.1	Pair-wise predator-prey interactions in a metapopulation.	83
5.2	Subpopulation structure over time at evolutionary equilibrium for spatial pair-wise predator prey interactions.	85
5.3	Example of subpopulation prey population dynamics in stochastic simulations.	86
5.4	Predicted within patch population dynamics for pair-wise predator-prey interactions.	87
5.5	Predicted within patch population dynamics for straight food chains.	88
A.1	Comparing methods of inferring evolutionary stable transmission rate for no transmission-virulence tradeoff.	101
E.1	Estimated host (or prey) intrinsic growth rates from spatial simulations and real systems.	113
E.2	Estimated pathogen basic reproduction number from spatial simulations.	114

LIST OF TABLES

Table

2.1	Predicted transmission rates (β) and virulence (α) for a set of spatial models.	18
2.2	A quantitative comparison of evolutionarily stable transmission rate (β) and virulence (α) in spatial and non-spatial models.	21
4.1	Metrics of the strength of local competition and their effect on predator attack rate.	62
E.1	Empirical estimates of R_0 for a range of human diseases.	110
E.2	Mean prey to predator body size ratios.	111

LIST OF APPENDICES

Appendix

A.	Inferring ES transmission rate from simulations	100
B.	Spatial Moment Equations	102
C.	Improved Pair Approximation (IPA)	104
D.	Solving for quasi-equilibrium $Q(S I)$	106
E.	Interpreting model parameter values	108
F.	Inclusive fitness framework for pathogens	115

ABSTRACT

Space: The final frontier of predator evolution?

by

Susanna M. Messinger

Chair: Associate Professor Annette Ostling

Interactions between individual organisms are often structured in space. Population spatial structure has important ecological consequences. Theoretical evidence suggests that the evolutionary effects can be equally significant, especially for exploitative species. With only a few exceptions, this theory focuses on pathogens. I review the existing literature to show that evolutionary spatial effects are strongest when host and pathogen dispersal are local and when host reproduction is relatively low. Under these conditions, the pathogen is subject to a competition-persistence tradeoff (increased competitive ability comes at the cost of decreased persistence) that favors the evolution of intermediate pathogen transmission rates.

Although existing literature clearly demonstrates that spatial structure impacts pathogen evolution, lacking is a comprehensive understanding of the role of host and pathogen ecology. Through comprehensive simulations of spatial host-pathogen models I show that the predicted pathogen transmission rate differs from the non-spatial prediction depending on the host reproduction rate, infected host death rate, and the shape or existence of a transmission-virulence tradeoff. In conjunction, I show that the effects of spatial structure cannot be fully understood through a commonly used quantitative method.

The effect of spatial structure on pathogens is postulated to extend to true predators. However, true predators are characterized by ecology that is unique relative to pathogens. Through additional simulations of spatial predator-prey models I show the influence of three unique aspects of ecology on true predator evolution: the prey conversion efficiency (the ratio of predators produced per prey consumed), the magnitude of predator death relative to the prey death rate, and the rate of predator

movement. Despite their unique ecology, however, there are consistent trends in the influence of common aspects of ecology.

Based on how spatial structure influences true predator evolution, spatial structure may also influence the evolution of entire food webs. Using simple population dynamic models I show that randomly constructed three and five species food webs are predicted to be evolutionarily unstable in both spatial and non-spatial contexts. However, I suggest spatial structure is still likely to play an important evolutionary role and should be considered more carefully in studies of evolutionary food web assembly.

CHAPTER I

Introduction

1.1 Background

The natural world is inherently spatial, at all levels of organization, with potentially important dynamical consequences. For instance, at the largest scale, there is substantial spatial variation in land cover across the globe (e.g. Fig. 1.1), which has important repercussions for climate change (Field et al. (2007); Marland et al. (2003); Pielke et al. (2011, 2002)). At a much smaller scale, the spatial coordination of individual stomata on the surface of leaves has been linked to the ability of the leaf to optimally adjust stomatal aperture to changing CO_2 concentrations and humidity (Peak et al. (2004)). Somewhere in between these two extremes is population-level spatial structure, where individuals in the same population or community do not interact randomly, but rather according to their spatial location. Population spatial structure is particularly interesting because it may modify the interaction between two species and thus has the potential to influence species coexistence and biodiversity (Amarasekare (2003); King and Hastings (2003); Tilman (1994)).

Population spatial structure is common in natural systems, whether imposed by external boundaries like local climate differences or geographic barriers or arising from the ecology of the organism itself (e.g. van der Heide et al. (2010); Komac et al. (2011); Rietkerk et al. (2004); Santini et al. (2011)). While the effects of population spatial structure on species coexistence and biodiversity have been relatively well explored over ecological time scales, the evolutionary effects have largely been ignored. There are a few exceptions, the most notable of which is the geographic mosaic theory of coevolution, which integrates the effects of population spatial structure and spatial heterogeneity on species coevolution (Thompson (2005)). Interest in the evolutionary effects of spatial structure has recently resurged, driven in a large part by the recognition that evolutionary dynamics can happen on timescales equivalent

to ecological dynamics (Carroll et al. (2007); Ellner et al. (2011); Fussmann et al. (2007); Pelletier et al. (2009)). Furthermore, in the absence of spatial structure, the integration of evolutionary and ecological dynamics has been shown to lead to novel predictions (Dieckmann et al. (2006); Urban and Skelly (2006); De Meester (2007); Fukami (2007); Hubbel (2006)).

The evolutionary influence of population spatial structure is particularly compelling because it bears on the fundamental evolutionary question of the emergence of cooperation. Theory suggests that spatial structure is a key requirement for the emergence of cooperation (Doebeli and Knowlton (1998); Killingback et al. (1999); Nowak and May (1992); Lion and Gandon (2009); Lehmann and Keller (2007); although see Hauert and Doebeli (2004)). One manifestation of cooperation, spatial structure appears to resolve the tragedy of the commons (Hardin (1968); Rankin and Lopez-Sepulcre (2005); Bargum (2007)). The tragedy is that among a group of consumers that share the same common resource, a selfish consumer that utilizes the resource to a greater extent than other consumers in the group should have a higher relative fitness. In other words, the benefits of increased resource use accrue to the individual while the costs are shared by all. However, by decreasing the amount of resources available, more selfish consumers will at the extreme cause extinction of both the resource and the consumers. Over evolutionary time, selection should lead to selfish behavior and subsequent extinction, a case of evolutionary suicide (Parvinen (2005); Rankin and Lopez-Sepulcre (2005)). Instead, when the consumer and resource are subject to spatial structure, consumers are more likely to evolve cooperative behavior that preserves the shared resource. The ability of spatial structure to resolve the tragedy of the commons not only informs our understanding of contemporary phenomena, but also historical phenomena like the major transitions in the history of life (see for example Szathmary (2001)).

The reasoning behind the tragedy of the commons is the same for the paradox of prudent predation, which applies when the common resource is a prey and the consumers are predators. A predator here is defined as any species that consumes or exploits another species in order to survive and reproduce, including pathogens, parasites, parasitoids, grazers and browsers, as well as true predators. The paradox is that in the natural world, we know that predator and prey stably coexist in nature even when heritable variation exists for traits involved in predator attack rates (e.g. Palkovacs and Post (2008); Forsman and Lindell (1993); Virol et al. (2003)), suggesting that evolutionary suicide is not inevitable. In this narrower context, the ability of spatial structure to resolve the paradox has implications for understanding the vir-

North American Environmental Atlas - Land Cover, 2005

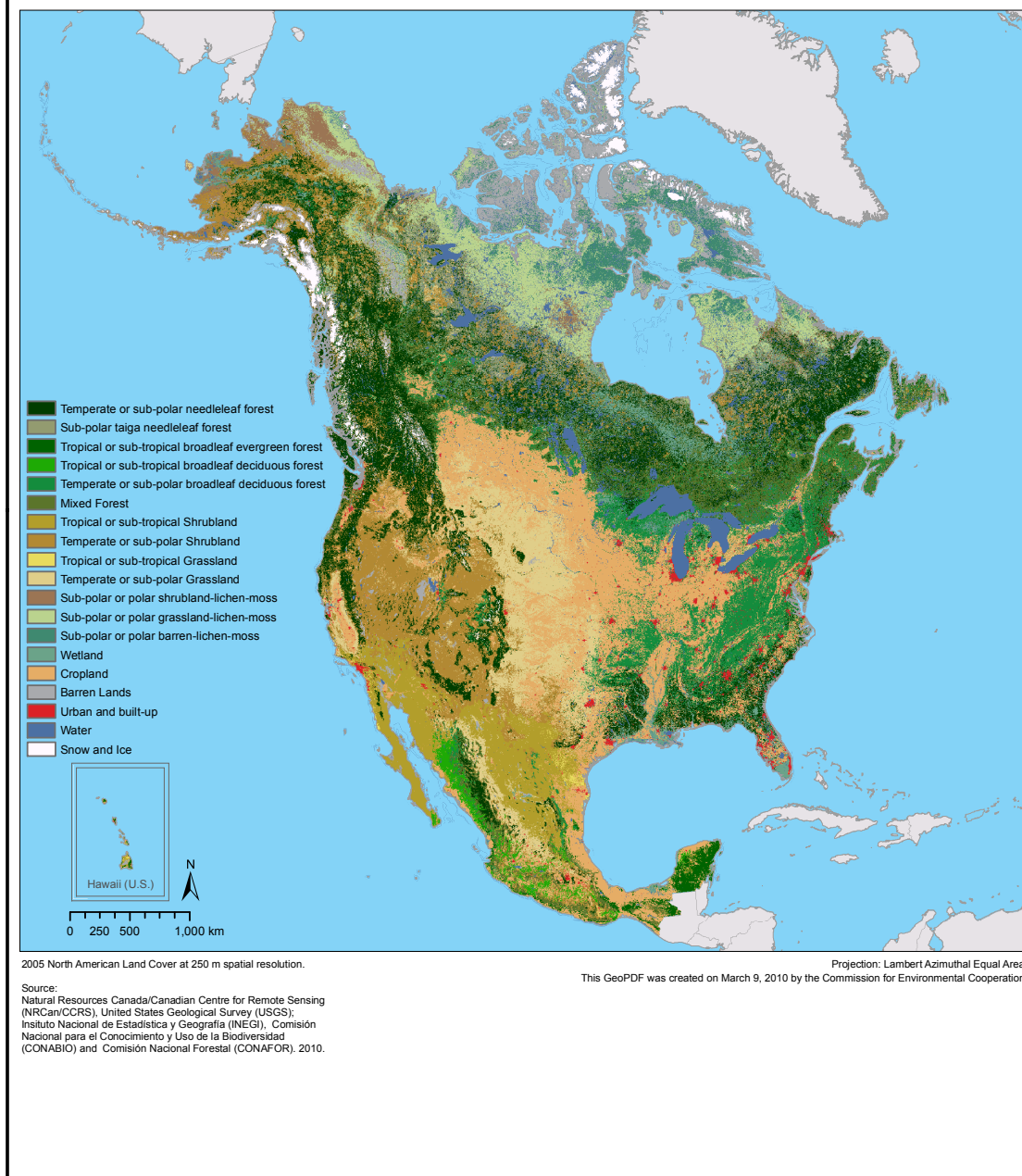


Figure 1.1: Spatial variation in land cover of North America in 2005. Map created by the Commission for Environmental Cooperation (www.CEC.org).

ulence of emerging infectious diseases (see for example Ewald (1998)) as well as the stability, dynamics, and energy flow in food webs. Despite these potentially important implications, our understanding of the influence of spatial structure on predator evolution is still in its nascency. In particular, the majority of studies exploring the impact of spatial structure on predator evolution has focused on pathogens. Few studies have addressed the influence of spatial structure on true predators, which are of primary relevance in understanding food webs. In addition, the expected influence of the interacting species' ecology on the predator's evolutionary trajectory has not been thoroughly addressed. Finally, it is not clear whether theory of pair-wise predator-prey interactions scales up to more complex multi-species communities.

1.2 Research Goals

Broadly, the goal of this research is to more carefully elucidate the evolutionary influence of spatial structure on predators, with an emphasis on how spatial structure alters the relationship between the species' ecology and their expected evolutionary trajectory. I begin by reviewing existing theory of the evolutionary effects of spatial structure on pathogens with the goal of outlining the type of spatial structure and other conditions which lead to strong spatial evolutionary effects. In addition, I assess the effect of spatial structure relative to the effect of a transmission-virulence tradeoff, which is often cited as an explanation for the emergence of prudent pathogens in the absence of spatial structure. Finally, I review spatial models which incorporate more complicated pathogen ecology, like co-infection, highlighting that the spatial context can alter the expected evolutionary role of a species ecology.

Building from the findings of this review, I explore in more detail how spatial structure alters the evolutionary role of pathogen and host ecology. Though prior studies show that the evolutionary influence of pathogen and host ecology can be significantly altered by the spatial context, a thorough exploration of the most basic aspects of pathogen and host ecology has not been done. I use evolutionary simulations of simple individual based lattice models of pathogen-host interactions. Although the type of spatial structure represented by this model is simple, since it has been shown to lead to strong evolutionary spatial effects, it is an ideal starting point for studying the impact of space on the relationship between species ecology and evolution. I perform extensive simulations to examine the expected evolutionary role of the host reproduction rate, host natural death rate, pathogen virulence, and the shape of the transmission-virulence tradeoff. Furthermore, I use the simulation

data to assess the accuracy of a commonly used quantitative framework for predicting pathogen evolution in a spatial context. Although this method has been shown to accurately predict the evolutionary effects of spatial structure in certain cases, it has been shown to fail in a few other cases. This assessment is the most thorough assessment of the method's accuracy to date.

I then similarly explore how spatial structure alters the evolutionary role of true predator and prey ecology. Very few studies have examined true predator evolution in a spatial context and none have explicitly addressed how the spatial context influences the evolutionary role of predator and prey ecology. Using the same basic modeling framework, I address the following questions. 1) How does predator ecology that is unique to true predators relative to pathogens influence predator evolution and 2) are there any consistent trends in the role of predator and prey ecology that are analogous with pathogens and their hosts? With reference to the first question, true predators have a lower prey conversion efficiency than pathogens—in other words, when a predator consumes a prey it does not necessarily result in a new predator whereas when a pathogen infects a susceptible host it necessarily becomes an infected host. In addition, true predators are likely to have a lower death rate than their prey, based on typical body size relationships (Cohen et al. (1993); Yodzis and Innes (1992)), whereas the reverse is true for pathogens. Finally, true predators are likely to have a larger range of movement than their prey. This last aspect of ecology is particularly interesting because non-spatial models offer no prediction as to its evolutionary role since it is exclusively a spatial process. With reference to the second question, it is possible that the host reproduction rate and prey reproduction rate have similar effects on pathogen and predator evolution. Similarly, the host natural death rate and predator death rate may comparably affect pathogen and predator evolution. I use the conceptual framework of inclusive fitness to qualitatively explain the trends reported.

In the last chapter I explore the possibility that the evolutionary effect of spatial structure on pair-wise predator prey interactions may extend to more complex multi-species communities. In particular, does spatial structure constrain the evolution of predator attack rates when other predators or prey are present? First I check the ability of three simple population dynamic models to predict pair-wise predator-prey evolutionary stability in a metapopulation context. These simple models are easily extendible to larger food webs but have not been demonstrated to predict evolutionary stability for the simplest case of pair-wise interactions. I then examine whether, like pair-wise predator-prey interactions, food webs are inherently unstable

in a non-spatial context without other stabilizing mechanisms like prey co-evolution, ecological, or allocation tradeoffs. Though intuition suggests this will be the case, it has not yet been demonstrated. Furthermore, studies of the evolution of three species food webs when other stabilizing mechanisms are present suggest that novel evolutionary dynamics can arise from the inclusion of more species. Finally I explore whether spatial structure can stabilize larger webs of three and five species. No studies have yet addressed food web evolution in a spatial context.

1.3 Broader Implications

A major challenge in ecology is to explain the incredible diversity of the natural world. By elucidating how population spatial structure influences the relationship between a species ecology and its evolutionary trajectory, this research may help explain observed natural variation among predators that is unexplainable by non-spatial models. Ultimately, this research highlights the need for ecological and evolutionary studies of interacting species to acknowledge each other as well as the spatial context of the interaction. In addition to contributing to our academic understanding the natural world, this research also has the potential to inform understanding of our own, often dramatic, impact on the natural world. Anthropogenic effects like habitat fragmentation from land use change (Dale et al. (2000)), climate change (Thomas et al. (2004)), and the rapid and long-distance transportation of organisms within and between habitats (Lee and Chown (2009); Ricciardi (2007)) have the potential to significantly alter the spatial structure of many species. To fully understand the consequences of these changes and arbitrate their impact on biodiversity we must incorporate the spatial context into our research paradigm. Finally, specific to pathogens, this research may inform our understanding of the evolution of pathogen virulence and improve our ability to predict and control infectious diseases. The emergence and re-emergence of infectious disease is a continual problem that will benefit from a better understanding of the factors that lead to the evolution of increased transmission rates and virulence.

CHAPTER II

The Consequences of Spatial Structure for the Evolution of Pathogen Transmission Rate and Virulence

2.1 Introduction

Far from the straightforward descriptions found in many traditional mathematical models, species interactions are frequently mediated by external factors. Classic examples include indirect mediation by a third species (Abrams (1995); Werner and Peacor (2003)) and direct mediation by the environment (Chesson (1985); Chesson et al. (2004); Taylor (1998)). Although often ignored, the spatial distribution of organisms can be an equally important mediator. Individuals within a population do not always mix randomly in space. Instead, interactions between individuals may be structured by extrinsic and intrinsic limitations on movement and dispersal. Besides potentially affecting the ecological dynamics of interacting species (reviewed in Gilpin and Hanski (1991); Kareiva (1990)), reciprocal feedback between ecological and evolutionary dynamics suggests that spatial structure may have equally significant evolutionary effects (Fussmann et al. (2007); Hoffmeister et al. (2005); Kokko and Lopez-Sepulcre (2007); Thompson (1998)).

To date, particular attention has been paid to the potential evolutionary effects of spatial structure on species involved in exploitative interactions, like predators and parasites. Interest in exploitative interactions stems from the long-standing paradox of ‘prudent predation’ or ‘the tragedy of the commons’ (Hardin (1968); Rankin et al. (2007)). Consider a group of consumers that share the same resource. If the consumers overexploit the resource they will drive it, and eventually themselves, to extinction. In contrast, if the consumers are prudent and conserve the resource they will ensure long-term survival. The paradox is that a selfish consumer that utilizes

the resource to a greater extent than other consumers has a higher relative fitness than non-selfish consumers. Over evolutionary time then, selfish behavior and subsequent extinction should be favored by selection (Lewontin (1970)). Spatial structure offers one possible resolution to this paradox, under certain conditions promoting the evolution of non-selfish, altruistic traits like prudence (Lion and van Baalen (2008)).

The evolutionary effects of spatial structure are likely to be especially relevant to pathogen-host interactions, one type of exploitative interaction. Pathogen populations are inherently structured in space by their division into discrete subpopulations within individual hosts. Although not necessarily so, host populations are also frequently spatially structured. Host population spatial structure arises when the opportunity for pathogen transmission between hosts depends on the spatial arrangement of hosts. In the case of an immobile host species like a plant, spatial structure may arise as a consequence of distance-limited pathogen dispersal (e.g. Moreno et al. (2007); Roumagnac et al. (2004)). Or, in the case of a mobile host species like an animal, spatial structure may be imposed by limitations on host movement or dispersal. For example, many animals have restricted home ranges such that only individuals with home ranges in close proximity are likely to interact and transmit disease (e.g. Fulford et al. (2002)).

Prudent predation is easily framed in the context of disease, with a prudent pathogen being one with an exploitation strategy that conserves susceptible hosts. A pathogen's exploitation strategy is largely determined by its virulence and transmission rate. Simple non-spatial models of disease dynamics predict that a pathogen will evolve to become avirulent and have infinitely fast transmission. However, many pathogens actually have intermediate to high virulence (like tuberculosis, malaria, and many others), leading to the hypothesis that pathogen virulence and transmission are related through the within-host population growth rate (Anderson and May (1982a); Lenski (1988); Levin et al. (1982); Levin and Pimentel (1981); May and Anderson (1982)). With this tradeoff incorporated, non-spatial models no longer predict avirulence. If the tradeoff is one of increasing returns in transmission as virulence increases, the pathogen is predicted to evolve both infinitely high virulence and infinitely fast transmission, a non-prudent strategy that will lead to extinction. If, however, the tradeoff is one of decreasing returns in transmission as virulence increases, the pathogen is instead predicted to evolve a more prudent strategy in the form of intermediate virulence and intermediate transmission rates.

Alternatively, a growing number of studies in the literature suggest that host population spatial structure can also lead to the evolution of intermediate trans-

mission rates and virulence. Here we review spatial structure as an explanation for the evolution of pathogen prudence. In the first section of our paper, we explain background concepts that the reader must be familiar with to understand our review: common mathematical approaches to modeling pathogen-host dynamics, methods for predicting pathogen evolution in spatial and non-spatial contexts, and the evolutionary effects of a transmission-virulence tradeoff and other aspects of host and pathogen ecology in a non-spatial context.

In the second section of our paper we provide an in depth review of spatial pathogen-host models from the literature, identifying key aspects of host and pathogen ecology that lead to the evolution of pathogen prudence, and comparing the potential effects of space with those of the transmission-virulence tradeoff. Although the general conditions that promote the evolution of altruism in a spatial context have been summarized (Lion and van Baalen (2008)), the conditions specific to pathogen-host interactions have not. By comparing and interpreting spatial pathogen-host models we show that spatially dependent host interactions (i.e. spatially dependent disease transmission), spatially dependent host dispersal, and relatively slow host reproduction can create spatial structure that enforces a competition-persistence tradeoff. We also point out that these models predict pathogen prudence regardless of the shape of the transmission-virulence tradeoff. Finally, we review the handful of spatial models from the literature that include more complex aspects of host and pathogen ecology (host immunity, more complicated host network structures, co-infection, super-infection, and free-living propagules) and discuss their potential importance for the evolution of pathogen transmission rate and virulence.

We conclude our paper by discussing three important directions for future research. First, it is essential to clarify and further develop our quantitative understanding of the evolutionary effects of spatial structure. The ability to quantitatively predict the evolutionary trajectory of a pathogen's transmission rate in a spatial context will potentially contribute to our ability to design appropriate intervention strategies for newly emerging infectious diseases (see for example Débarre et al. (2007)). Second, it is important to continue to develop existing, and create new, theoretical models of pathogen host interactions, improving and refining our understanding of both the overall dynamics and the individual causal factors. Finally, in order to practically apply the knowledge gained from theoretical models it is crucial to test the growing body of theoretical hypotheses both observationally and experimentally.

2.2 Background

2.2.1 Pathogen-host models

Non-spatial models. The canonical non-spatial pathogen-host model for horizontally transmitted diseases consists of a set of ordinary differential equations describing the population of susceptible hosts (S), the infected hosts (I), and hosts removed by recovery or death (R ; Anderson and May (1979); Diekmann and Heesterbeek (2000); Hethcote (2000)). A simple example, often used as the basic framework for many spatial and non-spatial models, is given by equations 2.1 and 2.2.

$$ds/dt = (\lambda - \mu) \cdot s - \beta \cdot i \cdot s \tag{2.1}$$

$$di/dt = \beta \cdot i \cdot s - (\alpha + \mu) \cdot i \tag{2.2}$$

In this formulation, $s = S/N$ and $i = I/N$ where N is the total population size such that s and i represent the fraction of the total population that is susceptible and infected, respectively. λ is the host birth rate, μ is the host death rate, β is the pathogen's transmission rate, and α is the pathogen's virulence. The fraction of hosts removed at a given time t is $r(t) = 1 - s(t) - i(t)$ and the amount of time an individual spends in the pool of infected hosts is $1/(\alpha + \mu)$.

This relatively simple model is only one of a large family of models characterized by different assumptions. All models in this family share some common features. First, the pathogen population is not explicitly modeled but inferred from the number of infected hosts. Second, each host is assumed to interact equally with all other hosts—pathogen transmission depends only on the relative numbers of infected and susceptible hosts in the population. Finally, the ability of a pathogen to invade a host population is determined by its basic reproductive ratio (R_0 ; Anderson and May (1979); May and Anderson (1979)).

The concept of R_0 (reviewed and discussed in Dieckmann (2002); Diekmann et al. (1990); Heesterbeek (2002); Heesterbeek and Dietz (1996); Heffernan et al. (2005); Hethcote (2000); Roberts (2007)) is closely related to the ecological and demographic concept of an individual's lifetime reproductive success (R). For a pathogen, R is the number of secondary infections caused by an average infected host or the number of secondary infections caused by a single infected individual per unit time ($\beta \cdot s(t)$) multiplied by the time spent in the infectious pool ($1/(\alpha + \mu)$). A more specific metric, R_0 is the lifetime reproductive success of a pathogen specifically when the

host population is entirely susceptible ($s(t) = 1$)

$$R_0 = \beta/(\alpha + \mu) \tag{2.3}$$

If $R_0 > 1$, then the pathogen will be able to successfully invade the host population.

Spatial Models. The majority of spatially explicit pathogen-host models are individual-based models (although see for example Débarre et al. (2007); House and Keeling (2008)) that track the state of individual hosts through time. Like non-spatial models, individual-based models (IBMs) track the pathogen population simply by its presence or absence in each host. Most individual based pathogen-host models assume fixed host location. These discrete state and space models are typically implemented as probabilistic cellular automata (PCA). By definition PCA treat the host population size as a discrete variable. In addition, since space is limiting, host reproduction is inherently density dependent. Finally, PCA are typically stochastic rather than deterministic.

Whether the host population in an IBM is spatially structured depends on how individual hosts interact. In this context, it is useful to think of the host population as a network where each node is an individual host and two nodes are connected if there is an opportunity for disease transmission between them. The connection kernel that describes the probability of interaction between nodes dictates the structural properties of the network and therefore the disease dynamics on that network (see for example Eames and Keeling (2006); Keeling (2005); Webb et al. (2007a)). If all individuals have an equal probability of interacting with, and transmitting disease to, every other individual in the population then it is randomly mixing and non-spatial. If however, each individual interacts with only a limited subset of other individuals, the population may not be randomly mixing. For example, if the probability of two hosts interacting depends on the physical distance between them then the population is spatially structured. If, on the other hand, the probability of two hosts interacting is random then the population is effectively randomly mixed. Complex spatial models of host-pathogen interactions may allow the number of connections per individual host to vary across the population or in time (e.g. Bansal et al. (2007); Volz and Meyers (2007)) or they may allow connections to be asymmetric such that the disease can be uni-directionally transmitted between hosts (e.g. Meyers et al. (2006)).

In general, there are two approaches to characterizing the dynamics of an IBM—simulation or correlation equations. In the former case, the dynamics are characterized by the statistical analysis of multiple independent simulations. In the latter case,

the dynamics are characterized by a set of differential equations that describe the spatial moments, or the spatial covariance, of the system. By using a pair approximation method the dynamics of the correlation equations are simplified such that they approximately describe correlations between pairs of neighboring hosts that can then be analyzed. Results obtained by simulation and pair approximation closely match each other (Haraguchi and Sasaki (2000); Kamo et al. (2007); Sato et al. (1994)). Recently it has been shown that including the effects of higher moments can improve the accuracy of the approximation (Peyrard et al. (2008)).

2.2.2 Predicting the evolution of pathogen transmission rate and virulence

For some non-spatial pathogen-host models the evolutionary stable transmission rate and virulence can be analytically determined by maximizing the pathogen's basic reproductive ratio (R_0 ; Bremermann and Thieme (1989); Roberts (2007)). In those cases, the pathogen with the highest initial growth rate, quantified by R_0 , is competitively superior to all other pathogens from the moment of invasion to equilibrium. Although attractive for its simplicity, the R_0 maximization approach to determining the evolutionary stable transmission rate and virulence is not without limitations. Perhaps the biggest limitation, this approach is only accurate if selection is not frequency dependent and the demographic and epidemiological rates are not density dependent (Dieckmann (2002)). In those cases, a pathogen with the highest initial growth rate may not be competitively superior later on, when the host population is not entirely susceptible. In addition, the R_0 maximization approach ignores short-term evolutionary dynamics giving only the long-term evolutionary end point. To avoid these limitations, a different approach is required. One commonly used alternative is an adaptive dynamics approach (Dieckmann (1997); Hofbauer and Sigmund (1990); Nowak and Sigmund (1990); Waxman and Gavrillets (2005)), which uses the pathogen's invasion fitness rather than R_0 to determine the evolutionary stable transmission rate and virulence, if one exists. Another, less-utilized alternative is a quantitative genetics approach (e.g. Day and Proulx (2004)).

Because of their complexity, the evolutionary dynamics of spatial host-pathogen models have to be analyzed using an adaptive dynamics approach, either utilizing pair correlation equations to derive a pathogen's invasion fitness (Matsuda et al. (1992); Sato et al. (1994)) or simulation. By simulation, the evolutionary stable transmission rate or virulence (again, if one exists) can be estimated using stochastic invasion sequences. Starting with host population in equilibrium with a resident pathogen

strain, a mutant strain with a trait value close to the resident strain is introduced. The process continues until a mutant strain with the evolutionary stable transmission rate or virulence invades so that the trait under selection no longer changes. To be accurate, such simulations should allow the system to reach equilibrium before new mutant strains are introduced. However, especially in large spatial systems equilibrium may take an inordinate amount of time and many authors instead infer the evolutionary stable trait value by averaging across all pathogen strains in the population at a given time. The evolutionary stable trait values estimated by simulation generally matches those estimated using correlation equations (Kamo et al. (2007)).

Transmission rate and virulence evolution in a non-spatial context Through the development of non-spatial models a multitude of potential controls on pathogen evolution have been identified. Perhaps the most prominent, and sometimes controversial aspect of pathogen ecology that can theoretically influence the evolution of a pathogen's transmission rate and virulence is a tradeoff between the two (Anderson and May (1982a); Lenski (1988); Levin et al. (1982); Levin and Pimentel (1981); Lipsitch and Moxon (1997); May and Anderson (1982)). The tradeoff theory of pathogen evolution arose from the observation that in simple disease models, selective maximization of R_0 should lead to the evolution of maximum transmission rates and minimal virulence (according to equation 2.3, maximum β and minimum α maximizes R_0). In reality, among the many known pathogens in the world, many exhibit intermediate to high virulence. The existence of a tradeoff between transmission and avirulence is one explanation for this variation. This tradeoff could arise due to a linkage between transmission and virulence through the within-host population growth rate of the pathogen, or due to other within-host mechanisms. A transmission-virulence tradeoff can take one of three basic shapes: linear, concave up, or concave down. A linear transmission-virulence tradeoff occurs for example if an increase in within host reproduction proportionally increases both transmission rate and virulence. In contrast, concave up tradeoff occurs when an increase in within host reproduction disproportionately increases transmission rate over virulence. Finally, a concave-down tradeoff occurs when an increase in within host reproduction disproportionately increases the virulence over the transmission rate. In other words, the benefits of an increased transmission rate are offset by the accelerating costs of virulence.

When the conditions for R_0 maximization are met, the evolutionary effects of different transmission-virulence tradeoff shapes can easily be assessed. Rather than avirulence and maximum transmission rates, both linear and concave up tradeoffs

lead to the evolution of maximal virulence and transmission rates. In contrast, a concave down tradeoff leads to the evolution of intermediate virulence and transmission rates, or prudence. When the conditions for R_0 maximization are not met, the evolutionary effects of different transmission-virulence tradeoff shapes may or may not differ from these general patterns (Dieckmann (2002)). For example, if the simple model presented in equations 2.1 and 2.2 is modified to include density dependent host reproduction, the evolutionary predictions generated by R_0 maximization and invasion analysis are quantitatively identical for all tradeoff shapes. In contrast, a similar model with density dependent host mortality and a concave up transmission-virulence tradeoff produces an evolutionary dimorphism not predicted by R_0 maximization (Pugliese (2002)).

Many other aspects of host and pathogen ecology have been shown to influence the evolution of a pathogen's transmission rate and virulence in a non-spatial context like the mode of transmission (Ewald (1993)), the ability of a pathogen to co-infect or super-infect already infected hosts (Bonhoeffer and Nowak (1994); Levin and Bull (1994); Levin and Pimentel (1981); Mosquera and Adler (1998); Nowak and Sigmund (2002)), disease life-history events like the time lag between the onset of transmission and the onset of pathogen-induced mortality (Day (2003)), host mortality (Anderson and May (1982a); Choo et al. (2003); Ebert and Weisser (1997); Kakehashi and Yoshinaga (1992); Lenski and May (1994)), and free-living propagule survival rate (Bonhoeffer et al. (1996a); Gandon and Michalakis (2000)).

More recently, theoretical evidence has been accumulating that host population spatial structure can also affect the evolution of a pathogen's transmission rate and virulence. In the following sections we review the results of several spatial pathogen-host models. By comparing these models with each other and their non-spatial counterpart, we find that the evolutionary effects of space are strongest when host interactions are local, host dispersal is local, and the host reproduction rate is low. Together, these conditions enforce a competition-persistence tradeoff.

2.3 Spatial models of the evolution of pathogen transmission and virulence

2.3.1 The competition-persistence tradeoff

Qualitatively, the effects of spatial structure on horizontally transmitted pathogens can best be understood in the framework of a tradeoff between a pathogen's com-

petitive ability and persistence. Decomposed, the lifetime reproductive success of a pathogen (R) is the pathogen’s basic reproductive ratio (R_0 , equation 2.3) multiplied by the fraction of susceptible hosts in the population ($s(t)$). The first component, R_0 , quantifies a pathogen’s competitive ability when host resources are not limiting—of two different pathogen strains introduced into the same host population, the one with the highest R_0 will have a competitive advantage. The second component, $s(t)$, determines the length of time the pathogen will persist in the population when resources are limiting (i.e. there is not a constant supply of susceptible hosts)—of two identical pathogen strains introduced into two different host populations of the same size, the one in the population with the highest fraction of susceptible hosts will persist longer.

A competition-persistence tradeoff arises when the factors that increase the pathogen’s competitive ability also decrease its persistence time. For example, in the model captured by equations 2.1 and 2.2, a higher transmission rate increases the pathogen’s competitive ability (R_0) but also decreases the size of the susceptible population ($s(t)$) and therefore the pathogen’s persistence time (see for example figure 1 in Keeling (2000)). Virulence, on the other hand, decreases the pathogen’s competitive ability and increases its persistence time by decreasing the size of the pool of infected hosts and thus the likelihood that a susceptible host will interact with an infected host. For this model then, a competition-persistence tradeoff has the potential to lead to the evolution of an intermediate transmission rate and virulence, with selection balancing the benefits of higher competitive ability with the costs of lower persistence times. It is important to note that in some cases, the effects of virulence on persistence are not so straightforward. For example, if infected hosts can reproduce, less virulent pathogens will increase persistence by maintaining a large pool of infected hosts to reproduce. Ultimately then, the effect of virulence on persistence will depend on the balance between the benefits and costs of maintaining a large pool of infected hosts.

Although a competition-persistence tradeoff conceptually exists in a non-spatial context, it does not affect the evolutionary trajectory of the pathogen because all pathogen strains share the same pool of susceptible hosts—if that shared pool disappears, all pathogen strains relying on it will go extinct. Therefore, in a non-spatial context, the persistence time of all pathogens is determined by the least persistent pathogen in the group. (A notable exception to this is when host population size is small enough that persistence time is influenced not just by the initial fraction of susceptibles, but also by the possibility of stochastic extinction due to fluctuations in the fraction of infected hosts inherent to host-pathogen dynamics, King et al. (2009)). In contrast, if the host population is spatially structured, two individuals infected by

different pathogen strains do not necessarily share the same pool of host resources—one particular pathogen strain may over-utilize its own pool of susceptible hosts and go extinct without also causing the extinction of every other pathogen strain. As a result, different pathogen strains can determine their own persistence time and selection can act on the competition-persistence tradeoff.

2.3.2 Simple models

By far, the most common spatial pathogen-host models in the literature are SI individual based PCA where co-infection and recovery are not allowed and the number of connections per host is constant across the population and fixed through time. These simple models are ideal for exploring the effects of a few basic aspects of host and pathogen ecology. Table 2.1 lists models of this type from the literature with their references, organized by the different aspects of host-pathogen ecology they capture including the range of host interactions, the range of host dispersal, the host reproduction rate, and the shape of the transmission-virulence tradeoff. The range of host interactions and the range of host dispersal can vary from local to random, the host reproduction rate can be high (empty sites in the PCA are instantaneously colonized by susceptible hosts) or low (colonization of empty sites by susceptible hosts is determined by the demography of the host population), and the shape of the tradeoff, if present, can be linear, concave up, or concave down. For each case of host-pathogen ecology, we indicate whether the model (or models) predicts the same or a different evolutionary outcome than a non-spatial model (i.e. model in equations 2.1 and 2.2) with the same type of tradeoff between transmission rate and virulence.

Note that in comparing the evolutionary dynamics of these spatial models with non-spatial models it is important to consider the potential effects of discrete population sizes and stochasticity, both of which are characteristic of PCA but not necessarily characteristic of non spatial models and both of which can have significant consequences (Durrett and Levin (1994); Read and Keeling (2007)). In the studies examined here, the authors have accounted for the potential effects of discreteness and stochasticity by comparing the dynamics of the spatial model with random mixing to the dynamics of an equivalent non-spatial, deterministic model. In the cases here, the dynamics are not significantly different, indicating that disparities that arise when other aspects of the spatial model are changed cannot be attributed to the effects of discreteness or stochasticity. Also important to consider, recall that density dependent host reproduction, implicit to PCA models, does not impact the evolutionary effects of different transmission-virulence tradeoff shapes.

By comparing across the models listed in table 2.1, some interesting patterns emerge. First, it is clear that the most evolutionarily significant aspects of host and pathogen ecology among those that vary across these models are the range of host interactions and the rate of host reproduction. Regardless of the presence or form of the transmission-virulence tradeoff or the range of host dispersal, if the host reproduction rate is low, local host interactions lead to the evolution of a lower transmission rate than either a non-spatial model (rows 1-3, and 7) or a similar model with a random interaction network (compare row 2 with 5, and row 7 with 9). However, the effects of local host interactions can be overridden by a high host reproduction rate. The evolutionary trajectory of a spatial model with local host interactions and a high host reproduction rate is no different than that of a non-spatial model (row 6).

Table 2.1 also reveals that, although not essential to the qualitative outcome, the range of host dispersal is quantitatively important to the evolutionary effects of spatial structure. When host interactions are local and host reproduction is low, localized host dispersal amplifies the effects of spatial structure (compare rows 2 and 3), leading to lower transmission rates and virulence than if host dispersal is random. By itself, however, local host dispersal does not lead to the evolution of a lower transmission rate than in a non-spatial model (row 9).

Interpreted in the context of a competition-persistence tradeoff it becomes clear why the evolutionary effects of spatial structure on pathogen transmission rate and virulence are strongest when the host reproduction rate is low, host interactions are local, and host dispersal is local. A low host reproduction in combination with local host interactions ensures that different pathogen strains do not often share the same pool of susceptible hosts such that selection can act on the competition-persistence tradeoff. Low host reproduction allows the host population to segregate into distinct patches separated by dead hosts and local host interactions limit the spread of the pathogen between patches so that each host patch is typically infected by only one pathogen strain. If the host reproduction rate is high, there is no opportunity for the formation of distinct host population patches and, whether host interactions are local or not, the end result is that different pathogen strains will frequently share the same pool of susceptible hosts such that selection cannot act on persistence. Note that these dynamics require that the space be large enough to contain multiple host patches. Otherwise, the dynamics are identical to a well-mixed system (Rauch and Bar-Yam (2006)).

Recall that we define high host reproduction as the instantaneous colonization of empty sites by susceptible hosts and low host reproduction as anything that is not

Table 2.1: Predicted transmission rates for a set of spatial models.

	Reference(s) ^a	Tradeoff Type	Host Interactions ^c	Host Rep. Rate	Host Dispersal ^d	β & α ^b
1	Rand et al. (1995) Haraguchi et al. (2000) Rauch et al. (2002)	None ^e	Local	Low	Local	Different
2	Boots et al. (1999) Haraguchi et al. (2000) Kamo et al. (2007) Boots et al. (2000)	Linear & Concave up Linear Linear Concave up	Local	Low	Local	Different
3	Boots et al. (2000)	Concave up	Local	Low	Random	Different ^f
4	Kamo et al. (2007) Boots et al. (1999)	Linear Concave up	Intermediate	Low	Local	Different
5	Kamo et al. (2007) Boots et al. (1999)	Linear Concave up	Random	Low	Local	Same
6	Claessens et al. (1995)	Concave down	Local	High	Local or Random ^g	Same

Continued on next page...

Table 2.1 — Continued

Reference(s)	Tradeoff Type	Host Interactions	Host Rep. Rate	Host Dispersal	β & α
7	Kamo et al. (2007)	Local	Low	Local	Different
8	Kamo et al. (2007)	Intermediate	Low	Local	Different ^h
9	Kamo et al. (2007)	Random	Low	Local	Same

^aAll models are PCA where the number of contacts per host (4) is constant both across the population and in time. Co-infection is not allowed. Models with similar host and pathogen ecologies are grouped together by line number.

^bIndicates whether the model qualitatively predicts the same transmission rate (β) as a non-spatial model with the same transmission-virulence tradeoff.

^cHost dispersal local when hosts reproduce only into directly adjacent sites and random when hosts reproduce into random sites.

^dHost interactions are local when interactions occur only between directly adjacent hosts and random when interactions occur randomly.

^eThe virulence is held fixed and only the transmission rate evolves.

^fThe predicted value is smaller than the non-spatial model predicts but larger than that predicted by row 2 models.

^gBecause of the high reproduction rate, there is no effective difference between the case of local or random host dispersal.

^hThe predicted value is larger than the equivalent non-spatial model.

high. This definition is especially imprecise with respect to low host reproduction. As such, although a low host reproduction rate as we define it allows the potential for the host population to segregate into distinct patches, whether it does depends on the reproduction rate relative to the host death rate, the pathogen's transmission rate, and the pathogen's virulence. In the studies reviewed here, the demographic and epidemiological rates are such that the host population dynamics are characterized by a patchy distribution in space, but this does not necessarily need to be the case. Also note that empty space (or population regulation by the pathogen) is one of the conditions that Lion and van Baalen (2008) cite as favorable to the evolution of altruistic traits.

Finally, given a low host reproduction and local host interactions, local host dispersal further enforces the competition-persistence tradeoff by restricting the effects of a particular pathogen strain to its own pool of susceptible hosts. Even if different pathogen strains do not share the same pool of susceptible hosts, host dispersal indirectly allows pathogen strains to influence pools of susceptible hosts other than their own. For example, random host dispersal from an area with a high density of susceptible hosts can replenish an area with a low density of susceptible hosts. However, because the effects are indirect, random host dispersal only weakens and cannot entirely negate the selective importance of the competition-persistence tradeoff.

Comparing across the models in table 2.1 additionally suggests that in a spatial context, given local host interactions, local host dispersal, and low host reproduction, the shape of the transmission-virulence tradeoff is not as critical as it is in a non-spatial context. In a non-spatial model, a linear or concave up transmission-virulence tradeoff leads to the evolution of infinite values of both while a concave down tradeoff leads to finite, intermediate values of both. In contrast, spatial models with local host interactions, local host dispersal, and low host reproduction qualitatively predict intermediate transmission rates and virulence lower than that predicted by a non-spatial model for all forms of the tradeoff and in the absence of a tradeoff altogether (compare rows 1, 2, and 7). Furthermore, a limited preliminary analysis of available results indicates that the quantitative difference in the evolutionary trajectory between spatial models with linear and concave down tradeoffs is small (see table 2.2). When spatial structure exists with local host interactions, local host dispersal, and low host reproduction, that spatial structure dominates over the form of transmission virulence tradeoff in determining pathogen transmission rate and virulence.

However, when host interactions are intermediate between local and random, the shape of the transmission-virulence tradeoff can have important consequences (see

Table 2.2: A quantitative comparison of evolutionarily stable transmission rate (β) and virulence (α) in spatial and non-spatial models.^a

Tradeoff Shape	Non-spatial Model		Spatial Model	
	α	β	α	β
Linear or Concave up	Max	Max	0.15	0.45
Concave down	0.145	0.29	0.1	0.21

^aThe virulence values for the spatial model were estimated from the cases with local host interactions (quantified by the parameter L ; $L = 0.0$) in figs. 1 and 5 in Kamo et al. (2007) and the transmission rates were calculated using the given tradeoff equations ($\beta = 3\alpha$, $\beta = 5 \cdot \log(\alpha + 1)$). The values for the non-spatial model were calculated by maximizing the expression for R_0 using the parameter values given for the spatial models: host death rate $d = 0.01$ and host reproduction rate $r = 3$.

row 4 and 8). For example, assuming a linear (Kamo et al. (2007)) or concave up (Boots and Sasaki (1999)) transmission-virulence tradeoff, at some intermediate connectivity between local and random (the ‘critical connectivity’) the evolutionary stable pathogen virulence quickly increases from an intermediate value to the value predicted by an equivalent non-spatial model. In contrast, assuming a concave down tradeoff, the evolutionary stable virulence initially increases with the probability of random interactions, reaches a maximum value at some intermediate connectivity, and then declines slightly to the virulence predicted by an equivalent non-spatial model (Kamo et al. (2007)). In addition, in the case of a linear tradeoff, there is evolutionary bi-stability on a small interval below the critical connectivity, behavior that is not evident when the tradeoff is concave down (Kamo et al. (2007)).

2.3.3 More complex models

The models reviewed above are relatively simple with respect to host and pathogen ecology. Here we briefly review a handful of spatial models that include more complicated aspects of host and pathogen ecology like host immunity, more complex host interaction networks, co-infection, super-infection, and propagule survival rate. While arguably more realistic, the complexity of these models makes it more difficult to interpret the dynamics in relation to the competition-persistence tradeoff. Also, because these aspects of host and pathogen ecology can be modeled in numerous ways, it is not clear to what degree the results of these models are generalizable.

Host immunity. Host immunity is an important aspect of host ecology that is not

often included into spatial models. In a model with local host interactions, local host dispersal, relatively low host reproduction, and a constant transmission rate, if the rate of recovery (and therefore the acquisition of immunity) is inversely related to the virulence of the pathogen then immunity leads to evolutionary bi-stability—high virulence or avirulence (Boots et al. (2004)). Which strategy is realized depends on the prevalence and spatial arrangement of immune hosts, which in addition to empty space, act as barriers to disease transmission. Because of the inverse relationship between virulence and the production of immune hosts, an initial epidemic caused by a low virulence pathogen leads to numerous, widespread immune hosts while a high virulence strain leads to fewer immune hosts and more empty space. In the former case, immune hosts retard the spread of all newly invading pathogen strains and, since high virulence strains are more likely to kill their host before they have an opportunity to spread, selection favors avirulence. In the latter case, newly invading less virulent pathogens surround themselves with immune hosts before they have an opportunity to spread and selection favors high virulence. Whether bi-stability occurs with other types of immunity (partial or temporary) or with other relationships between virulence and recovery has not yet been determined.

Host network structure. The simple spatial models reviewed earlier share the same basic host network structure where each host has the same number of connections and each connection is either local or random. Many other host network structures are possible, raising the question whether the evolutionary role of local host interactions in enforcing the competition-persistence tradeoff is consistent across all types of networks. Current evidence suggests that it may not be, at least in the context of pathogens for which there is permanent host immunity. In a model that includes permanent host immunity and a more complex host interaction structure, more local host interactions lead to higher virulence than global host interactions (Read and Keeling (2003)). In this model, after an initial epidemic the host population is fragmented into distinct host clusters separated from each other by barriers of immune hosts. When the network is structured locally, the clusters tend to be bigger (contain more hosts) and highly connected (hosts in the same cluster share many of the same contacts). As a consequence, new pathogen strains are more likely to arise in the same cluster and compete intensely. In essence, each cluster is an isolated, well-mixed system where competition, not persistence, drives the evolutionary dynamics.

Co-infection. One study (Claessen and deRoos (1995)) indicates that co-infection can allow for the evolution of reduced transmission and virulence even in the presence of high host reproduction. According to this model, the impact of co-infection on the

evolutionary trajectory of pathogens in a spatial context depends on the combined virulence of the pathogens. Assuming that the combined virulence and transmission rate of pathogens in doubly infected hosts is independent of the virulence of pathogens on their own, local host interactions, local host dispersal, a high host reproduction rate, and a concave down transmission-virulence tradeoff, this spatial model predicts that high combined virulence leads to the evolution of lower virulence, whereas low combined virulence leads to the evolution of high virulence. Like immune hosts or empty space, doubly infected hosts act as barriers to disease transmission because they cannot be infected a third time. When the virulence of doubly infected hosts is high, doubly infected hosts are not effective disease transmitters and the host population segregates into distinct patches of singly infected hosts separated by doubly infected hosts. This spatial structuring selects for lower virulence pathogens. When virulence of infected hosts is low infected hosts are less spatially segregated and higher virulence is selected.

Super-infection. Super-infection is a specific type of co-infection where higher virulence pathogens displace low virulence pathogens in doubly infected hosts. In a spatial model with local host interactions, local host dispersal, a relatively low host reproduction rate, and a linear tradeoff between pathogen transmission and virulence, super-infection leads to the evolution of a lower transmission rate and virulence than in a non-spatial context (Caraco et al. (2006)). These results are qualitatively identical to the predictions of a simple spatial model without super-infection (e.g. row 2 in Table 2.1) where local host interactions, local dispersal, and low host reproduction rates enforce a competition-persistence tradeoff. Further studies are needed to determine whether superinfection quantitatively affects the evolutionary stable transmission rate and virulence.

Free-living propagules. Many pathogens are able to persist for some amount of time outside their host. For those pathogens, the length of time the free-living propagules can persist and the means of dissemination can impact the evolution of pathogen transmission rates and virulence. Here we consider a spatial model with local host interactions, local host dispersal, a low host reproduction rate, and host recovery where infected hosts produce pathogen propagules that are disseminated (either throughout infection or upon the death of the infected host) to the site it occupies plus the sites that it is in contact with (Kamo and Boots (2004)). In this model, short-lived propagules lead to the evolution of higher, but still intermediate, transmission rates than long-lived propagules regardless of the shape or existence of a transmission-virulence tradeoff or the timing of propagule production. When there is a linear or

concave tradeoff, the same pattern holds for the evolution of virulence. However, if there is no tradeoff, the evolutionary stable virulence depends on the timing of propagule production. If the propagules are produced only when the host dies then long-lived propagules lead to the evolution of higher virulence. Otherwise, both long- and short-lived propagules lead to the evolution of avirulence.

With respect to the pathogen’s transmission rate, the results of this model are consistent with the results of the simple models already reviewed except that the particular transmission rate that optimally balances the benefits of increased competitive ability with the costs of decreased persistence depends on the lifespan of the free-living propagule. The evolutionary dynamics of virulence in this model are more complicated, partially because the model includes host recovery, an assumption that changes the relationship between virulence and pathogen persistence. Ultimately, the evolutionary stable virulence balances the effects of virulence and recovery on persistence with the effect of virulence on competitive ability.

2.3.4 Selection mechanism

Given the conditions that enforce a competition-persistence tradeoff, there are several ways to interpret the resulting evolutionary dynamics. Some authors attribute the dynamics to individual level selection (e.g. Boots and Sasaki (1999); Rauch et al. (2002)) and others to multilevel (kin or group) selection (e.g. Boerlijst et al. (1993) for a host-parasitoid interaction; Claessen and deRoos (1995); Haraguchi and Sasaki (2000)). Under both interpretations, the evolutionary driving force behind the dynamics is local feedback between the pathogen and the environment. Pathogens, or groups of pathogens, that reduce the local availability of susceptible hosts ultimately reduce their fitness. From the perspective of individual level selection, the fitness effects of the environmental feedback loop are assessed at the level of the individual—a single pathogen strain infecting a single host—and has variously been called ‘self-shading (Boots and Sasaki (1999, 2000); Haraguchi and Sasaki (2000)) or ‘time-dependent fitness (Rauch et al. (2003, 2002)). In contrast, from the perspective of multilevel selection, the fitness effects are assessed at the group level—a cluster of hosts, each infected by the same pathogen strain or closely related pathogen strains. Regardless of the interpretation, the key to these evolutionary dynamics is the spatial aggregation of pathogen types so that the environmental effects of a particular pathogen strain are experienced exclusively by it and similar or related pathogens. Importantly, spatial assortment been identified as the basis for the evolution of altruism in general (Fletcher and Doebeli (2009)).

It is important to note that the competition-persistence tradeoff induced by spatial structure is not the same as the tradeoff between a pathogen’s transmission rate and virulence. Because the two tradeoffs can have similar consequences (lower evolutionary stable pathogen transmission rates and virulence) it is tempting to assume that spatial structure is another explanation for the existence of a transmission-virulence tradeoff (see for example Johnson and Boerlijst (2002)). There is a critical distinction, however, between the two tradeoffs. A competition-persistence tradeoff is enforced at the level of the host population while the transmission-virulence tradeoff is enforced at the level of individual hosts.

2.4 Future Research

Theoretical work examining pathogen-host interactions has contributed significant insight into the effects of spatial structure on evolutionary dynamics. In particular, the importance of selected host and pathogen life history traits has been thoroughly explored. However, our understanding of the effects of spatial structure is still incomplete, offering opportunity for advancement in diverse directions. Below we identify and outline what we see as the next big steps.

2.4.1 Quantifying pathogen fitness

Currently, our ability to quantitatively predict pathogen evolution in a spatial context is limited to certain specific cases. For example, while the pathogen’s invasion fitness derived from pair correlation equations is an accurate predictor of the evolutionary stable transmission rate and virulence, it has only been developed for a narrow range of spatial models not including those with a variable number of contacts per host, either across the population or in time, or with more complicated host dispersal and connection kernels. Expanding the analytical framework within which we can quantitatively predict the evolution of pathogen transmission rate and virulence will be useful in the context of predicting the effects of newly emerging infectious diseases. Beyond successfully predicting the evolution of pathogen transmission rates and virulence, ultimately our understanding of the mechanism driving the evolution in a spatial context will depend on the quantitative development and subsequent comparison of the three possible interpretations of the dynamics as individual, kin, or group selection. It is possible that these three interpretations are indistinguishable, as argued by (Fletcher and Doebeli (2009)). To determine if they are distinguishable, each must 1) be associated with quantitatively different predictions of pathogen

evolution, and 2) be compared to simulation results.

To date, the mathematical argument for individual selection is the best developed. Based on the invasion fitness of individual pathogen strains derived from pair correlation equations, one can quantitatively and accurately predict a pathogen's evolutionary stable transmission rate and virulence without explicitly invoking either kin or group selection. However, because the invasion fitness derived in this way depends on the equilibrium density of susceptible hosts surrounding an invading pathogen, it is nonetheless suggestive of multilevel selection. In fact, by defining the relatedness of pathogens as a spatio-temporal variable and using the invasion fitness of the pathogen derived from the pair correlation equations, Hamilton's rule for the spread of altruism can easily be derived from the pair density dynamics (Lion and van Baalen (2008)). Although this formulation of Hamilton's rule does not immediately permit one to quantitatively predict a pathogen's transmission rate or virulence, it does suggest that such a prediction, reliant only on kin selection, is possible.

An alternative approach to quantitatively predicting a pathogen's evolutionary stable transmission rate and virulence based on the hypothesis of individual selection is to define the pathogen's invasion fitness as a function of time (Rauch et al. (2002)). In this way, the effect of the pathogen on its local environment can be incorporated into the selection dynamics without explicitly including it in the expression of pathogen fitness, thus eliminating the suggestion of multilevel selection. However, this approach is limited by the fact that the explicit shape of the time-dependent invasion fitness of a pathogen has so far only been estimated from simulations. As such, generating quantitative predictions that can be compared both to simulations and predictions generated by other approaches is so far impossible.

Group selection, an extension of kin selection, is the least mathematically developed hypothesis of the three. Although general formulations of group selection have been derived (see for example Chapter 10 in Rice (2004)), they have not been adapted specifically to pathogen transmission rate and virulence. Until these three hypotheses are sufficiently quantitatively developed, we will remain unsure which interpretation is correct and hence be limited in our understanding of the dynamics.

2.4.2 Modeling Developments

Continued exploration and development of spatial pathogen-host models will be invaluable. In addition to advancing our understanding of the factors that influence the evolution of pathogen transmission rate and virulence, models like those discussed in this review are useful tools for directing observational and experimental research.

This review suggests several interesting questions that can be addressed using existing models. First, is there a quantitative difference between the effects of spatial structure alone relative to the effects of a tradeoff between transmission rate and virulence? Although we suggest that spatial structure may have equally significant evolutionary effects as a tradeoff, the relative effects may differ depending on the details of the model or the shape of the tradeoff. As potentially alternative hypotheses to explain the evolution of pathogen prudence, a thorough exploration of the relative effects of both is important. Second, what is the shape of the relationship between the evolutionary stable transmission rate and the host reproduction rate? Although we present evidence that such a relationship exists, it is insufficient to determine whether it is smooth and continuous or if there is a critical threshold reproduction rate. Finally, are the conditions that enforce the competition persistence tradeoff consistent across different types of host interaction networks? Given that different network structures exhibit different disease dynamics they could also easily exhibit different evolutionary dynamics.

Many other questions can be addressed by further developing existing models. For example, while the co-evolutionary dynamics of pathogen-host interactions have been studied using non spatial models, and the evolution of host traits alone have been studied using spatially explicit models (Richards et al. (1999)), none so far have addressed co-evolution in a spatial context. Pathogen-host interactions are particularly good candidates for co-evolutionary change (Godfray et al. (1994)). It is likely that co-evolutionary relationships exist between host resistance and pathogen virulence, pathogen-avoidance and host-seeking behavior, and the hosts ability to clear infection and the pathogen's ability to evade host defenses (Woolhouse et al. (2002)). Undoubtedly, these co-evolutionary relationships will impact the effects of spatial structure on the evolution of pathogen transmission rate and virulence.

In addition, by using nested models (reviewed in Mideo et al. (2008)) the effects of spatial structure can more explicitly be related to the dynamics of the pathogen populations. For example, nested models have been used to examine the emergence of the hypothesized tradeoff between pathogen transmission rate and virulence (Alizon and van Baalen (2005); Antia et al. (1994); Gilchrist and Coombs (2006); Gilchrist and Sasaki (2002)). Nested models may be especially important when considering co-infection because they can explicitly treat competitive dynamics between pathogen strains in the same host (see for example Read and Keeling (2006)).

2.4.3 Experimental and Observational Validation

A perennial problem with modeling evolutionary dynamics is that the model predictions are usually very difficult to test experimentally. One of the advantages associated with modeling pathogen evolution is that, because of their ability to quickly adapt, they are exceptionally suited to experimental investigations. Two such studies have been done, one using moth larvae infected with their species-specific granulosis virus (Boots and Meador (2007)) and another using *Escherichia coli* and its T4 bacteriophage (Kerr et al. (2006)). Both studies supported the hypothesis that local host interactions in combination with local host dispersal can lead to reduced pathogen virulence. Future studies should test the effects of local interactions, local dispersal, and low host reproduction independently and together in varying degrees.

In addition to experimentation, it may be possible to observationally validate theoretical predictions using existing data. Comparison of the transmission rate and virulence of pathogens that affect host populations characterized by different ecologies may reveal consistent patterns. Ideally comparisons can be made between host populations infected with the same or closely related pathogen strains but in slightly different contexts. For example, comparing pathogen strains that infect two host populations, one that is more structured in space, perhaps due to landscape fragmentation, and one that is subject to fewer spatial constraints addresses the evolutionary importance of the range of host dispersal. Or, comparing pathogen strains that infect different species of animals, some more prolific than others, addresses the evolutionary importance of host reproduction rate.

2.5 Conclusions

Simple non-spatial models of pathogen evolution predict that natural selection should maximize the basic reproductive ratio (R_0). The particular pathogen virulence or transmission rate that maximizes R_0 depends on the existence and shape of the tradeoff between the transmission rate and virulence. If there is no tradeoff, selection leads to maximum transmission rate and minimal virulence. If the tradeoff is linear or concave up, selection leads to both maximum transmission rate and maximum virulence. If the tradeoff is concave down, selection leads to a finite and intermediate transmission rate and virulence. Alternatively, if the host population is spatially structured then the evolution of a pathogen's transmission rate can be constrained by a tradeoff between competitive ability and persistence. Pathogens with a higher transmission rate are more competitive but are more likely to cause their own

extinction by reducing their access to susceptible hosts. The models reviewed here suggest that the most important aspects of pathogen and host ecology in a spatial context are the range of host dispersal, the range of pathogen transmission, and the rate of host reproduction. All three factors enforce a competition-persistence tradeoff by inducing a spatially patchy host population structure.

As an explanation for the evolution of pathogen prudence, based on the results presented in this review, spatial structure offers several advantages over the transmission-virulence tradeoff theory. First, while some pathogens show evidence of a transmission-virulence tradeoff (Messenger et al. (1999); de Roode et al. (2005)), other pathogens do not (Bull (1994); Ebert and Bull (2003); Stewart et al. (2005)). In the absence of a transmission-virulence tradeoff, unlike non-spatial models, which predict infinitely fast transmission, spatial models can predict an intermediate transmission rate. An intermediate transmission rate is arguably a more realistic prediction and, more importantly, is in some cases a necessary component of prudence. Further, for pathogens that do exhibit a transmission-virulence tradeoff, whether it is one of decreasing returns is not clear. Unlike non-spatial models which require a tradeoff of decreasing returns to predict intermediate transmission rates and virulence, spatial models can predict the same regardless of the specific shape of the transmission-virulence tradeoff. Finally, while the explanatory power of a transmission-virulence tradeoff is specific to pathogen-host interactions, the evolutionary effects of spatial structure are likely to extend to other types of exploitative interactions (e.g. Rauch and Bar-Yam (2006)).

The continual, world-wide emergence of new, drug-resistant diseases and the ubiquity of spatial structure in human host populations emphasizes the critical importance of understanding the evolutionary effects of spatial structure on pathogen-host interactions. Future research should focus on quantifying pathogen fitness in a spatial context, further theoretical developments and exploration of spatial models, and experimental and observational validation of those models.

CHAPTER III

The influence of host demography, pathogen virulence, and relationships with virulence on the evolution of pathogen transmission in a spatial context

3.1 Introduction

A significant challenge in evolutionary ecology is to explain the extreme natural variation in pathogen transmission and virulence across pathogen species. A potentially important source of variation is host and pathogen ecology. For example, tuberculosis (*Mycobacterium tuberculosis*) is highly virulent (causes high host mortality) while pneumonia (*Mycoplasma pneumoniae*) is much less virulent (Walther and Ewald (2004)). One possible explanation is that the bacteria causing tuberculosis can survive upwards of 250 days in the environment while the bacteria causing pneumonia can survive less than 2 days in the environment (Bonhoeffer et al. (1996b); Walther and Ewald (2004)). Thus, the negative impact of virulence on pathogen fitness mediated by host mortality is less for tuberculosis than pneumonia. The evolutionary importance of environmental pathogen transmission has been more generally addressed in the literature (e.g. Roche et al. (2011); Gandon (1998); Day (2002)). Other highly cited ecological explanations for observed variation in pathogen transmission and virulence include the presence and shape of a transmission-virulence relationship (Anderson and May (1982b); Levin and Pimentel (1981); May and Anderson (1982)), the timing of transmission (Cooper et al. (2002); Day (2003); Osnas and Dobson (2010)), the mode of transmission (Ewald (1998, 1987); White et al. (2002)), and the occurrence of co-infection or super-infection (Bull (1994); Frank (1996); Levin and Bull (1994); Levin and Pimentel (1981); Mosquera and Adler (1998); Nowak and

Sigmund (2002)).

Our current understanding of the evolutionary influence of host and pathogen ecology is largely based on analysis of mathematical models or inference from observational studies (e.g. Ewald (1993)). Empirical studies are limited by the difficulty of isolating the evolutionary influence of one particular ecological factor on pathogen variation. As methods in the study of evolutionary ecology become more sophisticated, observational and theoretical predictions are increasingly being tested (e.g. de Roode et al. (2008); Eshelman et al. (2010)). Yet the mathematical theory being tested has been developed primarily from analysis of non-spatial pathogen-host models. Recent theoretical work suggests that spatial context can strongly influence the evolution of interacting species (Hansen et al. (2007); Johnson and Seinen (2002); Le Galliard et al. (2003); Prado and Kerr (2008)), including pathogens (Boerlijst and van Ballegooijen (2010); Boots and Sasaki (1999); Haraguchi and Sasaki (2000); Kamo et al. (2007); Kerr et al. (2006); Lion and van Baalen (2008); Messinger and Ostling (2009); Rauch et al. (2002)). This is especially relevant for pathogens since host populations are often naturally structured by intrinsic limitations on movement, ranging from immobility (e.g. plants) to restricted home ranges (e.g. many mammal species).

While some work has addressed the evolutionary impact of host and pathogen ecology in a spatial context (Boots et al. (2004); Caraco et al. (2006); Claessen and deRoos (1995); Kamo and Boots (2004); Kamo et al. (2007)), the impact of basic host demography on the evolution of pathogen transmission rate has not been thoroughly explored. Furthermore, we have only pieces of the whole picture regarding the impact of the shape of the relationship between the pathogen's transmission rate and virulence in a spatial context (see Boots and Sasaki (1999); Haraguchi and Sasaki (2000); Kamo et al. (2007)). In particular, lacking is a systematic exploration of the pathogen's ES transmission rate across both host demography and relationships between the pathogen's transmission and virulence. Also lacking is an exploration of the effect of pathogen virulence on the ES transmission rate when there is no transmission-virulence relationship. Given that these aspects of ecology are fundamental to all hosts and their pathogens, elucidating their effects in a spatial context may improve our understanding of trait variation across of a broad range of pathogen species.

Here I evaluate via simulations the effect of the shape of the pathogen's transmission-virulence relationship on the pathogen's evolutionary stable (ES) transmission rate. In addition, I evaluate the predicted effect of the host reproduction rate, host natu-

ral death rate, and pathogen virulence on the pathogen’s ES transmission rate for no transmission-virulence relationship and across a range of linear transmission-virulence relationships and concave-down transmission-virulence tradeoffs. I find that the ecological context set by these traits is an important determinant of the pathogen’s ES transmission rate even when the non-spatial model predicts they are not. Particularly important is host reproduction: high host reproduction leads to a higher ES transmission rate. In most cases, host death increases the ES transmission rate, but at high host reproduction rates the ES transmission rate can actually decline. Though in some cases the spatial and non-spatial models predict the same qualitative trends with ecology, the quantitative difference varies. In some ecological contexts the quantitative differences are substantial, suggesting that despite overarching qualitative consistency in the theoretical predictions of spatial and non-spatial models, the potential evolutionary effects of spatial structure should not be ignored.

Given the potential of these results to inform our understanding of pathogen evolution, as well as the computational difficulties associated with deriving them for all possible ecological contexts, I additionally evaluate the ability of existing analytical theory to predict them. Researchers have debated about the best way to quantify the effects of space on pathogen evolution and thus predict how it is influenced by the details of the spatial and ecological context (van Baalen and Rand (1998); Boots and Sasaki (1999); Slobodkin (1974); also compare interpretations of pathogen fitness in: Johnson and Boerlijst (2002); Kerr and Godfrey-Smith (2002); Rauch et al. (2002); and see Goodnight et al. (2008)). A recent key approach has been to quantify pathogen fitness through the use of spatial moment equations: coupled equations that describe the mean density and spatial arrangement of two or more types of individuals or populations. These equations enable one to deconstruct fitness into its spatial and non-spatial components and thus more clearly understand how spatial structure will influence the evolution of a particular trait as well as the effect of different ecological contexts. In particular, these equations have highlighted the evolutionary role of “self-shading”, when the growth of cheaters or over-exploiters is hindered by the depletion of local resources, and that host demography should play an important evolutionary role (Boots and Sasaki (1999); Lion and van Baalen (2008)).

Although conceptually insightful, the tractability of the fitness concept based on spatial moment equations for predicting the outcome of evolution depends on the use of a moment closure method. A frequently used method is a pair approximation (PA) (see Boots and Sasaki (2000); Caraco et al. (2006); Kamo and Boots (2006); Kamo et al. (2007); Wild et al. (2009)) that eliminates the infinite array of moments above

pairs of individual or population types (Harada and Iwasa (1994); Matsuda et al. (1992); Sato et al. (1994)). While it is common knowledge that pair approximations are not always accurate, it is not clear to what extent this is the case for host-pathogen interactions. A few recent suggestive studies have questioned the accuracy of the PA in predicting the pathogen’s ES transmission rate for the case that the pathogen is not subject to a transmission-virulence relationship (de Aguiar et al. (2004); Boots et al. (2006); Lion and Boots (2010)), demanding a more comprehensive evaluation.

Here I evaluate the ES transmission rate predicted using the improved pair approximation (IPA), which has commonly been used in studies of spatial pathogen-host dynamics, in comparison to the ES transmission rate predicted by spatial simulations. I find that predictions based on IPA can be qualitatively incorrect, and in particular fail to the largest degree when the effects of spatial structure are most significant. These results show that the previously unknown extent of the limitations of IPA in predicting the effect of spatial structure on pathogen evolution is substantial and advocate examination of the accuracy of other moment closure methods (e.g. Bauch (2005); Filipe and Maule (2003); Peyrard et al. (2008)). However, despite the limitations of the IPA, I find that the relationships with host and pathogen demography uncovered through simulation can still be conceptually understood within the framework of “self-shading.” I suggest that future work should explore new constructs for quantifying the effects of “self-shading.”

3.2 Materials and Methods

3.2.1 Non-spatial model

A standard non-spatial model of susceptible-infected host-pathogen dynamics is given by the following equations:

$$\frac{dS}{dt} = (r - d) \cdot S - \beta \cdot S \cdot I \tag{3.1}$$

$$\frac{dI}{dt} = \beta \cdot S \cdot I - (d + \alpha) \cdot I \tag{3.2}$$

In this model, S is the number of susceptible hosts, I is the number of infected hosts, d is the host natural death rate, r is the host reproduction rate, β is the infection rate per infected individual, and α is the pathogen virulence (the death rate of the host due to infection). The product of β and I is the infection rate. Thus, $\beta \cdot S \cdot I$ is the number of susceptible hosts that become infected per time assuming complete mixing of the

host population. This model assumes that infected hosts do not recover from infection but are removed from the population due to natural death or disease-induced death. Despite this apparently restrictive assumption, there are a number of real pathogen-host systems that conform to this assumption, ranging from very virulent pathogens like lethal yellowing disease to nearly avirulent pathogens like Herpes. In addition, the model assumes that hosts cannot be co-infected. As mentioned, co-infection has been shown to play an important role in pathogen evolution (Bull (1994); Frank (1996); Levin and Bull (1994); Levin and Pimentel (1981); Mosquera and Adler (1998); Nowak and Sigmund (2002)). Here, however, our goal is to more carefully explore the role of a limited set of basic host and pathogen ecology related only to demography. As such, I have chosen to build from a simple model that does not include evolutionary complexities like co-infection.

From this model, the pathogen's per-capita growth rate is:

$$\frac{1}{I} \cdot \frac{dI}{dt} = \beta \cdot \left[S - \frac{d + \alpha}{\beta} \right] = \beta \cdot [S - S^*] \quad (3.3)$$

where S^* is the equilibrium number of susceptible hosts in the population and is the inverse of the pathogen's epidemiological R_0 (the number of secondary infections caused per infected individual in a completely susceptible population).

$$R_0 = \frac{\beta}{d + \alpha} \quad (3.4)$$

Eq. 3.3 predicts that the pathogen population will grow if the number of susceptible hosts in the population at the time of invasion is bigger than the number at equilibrium. To understand the evolutionary dynamics predicted by this model, consider the ability of a pathogen to invade a host population that is already at equilibrium with a different resident pathogen strain. In this scenario, S from eq. 3.3 is set by the resident pathogen and will be equal to the number of susceptible hosts at equilibrium with the resident pathogen. Thus, an invading pathogen's per-capita growth rate is:

$$\frac{1}{I_{invader}} \cdot \frac{dI_{invader}}{dt} = \beta_{invader} \cdot [S_{resident}^* - S_{invader}^*] \quad (3.5)$$

Eq. 3.5 predicts that when the invader's S^* is less than the resident's the invasion will succeed. In terms of R_0 , the pathogen with the bigger R_0 can invade. Therefore, this model predicts that selection will maximize R_0 . Note that the pathogen's per-capita growth rate is no different if the host is assumed to have logistic rather than

exponential growth—the predictions arising from the following invasion analysis are not dependent on any assumptions about the host’s growth. This is important since our spatial model effectively regulates the host’s growth.

Since the non-spatial model predicts that evolution will maximize the pathogen’s R_0 (eq. 3.4), the evolutionary influence of host and pathogen ecology can be understood from the derivative of R_0 with respect to β and solving for the transmission rate that maximizes R_0 . Assuming there can be a relationship between the pathogen’s transmission rate and virulence ($\alpha = C \cdot \beta^z$), the evolutionarily stable transmission rate that maximizes R_0 is:

$$\beta = \sqrt[z]{\frac{d}{C \cdot (z - 1)}} \quad (3.6)$$

When there is no transmission-virulence relationship ($C = 0$) or if the relationship is linear ($z = 1$), the evolutionary stable (ES) transmission rate is undefined: R_0 is maximized by an infinite transmission rate (and virulence, in the case of a linear transmission-virulence relationship). In practice, the model predicts evolution to pathogen-driven host extinction. Only if there is a transmission-virulence tradeoff where $z > 1$ does the non-spatial model predict an intermediate ES transmission rate. It follows that when there is no transmission-virulence relationship or a linear transmission-virulence relationship, host and pathogen ecology are not predicted to play a role in pathogen evolution. When there is a transmission-virulence tradeoff, the ES transmission rate is predicted to increase with the constant of proportionality (C) and the tradeoff exponent (z). The host reproduction rate is not predicted to influence pathogen evolution when there is a transmission-virulence tradeoff (the parameter r does not even appear in eq. 3.6), and the ES transmission rate is predicted to increase with the host natural death rate (d).

3.2.2 Spatial model

Assuming the same basic susceptible-infected pathogen-host dynamics (no immunity or co-infection), I consider a relatively simple stochastic spatial model where the host population resides on a regular two-dimensional lattice (150 x 150). Lattice sites can be occupied or empty, hosts are fixed in space, and host reproduction and pathogen transmission only occur between directly adjacent lattice sites. The realized rate of host reproduction is determined by the product of r and the number of empty sites among the host’s four nearest-neighbor sites. Similarly, the realized rate of transmission is determined by the product of β and the number of susceptible hosts

among the infected hosts four nearest-neighbor sites. Otherwise, the dynamics are as described for the non-spatial model. I focus on this simple type of spatial structure because it captures the key elements of spatially-explicit host-pathogen dynamics, and has already been demonstrated to have significant evolutionary effects (Messinger and Ostling (2009)). Hence it provides a good starting point for understanding spatial effects on pathogen evolution. Furthermore, this type of spatial structure is potentially representative of several natural host populations, including plants, sedentary plant parasites like aphids and other scale insects, sessile marine animals like barnacles, or animals with limited movement like anemones, starfish, and some terrestrial invertebrates.

To find the ES transmission rate for the spatial model I simulate the dynamics as a Poisson process using the Gillespie algorithm (Gillespie (1977)). The algorithm computes the time interval between sequentially occurring events, which is exponentially distributed for a Poisson process. When an event occurs, the probability of a particular event (host birth, host death, and pathogen transmission) is equal to the rate at which that event should occur, divided by the total rate at which events occur. Each time a susceptible host is infected, there is some chance that the infecting strain will mutate and acquire a different transmission rate, slightly different than the parent strain. Starting from a low initial transmission rate, the average transmission rate of the pathogen population changes over time. When the average transmission rate is no longer changing over time, I run the simulation for an additional 2000 time steps and take the average over the last 2000 time steps as the ES transmission rate. Although this method has been used elsewhere (e.g. Best et al. (2011)), it is different than the method used in other papers (e.g. Kamo et al. (2007)). I compared three different methods of inferring the ES transmission rate and found no difference between them (Appendix A).

3.2.3 Spatial moment equations and improved pair approximation

One way to capture the effects of the type of spatial structure described above is via spatial moment equations that describe the time derivative of paired states on the lattice (Appendix B). Summing the appropriate state pair derivatives yields the time derivatives for infected hosts. From this analysis, a pathogen strain's per-capita growth rate is:

$$\frac{1}{I} \cdot \frac{dI}{dt} = \frac{\beta}{n} \cdot \left[Q(S|I) - \frac{d + \alpha}{\beta} \right] = \frac{\beta}{n} \cdot [Q(S|I) - Q^*(S|I)] \quad (3.7)$$

In this equation, $Q(S|I)$ is the average number of susceptible hosts in the neighborhood of an infected host, $Q^*(S|I)$ is the number at equilibrium (which, like S^* in the non-spatial model, is the inverse of the pathogen's epidemiological R_0), n is the number of lattice sites in the neighborhood of each host (here $n = 4$), and all other parameters are as defined for the mean-field model. Similar to the mean-field model, this model predicts that the pathogen population will grow if the number of susceptible hosts surrounding an infected host at the time of invasion is bigger than the number at equilibrium.

As with the mean-field model, to understand the evolutionary dynamics predicted by the spatial moment equations, I consider the ability of a pathogen to invade a host population that is already at equilibrium with a different resident pathogen strain. In that case, an invading pathogen's per-capita growth rate is:

$$\frac{1}{I_{invader}} \cdot \frac{dI_{invader}}{dt} = \frac{\beta_{invader}}{n} \cdot [Q^*(S|I_{resident}) - Q^*(S|I_{invader})] \quad (3.8)$$

This model predicts that the invasion will succeed when the invader's $Q^*(S|I)$ is smaller than the resident's $Q^*(S|I)$. This criterion is very similar to the criterion for invasion in the mean field model except that rather than depending on the number of susceptible hosts in the entire population, the success of the invasion depends only on the average number of susceptible hosts in the immediate vicinity of an infected host. This difference is important for the following reason. In the mean-field model a rare invading pathogen has only a small impact on the equilibrium number of susceptible hosts in the entire population, $S^*_{resident}$. But in the spatial model, even when rare, an invading pathogen can have a large impact on the number of susceptible hosts in its immediate vicinity, $Q^*(S|I_{resident})$. Thus, for the spatial model $Q^*(S|I_{resident})$ can be replaced with the invading pathogen's quasi-equilibrium $Q(S|I_{invader})$: the number of susceptible hosts surrounding hosts infected by the invading strain while it is still rare but after it has come to equilibrium with its neighborhood (Matsuda et al. (1992)). This yields instead

$$\frac{1}{I_{invader}} \cdot \frac{dI_{invader}}{dt} = \frac{\beta_{invader}}{n} \cdot [Q^0(S|I_{invader}) - Q^*(S|I_{invader})] \quad (3.9)$$

By this equation, the invasion will succeed if $Q^0(S|I_{invader})$ is greater than $Q^*(S|I_{invader})$. Note that even though this representation of the invasion fitness does not explicitly include the resident strain, the $Q^0(S|I_{invader})$ that the invading pathogen will achieve depends on how the resident pathogen has already shaped the host population. For

example, if there are very few susceptible hosts in the population to begin with, the invader is unlikely to realize a high $Q^0(S|I_{invader})$. In addition, note that this is a simplified version of the invasion fitness presented in previous papers (e.g. Boots and Sasaki (1999)).

Equation 3.9 provides a conceptual framework for explaining the effect of spatial structure on pathogen evolution. Because a highly transmissible pathogen quickly infects neighboring susceptible hosts, it will tend to have a lower $Q^0(S|I_{invader})$, thus diminishing its ability to invade the population. In effect, highly transmissible pathogens “self-shade” themselves. The risk of “self-shading” will vary depending on the invasion context. For example, if there are many susceptible hosts available upon invasion, the risk is lower than if there are few.

Although conceptually insightful, equation 3.9 is not closed: the average number of susceptible hosts next to infected hosts ($Q(S|I)$) depends on higher order spatial moments (e.g. $Q(S|IS)$). The dependencies continue upward in scale to the size of the entire lattice. Thus, in order to quantify pathogen fitness one must use a moment closure method. A simple moment closure method often used is the improved PA (IPA; Sato et al. (1994)). PAs take advantage of the fact that the number of state triples on a lattice can be written in terms of the two state pairs that it is composed of. If one makes certain assumptions about the distribution of state triples across the lattice (see Morris (1997)), the relationship between state triples and pairs simplifies so that correlations above pairs can be ignored. The IPA is a special PA that accounts for the aggregation of susceptible hosts in space due to local reproduction (Appendix C).

To infer the ES transmission rate predicted by an IPA of the spatial moment equations, for each transmission-virulence relationship and parameter set I numerically solve for the quasi-equilibrium $Q(S|I)$ (method described in Kamo et al. (2007); see Appendix D) and use it to calculate the invasion fitness for all pairs of resident and invading pathogens within a range of transmission rates. The transmission rate of the pathogen that cannot be invaded by any other pathogen strain is taken as the ES transmission rate. To find the predicted extinction threshold transmission rate and the invasion threshold transmission rate, I perform a stability analysis of the endemic equilibrium (methods described in Sato et al. (1994)).

3.2.4 Data analysis

I compare the pathogen’s ES transmission rate predicted from a non-spatial model to the ES transmission rate predicted by the spatial model. I also compare the spa-

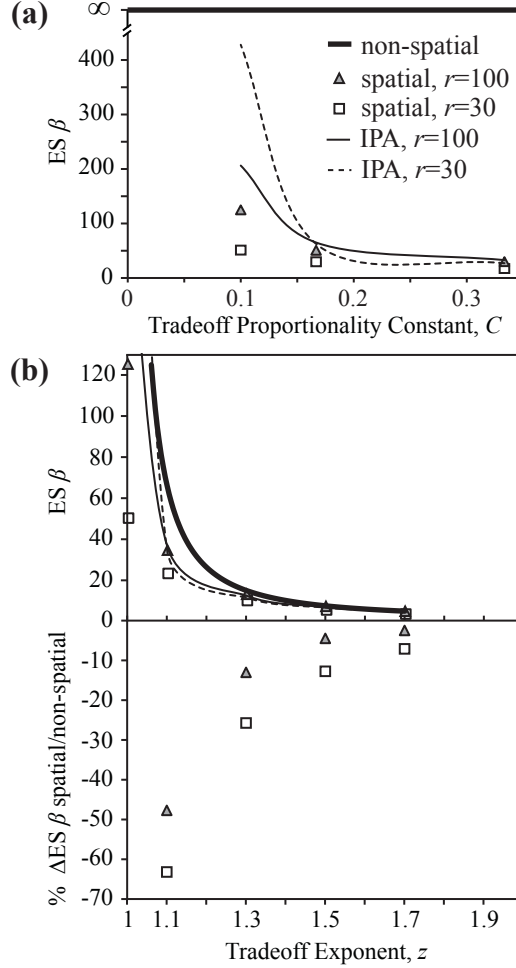


Figure 3.1: Evolutionary stable transmission rates across transmission-virulence relationship shapes. The evolutionary stable transmission rates (ES β) obtained from simulation (data points) and predictions from improved pair approximation (IPA; thin lines) and a non-spatial model (thick lines) are shown for different relationships and for two host reproduction rates ($r = 30$, squares and dashed line; $r = 100$, triangles and solid line). (a) linear transmission-virulence relationships, shape controlled by constant of proportionality C in $\alpha = C \cdot \beta^z$ when $z = 1$, (b) concave-down transmission-virulence tradeoff, shape controlled by tradeoff exponent z in $\alpha = C \cdot \beta^z$ when $C = 0.1$.

tial ES transmission rate to the ES transmission rate predicted from spatial moment equations closed with IPA. I make comparisons for the following cases: no transmission virulence relationship, three types of linear relationships ($\alpha = \beta/3$, $\alpha = \beta/6$, and $\alpha = \beta/10$), and four types of concave-down tradeoffs ($\alpha = \beta^{1.1}/10$, $\alpha = \beta^{1.3}/10$, $\alpha = \beta^{1.5}/10$, $\alpha = \beta^{1.7}/10$). Since little is known about the existence of shape of transmission-virulence relationships for real pathogens, these are chosen somewhat arbitrarily. However, they will provide a qualitative understanding of how the shape of the relationship can influence pathogen evolution. Furthermore, these relationships have commonly been used in previous literature. For each relationship, I examined a range of host reproduction rates (up to $r = 100$ in some cases) and natural host death rates (up to $d = 4$). For the case of no transmission-virulence relationship I also examined a range of pathogen virulence (up to $\alpha = 4$). For a biological interpretation of the parameter space explored, see Appendix E. For all parameter combinations I also show the extinction threshold transmission rate (above which the endemic equilibrium is unstable and the pathogen causes host extinction) and invasion threshold transmission rate (below which the endemic equilibrium is unstable and the pathogen cannot invade the host population) predicted from IPA. These predicted thresholds have been shown to be qualitatively accurate for the type of dynamics and spatial structure examined here (Boots and Sasaki (2000); Haraguchi and Sasaki (2000); Ohtsuka et al. (2006); Webb et al. (2007a,b)).

3.3 Results

Fig. 3.1 shows the spatial ES transmission rate, non-spatial ES transmission rate, and IPA ES transmission rate as a function of the transmission-virulence relationship shape. Fig. 3.1a shows data for a linear relationship and is plotted against the constant of proportionality (C in the equation $\alpha = C \cdot \beta^z$ when $z = 1$). Fig. 3.1b shows data for a concave-down tradeoff and is plotted against the tradeoff exponent (z in the equation $\alpha = C \cdot \beta^z$ when $C = 0.1$). In the case of a linear relationship, the non-spatial model predicts that the constant of proportionality does not influence pathogen evolution: the ES transmission rate is infinite for all values of C . In effect, the non-spatial model predicts evolution to pathogen-driven extinction. In contrast, the spatial model predicts that the ES transmission rate will decline with increasing values of C , for both low and high host reproduction rates, and that evolution will lead to endemism.

In the case of a concave-down tradeoff, both the spatial and non-spatial models

predict a decline in the ES transmission rate as the tradeoff becomes steeper (larger z), for low and high host reproduction rates. However, the spatial ES transmission rate is lower than the non-spatial expectation regardless of the steepness of the tradeoff. In addition, as the tradeoff becomes less steep, the non-spatial prediction diverges from the spatial prediction, approaching an infinite ES transmission rate and pathogen-driven extinction. Fig. 3.1b also shows the percent difference between the non-spatial and spatial ES transmission rate. The percent difference is greater for lower host reproduction rates. Further, as the tradeoff becomes steeper, the percent change between the spatial and non-spatial expectations diminishes. In other words, the evolutionary influence of spatial effects relative to the transmission-virulence tradeoff diminishes with the steepness of the tradeoff and with host reproduction. For a linear relationship, like the spatial model the IPA predicts that the ES transmission rate will decline with increasing values of C . However, especially for low host reproduction rates, the decline predicted by IPA is much steeper than the decline predicted by the spatial model. For a concave-down tradeoff, the IPA also predicts that the ES transmission rate will decline with increasing tradeoff steepness. However, like the non-spatial prediction, as the tradeoff becomes less steep, the IPA prediction diverges from the spatial prediction, approaching an infinite ES transmission rate and pathogen-driven extinction.

Fig. 3.2 shows the spatial ES transmission rate, non-spatial ES transmission rate, and IPA ES transmission rate as a function of the host reproduction rate when there is no relationship between β and α . The non-spatial model predicts an infinite ES transmission rate, and pathogen-driven extinction, across all host reproduction rates. In contrast, the spatial ES transmission rate predicted by simulation initially decreases and then increases with host reproduction rate for low host death rates ($d = 1, d = 2$) and pathogen virulence ($\alpha = 0, \alpha = 1$). For higher host death rates ($d = 3, d = 4$) and pathogen virulence ($\alpha = 2, \alpha = 3$), the ES transmission rate increases with host reproduction. Like the non-spatial model, the IPA predicts an infinite ES transmission rate and pathogen-driven extinction. Thus, the ES transmission rate predicted by IPA is both qualitatively and quantitatively inaccurate.

Fig. 3.3 shows the effect of increased host death rate and virulence on the spatial ES transmission rate, non-spatial ES transmission rate, and IPA ES transmission rate as a function of the host reproduction rate, when there is no transmission-virulence relationship. Again, the non-spatial model predicts an infinite ES transmission rate regardless of the host death rate and pathogen virulence. In contrast, the spatial ES transmission rate increases with the host death rate and virulence across low

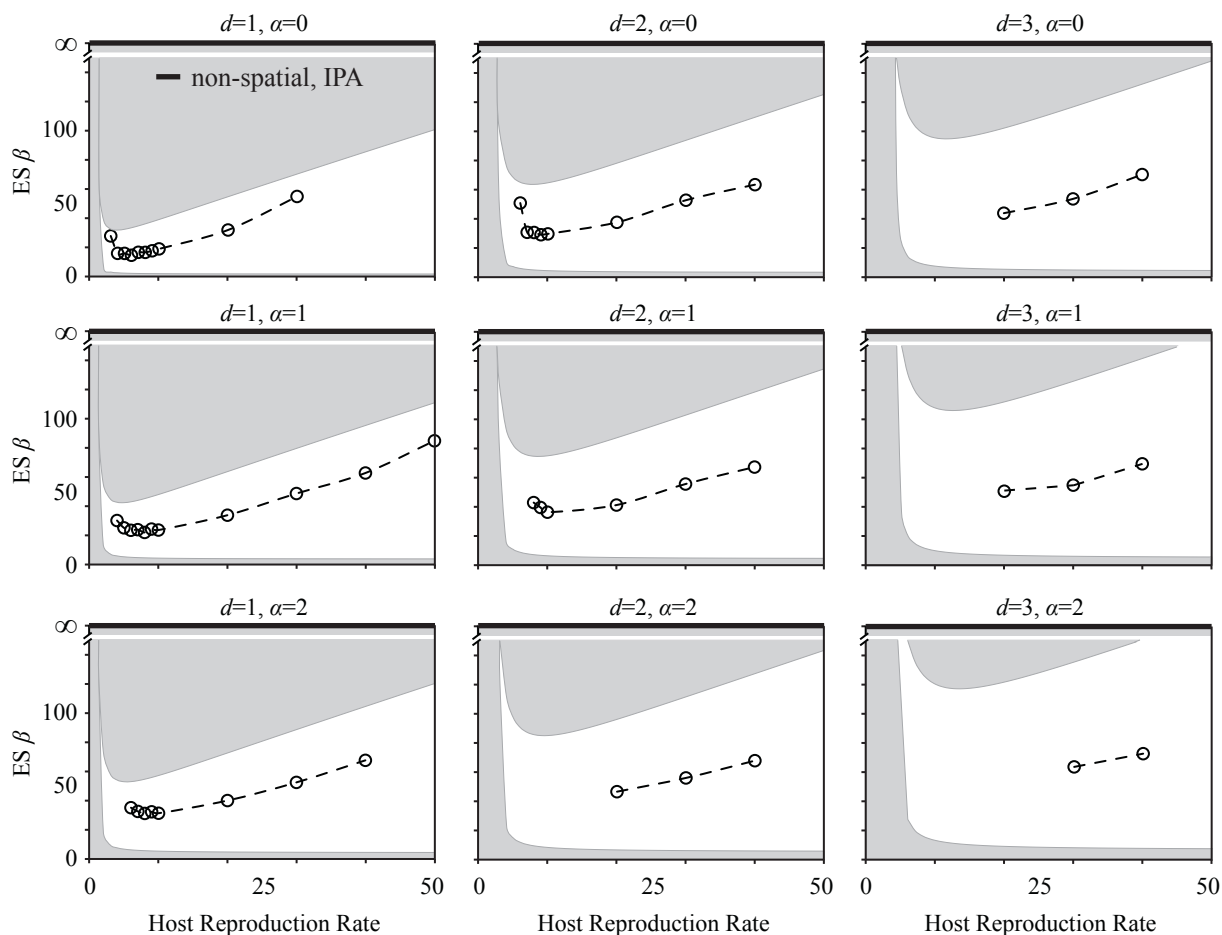


Figure 3.2: Effect of host reproduction rate on the evolutionary stable transmission rate for no transmission-virulence relationship. The evolutionary stable transmission rates (ES β) obtained from simulation (circles with dashed spline fit) are shown for a range of host reproduction rates, pathogen virulence, and host natural death rates along with predictions from the non-spatial model and improved pair approximation (IPA; thick lines). The shaded areas are regions where the IPA predicts extinction of the host, pathogen, or both. In the region to the left, the host will go extinct due to an insufficient reproduction rate. In the upper region the pathogen drives the host population and itself to extinction. In the lower region the pathogen cannot invade the host population due to an insufficient transmission rate. In some cases (high d or α) data could not be obtained for lower values of r , likely because the predicted invasion threshold is underestimated. For all cases, the non-spatial model and IPA predict evolution to pathogen-driven extinction.

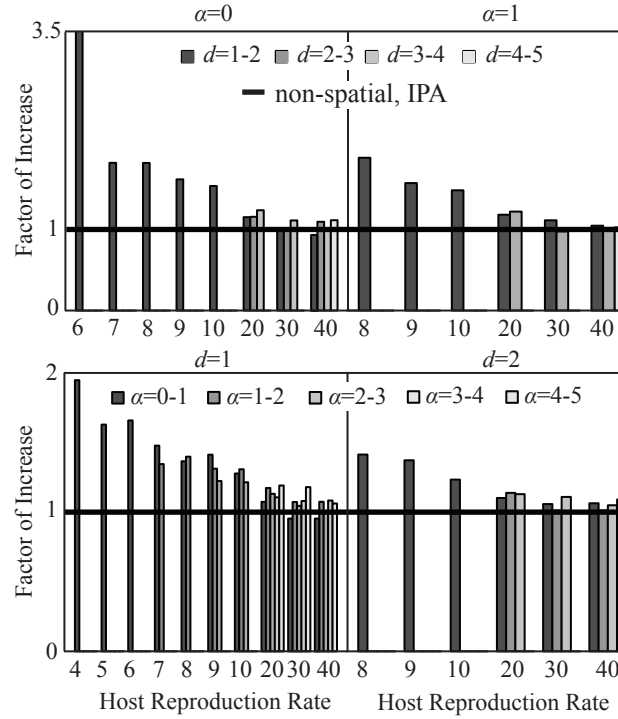


Figure 3.3: Effect of host death rate and virulence on the evolutionary stable transmission rate for no transmission-virulence relationship. The factor of increase in the evolutionary stable transmission rate (ES β) with a unit increase in the death rate (d ; top left panel $\alpha = 0$ and top right panel $\alpha = 1$) and virulence (α ; bottom left panel $d = 1$ and bottom right panel $d = 2$) from simulations (bars) along with predictions from the non-spatial model and improved pair approximation (IPA; thick lines) is shown for a range of host reproduction rates. A value of 1 represents no change in the ES β with death rate or virulence, a value greater than 1 is an increase, and a value less than 1 is a decrease. For example, the first bar in the top left graph (the $d = 1 - 2$ bar) indicates that when $\alpha = 0$ the ES transmission rate is 3.5 times higher when $d = 2$ than when $d = 1$. The non-spatial model and IPA predict no change across host reproduction rates.

to intermediate host reproduction rates. However, the effect of host death rate and virulence on the spatial ES transmission rate diminishes as the host reproduction rate increases and actually reverses at high host reproduction rates. In addition, the death rate has a larger effect than the virulence on the spatial ES transmission rate. Like the non-spatial model, IPA predicts an infinite ES transmission rate that does not depend on the host death rate or pathogen virulence. The IPA does not qualitatively or quantitatively correctly predict the trends of the ES transmission rate with host death rate or virulence.

Fig. 3.4 shows the spatial ES transmission rate, non-spatial ES transmission rate, and IPA ES transmission rate as a function of the host reproduction rate when there is a linear relationship between β and α . Again, the non-spatial model predicts an infinite ES transmission rate for all host reproduction rates and host death rates. In contrast, the spatial ES transmission rate is intermediate and increases with the host reproduction rate. Similar to the spatial ES transmission rate, the IPA predicts an intermediate ES transmission rate for all host reproduction rates. However, unlike the spatial ES transmission rate, the IPA ES transmission rate initially decreases then increases for steeper relationships ($\alpha = \beta/3$ and $\alpha = \beta/6$) and increases then decreases for the least steep relationship ($\alpha = \beta/10$, top panel of Fig. 3.4) and a range of low host reproduction rates, the IPA ES transmission rate is greater than the predicted extinction threshold transmission rate. Thus, the IPA effectively predicts pathogen-driven extinction and neither qualitatively nor quantitatively correctly predicts the trends of the ES transmission rate with host reproduction rate.

Fig. 3.6 shows the effect of the host death rate on the spatial ES transmission rate, non-spatial ES transmission rate, and IPA ES transmission rate as a function of the host reproduction rate for linear transmission-virulence relationships. The non-spatial model predicts an infinite ES transmission rate regardless of host death rate. In contrast, the spatial model predicts that the ES transmission rate should increase with host death rate. For all but the least steep relationship where the effect of the host death rate is largest for low host reproduction rates and diminishes with high host reproduction rates, the effect is relatively constant across host reproduction rates. For some parameter sets the IPA also predicts that the ES transmission rate should increase with host death rate; however, overall the predicted trends are qualitatively and quantitatively inaccurate.

Fig. 3.5 shows the spatial ES transmission rate, non-spatial ES transmission rate, and IPA ES transmission rate as a function of the host reproduction rate when there

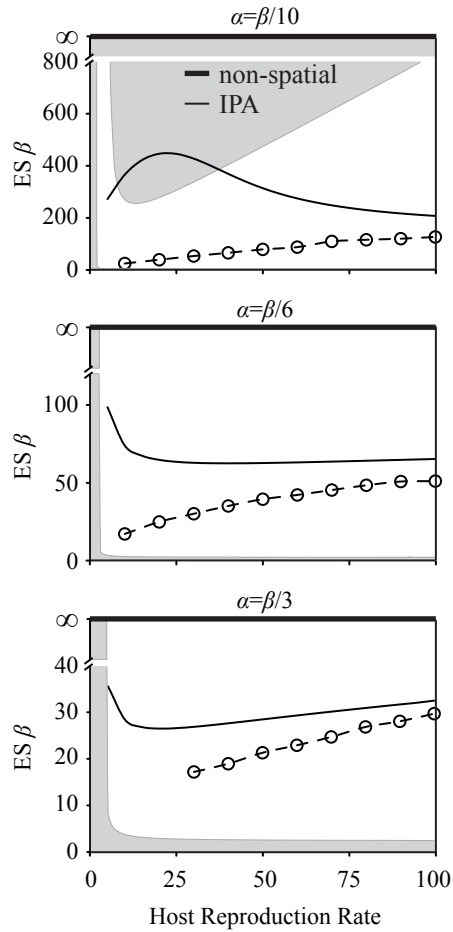


Figure 3.4: Effect of host reproduction rate on the evolutionary stable transmission rate for linear transmission-virulence relationships. The evolutionary stable transmission rates ($ES \beta$) obtained from simulation (circles with dashed spline fit) are shown across a range of host reproduction rates and relationship steepness, along with predictions from the non-spatial model (thick solid line) and improved pair approximation (IPA; thin solid line). The shaded areas are as in Fig. 3.1. Data could not be obtained for lower values of r , likely because the predicted invasion threshold is underestimated. For all graphs, $d = 1$.

is a concave-down transmission-virulence tradeoff. Both the non-spatial model and simulations predict an intermediate ES transmission rate and virulence below the extinction threshold transmission rate. However, the non-spatial model predicts the same ES transmission rate regardless of the host reproduction rate while the spatial ES transmission rate increases with host reproduction. Thus, the difference between the spatial and non-spatial predictions are largest for low host reproduction rates. Further, the difference is smaller for steeper tradeoffs.

The IPA also predicts an intermediate ES transmission rate across host reproduction rates. The trends in the ES transmission rate with host reproduction predicted by IPA are qualitatively similar to the trends predicted by simulation. Quantitatively, however, the relative difference between the ES transmission rate predicted by IPA and simulations varies depending on the steepness of the tradeoff as well as the host reproduction rate and natural death rate (Fig. 3.7). As the transmission-virulence tradeoff becomes steeper (higher z in $\alpha = C \cdot \beta^z$ where $C = 0.1$) the relative difference decreases. For the steepest tradeoff ($\alpha = 0.1 \cdot \beta^{1.7}$), the difference between predictions is nearly 0 across all host reproduction rates. For less steep tradeoffs, the relative difference is highest for low host reproduction rates, but decreases as host reproduction increases. Similar to less steep linear relationships, the relative difference decreases with increasing death rate for very low host reproduction rates.

The lower right panel of Fig. 3.6 shows the effect of host death rate on the spatial ES transmission rate, non-spatial ES transmission rate, and IPA ES transmission rate as a function of the host reproduction rate when there is a concave-down tradeoff. All three models (spatial, non-spatial, and IPA) predict that the ES transmission rate will increase with increasing host death rate. However, the non-spatial model and IPA predict stronger effects than the spatial model. Further, while the non-spatial model predicts that the effect of host death rate will not vary with host reproduction rate, the IPA predicts a slight decrease with host reproduction and the spatial model predicts a slight increase with host reproduction. However, the trends are not strong.

3.4 Discussion

3.4.1 Effects of host and pathogen ecology

Through extensive spatially-explicit simulations of host-pathogen interactions and comparison with non-spatial theory, I identified novel ways in which host and pathogen ecology can influence the pathogen’s ES transmission rate in a spatial context. In particular, I have shown that in a spatial context: 1) the shape of the transmission-

virulence relationship is important even when it is not an explicit tradeoff, 2) the host reproduction rate plays an important evolutionary role, 3) host mortality has a broader influence than expected in a non-spatial context (and can even have an influence opposite to that predicted by non-spatial models). In addition, for ecological contexts where the spatial and non-spatial models yield qualitatively consistent predictions, I have identified when space is still likely to have strong quantitative effects.

First, in contrast to non-spatial expectations, I found that in a spatial context the slope of the linear transmission-virulence relationship strongly influences the ES transmission rate: as the relationship becomes steeper, the ES transmission rate decreases. These results suggest that when the host population is spatially structured, the details of the transmission-virulence relationship can be important even when that relationship is not an explicit tradeoff. Space seems to induce an effective tradeoff between transmission and virulence even when the direct relationship between these traits is only linear. Furthermore, although when the relationship is a tradeoff the influence of the shape of the tradeoff on the ES transmission rate is qualitatively similar in a spatial and non-spatial context (the ES transmission rate declines with increasing tradeoff steepness), the quantitative difference between the spatial and non-spatial prediction increases and becomes substantial as the tradeoff gets shallower and as the host reproduction rate increases. These results imply that for pathogens with a shallow transmission-virulence tradeoff, consideration of space is particularly important for fully understanding pathogen evolution.

Second, I have shown that in space the ES transmission rate is influenced by the host reproduction rate, whereas in a non-spatial context it is predicted to have no influence. In particular, when the pathogen is subject to a transmission-virulence relationship, the ES transmission rate increases with the host reproduction rate. This trend was postulated based on other studies (Lion and Boots (2010); Messinger and Ostling (2009)) but was not comprehensively tested. In the case of no transmission-virulence relationship, I show that the ES transmission rate decreases then increases with host reproduction across a wide range of host death rates and virulence. This trend was previously shown only for one set of parameter values ($\alpha = 1$, $d = 1$; Haraguchi and Sasaki (2000)). When there is no transmission-virulence relationship, the ES transmission rate approaches the pathogen-driven extinction threshold at low and high host reproduction rates. Notably, the non-spatial model predicts that the host reproduction rate will not influence pathogen evolution, regardless of the presence or shape of a transmission-virulence relationship. Thus, a more complete theory

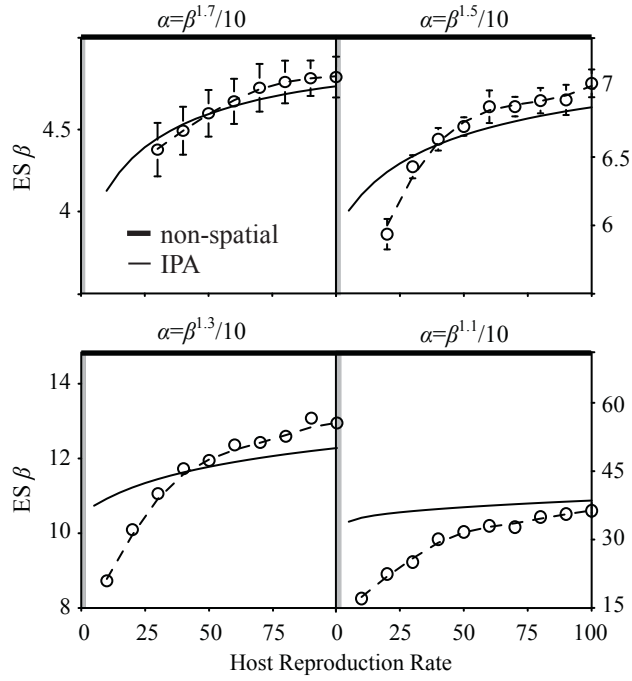


Figure 3.5: Effect of host reproduction rate on the evolutionary stable transmission rate for concave-down transmission-virulence tradeoffs. The evolutionary stable transmission rates ($ES \beta$) obtained from simulation (circles with dashed spline fit, error bars shown when larger than data points) are shown across a range of host reproduction rates and tradeoff steepness, along with predictions from the non-spatial model (thick solid line) and improved pair approximation (IPA; thin solid line). The shaded areas are as in Fig. 3.1.

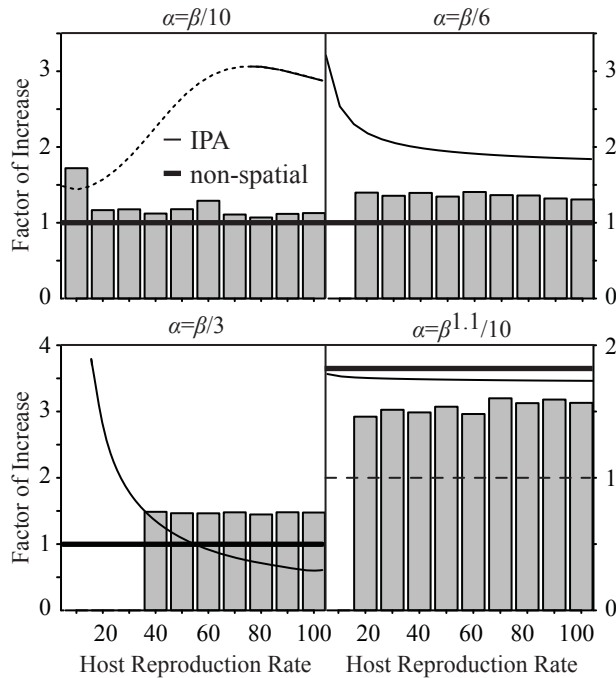


Figure 3.6: Effect of host death rate on the evolutionary stable transmission rate for transmission-virulence relationships. The factor of increase in the evolutionary stable transmission rate (ES β) with an increase in the death rate from $d = 1$ to $d = 2$ is shown for a range of host reproduction rates and relationship types: three linear and one concave-down (simulation data=bars, predictions from non-spatial model=thick solid line, predictions from IPA=thin solid line). The factor of increase predicted by simulations is always greater than or equal to 1 (dashed line). For the least steep linear tradeoff, the dotted portion of the curve indicates that the IPA predicts an ES β above the extinction threshold for $d = 1$ or $d = 2$ at that host reproduction rate.

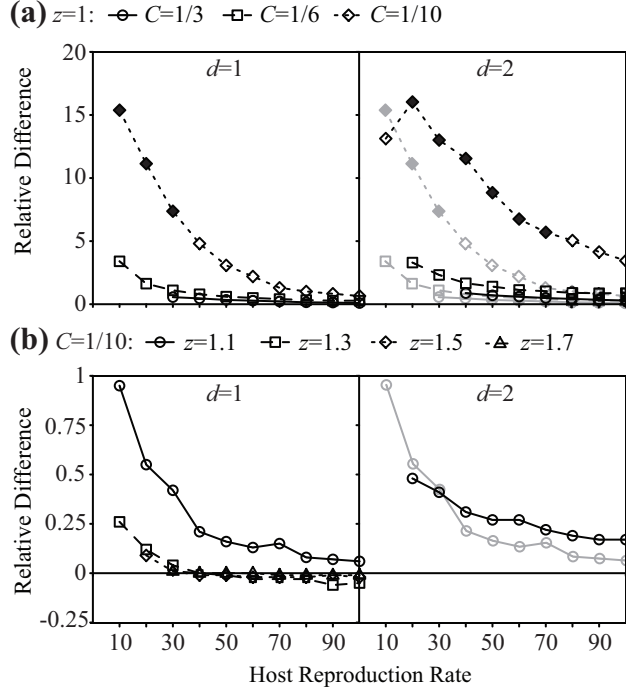


Figure 3.7: Relative difference between evolutionary stable transmission rate predicted by simulation and improved pair approximation for transmission-virulence relationships. Assuming a transmission-virulence relationship of the form $(\alpha = C \cdot \beta^z)$, data points are the relative difference between the evolutionary stable transmission rate (ES β) predicted by simulation and improved pair approximation (IPA) across host reproduction rates. The relative difference = $(\text{IPA ES } \beta - \text{simulation ES } \beta) / (\text{simulation ES } \beta)$. A negative value indicates that the simulation predicted a higher ES β . (a) Data for linear relationships with varying values of C when $z = 1$ and for $d = 1$ (upper left) and $d = 2$ (upper right, gray lines are data for $d = 1$ for ease of comparison). Filled data points indicate that the IPA predicts an ES β greater than the extinction threshold β . (b) Data for concave-down tradeoffs with varying values of z when $C = 0.1$ and for $d = 1$ (lower left) and $d = 2$ (lower right, gray lines are data for $d = 1$ for ease of comparison). For steep concave-down tradeoffs (high z), simulation data could not be obtained for $d = 2$ due to the narrow range of transmission rates that lead to endemism and high demographic stochasticity.

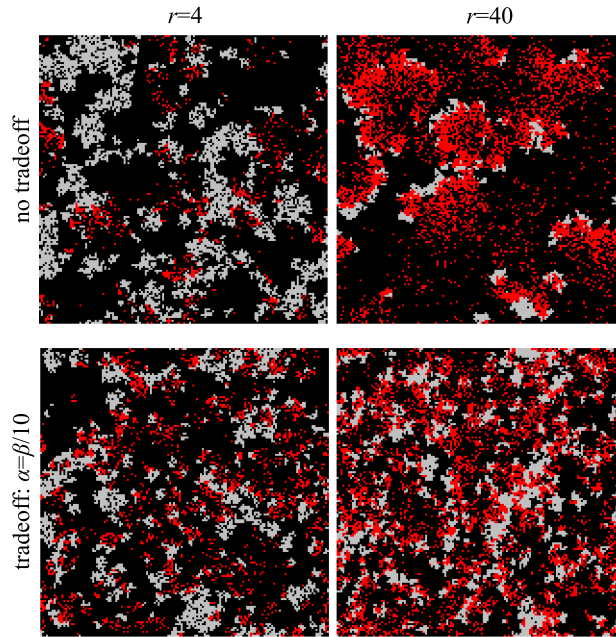


Figure 3.8: Population structure for lowest and highest host reproduction rates. Shown is the spatial distribution of empty sites (black), susceptible hosts (gray), and infected hosts (red) for low host reproduction (left column) and high host reproduction (right column) for no transmission-virulence relationship (top row) and a linear relationship of $\alpha = \beta/10$ (bottom row). In case of no relationship, when host reproduction is low, uninfected patches of susceptible hosts grow very large before becoming infected, actually reducing the risk of “self-shading”. This does not occur in the case of a linear relationship. Note that host reproduction is not chosen to be lower in the linear relationship case because the range of transmission rates leading to endemism (between the invasion and extinction threshold transmission rates) is very narrow and due to demographic stochasticity, simulation data could not be obtained. Other parameters: $d = 1$, and for no tradeoff $\alpha = 1$.

of pathogen evolution that considers the influence of space, predicts that existing variation in pathogen transmission rates may arise from differences in the intrinsic host reproduction rate.

Third, I find that in a spatial context the ES transmission rate typically increases with the host natural death rate for all transmission-virulence relationships and no relationship, but can actually decline with host death rate for high host reproduction rates in the case of no relationship. Importantly, the non-spatial model predicts that host death rate will influence pathogen evolution only in the case of a transmission-virulence tradeoff, and it never predicts a decline with host death rate. Furthermore, in the case of a transmission-virulence tradeoff, where the spatial and non-spatial models qualitatively agree regarding the influence of the death rate, the non-spatial predicted change in the ES transmission rate with host death is consistently greater than predicted by the spatial model. As host death rates increase, the spatial prediction diverges from the non-spatial prediction and in this sense spatial effects become strong (for example, given $\alpha = 0.1 \cdot \beta^{1.1}$, the spatial ES transmission rate is 66.8% lower than the non-spatial prediction for $d = 1$ and $r = 20$ but 74.2% lower for $d = 2$ and $r = 20$).

Interestingly, I also find an important interactive effect between the effects of the host's reproduction and death rates. Host reproduction seems to moderate the effects of other demographic rates. More specifically, for no transmission-virulence relationship or a less steep linear relationship, the spatial model predicts an increase in the ES transmission rate that diminishes with host reproduction. In other words, the host death rate has less influence on the evolutionary dynamics as host reproduction increases. This implies that an increased host reproduction rate not only directly influences the ES transmission rate (as seen in Figs. 3.2, 3.4, 3.5) but can also indirectly influence it through the impact of other demographic rates. This is a particularly relevant finding since host reproduction is not predicted to influence pathogen evolution at all in a non-spatial context. The indirect effects of host reproduction do not extend to steeper linear relationships and tradeoffs, where the influence of host death rate is fairly constant across reproduction rates.

Finally, the spatial model predicts a role for the pathogen's virulence that it does not play in the non-spatial model. For no transmission-virulence relationship, the pathogen virulence increases the ES transmission rate. In contrast, the non-spatial model predicts that pathogen virulence will not influence the ES transmission rate. As with the host death rate, the influence of pathogen virulence diminishes as host reproduction rate increases. Again, this suggests that the host reproduction rate

not only directly influences the ES transmission rate but also indirectly affects it by moderating the influence of other demographic rates.

3.4.2 Accuracy of the IPA

I demonstrate that the IPA does not always accurately predict the influence of host and pathogen ecology on pathogen evolution in a spatial context. In particular, I confirm for a wide range of host and pathogen ecology what has been hinted at in the literature for a few cases: the IPA is dramatically inaccurate when the pathogen is not subject to a transmission-virulence relationship, predicting pathogen-driven extinction while simulations predict endemism (de Aguiar et al. (2004); Boots et al. (2006); Lion and Boots (2010)). Perhaps more surprising, I show that the same can be true for less steep linear relationships, especially for low host reproduction rates and high host death rates. For steeper linear relationships the IPA correctly predicts endemism. This has previously been shown for similarly steep relationships, including $\alpha = 3 \cdot \beta$ where $d = 0.01$ and $r = 3$ (Boots and Sasaki (1999); Kamo et al. (2007)), as well as for $\alpha = C \cdot \beta$ where C ranges from 0.01-0.2, $d = 1$, and $r = 8$ (Haraguchi and Sasaki (2000)). However, I show that despite correctly predicting endemism, the IPA predicts different trends with increasing host reproduction and host death rate. Finally, I show that the IPA correctly predicts endemism for all tradeoffs and qualitatively predicts the correct trends with increasing host reproduction when there is transmission-virulence tradeoff. However, the less steep the tradeoff, the lower the reproduction rate, and the higher the host death rate, the greater the quantitative difference. Notably, these are the same conditions for which the spatial and non-spatial predictions diverge most, meaning that the IPA performs most poorly when spatial structure is most influential.

That the IPA is not always a good predictor of pathogen evolution is not surprising. However, its limitations appear to be more extensive than initially suspected. Especially in cases where the pathogen is not subject to a transmission-virulence relationship or when the relationship is linear and shallow, new analytical methods of quantifying pathogen fitness should be investigated. Forays in that direction have already been made (Bauch (2005); Filipe and Maule (2003); Peyrard et al. (2008)) and have shown some success in predicting equilibrium population densities. However, this does not necessarily suggest that these methods will be accurate predictors of evolutionary outcomes, since the improved pair approximation has also been shown to do well predicting equilibrium population densities and stability (Boots and Sasaki (2000); Haraguchi and Sasaki (2000); Ohtsuka et al. (2006); Sato et al. (1994); Webb

et al. (2007a,b)). A more careful examination of the spatial correlations in the cases where the IPA does not work well might suggest in particular why the IPA fails and inform the development of new methods. For example, Dieckmann and Law (Dieckmann and Law (2000)) suggest that larger scale spatial structure may be more appropriately modeled with diffusion approximations, which could potentially be combined with moment approximations to more accurately predict spatial effects.

3.4.3 Explaining the effects of ecology

Despite the quantitative limitations of the IPA, the influence of particular aspects of the host and pathogen ecologies on pathogen evolution can qualitatively be understood within the conceptual framework arising from spatial moment equations. The invasion fitness of a pathogen derived from spatial moment equations implicates “self-shading,” where the spread of more transmissible pathogens is impeded by the rapid depletion of the local supply of susceptible hosts, as an important evolutionary force in a spatial context. Examination of the spatially-explicit patch structure arising in different ecological contexts alludes to the relationship between “self-shading” and host and pathogen ecology. Consider host reproduction. Regardless of the transmission-virulence relationship, host reproduction increases local host availability. Therefore, when host reproduction is high the risk of “self-shading” is lower, resulting in a higher ES transmission rate. The trend of initially decreasing ES transmission rate with host reproduction when there is no relationship may arise because when the host reproduction rate is very low, the initial infecting pathogen strain creates a highly depauperate host population. Subsequently, most pathogens quickly go locally extinct but small, uninfected patches of susceptible hosts are free to grow. These patches can get very large before they come into contact with the sparsely occurring infected hosts (Fig. 3.8). The risk of “self-shading” in these large patches is low. Thus, it is the periodic formation of very large patches of susceptible hosts at lower host reproduction that favors a higher ES transmission rate. This does not occur when the pathogen is subject to a transmission-virulence relationship, most likely because the initial infection does not lead to such a large reduction in susceptible hosts because infected hosts die more quickly (Fig. 3.8).

The trends with host natural death rate and virulence are not immediately intuitive, but can also be understood within the framework of “self-shading” once the spatially explicit patch structure in different ecological contexts is identified. By reducing the availability of susceptible hosts, one might assume that the host natural death rate would increase the risk of “self-shading” and thus reduce the ES trans-

mission rate. However, empty sites are necessary for host reproduction. Thus, by creating space for new susceptible hosts, an increased host natural death rate may actually increase host availability and thus ultimately reduce the risk of “self-shading” (for example, the average number of susceptible hosts over 500 time steps during evolutionary equilibrium when there is no transmission-virulence relationship, $r = 10$, $\alpha = 1$, and $d = 1$ is $2,825 \pm 264.6$ while for $d = 2$ it is $3,999 \pm 446.2$). In addition, the host natural death rate applies to infected hosts: fewer infected hosts results in lower predation pressure and thus reduces the risk of “self-shading.” When there is no transmission-virulence relationship, by removing infected hosts virulence also creates space for new susceptible hosts and reduces the predation pressure. Thus, it similarly affects the ES transmission rate. However, because virulence only affects infected hosts it does not create as much empty space for new susceptible hosts and therefore has less of an effect on the ES transmission rate than the host natural death rate. Further, when host reproduction is high, the benefit of increased host natural death or virulence in terms of empty space relative to the direct cost to the pathogen in terms of decreasing susceptible and infected hosts is lower, potentially explaining the diminishing effect with host reproduction and eventual trend reversal for no transmission-virulence tradeoff.

3.4.4 Summary

In summary, host and pathogen ecology play an important role in the evolution of pathogen transmission rate when the population is spatially structured and may help explain variation among pathogens. I find that when there is no transmission-virulence relationship or when the relationship is linear and less steep, the host reproduction rate is a key determinant of pathogen evolution. Importantly, the non-spatial model predicts that the host reproduction rate should not influence the ES transmission rate. Understanding the effects of basic host demography and pathogen life-history will help to inform our understanding of the problematic emergence and re-emergence of infectious disease and the factors that increase the risk of such events. Although I show that the IPA is not a good method for quantifying self-shading and predicting these patterns, most notably in the cases where the effect of spatial structure is strongest, the conceptual framework of “self-shading” is still useful for gaining insights into the role of different ecological contexts. Thus, future work should focus on developing new approximations as well as alternative constructs for quantifying the effects of “self-shading.”

CHAPTER IV

Novel evolutionary effects of predator ecology in a spatial context

4.1 Introduction

Just as evolution shapes the ecology of a species, so can its ecology affect evolution. For example, life-history tradeoffs significantly influence a species' evolutionary trajectory. Although many theoretical studies of the evolutionary influence of a species ecology tacitly assume that the population dynamics occur in a non-spatial context, many organisms are subject to population spatial structure, where interactions between individuals are not random but rather dependent on their spatial location. An increasing number of theoretical studies suggest that population spatial structure can significantly influence evolution (e.g. North et al. (2011)), especially of interacting species (competing species: Johnson and Seinen (2002); Kinzig and Harte (1998); true predators: van Baalen and Sabelis (1995); Gilpin (1975); Pels et al. (2002); Rauch et al. (2002); pathogens: Debarre et al. (2012), reviewed in Lion and Boots (2010); Messinger and Ostling (2009); parasitoids: Boerlijst et al. (1993)). Further, for pathogen-host interactions, the influence of various aspects of host and pathogen ecology predicted by spatial models is incongruous with the influence predicted by non-spatial models (e.g. host recovery: Boots et al. (2004); superinfection: Caraco et al. (2006); coinfection: Claessen and deRoos (1995); free-living propagules: Kamo and Boots (2004); basic host and pathogen demography: Messinger and Ostling (view)). These studies highlight the importance of the spatial context for understanding the evolutionary influence of ecology.

To date, theoretical studies of evolution in a spatial context have focused largely on pathogen-host interactions, showing that host population spatial structure can lead to the evolution of a reduced pathogen transmission rate and/or virulence. The

evolutionary effect of population spatial structure on pathogens has been suggested to straightforwardly extend to other types of exploitative species (Rauch and Bar-Yam (2006)). Indeed, a handful of theoretical studies have demonstrated that spatial structure can lead to the evolution of a reduced attack rate for predators (van Baalen and Sabelis (1995); Gilpin (1975); Pels et al. (2002); Rauch et al. (2002)), and parasitoids (Boerlijst et al. (1993)). However, beyond the general similarity, it is not clear whether there are consistent patterns in the effect of ecology across exploitative species. Certainly, there are many aspects of ecology that are analogous across interaction types (like the pathogen transmission rate and predator or parasitoid attack rate) that may therefore analogously influence the evolution of exploitative species. Yet many other aspects of ecology are unique to the interaction type. In addition to impacting evolution in and of themselves, by changing the context of the interaction these unique aspects of ecology may alter the role of the aspects of ecology that are analogous across interaction types.

Here I use spatial simulations to examine the evolutionary impact of predator and prey ecology on predator evolution with the goals of determining 1) the predicted effect of unique aspects of predator and prey ecology on predator evolution relative to the non-spatial expectation and 2) whether, despite these unique aspects of ecology, the predicted effect of aspects of ecology that are analogous across predator-prey and pathogen-host interactions are consistent between interaction types. Predator evolution is of special interest because it may inform our understanding of the emergence of food-web structure and stability, which has been related to interaction strengths (Berlow et al. (2004)). I consider three aspects of predator and prey ecology that are unique relative to pathogen-host ecology. First, I consider the ratio of prey consumption to predator production, or the predator conversion efficiency. For pathogens the ratio is 1, but for predators the ratio can vary from 0 to 1. Second, I consider the magnitude of the predator death rate relative to the prey death rate. For pathogens, the infected host death rate is greater than or equal to the susceptible host death rate, but for predators the reverse is more likely based on relative body sizes (White et al. (2007); Yodzis and Innes (1992)). Finally, I consider predator movement. While infected hosts are rarely predicted to have a larger range of movement than susceptible hosts, predators often do, especially if the prey is relatively immobile (e.g. parasitoid wasps, flies, or beetles eating insect larvae or birds eating invertebrates). Even for mobile prey there is evidence that the predator may have a larger range of movement (Cronin et al. (2000); Jones et al. (1996)). I examine the role of these three aspects of ecology in reference to two additional aspects of ecology that are analogous between

predator-prey and pathogen-host interactions: the prey reproduction rate (analogous to the host reproduction rate) and the predator death rate (analogous to the infected host death rate) . For pathogen-host interactions, these two rates have been shown to significantly influence pathogen evolution in a spatial context, in ways not predicted by non-spatial models (Messinger and Ostling (view)).

In order to accurately compare the influence of ecology across the two types of interactions, I consider an individual-based lattice predator-prey model identical to that commonly used to model pathogen-host interactions. In addition to allowing comparison across interaction types, rather than representing population spatial structure induced by environmentally imposed boundaries, individual-based lattice models represent spatial structure resulting from the ecology of the organisms themselves. This type of spatial structure is commonly observed in natural systems (van der Heide et al. (2010); Komac et al. (2011); Rietkerk et al. (2004); Santini et al. (2011)). I find that the evolutionary stable (ES) predator attack rate declines with the predator conversion efficiency, demonstrating a power law-like relationship. In contrast, non-spatial theory predicts no evolutionary role for the predator conversion efficiency. I also find that decreasing the ratio of predator to prey death rate increases the ES attack rate. Again, non-spatial theory predicts no evolutionary dependence on the relative magnitudes of the two death rates. Finally, the predator movement rate increases or decreases the ES attack rate depending on the prey reproduction rate and the predator conversion efficiency. In general, the magnitude of the effect of predator movement relative to no movement is greater when the conversion efficiency is lower. Non-spatial theory does not yield predictions for the role of predator movement, since it is purely a spatial process. I find qualitatively similar patterns between the predator ES attack rate and prey reproduction rate compared to pathogen-host interactions, regardless of the predator conversion efficiency and death rate relative to the prey. Again no dependence on prey reproduction rate is predicted in a non-spatial context. However, the dependence predicted in the spatial model changes when the predator movement rate increases. I also find similar patterns between the ES attack rate and the predator death rate compared to pathogen-host interactions, regardless of the predator conversion efficiency.

Recently, inclusive fitness theory has been used to understand the influence of spatial structure on pathogen evolution (Lion and Boots (2010); Wild et al. (2009)). Within this framework, the evolutionary effect of spatial structure is determined by genetic and demographic spatial structuring, which influences the strength of local resource competition, both directly and indirectly (the latter through kin effects). This

approach, in combination with a mathematical approximation of spatial correlations, has been used to quantify the effect of pathogen and host ecology for individual-based lattice models like that used here (Lion and Boots (2010)). However, the accuracy of the approximation method is limited to the case that the pathogen has a transmission-virulence tradeoff (see Boots et al. (2006); Lion and Boots (2010); Messinger and Ostling (view)) and is thus of little use for predators. Despite these quantitative limitations, this framework offers a qualitative way to understand the impact of different aspects of ecology through their impact on the strength of local resource competition. To that end, I examine several metrics related to the genetic and demographic spatial distribution of the predator and prey from simulations and relate these to the strength of local competition to help understand the influence of the prey reproduction rate and predator movement rate.

4.2 Methods

4.2.1 Non-spatial Predator Evolution

In the absence of spatial structure, the population dynamics of a true predator and its prey can be described by the Lotka-Volterra (L-V) equations.

$$\frac{dN}{dt} = (r - d) \cdot N - \alpha \cdot N \cdot P \quad (4.1)$$

$$\frac{dP}{dt} = \alpha \cdot e \cdot N \cdot P - m \cdot P \quad (4.2)$$

In these equations, N is the prey population size, P is the predator population size, r is the prey reproduction rate, d is the prey death rate, α is the predator attack rate, e is the predator conversion efficiency (the ratio of predators produced per prey eaten), and m is the predator death rate. If the conversion efficiency is 1 and the predator death rate is an additive function of the prey death rate (i.e. $m = d + c$ where c is some positive constant), these equations are identical to a susceptible-infected model of pathogen-host interactions where the prey is the susceptible host population, the predator is the infected host population, and the attack rate is the pathogen transmission rate.

An invasion analysis using the L-V model yields the following. A predator's per-capita population growth rate is

$$\frac{1}{P} \cdot \frac{dP}{dt} = \alpha \cdot e \cdot N - m \quad (4.3)$$

When the predator is invading a prey population already at equilibrium with a resident predator, the per-capita population growth rate, and thus the predators invasion fitness, is

$$\frac{1}{P_I} \cdot \frac{dP_I}{dt} = \alpha_I \cdot e_I \cdot N_R^* - m_I \quad (4.4)$$

where the subscripts I and R refer to the invading and resident predator (respectively) and N^* is the prey population size at equilibrium, given by

$$N_R^* = \frac{m_R}{\alpha_R \cdot e_R} \quad (4.5)$$

Thus, a predator can invade a prey population at equilibrium with a resident predator when

$$\alpha_I \cdot e_I \cdot \left(\frac{m_R}{\alpha_R \cdot e_R} - \frac{m_I}{\alpha_I \cdot e_I} \right) > 0 \quad (4.6)$$

In other words, when the invader's equilibrium prey population size is less than the resident's equilibrium prey population size, the invasion will succeed. Because the equilibrium prey population size is inversely related to the predator attack rate, a predator with a higher attack rate than the resident can always invade. Over time, this model predicts that evolution will lead to higher predator attack rates. Eventually, however, the attack rate will be so high and the prey equilibrium population size so low that the prey population will be highly susceptible to extinction. And if the prey goes extinct, the predator will follow, a manifestation of evolutionary suicide (Parvinen (2005); Rankin and Lopez-Sepulcre (2005)). The same prediction arises from analysis of a basic susceptible-infected model of pathogen-host interactions (assuming no transmission-virulence relationship).

4.2.2 Spatial Predator Evolution

A variety of spatial L-V-like predator-prey models are possible. Here I consider the relatively simple case where the prey and predator populations reside on a regular two-dimensional lattice where lattice sites can be occupied or empty, prey are fixed in space, and prey reproduction, prey consumption, and predator reproduction only occur between directly adjacent lattice sites. In this model, the effective rate of prey reproduction is determined by r , the intrinsic host reproduction rate, and the number of empty sites among the prey's four nearest-neighbor sites. Similarly, the effective rate of prey consumption is determined by α , the maximum attack rate, and the number of prey among the predator's four nearest-neighbor sites. Each time a predator consumes a prey individual, the probability that it produces an offspring

is given by the conversion efficiency, e . When predator movement is allowed, the effective rate of movement depends on the maximum rate of movement, m_p , and the number of empty sites among the predator’s four nearest-neighboring sites. When multiple empty sites exist, the choice of destination sites is random. Otherwise, the dynamics are as described for the non-spatial L-V model.

To find the predator’s ES attack rate I simulate the dynamics as a Poisson process using the Gillespie algorithm (Gillespie (1977)). I assume that each time a predator reproduces there is some chance that the offspring is a mutant with an attack rate slightly different than the parent. The average attack rate of the predator population thus changes over time. When the average attack rate is no longer changing over time, I run the simulation for an additional 1000 time steps and take the average attack rate over the last 1000 time steps as the ES attack rate. In previous work I compared three different methods of inferring the ES strategy and found no difference between them (Messinger and Ostling (view)). I calculated the ES attack rate across a range of prey reproduction rates (up to $r = 100$), for several predator to prey death rate ratios ($d/m = 1/3, 1/2, 1,$ and 2), several predator conversion efficiencies ($e = 0.2, 0.5,$ and 1), and a range of predator movement rates (up to $m_p = 100$). For a biological interpretation of the parameter space explored, see Appendix E. I compared trends between the ES attack rate and different demographic rates with the special case of $e = 1, d/m = 0.5,$ and no predator movement, which corresponds to a pathogen-host-type interaction.

Progress has been made toward understanding the impact of individual based spatial structure on pathogen evolution using an inclusive fitness framework (Lion and Boots (2010)). In particular, when there is no tradeoff between the pathogen’s transmission rate and virulence, the selection gradient for increased transmission has two components: direct benefits and both direct and indirect costs due to local competition (Appendix F). When the direct benefits outweigh the costs, the selection gradient is positive and the pathogen will evolve an increased transmission rate. The costs due to local competition are influenced by the ecology of the interaction. For example, mathematically, recovery from infection is predicted to reduce the strength of local competition, ostensibly by increasing the local availability of susceptible hosts (Lion and Boots (2010)). Furthermore, there are direct and indirect components of local competition, where the direct costs are due to the effects of competition on the focal individual and the indirect costs are due to the effects of kin competition. With this framework in mind, I examine several metrics of the spatial distribution and dynamics of the predator and prey population that likely influence the strength

Table 4.1: Metrics of the strength of local competition and their effect on predator attack rate.

Metric	Measure Of	Local Competition	Attack Rate
Average prey cluster size	Local prey availability in space	↓	↑
Prey cluster join rate	Local prey availability through time	↓	↑
Average global prey density ^a	Local prey availability in space and time	↓	↑
Number of local predator types	Local kin competition	↓	↑
Predator movement	Local prey availability through time	↓	↑

^aFor a fixed host reproduction rate

of local competition (and thus the costs of an increased attack rate) to qualitatively understand some of the trends I report. Table 4.1 summarizes the metrics, their proposed effect on local competition, and the effect on the ES attack rate.

To help understand the trends of the ES attack rate with the prey reproduction rate, I examine the spatial distribution and dynamics of the prey population at evolutionary equilibrium as a function of the prey reproduction rate. At equilibrium, the prey and predator population is fragmented into distinct clusters of prey and predators. These clusters are dynamic, growing and shrinking as well as moving across the lattice. I look at two metrics related to the spatial distribution and dynamics of the prey population, which should influence the strength of local competition. First I look at the average prey cluster size at equilibrium. Larger clusters should indicate weaker local competition: local competition is strongest when few prey individuals are locally available. Second, I look at the rate at which prey clusters come together through time. More frequent joining of prey clusters should also indicate weak local competition: local competition is strongest when prey clusters are more isolated from one another.

To calculate the average prey cluster size at evolutionary equilibrium, I sampled the population at 10 different time points during equilibrium, separated by 50 time

steps to reduce correlation between samples. At each sampling time, prey clusters were identified as contiguous lattice sites that contained prey individuals. The number of prey within each unique cluster was recorded and the average cluster size was then calculated both within a single sampling time and across the 10 different sampling times. To calculate the average rate at which prey clusters come together through time at evolutionary equilibrium, a single, isolated prey individual was randomly chosen. As the population dynamics proceeded, I tracked the number of prey in the contiguous neighborhood of the chosen prey individual. In the case that the target individual died, I selected a new target individual that was within the contiguous neighborhood. When the target cluster grew by more than one prey individual, I counted the event as the joining of two prey clusters. After the target cluster disappeared, I picked a new target prey individual and repeated the process until I had collected data for at least 100 independent clusters. I then averaged the rate of cluster coalescence across the 100 samples.

To help understand the trends in the ES attack rate with the predator movement rate, I examined the average global prey density at evolutionary equilibrium as well as the average number of predator types found within small local areas across the lattice. I take the global prey density as an indicator of both the dynamics and spatial distribution of the prey population. When the host reproduction is the same, fewer prey indicate more empty space between clusters and thus greater the isolation. In addition, fewer prey indicate smaller average cluster sizes. As mentioned above, greater isolation between prey clusters as well as smaller average cluster size should indicate stronger local competition. I take the average number of predator types within a small local area as reflective of predator relatedness within a prey cluster: fewer types correspond to higher relatedness. Greater relatedness within a cluster should increase the strength of the indirect effects of local competition. Overall, predator movement should decrease the strength of local competition by allowing predators access to more prey than are necessarily available within a single cluster.

To calculate the average global prey density at evolutionary equilibrium I recorded the total number of prey in the population at 10 different time points during equilibrium, separated by 50 time steps to reduce correlation between samples. I then averaged the total number of prey across the 10 samples. To calculate the average number of predator types found within a small local area at evolutionary equilibrium, at 30 different time points during equilibrium, separated by 100 time steps, I randomly sub-sampled 800 n by n squares across the lattice to find the average number of predator types per area ($n = 5, 10, 15, 20, 25, 30$). I then averaged across the 30

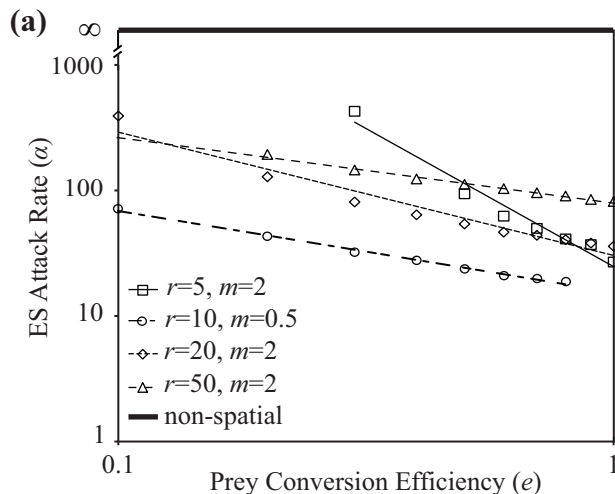


Figure 4.1: Effect of predator conversion efficiency on the evolutionary stable attack rate. Data points are the evolutionary stable attack rate (ES α) predicted from spatial simulations and the thick line is the ES α predicted by the non-spatial model. Simulation data are fit with a power law ($r = 5$: $\alpha = 24.74 \cdot e^{-2.2}$, $R^2 = 0.96865$; $r = 10$: $\alpha = 15.52 \cdot e^{-0.65}$, $R^2 = 0.99442$; $r = 20$: $\alpha = 30.38 \cdot e^{-0.982}$, $R^2 = 0.95168$; $r = 50$: $\alpha = 79.725 \cdot e^{-0.52}$, $R^2 = 0.9906$).

samples.

4.3 Results

4.3.1 Predator Conversion Efficiency

In the absence of predator movement, the relationship between the ES attack rate and the prey conversion efficiency is power law-like; lower conversion efficiencies lead to higher ES attack rates (Fig. 4.1). In contrast, an equivalent non-spatial model predicts no relationship between the ES attack rate and the conversion efficiency: all predators evolve a maximal attack rate. Neither the host reproduction rate (Fig. 4.1a) nor the magnitude of the predator death rate relative to the prey death rate change the qualitative shape of the relationship, though the steepness appears to increase with lower host reproduction rates and the ratio of predator to prey death rate. Across conversion efficiencies the ES attack rate is well below the predator-driven extinction threshold (Fig. 4.2). Thus, evolution is not driving the predator to the extinction threshold, suggesting that the evolutionary outcome will be somewhat robust to external perturbations. Furthermore, the ES attack rate does not seem to approach the extinction threshold at the extremes.

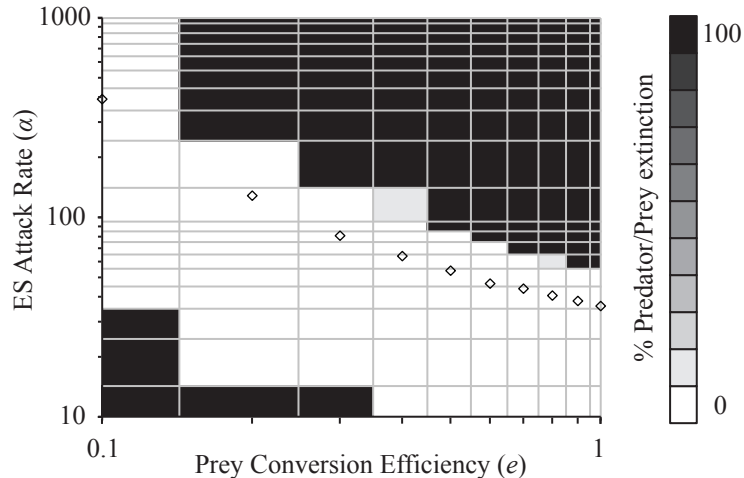


Figure 4.2: The evolutionary stable attack rate relative to extinction thresholds. Data points are the evolutionary stable attack rate (ES α) predicted from spatial simulations. Shading represents the percentage (out of 10) of non-evolutionary spatial simulations with the given attack rate and conversion efficiency where the predator and prey go extinct. In the lower left corner, the predator goes extinct and the prey persists. In the upper right corner, the predator drives prey extinction. The ES α is consistently below the predator-driven prey extinction threshold. Other parameters: $d = 1$, $m = 2$, and $r = 20$.

4.3.2 Prey reproduction rate

In the absence of predator movement, the prey reproduction rate first decreases then increases the ES attack rate (Fig. 4.3). In contrast, an equivalent non-spatial model predicts that the prey reproduction rate will not influence predator evolution: all predators evolve a maximal attack rate. The qualitative relationship between the ES attack rate and the prey reproduction rate is the same for a prey conversion efficiency of 1 and a prey conversion efficiency less than 1 (Fig. 4.3a). The ES attack rate initially declines with the prey reproduction rate but at a critical point begins to increase with prey reproduction. However, certain features of the relationship are shifted or magnified when the conversion efficiency is less than 1. Notably, the range of ES attack rates between the lowest host reproduction rate and the critical point where the ES attack rate begins to increase is larger for low efficiencies (e.g. in Fig. 4.3a, for $e = 1$, the range is 6.84, for $e = 0.5$ the range is 26.98, and for $e = 0.2$, the range is 44.75). In addition, the critical point where the ES attack rate begins to increase is shifted to higher reproduction rates (e.g. in Fig. 4.3a, for $e = 1$, the critical point is $r \approx 8$, for $e = 0.5$ $r \approx 10$, and for $e = 0.2$ $r \approx 20$).

The relationship between the ES attack rate and the prey reproduction rate is

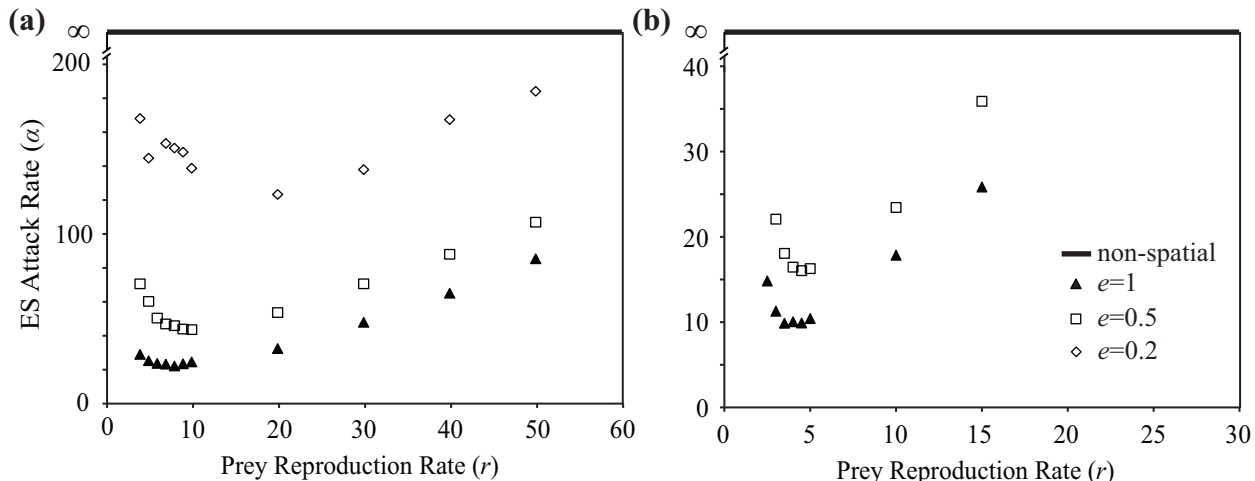


Figure 4.3: Effect of prey reproduction rate on the evolutionary stable attack rate. Data points are the evolutionary stable attack rate (ES α) predicted from spatial simulations and the thick line is the ES attack rate predicted by the non-spatial model. Simulations predict that the ES α initially declines and then increases with the prey reproduction rate regardless of the conversion efficiency or magnitude of predator death rate relative to prey death rate. Other parameters: (a) $d = 1$, $m = 2$; (b) $d = 1$, $m = 0.5$.

also qualitatively similar when the predator death rate is less than the prey death rate. However, while the range of ES attack rates between the lowest host reproduction rate and the critical point is still higher for lower efficiencies, the difference is less pronounced. Furthermore, the location of the critical point is similar between efficiencies. In addition, compared to the case when the prey death rate is less than the predator death rate, both the initial decrease and subsequent increase of the ES attack rate with prey reproduction is much steeper (Fig. 4.3b).

For both high and low predator conversion efficiencies, the rate at which prey clusters come together initially declines sharply with reproduction but subsequently increases (Fig. 4.4a). Thus, it appears that the degree of isolation between prey clusters, and thus the strength of local competition, initially increases with reproduction and then decreases. This may help explain why the ES attack rate initially decreases then increases with the prey reproduction rate: local competition is minimized at an intermediate reproduction rate. Prey cluster size decreases with increasing host reproduction rate, for both a low and high predator conversion efficiencies (Fig. 4.4b). The instantaneous local availability of prey declines with prey reproduction, and thus the strength of local competition increases with host reproduction. While this helps explain why the ES attack rate initially decreases with the prey reproduction rate (increased local competition), it does not help explain the subsequent increase, which

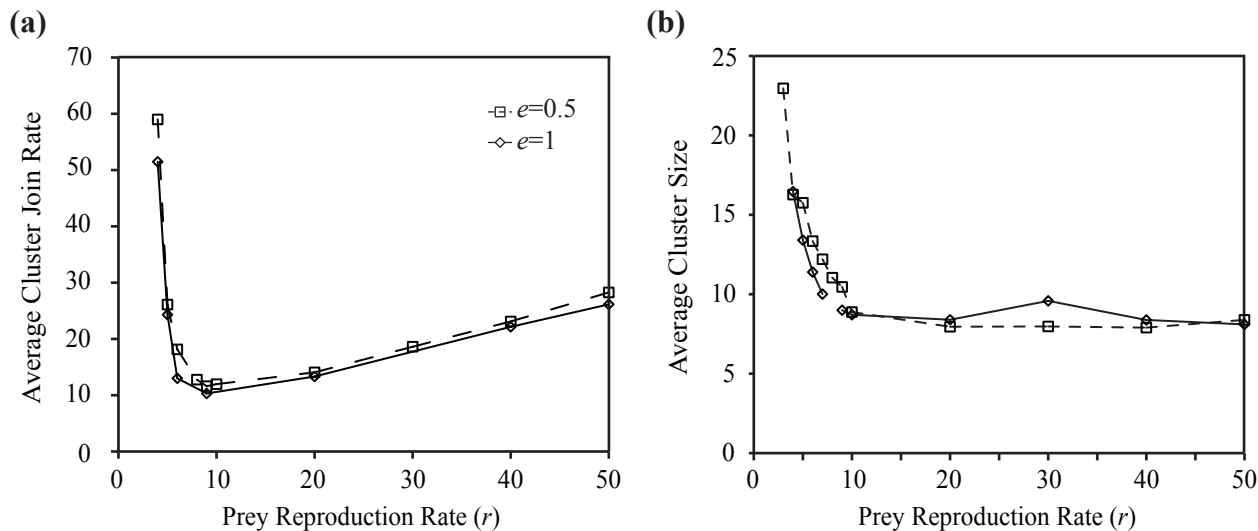


Figure 4.4: Effect of prey reproduction rate on the spatial distribution and dynamics of the prey population. (a) Data points are the average number of times two prey clusters join together per cluster per time at evolutionary equilibrium for two different predator conversion efficiencies and a range of host reproduction rates. Each data point is the average of over 100 independent clusters. The rate of prey cluster convergence declines and then increases with host reproduction rate regardless of the predator conversion efficiency. (b) Data points are the average size of prey clusters across the lattice at evolutionary equilibrium for two different predator conversion efficiencies and a range of host reproduction rates. Each data point is the average across 10 time samples separated by 50 time steps. Other parameters: $d = 1$, $m = 2$.

may be driven instead by the dynamics of the prey population in space. Furthermore, there is very little difference in either the prey cluster join rate or the average prey cluster size between a predator conversion efficiency of 1 and 0.5. Thus, the distribution and dynamics of the prey population cannot explain why the ES attack rate is higher for lower conversion efficiencies. Instead, the distribution and dynamics of the predator may be responsible.

4.3.3 Predator death rate

Increasing the predator death rate increases the ES attack rate for low host reproduction rates and decreases it for high reproduction rates (Fig. 4.5), regardless of the relative magnitude of the predator death rate relative to the prey death rate. In contrast, the equivalent non-spatial model predicts that the predator death rate will not influence predator evolution. The qualitative effect of the predator death rate on the ES attack rate is the same for a prey conversion efficiency of 1 and 0.5. In both cases, increasing the predator death rate increases the ES attack rate for

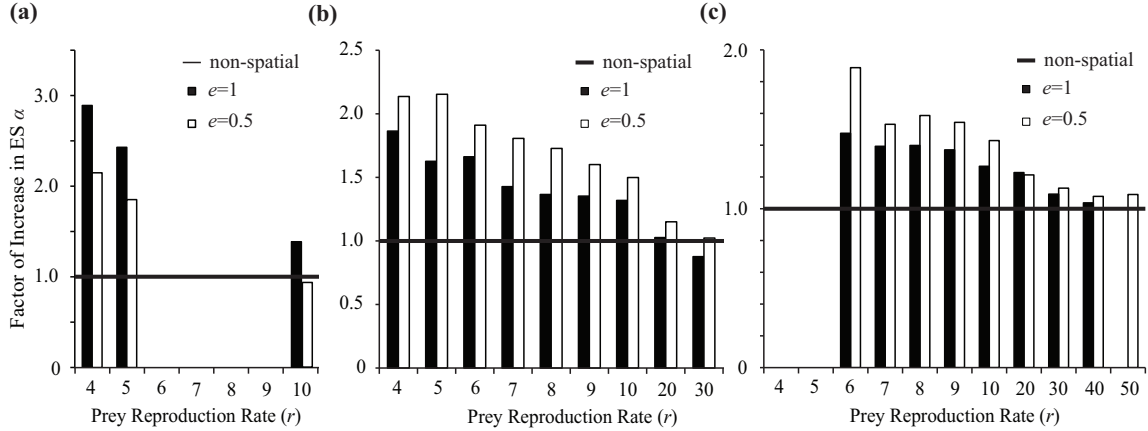


Figure 4.5: Effect of predator death rate on the evolutionary stable attack rate. The factor of increase in the evolutionary stable attack rate (ES α) is shown for an increase in the predator death rate from (a) $m = 0.5$ to $m = 1$, (b) $m = 1$ to $m = 2$, and (c) $m = 2$ to $m = 3$ across prey reproduction rates. A factor of increase of 1 means the ES α did not change. The non-spatial model predicts a factor of increase of 1 (in other words, no evolutionary effect) for all prey reproduction rates and predator conversion efficiencies. Other parameters: $d = 1$, $r = 20$.

low to intermediate prey reproduction rates. However, the effect diminishes as the prey reproduction rate increases and eventually reverses such that the ES attack rate decreases. Finally, the increase in the ES attack rate is greater for a lower efficiency across all prey reproduction rates only when the ratio of prey to predator death rates is less than 1. When the predator death rate increases and the ratio of prey to predator death rates is greater than 1, the reverse is true (compare Fig. 4.5b and c to Fig. 4.5a).

A comparison of the average prey cluster size for different predator death rates across prey reproduction rates shows that for low prey reproduction rates, the average cluster size is slightly larger for higher predator death rates. The difference in cluster size between death rates diminishes as the prey reproduction rate increases. This suggests that local competition may be stronger for lower predator death rates where there are fewer prey per cluster, especially for low prey reproduction rates. The trend helps explain the pattern of increasing ES attack rate with increasing predator death rate: local competition is weakened as death rate increases, thus leading to a higher ES attack rate. It also helps explain why the effect of the predator death rate diminishes with increasing prey reproduction: local competition is the same for all predator death rates when prey reproduction is high. However, it is likely that the

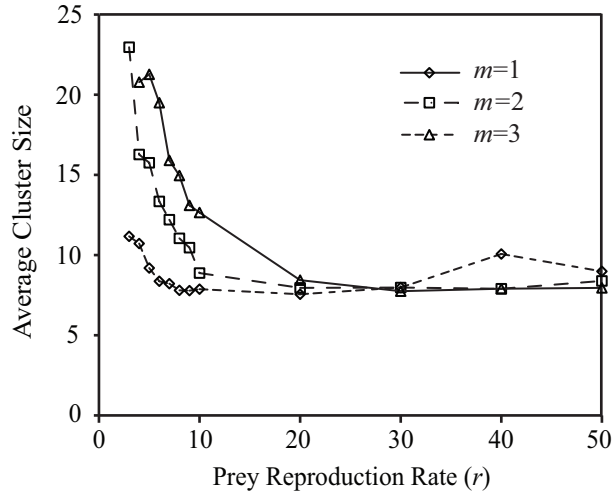


Figure 4.6: Effect of predator death rate on the spatial distribution of the prey population. Data points are the average size of prey clusters across the lattice at evolutionary equilibrium for two different predator death rates (m) and a range of host reproduction rates. Each data point is the average across more than 10 time samples separated by 100 time steps. Other parameters: $e = 0.5$, $d = 1$.

predator distribution and dynamics would also help explain the pattern.

4.3.4 Predator movement

Predator movement can significantly influence the ES attack rate (Fig. 4.7). Because movement is strictly a spatial process, equivalent non-spatial models do not predict an evolutionary role for predator movement. The relationship between movement and the ES attack rate differs depending on the prey reproduction rate and predator conversion efficiency. For intermediate prey reproduction rates ($r = 10$ and 20) and a low efficiency, predator movement strictly increases the predator attack rate. For high prey reproduction rates and a conversion efficiency of 1, the ES attack rate actually decreases with predator movement. Across prey reproduction rates, the range of the ES attack rate across predator movement rates is smaller ($\sim 2x$) for an efficiency of 0.5 than for an efficiency of 1, except for the case of $r = 50$.

Predator movement decreases the global density of prey across the lattice (Fig. 4.8; top panels) for all reproduction rates and a predator conversion efficiency of 1 (Fig. 4.8a) and 0.5 (Fig. 4.8b). I assume that given the same prey reproduction rate, differences in the global density of prey reflects both the dynamics and distribution of the prey population: as global prey density declines, prey clusters become smaller and more spatially distant, likely decreasing the rate at which they join together. Visually,

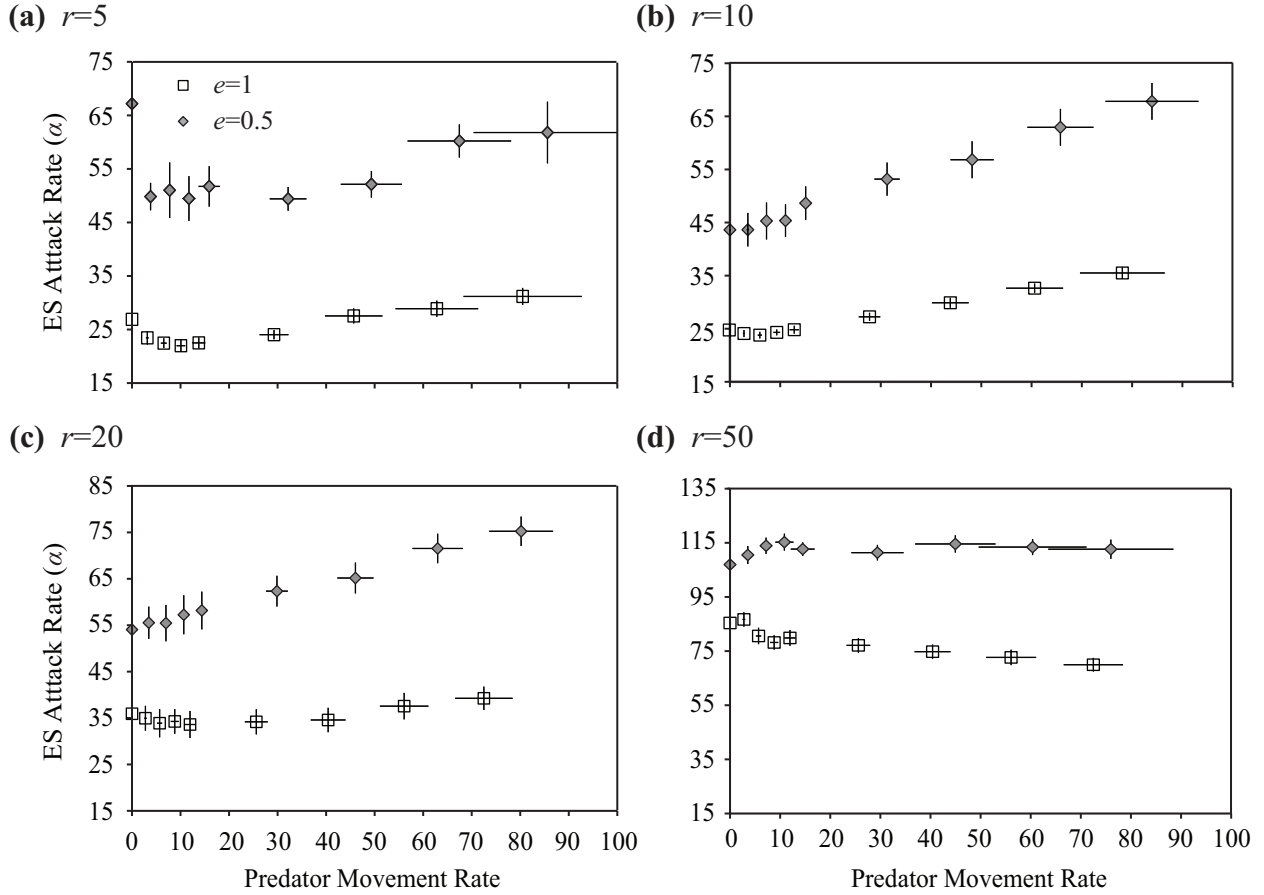


Figure 4.7: Effect of predator movement on the evolutionary stable attack rate. Each panel shows data for a different prey reproduction rate (r). Data points are the evolutionary stable attack rate (ES α) from spatial simulations for different predator conversion efficiencies. Data are plotted against the average actual predator movement rate, which is lower than the maximum possible movement rate (m_p). Error bars show the standard deviation in the ES α as well as the movement rate. Other parameters: $d = 1$, $m = 2$.

this appears to be true (see Fig. 4.8; bottom panels). Local competition is likely to be strongest when prey clusters are small and highly isolated. However, predator movement by itself decreases the strength of local competition by increasing the prey availability to a predator in both space and time. Predator movement should also tend to increase the number of predator types found within a local area on the lattice (Fig. 4.8; middle panels). The strength of local competition through indirect kin effects is likely to be strongest when predator types are clustered together (reflecting a high relatedness within prey clusters). Thus, the strength of local competition should be stronger when predator types are highly clustered together (low rates of predator movement). All together then, predator movement has several competing effects on

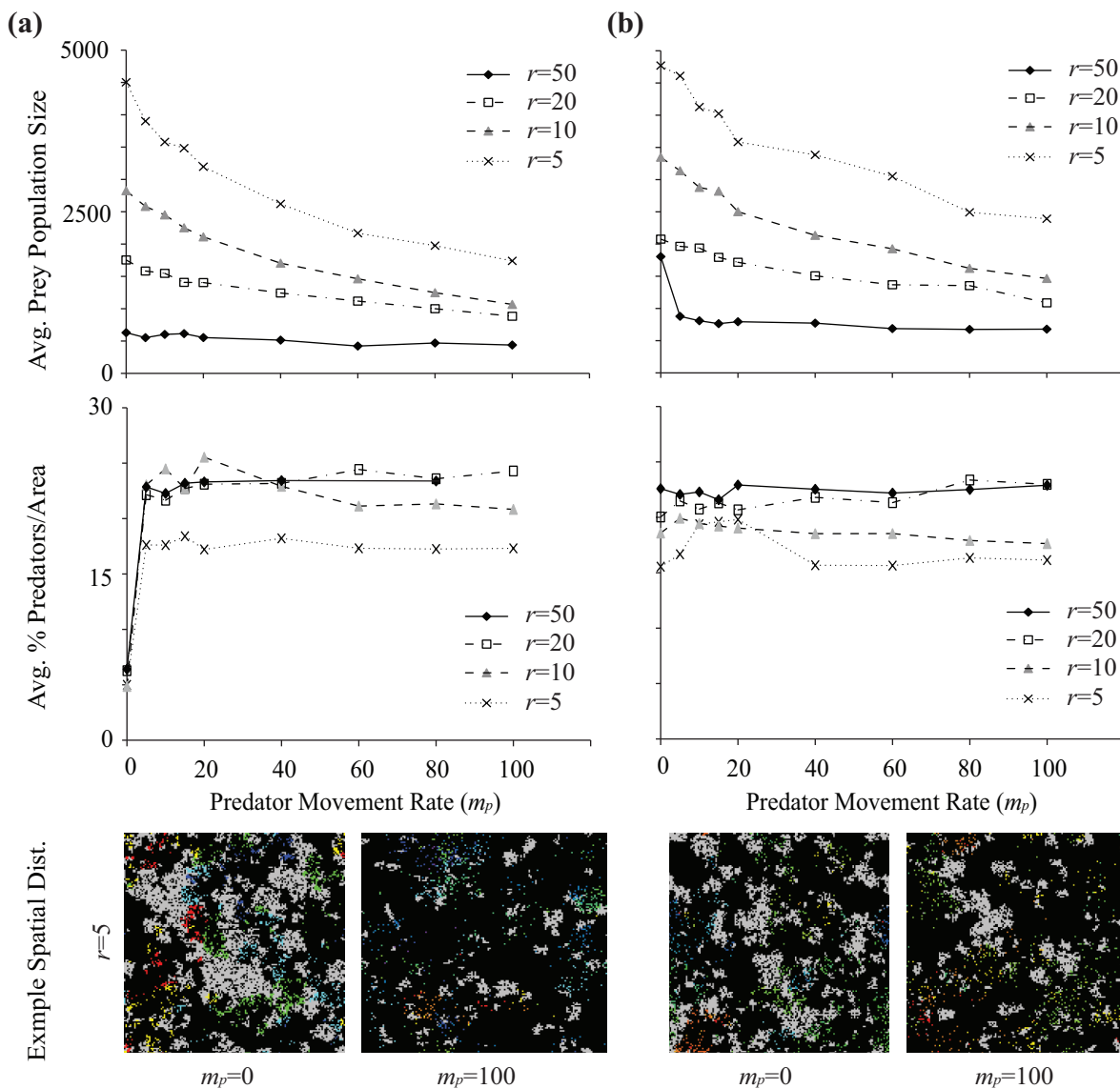


Figure 4.8: Effect of predator movement rate on global prey density and predator type distribution. (a) shows data for predator conversion efficiency (e) of 1 and (b) for $e = 0.5$. The top panels show the average prey density across at least 500 time steps at evolutionary equilibrium as a function of the predator movement rate (m_p) for different prey reproduction rates (r). In all cases, prey population size declines with increasing predator movement rates. The second panels show the average percent of the total number of predator types (identified by their attack rate) present in 800 randomly sub-sampled areas across the lattice (30 by 30 lattice sites; the trends are the same for smaller area sizes). The % predators per area either increases or remains similar across predator movement rates. The bottom panels show two snapshots of the lattice for one prey reproduction rate ($r = 5$) and two different predator movement rates ($m_p = 0$ and 100). In the images, gray sites are occupied by prey, colored sites are occupied by predators (where the color represents a particular attack rate), and black sites are empty. Other parameters: $d = 1$, $m = 2$.

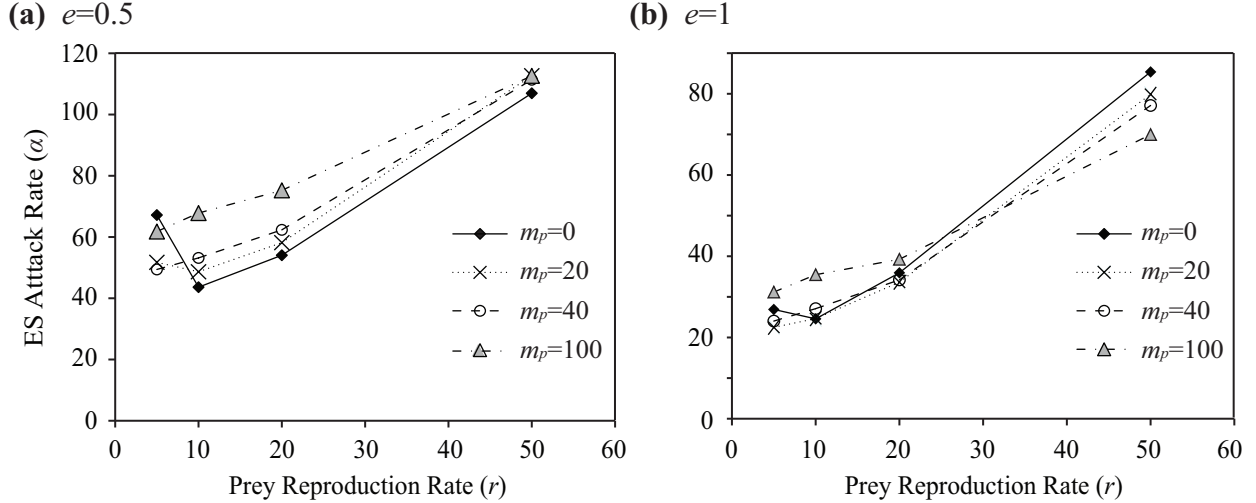


Figure 4.9: Effect of predator movement rate on the relationship between prey reproduction rate and the evolutionary stable attack rate. Data points show the evolutionary stable attack rate (ES α) predicted by spatial simulations across prey reproduction rates (r) for different predator movement rates (m_p). When $m_p = 0$, the ES α initially decreases with prey reproduction and then increases. As m_p increases, the initial dip disappears. Other parameters: (a) $d = 1$, $m = 2$, $r = 20$, $e = 0.5$; (b) $d = 1$, $m = 2$, $r = 20$, $e = 1$.

the strength of local competition: it increases local competition through the distribution of the prey population, decreases local competition through the direct effect of movement, and decreases it through the distribution of the predator population.

An important consequence of predator movement is that it changes the qualitative relationship between the prey reproduction rate and the ES attack rate (Fig. 4.9), demonstrating that different aspects of ecology can interact to influence the evolutionary dynamics. As the predator movement rate increases, the characteristic initial decline in the evolutionary stable attack rate with prey reproduction disappears. This is consistent for low and high conversion efficiencies. Furthermore, for an efficiency of 1, as the predator movement rate increases the ES attack rate at the highest prey reproduction rate ($r = 50$) declines (Fig. 4.9b). However, although the relationship is changed, there is still a significant relationship, which is not predicted by an equivalent non-spatial model.

4.4 Discussion

Population spatial structure has been shown to influence pathogen evolution (reviewed in Messinger and Ostling (2009); Lion and Boots (2010)), and, in many cases,

to alter the influence of various aspects of pathogen and host ecology. Population spatial structure can similarly influence predator evolution. In particular, two studies have shown that when the predator and prey populations are spatially structured into a metapopulation the predator may evolve an intermediate ES attack rate, below the extinction threshold (Gilpin (1975); Pels et al. (2002)). Although one study has nominally examined the effects of individual level spatial structure on the evolution of true predators, the authors do not examine the dynamics for parameter sets that would distinguish the interaction from a pathogen-host interaction (Rauch and Bar-Yam (2006)). Regardless of the type of spatial structure, prior to this study, the influence of predator and prey ecology had not been thoroughly explored. Of particular interest is: 1) the predicted effect of unique aspects of predator and prey ecology on predator evolution relative to the non-spatial expectation and 2) whether, despite these unique aspects of ecology, there are consistent patterns predicted in the effect of aspects of predator and prey ecology that are analogous with pathogen and host ecology. Here I show the influence of three aspects of predator and prey ecology (conversion efficiency, relative magnitude of predator and prey death rate, and predator movement) on predator evolution in reference to two non-interaction-specific aspects of ecology that are analogous to aspects of pathogen and host ecology (prey reproduction rate and predator death rate).

First, at a very general level, I show that for predators with ecology unique relative to pathogens, individual-level spatial structure can lead to an intermediate attack rate lower than the extinction threshold attack rate. I then show how different aspects of ecology influence the evolutionary dynamics relative to the non-spatial expectation. I find that the ES attack rate declines with increasing predator conversion efficiency, regardless of prey reproduction rate and the relative rates of predator and prey death. In contrast, non-spatial theory predicts no relationship with the predator's conversion efficiency. In addition, the ES attack rate is below the predator-driven extinction threshold across predator conversion efficiencies (see Fig. 4.2). Since the predicted ES attack rate for low conversion efficiencies can be quite large (e.g. for $e = 0.1$, $r = 20$, $d = 1$, and $m = 2$ the ES attack rate is ≈ 392) it may be that other mechanisms of constraint will come into play before the predator achieves the ES attack rate predicted from spatial effects alone. However, these results demonstrate that predator ecology can have significant evolutionary effects when space is considered.

I also find that the predicted effect of prey reproduction and predator death rate on predator evolution are similar to the predicted effect of host reproduction and infected host death rate on pathogen evolution, regardless of the conversion efficiency or ratio

of prey to predator death rate. The predators ES attack rate initially declines and then increases with the prey reproduction rate and increases with increasing predator death rate. The evolutionary effect of increasing the predator death rate declines as the prey reproduction rate increases and is generally larger for lower predator conversion efficiencies. Non-spatial models predict that neither the reproduction nor death rate will influence predator evolution. The consistency in the trends of the ES attack rate with these two demographic rates between pathogens and true predators suggests they may play a key role in the evolution of all types of exploitative species. Even though unique aspects of ecology, like predator movement, may qualitatively alter the trends, they will likely still play an important evolutionary role.

I suggest that the evolutionary effect of the prey reproduction and predator death rates can be qualitatively understood from the spatial dynamics and distribution of the prey population. In particular, when the prey population is spatially segregated into distinct clusters, the rate at which those clusters join together and their average size is likely to influence the strength of local competition. Within an inclusive fitness framework, stronger local competition leads to a reduced predator attack rate. The prey reproduction rate initially increases the strength of local competition by decreasing the average prey cluster size and the rate at which prey clusters join together. Subsequently, the prey reproduction rate increases the rate at which prey clusters join together, weakening local competition and resulting in the evolution of a higher ES attack rate. It is likely that the distribution and dynamics of the predator population are also important, especially in understanding the influence of the predator death rate.

Finally, I demonstrate that when spatial structure is at the individual level, predator movement matters. However, the effect of movement is not clear-cut. Rather than simply increasing or decreasing the ES attack rate, its effect depends on the prey reproduction rate and predator conversion efficiency. I suggest that the evolutionary effect of predator movement can also be qualitatively understood from the spatial dynamics and distribution of the prey population as well as the distribution of the predator population. Predator movement decreases both prey cluster size and the rate at which prey clusters join together, strengthening local competition. However, predator movement intrinsically decreases local competition by allowing predators to move to different prey clusters. Movement also decreases the clustering of predator types in space, or the relatedness of predators within a cluster, weakening local competition through kin effects. Thus, the ES attack rate is ultimately a balance of the dual and contradictory effects of predator movement on the strength of local

competition. The weakening effects of movement appear to be more important when the efficiency is low and prey reproduction is intermediate. In that case, predator movement strictly increases the ES attack rate.

While these results demonstrate that predator movement is evolutionarily important, our model is quite simplistic. In reality, predators are likely to move in response to prey density. This added realism is likely to influence predator evolution because it will alter the spatial distribution of both predator and prey. Likely, predators will be more clustered around prey, amplifying local competition. A priori, it is not clear that density dependent movement will change the spatial genetic structuring of the predator population relative to random movement, implying that density dependent movement will still weaken the strength of local competition through indirect kin effects.

The results presented here clearly show that spatial structure can strongly influence the evolutionary role of predator and prey ecology. Many aspects of ecology that are not predicted to influence predator evolution in a non-spatial context have a strong influence when space is considered. Ultimately, our findings emphasize that spatial context is a key evolutionary influence that cannot safely be ignored. Furthermore, the fact that spatial structure can influence predator evolution has important implications for our understanding of the evolutionary stability of entire food webs. Spatial structure may be a key force shaping food web structure over evolutionary time, influencing biodiversity and species turnover.

CHAPTER V

Evolutionary stability of food webs arising from spatial structure

5.1 Introduction

Theory suggests that pair-wise predator-prey interactions are inherently evolutionarily unstable. Over evolutionary time, the predator is predicted to evolve an increased attack rate. Concurrently, the prey population size will decrease, eventually to the point that it is highly susceptible to extinction. Building from this critical prediction, additional theory has shown that the inclusion of ecological or allocation tradeoffs or prey co-evolution can stabilize predator-prey interactions (Abrams (1991)). More recent theory has shown that without tradeoffs or co-evolution, population spatial structure, where individual organisms do not interact randomly but rather according to their spatial location, can also stabilize predator-prey interactions (van Baalen and Sabelis (1995); Gilpin (1975); Pels et al. (2002); Rauch et al. (2002)). Furthermore, spatial structure has already been shown to play an important role in the dynamic stability and the complexity of entire food webs in the absence of evolution (e.g. Pillai et al. (2011)). A natural conjecture is that spatial structure may also play an important role in the evolutionary stability of larger food webs. However, to date no studies have examined the effect of spatial structure alone on the evolutionary stability of food webs (see Figure 1 in Urban and Skelly (2006)).

The evolutionary instability of pair-wise predator-prey interactions is at least naively expected to extend to the evolutionary stability of whole food webs if the feeding interactions are fixed (i.e. there is no prey switching). In the absence of other stabilizing mechanisms including spatial structure, each predator should evolve increased attack rates to the point of prey extinction and the web should collapse. Though intuitive, to my knowledge this has not been demonstrated, even for simple

three species food chains. Based on studies of the evolution of three species food webs when there are other stabilizing mechanisms at work, there is good reason to test this naive expectation. For a co-evolving predator and prey, the inclusion of just a single additional species (either another predator or prey) can significantly alter the evolutionary trajectory of the system (Abrams (1991); Dercole et al. (2010); Mougi (2010); Mougi and Nishimura (2009)). While a small number of studies have examined the evolutionary assembly of larger food webs or whole interaction webs in a non-spatial context, none clearly explore whether food webs are inherently evolutionarily unstable. Most existing models allow the network structure itself to evolve and are consequently characterized by constant species turnover (e.g. the Tangled Nature model, Murase et al. (2010); Rikvold and Sevim (2007); Rikvold and Zia (2003); Rikvold (2007), the Web World model, Caldarelli et al. (1998); Drossel (2004), and other models, Brown and Vincent (1992); Mithen and Lawton (1986); Post and Pimm (1983)). While these models produce realistic average food-web structures and properties, they do not provide insight into the non-spatial evolution of each predator over time. Presumably, the constant species turnover results from the continuous evolutionary destabilization of existing interactions and the introduction of new interactions, but this has not been explicitly shown. A more recent study examined the stability consequences of a single evolutionary change within a community, which allows more careful dissection of predator evolution within a community (Loeuille (2010)). However, this study also assumed ecological or allocation tradeoffs, which are stabilizing mechanisms in and of themselves.

Here I use three simple population dynamic models of predator-prey interactions implemented in a metapopulation context to determine whether they predict evolutionary stability for pair-wise predator-prey interactions. Prior metapopulation models that predict evolutionary stability of pair-wise predator-prey interactions (van Baalen and Sabelis (1995); Gilpin (1975); Pels et al. (2002)) are relatively more system specific and thus do not easily scale up to entire food webs like the models tested here. I find that all three models predict evolutionary stability for pair-wise interactions. However, I suggest that the evolutionary mechanism at work differs between models. Importantly, the evolutionary stability that arises from the stochastic model is more robust than for deterministic models. I then use the stochastic model to determine the evolutionary stability of three and five species food webs in spatial and non-spatial contexts. I show that in the absence of spatial structure, without other stabilizing mechanisms, three species food chains and five species webs are indeed evolutionarily unstable: the predators evolve to either predator or prey extinction.

Furthermore, the time to extinction declines with the number of species in the web. I finally show that three species food chains and five species webs are also evolutionarily unstable in a spatial context. For three species webs, only one predator goes extinct—the top predator for straight food chains and the middle predator for food chains with omnivory (where the top predator also eats the basal species). For five species webs, 50% of the time all predators and/or prey go extinct and 50% of the time one predator remains, stably coexisting with the prey.

My results have several important implications. First, non-spatial models of food-webs used to explore ecological phenomena ought to include evolutionary stabilizing mechanisms like prey co-evolution, ecological or allocation tradeoffs. Without these mechanisms, the web will be evolutionarily unstable and predictions arising from the model will have limited scope. Second, very simple predator-prey population dynamic models can predict evolutionary stability in a metapopulation context. However, stochastic models are likely to produce robust stability, suggesting that demographic stochasticity is an important evolutionary force. Finally, though the particular model used here does not predict that spatial structure will stabilize food webs, this does not preclude the possibility. Other regions of parameter space or a model with more biological realism may predict otherwise. However, if spatial structure alone cannot stabilize entire webs, one might conclude that the constant species turnover predicted by existing non-spatial evolutionary community assembly models may also characterize spatial evolutionary community assembly. A small but key difference may simply be that without spatial structure, the entire web may from time to time collapse while in a spatial context, at least one predator and prey will likely persist, providing a base from which to build up another web.

5.2 Methods

Choosing an appropriate model to explore the evolutionary effects of spatial structure is not trivial. The model framework should be suitable to induce evolutionary stability of pair-wise interactions and at the same time realistic for scaling up to entire food webs. For large food webs, a metapopulation model is a natural choice. However, a significant portion of the theory regarding the ability of spatial structure to stabilize pair-wise predator-prey interactions is founded in individual based lattice models (e.g. Rauch et al. (2002)). Other theory based on metapopulation models include system-specific complexities that preclude scaling the dynamics to entire food webs. For example, the metapopulation model published by Pels et al. (2002) is specifically

constructed to model predatory mites so that many of the model details are specific to that organism. The model published by Gilpin (1975) includes social interactions and assumes the attack rate is a two allele trait.

Here I compare the predictions of three types of very general population dynamic models of pair-wise predator-prey interactions, both within a metapopulation context and in a non-spatial context. The three models are 1) deterministic with logistic prey growth, 2) deterministic with exponential prey growth, and 3) stochastic with exponential prey growth. Based on the model predictions for pair-wise interactions, I then use the stochastic model to explore the evolution of three and five species food webs in a spatial and non-spatial context.

5.2.1 Deterministic, logistic growth model

The population dynamics of prey (B) and predator (P) species are governed by the following equations

$$B : \frac{dN_{i,k}}{dt} = r_i \cdot N_{i,k} \cdot (1 - N_{i,k}) + \sum_{i,j \in S, i \neq j} \alpha_{i,j} \cdot N_{i,k} \cdot N_{j,k} - \sum_{n \in N} m \cdot (N_{i,k} - 0.25 \cdot N_{i,n}) \quad (5.1)$$

$$P : \frac{dN_{i,k}}{dt} = \sum_{i,j \in S, i \neq j} \alpha_{i,j} \cdot N_{i,k} \cdot N_{j,k} - d_i \cdot N_{i,k} - \sum_{n \in N} m \cdot (N_{i,k} - 0.25 \cdot N_{i,n}) \quad (5.2)$$

where $N_{i,k}$ is the population size of species i in subpopulation k , r_i is the intrinsic growth rate of species i ($r_i = 1$), N is the set of four subpopulations directly adjacent to subpopulation k , m is the migration rate, α_{ij} is the effect of species j on species i ($\alpha_{ij} < 0$ when j eats i), and d_i is the predator death rate ($d_i = 0.1$). Here I refer to α_{ij} as the attack rate of species j . The carrying capacity of the prey is 1. In the case of one predator and one prey, there is a stable equilibrium at $P^* = r/\alpha - d/\alpha^2$ and $B^* = d/\alpha$. In the non-spatial model, $m = 0$. If the population size of a particular species drops below 0.01 (1% of the carrying capacity in the case of basal species) then it is removed from the simulation. Note that time is scaled to the prey intrinsic reproduction rate and that the default parameter choices are somewhat arbitrary, not chosen to reflect any particular type of natural system. This study is intended as a proof of concept to stimulate future studies.

5.2.2 Deterministic, exponential growth model

The population dynamics of prey (B) and predator (P) species are governed by the following equations

$$B : \frac{dN_{i,k}}{dt} = r_i \cdot N_{i,k} + \sum_{i,j \in S, i \neq j} \alpha_{i,j} \cdot N_{i,k} \cdot N_{j,k} - \sum_{n \in N} m \cdot (N_{i,k} - 0.25 \cdot N_{i,n}) \quad (5.3)$$

$$P : \frac{dN_{i,k}}{dt} = \sum_{i,j \in S, i \neq j} \alpha_{i,j} \cdot N_{i,k} \cdot N_{j,k} - d_i \cdot N_{i,k} - \sum_{n \in N} m \cdot (N_{i,k} - 0.25 \cdot N_{i,n}) \quad (5.4)$$

where all parameters have the same meaning and default values as in the deterministic logistic model. However, in this model the prey experiences unregulated exponential growth in the absence of predators. In the spatial simulations, an artificial cap is set on the prey population size so that the prey cannot grow unbounded in patches without predators (here set to 2). In the case of one predator and one prey, there are neutrally stable limit cycles centered at $P^* = r/\alpha$ and $B^* = d/\alpha$. Again, if the population size of a particular species drops below 0.01 then it is removed from the simulation.

5.2.3 Stochastic, exponential growth model

I simulated the population dynamics of the deterministic exponential growth model in discrete state space such that population sizes could only take on integer values. I used the Gillespie algorithm to simulate the dynamics (Gillespie (1977)). As with the deterministic exponential growth model, in the spatial simulations an artificial cap is set on the prey population size to prevent unbounded growth in predator-free patches (here set to 200 for two and three species webs and 10,000 for five species webs). In these simulations the default prey reproduction rate is 1.5 and the predator death rate is 1. Thus, time is scaled to the predator death rate in the stochastic simulations rather than the prey reproduction rate. This parameter choice prevents direct comparison of time scales between the deterministic and stochastic models. However, I can compare time scales between the spatial and non-spatial versions of each population model.

5.2.4 Food web construction

To examine the impact of space on entire food webs it is necessary to construct them. Historically, many food web studies are based on randomly assembled webs

(e.g. May (1971)). Though webs constructed this way are not realistic, a number of important hypotheses have been generated from them that are still discussed today (e.g. the relationship between diversity and stability in food webs; see McCann (2000)). Since then, many other food web assembly models have been developed and found to create realistic food web structures. Though the latter types of food webs offer increased realism, they come with added complexity. For example, structuring in the cascade model (Cohen et al. (1990)) is based on body size relationships between predator and prey. In addition to food web structure, body size relationships influence the population dynamics of the predator and prey (Brose et al. (2006); Yodzis and Innes (1992)), which can have important ecological (Jonsson and Ebenman (1998)) and evolutionary consequences (Brose et al. (2006); Weitz and Levin (2006)). Thus, as a first test of the potential role of spatial structure alone in evolutionarily stabilizing food webs, here I use more simple randomly constructed webs. Furthermore, for small numbers of species modeled here, randomly constructed webs are not unrealistic—for example, there are many examples of naturally occurring food chains.

Webs are constructed with P predators and B basal species for a total of $S = P + B$ species. Only feasible (equilibrium population sizes > 0) and dynamically stable (all species stably coexist for 500 time units) webs are used. To assemble the webs, attack rates are assigned a value of 0 with probability $1-C$, where C is the food web connectance. Feeding links are symmetrical such that $\alpha_{ij} = -\alpha_{ji}$. Non-zero interaction strengths are drawn from a uniform random distribution. For three species webs, the distribution ranges from 0 to 0.01. For five species webs, the distribution ranges from 0 to 0.002. For simplicity, community structures are restricted to those that do not contain intransitive loops (species a eats species b , species b eats species c , and species c eats species a). I randomly constructed 50 different feasible and dynamically stable three species webs (either food chains or food chains with omnivory) and 10 different feasible and dynamically stable five species webs.

5.2.5 Evolutionary dynamics

In both spatial and non-spatial simulations, at regular intervals there is some probability (p_{mut}) that a single predator will mutate. Mutations affect only one predator and only one attack rate at a time in the case that the predator has more than one prey species. A mutation can either increase or decrease the attack rate of that interaction by some small amount ($\Delta\alpha = 0.5$ for deterministic models and $\Delta\alpha = 0.01$ for the stochastic model). If the original attack rate was positive, the

mutant attack rate is constrained to also be positive. Thus, mutant predators have the same feeding links as their parents and mutation does not lead to new species, here defined by their trophic interactions. Mutant predators begin with a population size of 0.01 for the deterministic models and 1 for the stochastic model. Over time, the average attack rate of predators in the community changes. A predator's average attack rate is calculated across all its feeding links.

5.3 Results

5.3.1 Two species

When predator and prey populations are spatially structured in a metapopulation the predator may evolve an evolutionary stable attack rate that allows stable predator-prey coexistence (Fig. 5.1). Furthermore, the evolutionary constraint induced by spatial structure is independent of the type of population dynamic model used, occurring for both deterministic and stochastic models and different modes of prey growth (logistic or exponential). However, the evolutionary outcome for the deterministic population models appears to arise from a fundamentally different mechanism than the stochastic population model. For both deterministic models, the predator evolves an attack rate that pushes the prey population very close to the extinction threshold. Averaged over 100 time steps near the end of each simulation shown in Fig. 5.1, the average prey population is 0.01417 ($s.d. < 10^{-4}$) for the deterministic logistic growth model, and 0.0145 ($s.d. < 10^{-4}$) for the deterministic exponential growth model. In contrast, for the stochastic model the average prey population size is 33.73 ($s.d. = 10.034$). Recall that for the two deterministic models, the extinction cutoff is 0.01 and for the stochastic model it is 1. Further evidence that the evolutionary mechanism at work in the deterministic and stochastic models are different, at evolutionary equilibrium in the stochastic model the predator and prey are dynamically moving between patches. In contrast, in the two deterministic models the patch occupancy is fixed through time once evolutionary equilibrium is reached (Fig. 5.2).

To elucidate the evolutionary dynamics in the two deterministic models, I calculate the population growth rate of a predator invading a prey population at equilibrium with a resident predator. At metapopulation equilibrium, there is no net migration of predator or prey between subpopulations, which leads to static subpopulation occupancy. In this scenario, the growth rate of an invading predator (denoted with the subscript I) in a single subpopulation with prey (denoted with subscript V) and

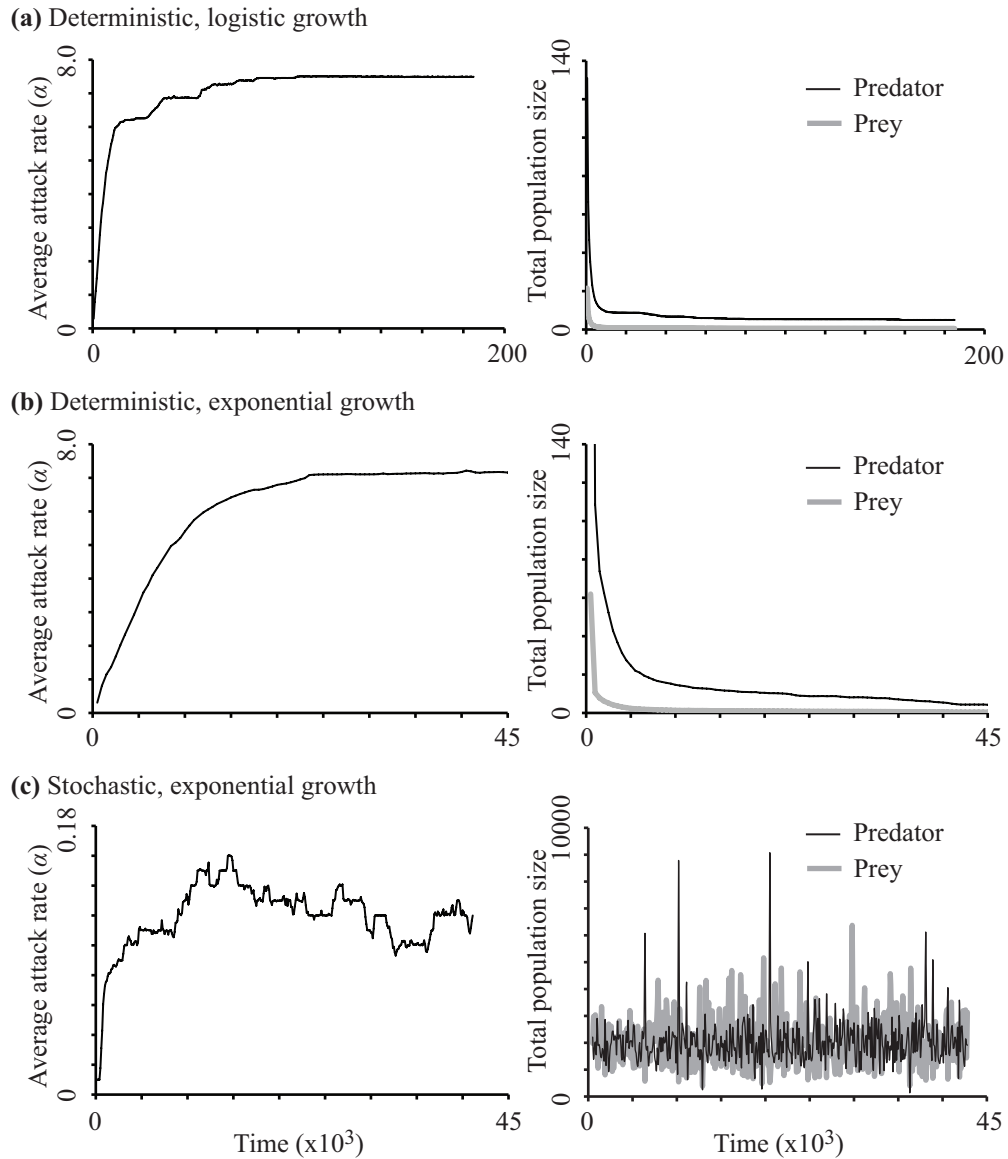


Figure 5.1: Pair-wise predator-prey interactions in a metapopulation. Data are shown for three different population dynamic models. The left column of graphs is the average predator attack rate over time. For the two deterministic models (a & b) time is scaled to the prey reproduction rate. For the stochastic model (c) time is scaled to the predator death rate. The right column of graphs shows the total population size of the predator and prey over time. Other parameters are as defined in the methods.

a resident predator (denoted with subscript R) is

$$\frac{dN_I}{dt} = \alpha_I \cdot N_V^* \cdot N_I - d \cdot N_I - 4 \cdot m \cdot N_I \quad (5.5)$$

The population growth rate of the invading predator will be positive when

$$\alpha_I > \frac{d + 4 \cdot m}{N_V^*} \quad (5.6)$$

Plugging in the equilibrium prey population size ($N_V^* = d/\alpha_R$), this is

$$\alpha_I > \frac{\alpha_R \cdot (d + 4 \cdot m)}{d} \quad (5.7)$$

In essence, the predator can only invade if its rate of growth due to eating the prey is greater than its rate of decline due to death and migration to surrounding patches. Once a resident strain comes into equilibrium with the prey such that there is no net migration, the invading predator must have an attack rate $(4 \cdot m + d)/d$ times larger than the resident to invade. Thus, the migration rate will dictate what mutation size is required for successful invasion. For the parameters used here, the invading predator needs an attack rate 1.4 times larger than the resident.

In contrast to the deterministic simulations in which the metapopulation comes to an equilibrium characterized by a single predator and the prey, stochastic simulations are characterized by continual population turnover within each subpopulation. Over time, the prey within a subpopulation periodically go extinct but subsequently reinvade (see Fig. 5.3). The amount of time between prey colonization events within a given patch increases as the average predator attack rate increases. Compare Fig. 5.3a and Fig. 5.3b, which show the prey population size within the same patch over the same amount of time. In a, the average attack rate is ≈ 0.02 and in b it is ≈ 0.08 . When the attack rate is low (Fig. 5.3a) the number of time points where the patch is empty is 21 and when the attack rate is high (Fig. 5.3b) the number of time points is 97. These dynamics suggest that empty patches are first colonized by the prey and subsequently colonized by a predator. The patch may then be colonized by another predator, which, given a high enough attack rate, could lead to prey and predator extinction. The reason evolution leads to an intermediate predator attack rate is likely related to the average prey population size prior to extinction. The peak predator and prey population size is larger when the average attack rate is lower. This can be seen in Fig. 5.3. In Fig. 5.3a, the average peak prey population size is 96.375 (s.d. =

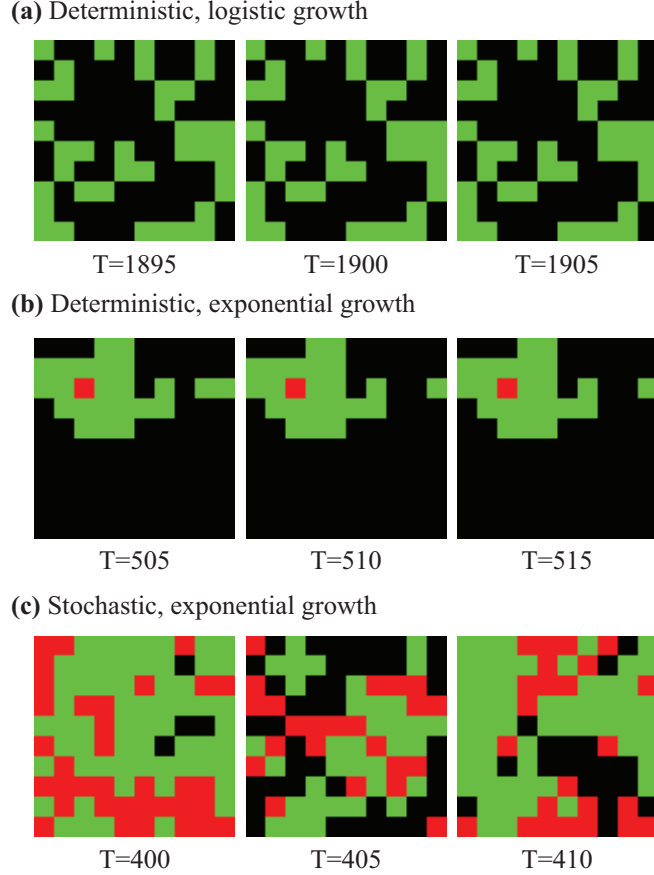


Figure 5.2: Subpopulation structure over time for spatial pair-wise predator prey interactions. Three example time points are shown for each of the three types of population models. In the image, black squares are empty, green squares have both predator and prey, and red squares have only predators. Time units are $T \times 10^3$. All three time points are from evolutionary equilibrium (when the predator average attack rate is not increasing over time).

42.53) and in Fig. 5.3b it is 67.3125 (s.d.=55.662); $t=1.659$, significant at $\alpha = 0.1$). A non-spatial deterministic predator-prey model supports this hypothesis. Fig. 5.4 shows the predicted population dynamics of a prey and two different predators, one with a high attack rate ($\alpha = 0.05$) and one with a low attack rate ($\alpha = 0.02$). in Fig. 5.4a all three occupy the same patch. The high attack rate predator clearly out-competes the low attack rate predator. However, on their own (Fig. 5.4b and c), the low attack rate predator achieves a higher peak population size than the high attack rate predator. In conjunction, the peak prey population size is larger with the low attack rate predator than the high attack rate predator. In essence, a predator with a high attack rate achieves a within-patch competitive advantage, but a predator with a low attack rate achieves a between patch population advantage. Thus, the

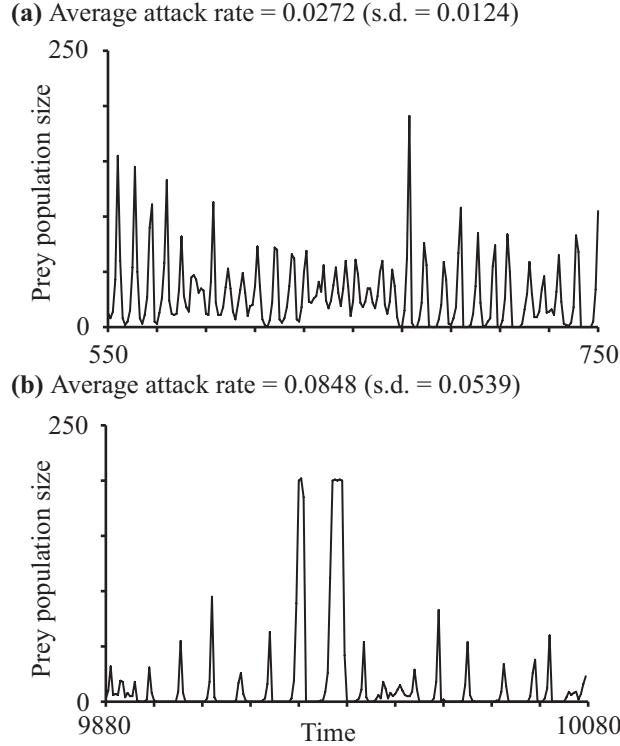


Figure 5.3: Example of subpopulation prey population dynamics in stochastic simulations. Shown is the prey population size over time within a single subpopulation at two different time intervals. In (a) the data is early in the simulation when the average attack rate is 0.02 and in (b) the data is later in the simulation when the average attack rate is 0.08. The peaks are more frequent and higher when the average attack rate is 0.02 compared to 0.08.

evolutionary stable attack rate is intermediate, balancing the benefits of competitive ability with the costs of small populations and resulting low migration.

5.3.2 Three species

Given the fragile and somewhat artificial evolutionary outcome of the two deterministic models for pair-wise interactions in space, I use the stochastic model to explore the effect of space on the evolution of three and five species food webs. There are only two types of three-species food webs where each of the two predators has a unique set of feeding interactions. The first is a strict food-chain and the second is a food chain where the top predator is an omnivore (also eats the basal species).

In a non-spatial context, all randomly assembled three-species food webs are evolutionarily unstable—in all cases, all predators or predators and prey go extinct. I tested 50 different dynamically stable random webs, of which 36 were food chains with

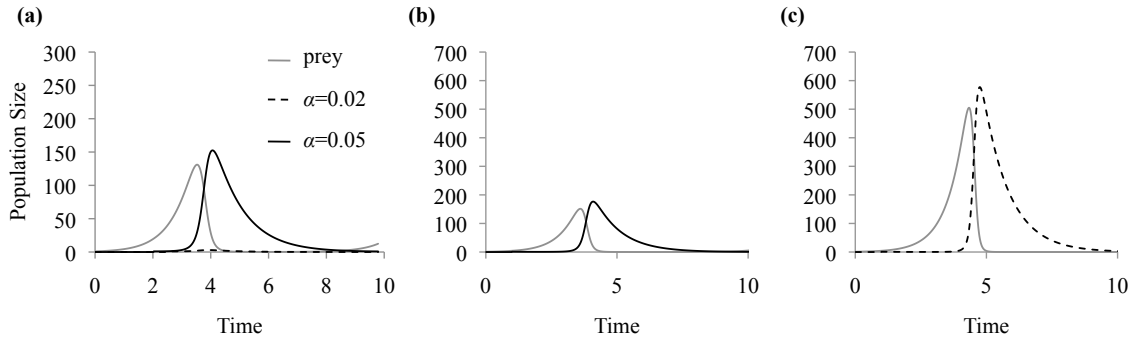


Figure 5.4: Predicted within patch population dynamics for pair-wise predator-prey interactions. Lines show the predicted deterministic population dynamics for a prey with two shared predators ($\alpha = 0.02$ and $\alpha = 0.05$) within a single subpopulation. (a) shows the prey with both predators, (b) shows the prey with only the high attack rate predator, and (c) shows the prey with only the low attack rate predator. Time is scaled to the predator death rate and other parameters are as defined in the methods.

omnivory and 14 were straight food chains. The average time to extinction was 30.32 (s.d.=19.11). There were no significant trends in the order of species extinctions. Surprisingly, food web collapse was not always characterized by prey extinction. In approximately half the simulations the predators went extinct first.

In a spatial context, all randomly assembled three species food webs are still evolutionarily stable—one predator species always goes extinct. I tested a subset of 12 different three species webs, 6 each of straight food chains and food chains with omnivory. In straight food chains the top predator always went extinct first. In food chains with omnivory, in 5 cases the middle predator went extinct first and only in one case did the top predator go extinct and the middle predator persist. In general, the first extinction occurred within 50 time steps. Notably, though the entire food web does not persist, neither does the entire web collapse, as it did in a non-spatial context. Instead, it reduces to an evolutionarily stable pair-wise interaction.

To elucidate why spatial structure cannot stabilize three species food chains, I examined the deterministic population dynamics of straight food chains with different combinations of predator attack rates. Fig. 5.5 shows the peak population size of the top and middle predators for different combinations of predator attack rates. In contrast to the case with pair-wise predator-prey interactions, as the attack rate of the top predator increases, there is not an immediate decline in its peak population size, though it does eventually decline. In addition, at the highest middle predator attack rate (which is approximately the evolutionarily stable attack rate for pair-

wise interactions), the peak population size of the top predator is very small. This suggests that if the middle predator reaches its evolutionary equilibrium first, the top predator is likely to go extinct due to stochasticity. This explains why the top predator always goes extinct first in straight food chains.

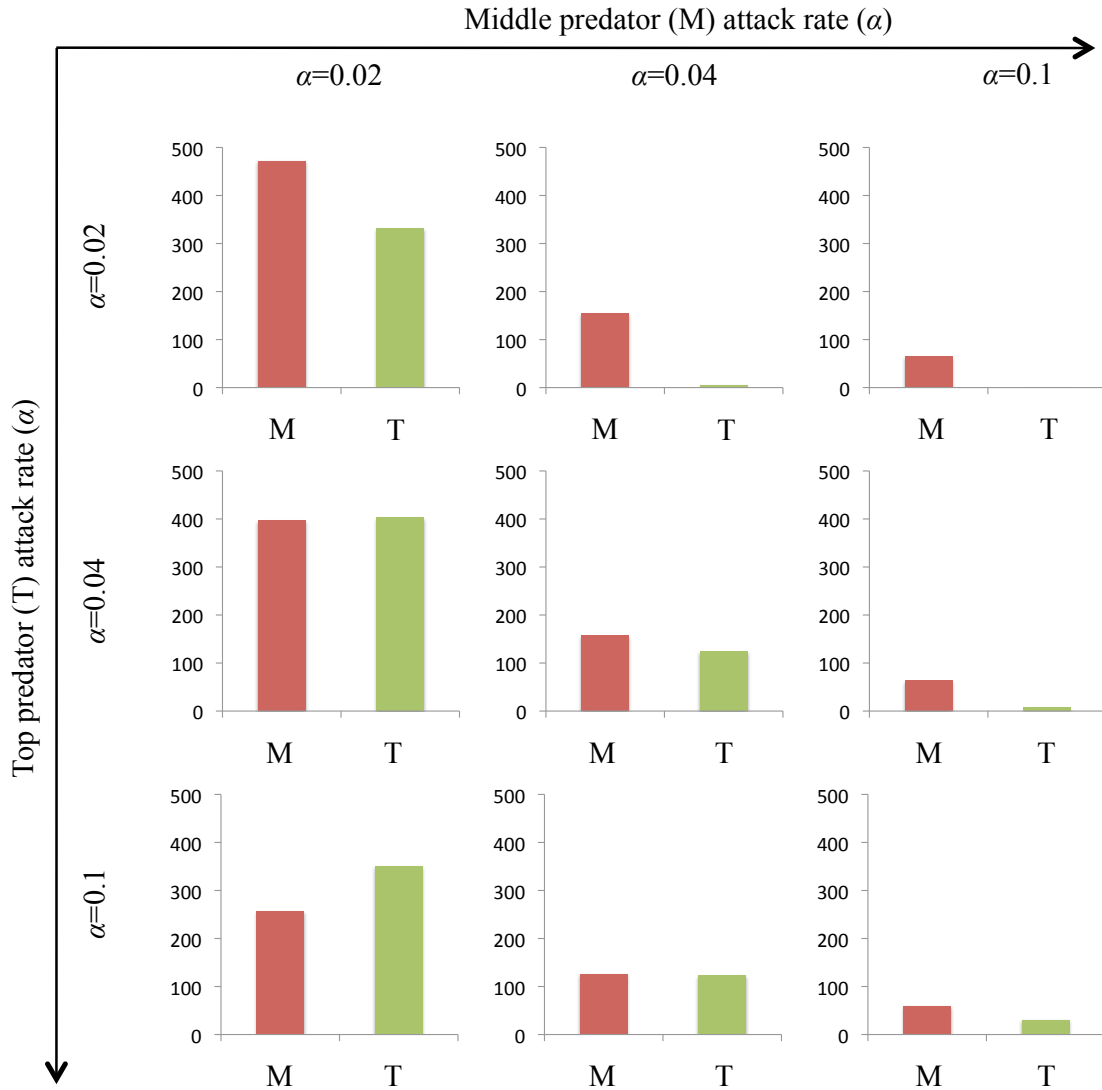


Figure 5.5: Predicted within patch population dynamics for straight food chains. Bars show the peak population size of predators in a straight food chain within a single subpopulation predicted from a deterministic predator-prey model. The middle predator's attack rate increases from right to left and the top predator's attack rate increases from top to bottom. Time is scaled to the predator death rate and other parameters are as defined in the methods.

5.3.3 Five species

In a non-spatial context, randomly generated five species webs (constrained to consist of four predators and one prey) are also evolutionarily unstable—all predators or all predators and the prey go extinct. I tested 11 dynamically stable random food webs. The average time to extinction was shorter than for three-species webs: 6.05 (s.d. = 4.566). This is a 19% difference.

In a spatial context, the same randomly generated 5 species webs are also evolutionarily unstable. In 6 cases the web collapsed to a single predator and the prey and in 5 cases all predator species went extinct, leaving only the prey species. The average time to extinction for those 5 webs was 39 (s.d.=8.72). In the webs where one predator persisted, the average time to extinction of all other predator species was 38.2 (s.d.=16.87).

5.4 Discussion

Spatial structure has been shown to play an important role shaping the evolution of predators. In particular, theory suggests that spatial structure can lead to the evolution of a reduced predator attack rate and evolutionarily stable predator-prey coexistence (van Baalen and Sabelis (1995); Gilpin (1975); Pels et al. (2002); Rauch et al. (2002)). Whether spatial structure can stabilize predator-prey interactions embedded in a more complex multi-species assemblage is an open question. Here I first demonstrate that for pair-wise interactions evolutionary stability can arise from very simple spatial population dynamic models. Only a few studies have shown that metapopulation spatial structure can induce evolutionary stability for pair-wise predator-prey interactions (van Baalen and Sabelis (1995); Gilpin (1975); Pels et al. (2002)). However, the population dynamic models used do not lend themselves well to scaling up to general food web dynamics. Using three population dynamic models that easily scale up to entire food webs, I show that both deterministic and stochastic spatial metapopulation models with local migration between subpopulations predict evolution of reduced predator attack rates and thus evolutionary stability.

The mechanism constraining evolution differs between deterministic and stochastic population models. The deterministic models (either with logistic or exponential prey growth) predict that the system will evolve to a stable equilibrium with a single predator. The equilibrium is static in the sense that the distribution of the prey and predator populations among the subpopulations is fixed through time. Furthermore, at equilibrium the prey population size within each subpopulation is very near the

extinction threshold. I show that the invasibility of this equilibrium depends on the migration rate between subpopulations as well as the allowable mutation size. If the migration rate is small and mutations large, the equilibrium can be invaded by higher attack rate predators that would drive the prey population below the extinction threshold. Thus, the deterministic models predict an evolutionary equilibrium that is fragile in the sense that the prey population is close to extinction and artificial in the sense that the invasibility of the equilibrium is sensitive to model assumptions. As a consequence, these models are not likely to explain evolutionary stability of predator-prey interactions in the real world.

In contrast to the deterministic population models, the evolutionary equilibrium predicted by the stochastic model is more robust. Within the metapopulation, each subpopulation undergoes cyclic extinction and recolonization dynamics, even at evolutionary equilibrium. I show evidence that the reason the predator attack rate does not increase to the point of global prey extinction is related to the predator and prey population sizes achieved within a subpopulation before prey extinction. High attack rate predators cannot invade the metapopulation because within a single patch, before prey extinction, they do not reach as large a population size as the low attack rate predators. As a result, low attack rate predators produce more migrants which can colonize neighboring subpopulations. In addition, subpopulations with lower attack rate predators will have higher prey population sizes resulting in more prey migrants and increasing the likelihood that migrating predators will land in a subpopulation already colonized by prey. Thus, though high attack rate predators have a competitive advantage within a single subpopulation, they are at a competitive disadvantage within the metapopulation as a whole. This is the same mechanism driving the evolution of intermediate attack rates in the metapopulation model studied by Pels et al. (2002), suggesting some level of generality.

Given the mechanism driving evolutionary stability, it may be that local predator and prey migration is not a requirement (indeed, in Pels et al. (2002) migration is global). However, in larger metapopulations with local migration, it is possible that the advantage of low attack rate predators will be amplified. If predator types are spatially restricted so that the benefits of increased prey migration are exclusively experienced by the low attack rate predators in the area, and conversely the cost of decreased prey migration are exclusively experienced by the high attack rate predators in the area, then the evolutionary stable attack rate may be even lower than predicted in the relatively small metapopulation model used here. In addition, the carrying capacity of the prey will likely influence the peak predator and prey popu-

lation sizes achieved in a subpopulation, in particular potentially limiting the peak of lower attack rate predators. This may shift the evolutionary stable attack rate. However, regardless of the prey carrying capacity, there will always be a relative difference between the maximum population sizes achieved by predators with different attack rates within a single subpopulation.

The differences between the continuous and stochastic models are consistent with the findings of other studies. Murase et al. (2010) showed that demographic stochasticity can significantly alter the predictions arising from models of community assembly over evolutionary time. In addition, Rohani et al. (1996) showed that when the population equilibrium is identical across subpopulations because of a balance in dispersal, the metapopulation equilibrium expectations will be identical to the subpopulation equilibrium. In an evolutionary context, this implies that the evolutionary expectations will also be identical, predicting evolution to extinction.

Because of the fragility and somewhat artificial nature of the evolutionary equilibrium predicted by the two deterministic population models, I use the spatial stochastic model to explore the evolutionary stability of larger food webs in non-spatial and spatial contexts. While the evolutionary stability of simple food chains in a non-spatial context has been discussed in the literature, the meaning of evolutionary stability differs from what we consider here. For example, Hutchinson (1959) proposed that food chains longer than three species would be evolutionarily unstable because it is more energy efficiency for higher trophic levels to feed on lower trophic levels, an idea more rigorously supported later (Hastings and Conrad (1979)). Although informative for understanding why a particular feeding link would arise in the first place, these studies do not inform our understanding of how the feeding link itself, once it exists, will evolve. Others have inferred the evolutionary stability of food chains from the ecological dynamics of the web. For example, Pimm and Lawton (1977) suggest that longer food chains will be less evolutionarily stable because they have longer return times to dynamic equilibrium. A few studies have directly examined the evolutionary trajectory of predators and prey in simple three-species food chains (Abrams (1991); Abrams et al. (1993); Dercole et al. (2010); Mougi (2010); Mougi and Nishimura (2009)). However, these latter studies typically assume prey co-evolution and/or other tradeoffs that are known to induce evolutionary stability.

For more complex webs, very few studies have explicitly explored evolutionary stability in a non-spatial context. Most models assume that the structure of the web may change over time and thus do not inform our understanding of evolution within a particular web structure. Two studies have shown that food webs assembled from

a larger species pool can be evolutionarily stable to invasion specifically by other species in the larger species pool (Bell (2007); Law and Morton (1996)). However, the invading species may have different feeding links than the species already present in the web. Thus, whether this type evolutionary stability generalizes to invasion by mutants of the existing species is unclear. Here I consider evolutionary stability under the assumption that a predator's feeding links are fixed through time (who eats who is not subject to evolutionary change). I demonstrate here that three species food chains, with and without omnivory, and random five species food webs are inherently evolutionarily unstable in a non-spatial context, always collapsing to either the prey alone or no species at all. Perhaps counter-intuitively, the larger five species webs collapse faster than the three species webs. Though the time scale of collapse will likely be affected by the mutation rate and mutation size, the relative difference is likely to hold.

With the knowledge that at least small food webs are evolutionary unstable in non-spatial contexts, I then show that the evolutionary stability of pair-wise interactions in a metapopulation does not necessarily extend to food-webs with more species. The model predicts that for all randomly assembled three-species webs (food chains and food chains with omnivory), at least one of the predator species will go extinct. The remaining predator may come into evolutionary equilibrium with the prey species via the mechanisms described above, or in fewer cases, may also go extinct. The inability of spatial structure to stabilize food chains without omnivory is likely due to the fact that within the parameter space explored here, the top predator's peak population size is very small when the middle predator has an intermediate attack rate. For food chains with omnivory, where the middle predator goes extinct first, it is likely that the middle predator's population size is very small when the top predator has an intermediate attack rate. It is possible that in other regions of parameter space this would not necessarily be the case. For example, allowing the predators to have different death rates or conversion efficiencies might lead to evolutionarily stable three species food chains. Alternatively, evolutionary stability might be achieved if the attack rates of the two predators are coupled. While at first pass this seems unrealistic, there is some experimental evidence that tri-trophic interactions can be linked such that they represent a heritable unit (Bailey (2006)).

Perhaps not surprisingly, the evolutionary instability of three species webs extends to randomly assembled five species webs. However, the larger webs are more likely to collapse entirely (all species go extinct) rather than collapse to an evolutionarily stable pair-wise interaction. In the case that the web does collapse, it happens very

quickly, though it takes longer than in the non-spatial context. Again, the mutation rate and size is likely to influence the time scale of collapse, but the relative difference ought to remain.

The non-spatial evolutionary stability of food webs with more than 5 species bears further consideration, though it seems unlikely that under the same model assumptions larger webs will be stable. Studies that show that food webs can be evolutionarily stable to invasion from a fixed species pool also show that this outcome is much less likely for larger food webs (Bell (2007); Law and Morton (1996)). An obvious though important implication of the evolutionary instability of simple food webs in a non-spatial context is that to be realistic, non spatial food web models should include other evolutionary stabilizing mechanisms like prey co-evolution, ecological or allocation tradeoffs, or adaptive foraging (Kondoh (2003)). Otherwise, the scope of the model predictions are limited to ecological time scales.

Though the results of this study suggest that population spatial structure may not be enough to induce the evolutionary stability of entire food webs, spatial considerations are still likely to be important, even when other stabilizing mechanisms are at work. Assuming that food webs are indeed characterized by constant species turnover, spatial structure may alter the rate of turnover or the structure of the web through time. The ubiquity of population spatial structure, both at the individual level and at the level of populations and communities, and the ability of spatial structure to fundamentally alter population dynamics suggests that it is likely to play a significant evolutionary role. Thus, consideration of space will be an important ingredient in future studies of the influence of ecology on the evolutionary dynamics of food webs.

CHAPTER VI

Conclusion

6.1 Introduction

Spatial structure is ubiquitous in the natural world, from the level of the landscape to individual organisms. This structure can have important dynamical consequences. Population level spatial structure where organisms in a population do not interact randomly but rather according to their spatial location is particularly interesting. A large body of research has shown that population spatial structure can have important ecological consequences, leading to the coexistence of species and contributing to the maintenance of biodiversity (Amarasekare (2003); King and Hastings (2003); Tilman (1994)). However, the evolutionary consequences are less well known. Theory and experiments suggest that novel insight into the natural world can arise from considering ecology and evolution are together (Dieckmann et al. (2006); Urban and Skelly (2006); De Meester (2007); Fukami (2007); Hubbel (2006)). In addition, population spatial structure has been shown to promote the evolution of cooperation (Doebeli and Knowlton (1998); Killingback et al. (1999); Nowak and May (1992); Lion and Gandon (2009); Lehmann and Keller (2007)), resolving the tragedy of the commons (Hardin (1968); Rankin and Lopez-Sepulcre (2005); Bargum (2007)), and perhaps explaining the major transitions between life forms (e.g. Szathmary (2001)). A more specific case of the tragedy of the commons, population spatial structure can also resolve the paradox of prudent predation, where the consumer is specifically a predator and the resource their prey.

The goal of this research was to more carefully elucidate the evolutionary influence of spatial structure on predators, with an emphasis on how spatial structure alters the relationship between the species' ecology and their expected evolutionary trajectory.

6.2 Summary of Findings

In Chapter 1 I review existing theory of the evolutionary effects of spatial structure on pathogens to outline the conditions necessary for strong spatial effects. I find that local host interactions, local pathogen dispersal, and slow host reproduction relative to pathogen transmission lead to the strongest spatial effects: a lower pathogen transmission rate or virulence than predicted by a non-spatial model. I explain this finding in the context of a competition-persistence tradeoff, where the high transmission rate pathogens are more competitive but less persistent. Spatial structure allows selection on this tradeoff because the host population can become spatially segregated into distinct clusters. I assess the relative influence of spatial structure compared to the oft cited transmission-virulence tradeoff on pathogen evolution and found evidence that spatial structure can in some cases supersede the influence of the transmission-virulence tradeoff. I also review a handful of models that include more complex aspects of host or pathogen ecology and discuss their potential importance for pathogen evolution. Finally, I suggest three important directions for future research, including developing quantitative methods for predicting pathogen evolution in a spatial context, to develop and create new models of pathogen host interactions, and to observationally or experimentally validate existing theoretical hypotheses of the influence of spatial structure on pathogen evolution.

In Chapter 2 I build from the findings in Chapter 1 and use spatial simulations to more carefully explore how spatial structure alters the evolutionary influence of host and pathogen ecology, in particular for the most basic aspects of ecology. I find that the spatial context significantly alters the expected influence of the host reproduction rate, host death rate, pathogen virulence, and the shape of the transmission virulence tradeoff. Of particular importance is the host reproduction rate: regardless of the existence or shape of a transmission-virulence tradeoff, non-spatial models predict no evolutionary role for the host reproduction rate but in spatial models it is a key parameter, significantly increasing or decreasing the predicted evolutionary stable transmission rate. I also assess the accuracy of a commonly used quantitative framework to predict the influence of these aspects of host and pathogen ecology. While this framework is known to be limited, I show that its limitations are quite extensive, in particular when there is no transmission-virulence tradeoff or a linear tradeoff.

In Chapter 3 I examine how spatial structure alters the evolutionary influence of true predator and prey ecology. I address the following questions: 1) What is the

role of predator ecology that is unique to true predators relative to pathogens and 2) are there any consistent trends in the role of predator and prey ecology that are analogous with pathogens and their hosts. I find that like pathogen-host interactions, the spatial context can significantly influence the evolutionary role of predator and prey ecology. In particular, though non-spatial models predict no evolutionary role for the prey conversion efficiency, the magnitude of the predator death rate relative to the prey death rate, or predator movement, all three can significantly influence predator evolution in a spatial context. In addition, as with pathogen-host interactions, the prey reproduction rate and predator death rate strongly influence predator evolution in a spatial context. Furthermore, even with differences in the prey conversion efficiency and the relative magnitude of predator and prey death rates, the trends are similar between predator-prey and pathogen-host interactions. However, with predator movement, the shape of the trend subtly changes. I qualitatively explain the influence of prey reproduction rate in the absence of predator movement and predator movement alone within the framework of inclusive fitness, where the genetic and spatial distribution of the predator and prey influence the strength of local competition.

In Chapter 4 I explore the potential for the evolutionary effects of spatial structure on pair-wise predator prey interactions to extend to larger, more complex food webs. In particular, does spatial structure constrain the evolution of predator attack rates when other predators or prey are present? First I test the whether three simple population dynamic models that can easily be scaled up to complex food web dynamics predict the evolution of reduced predator attack rates in a metapopulation context for pair-wise predator-prey interactions. I find that while all three models predict evolutionary stability and coexistence of the predator and prey, the evolutionary outcome of the two deterministic models is both fragile and artificial in nature. Thus, for the remainder of the study I use the stochastic population dynamic model. I then test whether the model predicts evolutionary instability of food webs in a non-spatial context. I find that randomly assembled three and five species webs are indeed evolutionarily unstable in a non-spatial context. Further, the five species webs collapse to extinction earlier than the three species webs. Finally, I test whether spatial structure can stabilize food webs. I find that neither three nor five species webs are stable in a spatial context. However, while in a non-spatial context the entire web collapses such that all species go extinct, in a spatial context the web frequently collapses just to a single pair-wise interaction. However, the probability that the entire web will collapse increases with the number of species in the web.

6.3 Conclusions

This research contributes to our understanding of the influence of spatial structure on predator evolution. In particular, it highlights that the spatial context of the interaction has important implications for the relationship between a species' ecology and its evolutionary trajectory. The evolutionary effect of even the most basic aspects of the species' ecology can change depending on the spatial context. For pathogens, understanding the effects of basic host demography and pathogen life-history will help to inform our ability to predict and control the problematic emergence and re-emergence of infectious disease. For other predators, these findings may help us better understand the consequences of anthropogenic changes like habitat fragmentation, climate change, and facilitated transport of organisms between habitats. Finally, this research gives us insight into the mechanisms that lead to the evolutionary stability of entire food webs.

6.4 Future Directions

While this research makes a significant step toward understanding the evolutionary influence of spatial structure on predators, there is much more to be done. Of primary importance is testing the predictions that are presented here. Is there evidence that spatial structure has played an important role in the evolution of current day systems? Can we observe the evolutionary influence of spatial structure in experimental systems? Furthermore, this research focuses on fairly simple spatial structure, where there is no variation in the spatial dependence of interactions. Very few systems are likely to be subject to such strict, regular structuring. For pathogens in particular, studies incorporating more complex population spatial structuring has led to novel predictions (e.g. Read and Keeling (2003)). Likely, more complex spatial structuring will also lead to novel predictions for true predators.

Furthermore, the focus of this research is predators. However, as mentioned in the background, spatial structure is predicted to play an important role in general in the emergence of cooperation. Already, some studies have examined what ecological contexts support the evolution of facilitation between potential competitors Kefi et al. (2008); Kinzig and Harte (1998); Johnson and Seinen (2002); Champagnat and S. (2007); Prado and Kerr (2008). Future studies building from the findings here could lend more valuable insight into the transition from predation to mutualism and the conditions that promote such transitions. This could subsequently improve our

understanding of biodiversity, which has been linked to the ratio of antagonistic and mutualistic interactions in a community Melian et al. (2009). There may be interesting general patterns in the effect of spatial structure on a broad set of interactions beyond consumer-resource interactions.

Finally, though the results of this study suggest that population spatial structure alone may not induce the evolutionary stability of entire food webs, spatial considerations are still likely to be important. For one thing, the spatial context may be important in determining the evolution of food web structure when other stabilizing mechanisms are at work. Alternatively, spatial structure may influence the rate of species turnover, species diversity, and trophic structure within an evolving food web.

APPENDICES

APPENDIX A

Inferring ES transmission rate from simulations

By definition, the ES transmission rate is the transmission rate that cannot be invaded by any other transmission rate. Using simulations, one can infer the ES transmission rate from the results of a multitude of discrete pair-wise invasions (see for example Kamo et al. (2007)). The ability of one pathogen strain to invade another is taken as the average number of successful invasions out of some number of trial invasions. One can also infer the ES transmission rate from the results of continuous invasion by mutation (see for example Webb et al. (2007a)). Once the pathogen strain with the ES transmission rate invades, no other mutant strain will be able to invade and the average transmission rate in the population will stabilize at the ES value. The notable, and potentially important difference between the two methods is that the under pair-wise invasion there are never more than two pathogen strains in the population at one time while under continuous invasion many strains are present. To be sure our results were not dependent on our method of inference, we tested three different methods of inferring the ES transmission rate from simulations: pair-wise invasion, continuous invasion by small mutations, and continuous invasion by random mutation.

For the pair-wise invasion method we started the host population with a single resident strain at equilibrium. We then allowed a second pathogen strain with a random transmission rate to invade. Once either the invading or resident strain had been excluded from the host population, the process was repeated. Although this method is not exactly the same as a complete pair-wise invasion analysis, it does capture the essential feature that only two pathogen strains reside in the population at any given time. For the two continuous invasion methods, the ES transmission rate is taken as the average transmission rate of the pathogen population when it

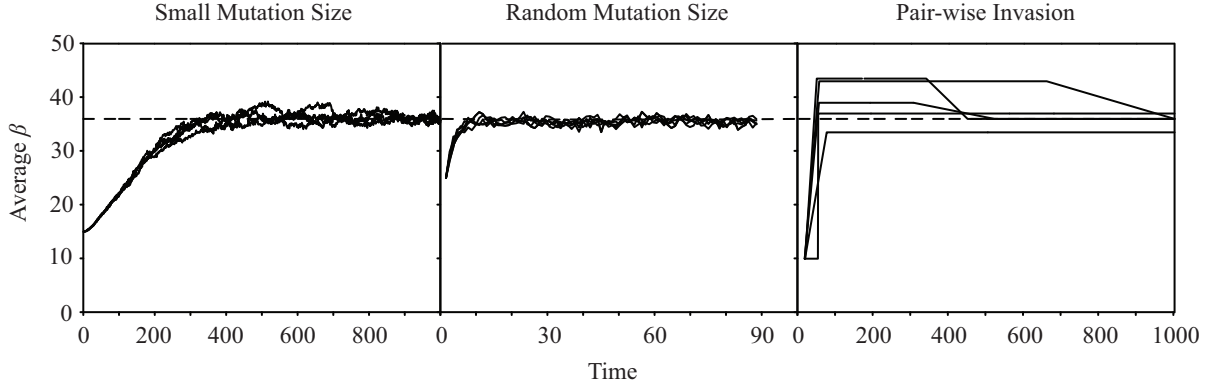


Figure A.1: Comparing methods of inferring evolutionary stable transmission rate for no transmission-virulence tradeoff. The left panel shows the average pathogen transmission rate (β) over time for six different stochastic simulations where evolution is modeled as continuous evolution by small mutations. The middle panel shows the same for continuous evolution with randomly sized mutations. The right panel shows the average β over time for simulations consisting of a sequence of pair-wise invasions—there are only ever two pathogen strains in the population at one time. The dashed line shows the evolutionary stable (ES) β inferred by averaging across the last 500 time steps of the continuous evolution by small mutation data. In the analyses here we found no substantial difference in the ES β obtained across these methods. Other parameters are $r = 20$, $\alpha = 1$, and $d = 1$.

is no longer changing over time. When the average transmission rate was no longer changing over time, we ran the simulation for an additional 2000 time steps. We then took the average transmission rate over the last 2000 time steps as the ES transmission rate. For the continuous invasion by random mutation method, we allowed mutant pathogens to differ randomly (rather than only by a small amount) from the parent strain.

To determine whether the methods yielded different results, we compared the ES transmission rate across multiple realizations of each method for the case of no transmission-virulence tradeoff. The three methods did not give significantly different predictions (Fig. A.1). Thus, using the ES transmission rate predicted by the less computationally intensive continuous evolution method is an accurate comparison point for the ES transmission rate predicted by an IPA of the spatial moment equations.

APPENDIX B

Spatial Moment Equations

On a regular two-dimensional lattice where sites can be occupied by a susceptible host (S), an infected host (I), or be empty (O), the change in the number of paired states on the lattice (e.g. SO pairs) can be described by the following set of equations.

$$\frac{d[SS]}{dt} = 2 \cdot \frac{r}{n} \cdot Q(S|OS) \cdot [SO] - \left(2 \cdot d + 2 \cdot \frac{\beta}{n} \cdot Q(I|SS) \right) \cdot [SS] \quad (\text{B.1})$$

$$\begin{aligned} \frac{d[SO]}{dt} = \frac{r}{n} \cdot Q(S|OO) \cdot [OO] + d \cdot [SS] + (d + \alpha) \cdot [IS] \\ - \left(d + \frac{r}{n} \cdot Q(S|OS) + \frac{\beta}{n} \cdot Q(I|OS) \right) \cdot [SO] \end{aligned} \quad (\text{B.2})$$

$$\frac{d[OO]}{dt} = 2 \cdot d \cdot [SO] + 2 \cdot (d + \alpha) \cdot [IO] + 2 \cdot \frac{r}{n} \cdot Q(S|OO) \cdot [OO] \quad (\text{B.3})$$

$$\frac{d[II]}{dt} = 2 \cdot \frac{\beta}{n} \cdot Q(I|SI) \cdot [SI] - 2 \cdot (d + \alpha) \cdot [II] \quad (\text{B.4})$$

$$\frac{d[IS]}{dt} = \frac{r}{n} \cdot Q(S|OI) \cdot [IO] + \frac{\beta}{n} \cdot Q(I|SS) \cdot [SS] - \left(2 \cdot d + \alpha + \frac{\beta}{n} \cdot Q(I|SI) \right) \cdot [IS] \quad (\text{B.5})$$

$$\frac{d[IO]}{dt} = \frac{\beta}{n} \cdot Q(I|SO) \cdot [SO] + d \cdot [IS] + (d + \alpha) \cdot [II] - \left(d + \alpha + \frac{r}{n} \cdot Q(S|OI) \right) \cdot [OI] \quad (\text{B.6})$$

In these equations, r is the host reproduction rate, d is the natural host death rate, α is the pathogen virulence, β is the pathogen transmission rate, and n is the neighborhood size. $Q(X|YZ)$ is the number of lattice sites in state X in the neighborhood of a site in state Y with a neighboring lattice site in state Z . This set of equations does not incorporate any approximations but is not closed. Further,

these equations can be scaled to the size of the lattice and interaction neighborhood to represent the proportion of state pairs on the lattice. Summing equations B.1, B.2, and B.5 yields an equation for the time derivative of the number of susceptible hosts on the lattice, summing equations B.4- B.6 yields the time derivative of the number of infected hosts, and summing equations B.2, B.3, and B.6 yields the time derivative of the number of empty sites.

APPENDIX C

Improved Pair Approximation (IPA)

Equations B.1 - B.6 are not closed. Quantities involving state triples ($Q(X|YZ)$) depend on higher order state combinations. To solve these equations, a moment closure method is required. An ordinary pair approximation (OPA) simply assumes that the presence of a site in state X next to a site in state Y does not depend on the state of other sites in the neighborhood of Y . Thus,

$$Q(X|YZ) = (1 - \theta) \cdot Q(X|Y) \tag{C.1}$$

$$Q(X|YX) = (1 - \theta) \cdot Q(X|Y) + \theta \tag{C.2}$$

where θ is $1/n$ and scales the relationship to account for the fact that the maximum $Q(X|Y)$ is 4 but the maximum $Q(X|YZ)$ is 3. However, when host reproduction is local, $Q(S|OO)$ should be smaller than $Q(S|O)$ and $Q(S|OS)$ should be larger than $Q(S|O)$ because susceptible hosts will tend to cluster in space. The improved pair approximation (IPA) takes this clustering into account. When the size of the neighborhood on the lattice is 4, the ratio of $Q(S|OO)$ to $Q(S|O)$ has been shown to be approximately 0.8093. Thus, the IPA assumes that

$$Q(S|OO) = 0.8093 \cdot (1 - \theta) \cdot Q(S|O) \tag{C.3}$$

Using the relationship in equation B.3 and the following identity relationship

$$Q(S|OS) \cdot Q(S|O) + Q(S|OO) \cdot Q(O|O) + Q(S|OI) \cdot Q(I|O) = Q(S|O) \tag{C.4}$$

the IPA also assumes that

$$Q(S|OS) = n - (1 - \theta) \cdot Q(I|O) - 0.89093 \cdot (1 - \theta) \cdot Q(O|O) \quad (\text{C.5})$$

APPENDIX D

Solving for quasi-equilibrium $Q(S|I)$

The quasi-equilibrium $Q(S|I)$ for a pathogen strain invading a resident strain in equilibrium with the host population must be obtained numerically. Using IPA, for two pathogen strains J and K, where J is the invading strain and K is the resident strain, the time derivatives of paired states involving strain J are:

$$\begin{aligned} \frac{d[I_J S]}{dt} = & \frac{r}{n} \cdot (1 - \theta) \cdot Q(S|O) \cdot [I_J O] + \frac{\beta_J}{n} \cdot (1 - \theta) \cdot Q(I_J|S) \cdot [SS] \\ & - \left(2 \cdot d + \alpha_J + \frac{\beta_K}{n} \cdot Q(I_K|S) + \frac{\beta_J}{n} \cdot (1 + (1 - \theta) \cdot Q(I_K|S)) \right) \cdot [I_J S] \quad (\text{D.1}) \end{aligned}$$

$$\begin{aligned} \frac{d[I_J O]}{dt} = & \frac{\beta_J}{n} \cdot (1 - \theta) \cdot Q(I_J|S) \cdot [SO] + d \cdot [I_J S] + (d + \alpha_J) \cdot [I_J I_J] + (d + \alpha_K) \cdot [I_K I_J] \\ & - \left(d + \alpha_J + \frac{r}{n} \cdot (1 - \theta) \cdot Q(S|O) \right) \cdot [O I_J] \quad (\text{D.2}) \end{aligned}$$

$$\frac{d[I_J I_J]}{dt} = 2 \cdot \frac{\beta_J}{n} \cdot (1 + (1 - \theta) \cdot Q(I_J|S)) \cdot [S I_J] - 2 \cdot (d + \alpha_J) \cdot [I_J I_J] \quad (\text{D.3})$$

$$\begin{aligned} \frac{d[I_J I_K]}{dt} = & \frac{\beta_J}{n} \cdot (1 - \theta) \cdot Q(I_J|S) \cdot [S I_K] + \frac{\beta_K}{n} \cdot (1 - \theta) \cdot Q(I_K|S) \cdot [S I_J] \\ & - (2 \cdot d + \alpha_J + \alpha_K) \cdot [I_J I_K] \quad (\text{D.4}) \end{aligned}$$

Parameters are as defined in Appendix B and θ is $1/n$. Numerically solving these equations assuming equilibrium values for all pairs and $Q(X|Y)$ that do not involve strain J (e.g. in equation D.1, $[SS]$, $Q(S|O)$, and $Q(I_K|S)$), yields the quasi-equilibrium number of state pairs for the invading pathogen. The quasi-equilibrium

QS/I for strain J can then be calculated as

$$Q^0(S|I_J) = \frac{[SI_J]^0}{[I_J]^0} \quad (\text{D.5})$$

APPENDIX E

Interpreting model parameter values

Here I analyze simulation data using empirical methods in order to compare model parameter values with the demographic rates of real systems. This provides important perspective on the types of systems represented by the spatial models examined.

Host/prey reproduction rate The lowest host or prey reproduction rate used in spatial simulations is 4 and the maximum is 100 (per host generation). In the absence of the pathogen or predator, the host or prey population is predicted to grow exponentially at a rate equal to $r - d$ (called r_{max}) where r is the reproduction rate and d is the host natural death rate. Thus, scaling time to be measured in host (or prey) generations (i.e. setting $d = 1$), the minimum r_{max} is 3/generation and the maximum is 99/generation. However, in the spatial models, the realized r_{max} is much lower because of the limited availability of empty sites for host (or prey) offspring to colonize. To determine the relationship between the realized r_{max} and the host reproduction rate parameter, I analyze simulation data using the same method often used to estimate r_{max} from observational data. In natural populations, r_{max} can be estimated from population size data over time when the population starts from rarity. I derive an equivalent “empirical” estimate from spatial simulation data by starting the simulation with no pathogen (or predator) individuals and only one host (or prey) individual. This yields population size data over time starting from rarity, which can be fit with an exponential curve to estimate r_{max} .

Fig. E.1 shows the “empirical” estimate of the intrinsic growth rate of the host (or prey) per generation from spatial model simulations as a function of the host reproduction rate parameter. Also shown are the intrinsic growth rates (per generation) of a variety of species from the literature. The empirical estimates of r_{max} from simulations are well within the range of those expected in natural systems. The

higher reproduction rates tend to correspond to plants and arthropods (high reproductive output or long generation times), while the lower reproduction rates tend to correspond to bacteria and protozoans (low reproductive output or short generation times).

Pathogen transmission rate The ES transmission rate predicted by the spatial pathogen-host model ranges from a minimum of just under 4 to a maximum around 150 (per host generation). It is problematic to directly compare these values to real diseases because the transmission parameter is notably the most difficult to estimate for real pathogens. Instead, real pathogens are often characterized by their basic reproduction number (R_0), or the average number of secondary infections caused by a single infected individual over its infectious period (Heffernan et al. (2005)). R_0 is proportional to the pathogens transmission rate and thus can provide perspective on the range of transmission rates arising from the spatial models.

R_0 is often estimated in real systems from incidence data. Assuming that the pathogen is at an endemic equilibrium with the host, the pathogen's R_0 is equal to $1/s$, where s is the proportion of host-host contacts that can result in infection and is often assumed to be equal to the proportion of susceptible hosts in the population (Mollison (1995)). Using this relationship, one can derive an equivalent "empirical" estimate of the pathogen's R_0 from simulation data. Fig.E2 shows the "empirical" R_0 of a pathogen (derived from incidence data at equilibrium) as a function of the transmission rate parameter for the spatial pathogen-host model with no transmission-virulence relationship. The resulting R_0 values are well within the range of real pathogens. Table E.1 gives the estimated R_0 of a number of well-known human diseases for comparison. Note that the ES transmission rate arising from simulations can be higher than the range shown in Fig. E.2a (e.g. for a host reproduction rate of 50 and virulence of 1, the ES transmission rate is 80) potentially encompassing R_0 values in the range of measles, one of the most infectious childhood diseases.

The relationship between the "empirical" R_0 and the transmission rate differs when there is a transmission-virulence relationship. With a transmission-virulence relationship, an increase in transmission also results in an increase in virulence. Since R_0 is inversely related to virulence, the relationship between the empirical estimate of R_0 and the transmission rate will not necessarily be positive. See for example Fig. E.2b, which shows the relationship between the "empirical" R_0 and the transmission rate for two linear transmission-virulence relationships. In both cases, the "empirical" R_0 declines with the transmission rate.

Prey conversion efficiency I performed spatial simulations for prey conversion

Table E.1: Empirical estimates of R_0 for a range of human diseases. Data reproduced from Hethcote (2008).

Disease	Location	R_0
Measles	England and Wales	15.6
	USA	12.3
Chickenpox	Nigeria	17.0
	Maryland, USA	11.3
Mumps	Maryland, USA	8.1
Rubella	England and Wales	7.0
	West Germany	7.7
Poliomyelitis	USA	4.9
	Netherlands	4.3
Smallpox	India	5.2

efficiencies of 0.2, 0.5 and 1. Empirical quantification of the prey conversion efficiency defined as the ratio of prey eaten to predator offspring produced is uncommon in the literature. More common are estimates of the energy conversion efficiency, or the proportion of prey mass consumed that is converted into predator body mass and used for individual predator growth. However, allometric scaling theory provides a framework within which the prey conversion efficiency can be estimated. It has been proposed that the prey conversion efficiency is proportional to the ratio of the prey to predator body size (Yodzis and Innes (1992)). Using published body size data for a variety of predator and prey species (Cohen et al. (1993)) I calculated the mean prey to predator body size ratio for broad classes of predator and prey (Table E.2). This data does not provide exact prey conversion efficiencies and cannot be directly compared to the conversion efficiencies used in the spatial predator-prey model; however, it does provide a relative understanding of how the conversion efficiency varies between different types of predator-prey interactions.

The greatest conversion efficiencies are for invertebrates eating invertebrates and vertebrates eating vertebrates (with endotherm predators of either endotherm or ectotherm prey having a slightly higher efficiency). Not surprisingly, the lowest conversion efficiencies are for vertebrate predators eating invertebrate prey (vertebrates are on average much larger than invertebrates). Given that the spatial model predicts that the ES attack rate declines with increasing conversion efficiency, the implication is that in a spatial context, large vertebrates eating small invertebrates will evolve a higher attack rate than invertebrates eating equally sized invertebrates.

Table E.2: Mean prey to predator body size ratios. Mean body size data (first value based on body length in *cm*, second value based on body size in *g*) were obtained from Cohen et al. (1993).

Prey	Predator			
	Invertebrate	Vertebrate Ectotherm	Vertebrate Endotherm	
Invertebrate	0.499, 0.02	0.035, 0.0002	0.045, 0.000027	
Vertebrate Ectotherm		0.242, 0.032	0.168, 0.116	
Vertebrate Endotherm			0.336, 0.12	

Predator attack rate The ES predator attack rate predicted by the spatial models used here range from 10 to 200 (per prey generation). The attack rate determines the per-capita prey consumption rate (number of prey consumed per predator per time). Specifically, at equilibrium the per-capita prey consumption rate is equal to the attack rate times the mean number of predator-prey interactions per predator. In a spatial context, the maximum number of predator-prey interactions per predator is 4 (since each lattice site has only 4 neighboring sites) and the minimum can be much less than 1. Thus, the minimum ES per-capita consumption rate predicted by the spatial model is nearly 0 and the maximum is 800 (per prey generation).

In the literature, the majority of estimates of per-capita consumption rates are for insect predators. For example, after 24 hours of starvation and with unlimited prey, *Cheilomenes sexmaculata* (a ladybug) can consume up to 200 *Aphis craccivora* (aphids) per day (Pervez and Omkar (2005)). Assuming an aphid generation time of about 5.8 days (Gutierrez et al. (1971)), this is equivalent to a maximum per-capita consumption rate of over 1000 prey/predator/prey generation. A rare non-insect example, after 24 hours of starvation and with unlimited prey, *Cancer irroratus* (Atlantic rock crab) can consume 3 *Placopecten magellanicus* (Atlantic sea scallop) per day (Wong and Barbeau (2006)). Assuming a scallop generation time of 5 years (Ansell et al. (1991)) yields a maximum per-capita consumption rate of 5,475 prey/predator /prey generation. In reality, the per-capita consumption rates of these organisms will likely be lower because of limited prey availability and predator satiation. However, these estimates give some perspective on the types of predators that represent the upper range of ES attack rates predicted by the spatial model. At the other end of the spectrum, a field study of *Crotalus viridis* (the Western rattlesnake) found that individual snakes consume about 6 prey items (including

squirrels, rats, rabbits and mice) per year (Diller and Johnson (1988)). Assuming a rodent generation time of around 150 days (Pianka (2000)) yields an attack rate of 2.5 prey/predator/prey generation.

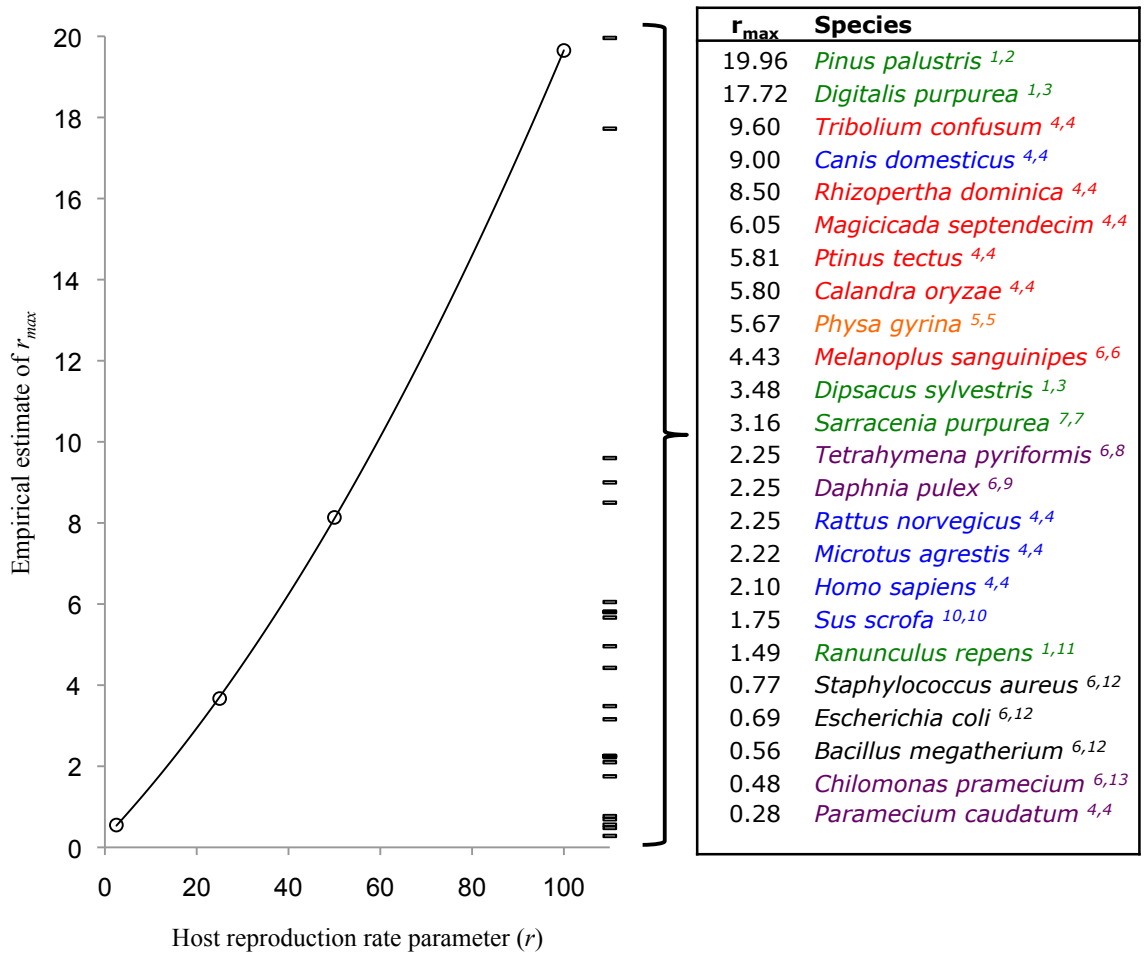


Figure E.1: Estimated host (or prey) intrinsic growth rates from spatial simulations and real systems. Data points (with spline fit) show the empirical estimate of the intrinsic growth rate (r_{max}) from spatial simulations as a function of the host reproduction rate parameter (r). The dashes to the right of the graph are empirically derived values of r_{max} for a variety of species (text colored by type of organism: black=bacteria; purple=protozoa; red=arthropods; orange=mollusks; blue=mammals; green=plants; superscripts refer to source for r_{max} and generation time). All rates are scaled to the generation time of the host (or prey; $1/d$).

¹ Silvertown et al. (1993), ² Platt et al. (1988); conservative estimate based on age of first reproduction, ³ Based on the biennial life-cycle and first flowering in the second year, generation time is estimated at 1.5 years, ⁴ Pianka (2000), ⁵ DeWitt (1954), ⁶ Fenchel (1974), ⁷ Schwaegerle (1983), ⁸ Rachid et al. (2008), ⁹ Grigoriev et al. (2011), ¹⁰ Pech and Hone (1988), ¹¹ Sarukhan and Harper (1973), ¹² Todar (2008), ¹³ Ducoff (1957).

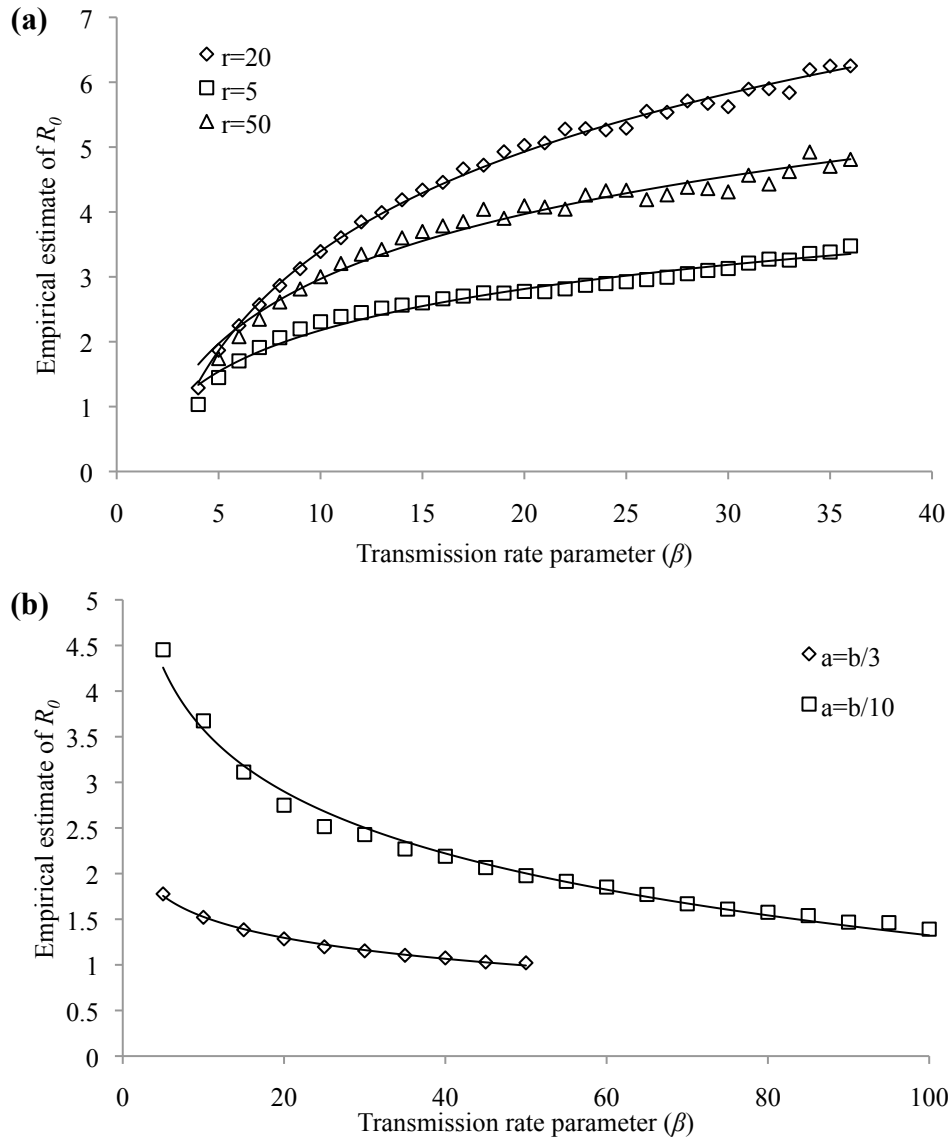


Figure E.2: Estimated pathogen basic reproduction number from spatial simulations. Data points (with logistic fit) show the “empirical” estimate of the pathogen’s R_0 as a function of the transmission rate parameter (β). (a) the model assumes no transmission-virulence relationship. The host natural death rate (d) is 1 and the pathogen virulence (α) is 1. (b) the model assumes a linear transmission-virulence relationship of $\alpha = \beta/3$ and $\alpha = \beta/10$. The host natural death rate (d) is 1.

APPENDIX F

Inclusive fitness framework for pathogens

The inclusive fitness of a pathogen in a spatial context where pathogen transmission and host dispersal are local is

$$\Delta\lambda_J \propto \frac{\Delta\beta}{\beta} - \frac{\Delta\alpha}{d + \alpha} + \frac{\beta}{d + \alpha} \cdot \Delta q_{S|J} \quad (\text{F.1})$$

where $\Delta\lambda_J$ is the selection gradient of pathogen strain J , β is the pathogen transmission rate, α is the pathogen virulence, d is the host natural death rate, and $q_{S|J}$ is the average density of susceptible hosts around a host infected with strain J . If the selection gradient is greater than 0, selection will favor an increase in the pathogen's transmission rate. There are three components to the pathogen's selection gradient. The first component, $\Delta\beta/\beta$, is the direct benefit of increasing the transmission rate. The second component, $\Delta\alpha/(d + \alpha)$, is the direct cost of increasing the transmission rate due to increased host death by virulence. This only comes into play when the pathogen is subject to a tradeoff between its transmission rate and virulence, such that an increase in β results in an increase in α . The final component, $\beta/(d + \alpha) \cdot \Delta q_{S|J}$, is the indirect cost of increasing the transmission rate due to increased local competition for susceptible hosts because of decreased density of susceptible hosts around infected hosts.

BIBLIOGRAPHY

BIBLIOGRAPHY

- Abrams, P. A. (1991). The effects of interacting species on predator-prey coevolution. *Theoretical Population Biology*, 39(3):241–262.
- Abrams, P. A. (1995). Implications of dynamically variable traits for identifying, classifying, and measuring direct and indirect effects in ecological communities. *The American Naturalist*, 146(1):112–134.
- Abrams, P. A., Matsuda, H., and Harada, Y. (1993). Evolutionarily unstable fitness maxima and stable fitness minima of continuous traits. *Evolutionary Ecology*, 7(5):465–487.
- Alizon, S. and van Baalen, M. (2005). Emergence of a convex trade-off between transmission and virulence. *American Naturalist*, 165(6):E155–E167.
- Amarasekare, P. (2003). Competitive coexistence in spatially structured environments: a synthesis. *Ecology Letters*, 6(12):1109–1122.
- Anderson, R. M. and May, R. M. (1979). Population biology of infectious-diseases. 1. *Nature*, 280(5721):361–367.
- Anderson, R. M. and May, R. M. (1982a). Coevolution of hosts and parasites. *Parasitology*, 85:411–426.
- Anderson, R. M. and May, R. M. (1982b). Coevolution of hosts and parasites. *Parasitology*, 85:411–426.
- Ansell, A. D., Dao, J.-C., and Mason, J. (1991). Three european scallops: *Pecten maximus*, *chlamys (aequipecten) opercularis* and *c. (chlamys) varia*. In Shumway, S. E., editor, *Scallops: biology, ecology and aquaculture*. Elsevier.
- Antia, R., Levin, B. R., and May, R. M. (1994). Within-host population-dynamics and the evolution and maintenance of microparasite virulence. *The American Naturalist*, 144(3):457–472.
- Bailey, J. K. (2006). Importance of species interactions to community heritability: a genetic basis to trophic-level interactions. *Ecology Letters*, 9(1):78–85.
- Bansal, S., Grenfell, B. T., and Meyers, L. A. (2007). When individual behaviour matters: homogeneous and network models in epidemiology. *Journal of the Royal Society Interface*, 4(16):879–891.

- Bargum, K. (2007). Multiple breeders, breeder shifts and inclusive fitness returns in an ant. *Proceedings of the Royal Society B-Biological Sciences*, 274(1617):1547–1551.
- Bauch, C. T. (2005). The spread of infectious diseases in spatially structured populations: An invasy pair approximation. *Mathematical Biosciences*, 198(2):217–237.
- Bell, G. (2007). The evolution of trophic structure. *Heredity*, 99:1–12.
- Berlow, E. L., Neutel, A. M., Cohen, J. E., de Ruiter, P. C., Ebenman, B., Emmerson, M., Fox, J. W., Jansen, V. A. A., Jones, J. I., Kokkoris, G. D., Logofet, D. O., McKane, A. J., Montoya, J. M., and Petchey, O. (2004). Interaction strengths in food webs: issues and opportunities. *Journal of Animal Ecology*, 73(3):585–598.
- Best, A., Webb, S., White, A., and Boots, M. (2011). Host resistance and coevolution in spatially structured populations. *Proceedings of the Royal Society B-Biological Sciences*, 278(1715):2216–2222.
- Boerlijst, M. C., Lamers, M. E., and Hogeweg, P. (1993). Evolutionary consequences of sprial waves in a host parasitoid system. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 253(1336):15–18.
- Boerlijst, M. C. and van Ballegooijen, W. M. (2010). Spatial pattern switching enables cyclic evolution in spatial epidemics. *Plos Computational Biology*, 6(12).
- Bonhoeffer, S., Lenski, R. E., and Ebert, D. (1996a). The curse of the pharaoh: The evolution of virulence in pathogens with long living propagules. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 263(1371):715–721.
- Bonhoeffer, S., Lenski, R. E., and Ebert, D. (1996b). The curse of the pharaoh: The evolution of virulence in pathogens with long living propagules. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 263(1371):715–721.
- Bonhoeffer, S. and Nowak, M. A. (1994). Mutation and the evolution of virulence. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 258(1352):133–140.
- Boots, M., Hudson, P. J., and Sasaki, A. (2004). Large shifts in pathogen virulence relate to host population structure. *Science*, 303(5659):842–844.
- Boots, M., Kamo, M., and Sasaki, A. (2006). The implications of spatial structure within populations to the evolution of parasites. In Feng, Z., Dieckmann, U., and Levin, S. A., editors, *Disease evolution: models, concepts, and data analyses*, DIMACS Series in Discrete Mathematics and Theoretical Computer Science, page 297. American Mathematical Society, Providence, R.I.
- Boots, M. and Meador, M. (2007). Local interactions select for lower pathogen infectivity. *Science*, 315(5816):1284–1286.

- Boots, M. and Sasaki, A. (1999). 'small worlds' and the evolution of virulence: infection occurs locally and at a distance. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 266(1432):1933–1938.
- Boots, M. and Sasaki, A. (2000). The evolutionary dynamics of local infection and global reproduction in host-parasite interactions. *Ecology Letters*, 3(3):181–185.
- Bremermann, H. J. and Thieme, H. R. (1989). A competitive exclusion principle for pathogen virulence. *Journal of Mathematical Biology*, 27:179–190.
- Brose, U., Jonsson, T., Berlow, E. L., Warren, P., Banasek-Richter, C., Bersier, L. F., Blanchard, J. L., Brey, T., Carpenter, S. R., Blandenier, M. F. C., Cushing, L., Dawah, H. A., Dell, T., Edwards, F., Harper-Smith, S., Jacob, U., Ledger, M. E., Martinez, N. D., Memmott, J., Mintenbeck, K., Pinnegar, J. K., Rall, B. C., Rayner, T. S., Reuman, D. C., Ruess, L., Ulrich, W., Williams, R. J., Woodward, G., and Cohen, J. E. (2006). Consumer-resource body-size relationships in natural food webs. *Ecology*, 87(10):2411–2417.
- Brown, J. S. and Vincent, T. L. (1992). Organization of predator-prey communities as an evolutionary game. *Evolution*, 46(5):1269–1283.
- Bull, J. J. (1994). Virulence. *Evolution*, 48:1423–1437.
- Caldarelli, G., Higgs, P. G., and McKane, A. J. (1998). Modelling coevolution in multispecies communities. *Journal of Theoretical Biology*, 193(2):345–358.
- Caraco, T., Glavanakov, S., Li, S. G., Maniatty, W., and Szymanski, B. K. (2006). Spatially structured superinfection and the evolution of disease virulence. *Theoretical Population Biology*, 69(4):367–384.
- Carroll, S. P., Hendry, A. P., Reznick, D. N., and Fox, C. W. (2007). Evolution on ecological time-scales. *Functional Ecology*, 21(3):387–393.
- Champagnat, N. and S., M. (2007). Invasion and adaptive evolution for individual-based spatially structured populations. *Journal of Mathematical Biology*, 55(2):147–188.
- Chesson, P. (1985). Coexistence of competitors in spatially and temporally varying environments: a look at the combined effects of different sorts of variability. *Theoretical Population Biology*, 28:263–287.
- Chesson, P., Gebauer, R. L. E., Schwinning, S., Huntly, N., Wiegand, K., Ernest, M. S. K., Sher, A., Novoplansky, A., and Weltzin, J. F. (2004). Resource pulses, species interactions, and diversity maintenance in arid and semi-arid environments. *Oecologia*, 141(2):236–253.
- Choo, K., Williams, P. D., and Day, T. (2003). Host mortality, predation and the evolution of parasite virulence. *Ecology Letters*, 6(4):310–315.

- Claessen, D. and deRoos, A. M. (1995). Evolution of virulence in a host-pathogen system with local pathogen transmission. *Oikos*, 74(3):401–413.
- Cohen, J. E., Luczak, T., Newman, C. M., and Zhou, Z. M. (1990). Stochastic structure and nonlinear dynamics of food webs: Qualitative stability in a lotka-volterra cascade model. *Proceedings of the Royal Society B: Biological Sciences*, 240(1299):607–627.
- Cohen, J. E., Pimm, S. L., Yodzis, P., and Saldana, J. (1993). Body sizes of animal predators and animal prey in food webs. *The Journal of Animal Ecology*, 62(1):67–78.
- Cooper, V. S., Reiskind, M. H., Miller, J. A., Shelton, K. A., Walther, B. A., Elkinton, J. S., and Ewald, P. W. (2002). Timing of transmission and the evolution of virulence of an insect virus. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 269(1496):1161–1165.
- Cronin, J. T., Reeve, J. D., Wilkens, R., and Turchin, P. (2000). The pattern and range of movement of a checkered beetle predator relative to its bark beetle prey. *Oikos*, 90(1):127–138.
- Dale, V. H., Brown, S., Haeuber, R. A., Hobbs, N. T., Huntly, N., Naiman, R. J., Riebsame, W. E., Turner, M. G., and Valone, T. J. (2000). Ecological principles and guidelines for managing the use of land. *Ecological Applications*, 10(3):639–670.
- Day, T. (2002). Virulence evolution via host exploitation and toxin production in spore-producing pathogens. *Ecology Letters*, 5(4):471–476.
- Day, T. (2003). Virulence evolution and the timing of disease life-history events. *Trends in Ecology and Evolution*, 18(3):113–118.
- Day, T. and Proulx, S. R. (2004). A general theory for the evolutionary dynamics of virulence. *The American Naturalist*, 163(4):E40–E63.
- de Aguiar, M. A. M., Rauch, E. M., and Bar-Yam, Y. (2004). Invasion and extinction in the mean field approximation for a spatial host-pathogen model. *Journal of Statistical Physics*, 114(5-6):1417–1451.
- De Meester, L. (2007). Genetic composition of resident populations influences establishment success of immigrant species. *Oecologia*, 153(2):431–440.
- de Roode, J. C., Pansini, R., Cheesman, S. J., Helinski, M. E. H., Huijben, S., Wargo, A. R., Bell, A. S., Chan, B. H. K., Walliker, D., and Read, A. F. (2005). Virulence and competitive ability in genetically diverse malaria infections. *Proceedings of the National Academy of Sciences of the United States of America*, 102(21):7624–7628.
- de Roode, J. C., Yates, A. J., and Altizer, S. (2008). Virulence-transmission trade-offs and population divergence in virulence in a naturally occurring butterfly parasite. *Proceedings of the National Academy of Sciences*, 105(21):7489–7494.

- Débarre, F., Bonhoeffer, S., and Regoes, R. R. (2007). The effect of population structure on the emergence of drug resistance during influenza pandemics. *Journal of the Royal Society Interface*, 4:893–906.
- Debarre, F., Lion, S., van Baalen, M., and Gandon, S. (2012). Evolution of host life-history traits in a spatially structured host-parasite system. *American Naturalist*, 179(1):52–63.
- Dercole, F., Ferriere, R., and Rinaldi, S. (2010). Chaotic red queen coevolution in three-species food chains. *Proceedings of the Royal Society B-Biological Sciences*, 277(1692):2321–2330.
- DeWitt, R. M. (1954). The intrinsic rate of natural increase in a pond snail (*Physa gyrina* say). *The American Naturalist*, 88(842):353–359.
- Dieckmann, U. (1997). Can adaptive dynamics invade? *Trends in Ecology and Evolution*, 12(4):128–131.
- Dieckmann, U. (2002). Adaptive dynamics of pathogen-host interactions. In Dieckmann, U., Metz, J. A. J., Sabelis, M. W., and Sigmund, K., editors, *Adaptive dynamics of infectious diseases: In pursuit of virulence management*, pages 39–59. Cambridge University Press, Cambridge.
- Dieckmann, U., Heino, M., and Parvinen, K. (2006). The adaptive dynamics of function-valued traits. *Journal of Theoretical Biology*, 241(2):370–389.
- Dieckmann, U. and Law, R. (2000). Moment approximations of individual-based models. In Dieckmann, U., Law, R., and Metz, J. A. J., editors, *The Geometry of Ecological Interactions: Simplifying Spatial Complexity*, pages 252–270. Cambridge University Press, Cambridge, UK.
- Diekmann, O. and Heesterbeek, J. A. P. (2000). *Mathematical Epidemiology of Infectious Diseases: model building, analysis and interpretation*. John Wiley and Sons, Chichester.
- Diekmann, O., Heesterbeek, J. A. P., and Metz, J. A. J. (1990). On the definition and the computation of the basic reproduction ratio r_0 in models for infectious-diseases in heterogeneous populations. *Journal of Mathematical Biology*, 28(4):365–382.
- Diller, L. V. and Johnson, D. R. (1988). Food habits, consumption rates, and predation rates of western rattlesnakes and gopher snakes in southwestern idaho. *Herpetologica*, 44:228–233.
- Doebeli, M. and Knowlton, N. (1998). The evolution of interspecific mutualisms. *Proceedings of the National Academy of Sciences*, 95(15):8676–8680.
- Drossel, B. (2004). The impact of nonlinear functional responses on the long-term evolution of food web structure. *Journal of Theoretical Biology*, 229(4):539–548.

- Ducoff, H. S. (1957). Factors affecting radiation-induced division delay in *Chlamydomonas paramecium*. *Physiological Zoology*, 30(3):268–280.
- Durrett, R. and Levin, S. (1994). The importance of being discrete (and spatial). *Theoretical Population Biology*, 46(3):363–394.
- Eames, K. T. D. and Keeling, M. J. (2006). Coexistence and specialization of pathogen strains on contact networks. *The American Naturalist*, 168(2):230–241.
- Ebert, D. and Bull, J. J. (2003). Challenging the trade-off model for the evolution of virulence: is virulence management feasible? *Trends in Microbiology*, 11(1):15–20.
- Ebert, D. and Weisser, W. W. (1997). Optimal killing for obligate killers: The evolution of life histories and virulence of semelparous parasites. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 264(1384):985–991.
- Ellner, S. P., Geber, M. A., and Hairston, N. G. (2011). Does rapid evolution matter? measuring the rate of contemporary evolution and its impacts on ecological dynamics. *Ecology Letters*, 14(6):603–614.
- Eshelman, C. M., Vouk, R., Stewart, J. L., Halsne, E., Lindsey, H. A., Schneider, S., Gualu, M., Dean, A. M., and Kerr, B. (2010). Unrestricted migration favours virulent pathogens in experimental metapopulations: Evolutionary genetics of a rapacious life history. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences*, 365(1552):2503–2513.
- Ewald, P. W. (1987). Transmission modes and evolution of the parasitism-mutualism continuum. *Annals of the New York Academy of Sciences*, 503:295–306.
- Ewald, P. W. (1993). The evolution of virulence. *Scientific American*, 268(4):86.
- Ewald, P. W. (1998). The evolution of virulence and emerging diseases. *Journal of Urban Health-Bulletin of the New York Academy of Medicine*, 75(3):480–491.
- Fenchel, T. (1974). Intrinsic rate of natural increase: The relationship with body size. *Oecologia*, 14(317-326).
- Field, C. B., Lobell, D. B., Peters, H. A., and Chiariello, N. R. (2007). Feedbacks of terrestrial ecosystems to climate change. In *Annual Review of Environment and Resources*, volume 32 of *Annual Review of Environment and Resources*, pages 1–29. Annual Reviews, Palo Alto.
- Filipe, J. A. N. and Maule, M. M. (2003). Analytical methods for predicting the behaviour of population models with general spatial interactions. *Mathematical Biosciences*, 183(1):15–35.
- Fletcher, J. A. and Doebeli, M. (2009). A simple and general explanation for the evolution of altruism. *Proceedings of the Royal Society B-Biological Sciences*, 276(1654):13–19.

- Forsman, A. and Lindell, L. E. (1993). The advantage of a big head—swallowing performance in adders, *Vipera berus*. *Functional Ecology*, 7(2):183–189.
- Frank, S. A. (1996). Models of parasite virulence. *Quarterly Review of Biology*, 71(1):37–78.
- Fukami, T. (2007). Immigration history controls diversification in experimental adaptive radiation. *Nature*, 446(7134):436–439.
- Fulford, G. R., Roberts, M. G., and Heesterbeek, J. A. P. (2002). The metapopulation dynamics of an infectious disease: Tuberculosis in possums. *Theoretical Population Biology*, 61(1):15–29.
- Fussmann, G. F., Loreau, M., and Abrams, P. A. (2007). Eco-evolutionary dynamics of communities and ecosystems. *Functional Ecology*, 21(3):465–477.
- Gandon, S. (1998). The curse of the pharaoh hypothesis. *Proceedings of the Royal Society B: Biological Sciences*, 265(1405):1545–1552.
- Gandon, S. and Michalakis, Y. (2000). Evolution of parasite virulence against qualitative or quantitative host resistance. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 267(1447):985–990.
- Gilchrist, M. A. and Coombs, D. (2006). Evolution of virulence: Interdependence, constraints, and selection using nested models. *Theoretical Population Biology*, 69(2):145–153.
- Gilchrist, M. A. and Sasaki, A. (2002). Modeling host-parasite coevolution: A nested approach based on mechanistic models. *Journal of Theoretical Biology*, 218(3):289–308.
- Gillespie, D. T. (1977). Exact stochastic simulation of coupled chemical-reactions. *Journal of Physical Chemistry*, 81(25):2340–2361.
- Gilpin, M. and Hanski, I. (1991). Metapopulation dynamics: empirical and theoretical investigations. *Biological Journal of the Linnean Society*, 42(1-2).
- Gilpin, M. E. (1975). *Group selection in predator-prey communities*. Princeton University Press, Princeton, NJ.
- Godfray, H. C. J., Hassell, M. P., and Holt, R. D. (1994). The population-dynamic consequences of phenological asynchrony between parasitoids and their hosts. *Journal of Animal Ecology*, 63(1):1–10.
- Goodnight, C., Rauch, E., Sayama, H., De Aguiar, M. A. M., Baranger, M., and Bar-Yam, Y. (2008). Evolution in spatial predator-prey models and the "prudent predator": The inadequacy of steady-state organism fitness and the concept of individual and group selection. *Complexity*, 13(5):23–44.

- Grigoriev, I. V., Nordberg, H., Shabalov, I., Aerts, A., Cantor, M., Goodstein, D., Kuo, A., Minovitsky, S., Nikitin, R., Ohm, R. A., Otilar, R., Poliakov, A., Ratnere, I., Riley, R., Smirnova, T., Rokhsar, D., and Dubchak, I. (2011). The genome portal of the department of energy joint genome institute. <http://genome.jgi-psf.org/Dappu1/Dappu1.home.html>.
- Gutierrez, A. P., Morgan, D. J., and Haven-Stein, D. E. (1971). The ecology of aphid *cracivora koch* and subterranean clover stunt virus. i. the phenology of aphid populations and the epidemiology of virus in pastures in south-east australia. *Journal of Applied Ecology*, 8:699–721.
- Hansen, S. K., Rainey, P. B., Haagensen, J. A. J., and Molin, S. (2007). Evolution of species interactions in a biofilm community. *Nature*, 445(7127):533–536.
- Harada, Y. and Iwasa, Y. (1994). Lattice population-dynamics for plants with dispersing seeds and vegetative propagation. *Researches on Population Ecology*, 36(2):237–249.
- Haraguchi, Y. and Sasaki, A. (2000). The evolution of parasite virulence and transmission rate in a spatially structured population. *Journal of Theoretical Biology*, 203(2):85–96.
- Hardin, G. (1968). The tragedy of the commons. *Science*, 162(3859):1243–1248.
- Hastings, H. M. and Conrad, M. (1979). Length and evolutionary stability of food-chains. *Nature*, 282(5741):838–839.
- Hauert, C. and Doebeli, M. (2004). Spatial structure often inhibits the evolution of cooperation in the snowdrift game. *Nature*, 428(6983):643–646.
- Heesterbeek, J. A. P. (2002). A brief history of r_0 and a recipe for its calculation. *Acta Biotheoretica*, 50(3):189–204.
- Heesterbeek, J. A. P. and Dietz, K. (1996). The concept of r_0 in epidemic theory. *Statistica Neerlandica*, 50(1):89–110.
- Heffernan, J. M., Smith, R. J., and Wahl, L. M. (2005). Perspectives on the basic reproductive ratio. *Journal of the Royal Society Interface*, 2(4):281–293.
- Hethcote, H. W. (2000). The mathematics of infectious diseases. *Siam Review*, 42(4):599–653.
- Hethcote, H. W. (2008). The basic epidemiology models: Models, expressions for r_0 , parameter estimation, and application. In Ma, S. and Xia, Y., editors, *Mathematical understanding of infectious disease dynamics*, volume 16 of *Lecture Notes Series, Institute for Mathematical Sciences, National University of Singapore*. World Scientific Publishing Co. Pte. Ltd.

- Hofbauer, J. and Sigmund, K. (1990). Adaptive dynamics and evolutionary stability. *Applied Mathematics Letters*, 3(4):75–79.
- Hoffmeister, T. S., Vet, L. E. M., Biere, A., Holsinger, K., and Filser, J. (2005). Ecological and evolutionary consequences of biological invasion and habitat fragmentation. *Ecosystems*, 8(6):657–667.
- House, T. and Keeling, M. J. (2008). Deterministic epidemic models with explicit household structure. *Mathematical Biosciences*, 213(1):29–39.
- Hubbel, S. P. (2006). Neutral theory and the evolution of ecological equivalence. *Ecology*, 87(6):1387–1398.
- Hutchinson, G. E. (1959). Homage to santa rosalia or why are there so many kinds of animals? *The American Naturalist*, 43(870):145–159.
- Johnson, C. R. and Boerlijst, M. C. (2002). Selection at the level of the community: the importance of spatial structure. *Trends in Ecology and Evolution*, 17(2):83–90.
- Johnson, C. R. and Seinen, I. (2002). Selection for restraint in competitive ability in spatial competition systems. *Proceedings of the Royal Society B-Biological Sciences*, 269:655–663.
- Jones, T. H., Godfray, H. C. J., and Hassell, M. P. (1996). Relative movement patterns of a tephritid fly and its parasitoid wasps. *Oecologia*, 106(3):317–324.
- Jonsson, T. and Ebenman, B. (1998). Effects of predator-prey body size ratios on the stability of food chains. *Journal of Theoretical Biology*, 193(3):407–417.
- Takehashi, M. and Yoshinaga, F. (1992). Evolution of airborne infectious diseases according to changes in the characteristics of the host population. *Ecological Research*, 7:235–243.
- Kamo, M. and Boots, M. (2004). The curse of the pharaoh in space: free-living infectious stages and the evolution of virulence in spatially explicit populations. *Journal of Theoretical Biology*, 231(3):435–441.
- Kamo, M. and Boots, M. (2006). The evolution of parasite dispersal, transmission, and virulence in spatial host populations. *Evolutionary Ecology Research*, 8(7):1333–1347.
- Kamo, M., Sasaki, A., and Boots, M. (2007). The role of trade-off shapes in the evolution of parasites in spatial host populations: An approximate analytical approach. *Journal of Theoretical Biology*, 244(4):588–596.
- Kareiva, P. (1990). Population dynamics in spatially complex environments - theory and data. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences*, 330(1257):175–190.

- Keeling, M. (2000). Evolutionary trade-offs at two time-scales: competition versus persistence. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 267(1441):385–391.
- Keeling, M. (2005). The implications of network structure for epidemic dynamics. *Theoretical Population Biology*, 67(1):1–8.
- Kefi, S., van Baalen, M., Rietkerk, M., and Loreau, M. (2008). Evolution of local facilitation in arid ecosystems. *American Naturalist*, 172(1):E1–E17.
- Kerr, B. and Godfrey-Smith, P. (2002). Individualist and multi-level perspectives on selection in structured populations. *Biology and Philosophy*, 17(4):477–517.
- Kerr, B., Neuhauser, C., Bohannan, B. J. M., and Dean, A. M. (2006). Local migration promotes competitive restraint in a host-pathogen 'tragedy of the commons'. *Nature*, 442(7098):75–78.
- Killingback, T., Doebeli, M., and Knowlton, N. (1999). Variable investment, the continuous prisoner's dilemma, and the origin of cooperation. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, 266(1430):1723–1728.
- King, A. A. and Hastings, A. (2003). Spatial mechanisms for coexistence of species sharing a common natural enemy. *Theoretical Population Biology*, 64(4):431–438.
- King, A. A., Shrestha, S., Harvill, E. T., and Bjornstad, O. N. (2009). Evolution of acute infections and the invasion-persistence trade-off. *American Naturalist*, 173(4):446–455.
- Kinzig, A. P. and Harte, J. (1998). Selection of micro-organisms in a spatially explicit environment and implications for plant access to nitrogen. *The Journal of Ecology*, 86(5):841–853.
- Kokko, H. and Lopez-Sepulcre, A. (2007). The ecogenetic link between demography and evolution: can we bridge the gap between theory and data? *Ecology Letters*, 10(9):773–782.
- Komac, B., Alados, C. L., Bueno, C. G., and Gomez, D. (2011). Spatial patterns of species distributions in grazed subalpine grasslands. *Plant Ecology*, 212(3):519–529.
- Kondoh, M. (2003). Foraging adaptation and the relationship between food-web complexity and stability. *Science*, 299(5611):1388–1391.
- Law, R. and Morton, R. D. (1996). Permanence and the assembly of ecological communities. *Ecology*, 77(3):762–775.
- Le Galliard, J. F., Ferriere, R., and Dieckmann, U. (2003). The adaptive dynamics of altruism in spatially heterogeneous populations. *Evolution*, 57(1):1–17.
- Lee, J. E. and Chown, S. L. (2009). Breaching the dispersal barrier to invasion: quantification and management. *Ecological Applications*, 19(7):1944–1959.

- Lehmann, L. and Keller, L. (2007). The evolution of helping and harming on graphs: the return of the inclusive fitness effect. *Journal of Evolutionary Biology*, 20(6):2284–2295.
- Lenski, R. E. (1988). Evolution of plague virulence. *Nature*, 334:473–474.
- Lenski, R. E. and May, R. M. (1994). The evolution of virulence in parasites and pathogens - reconciliation between two competing hypotheses. *Journal of Theoretical Biology*, 169(3):253–265.
- Levin, B. R., Allison, A. C., Bremermann, H. J., Cavalli-Sforza, L. L., Clarke, B. C., Frenzel-Beyme, R., Hamilton, W. D., Levin, S. A., May, R. M., and Thieme, H. R. (1982). Evolution of parasites and hosts (group report). In Anderson, R. M. and May, R. M., editors, *Population biology of infectious diseases*, pages 213–243. Springer-Verlag, Berlin, Heidelberg, New York.
- Levin, B. R. and Bull, J. J. (1994). Short-sighted evolution and the virulence of pathogenic microorganisms. *Trends in Microbiology*, 2(3):76–81.
- Levin, S. and Pimentel, D. (1981). Selection of intermediate rates of increase in parasite-host systems. *The American Naturalist*, 117(3):308–315.
- Lewontin, R. C. (1970). The units of selection. *Annual Review of Ecology and Systematics*, 1(1):1–18.
- Lion, S. and Boots, M. (2010). Are parasites "prudent" in space? *Ecology Letters*, 13(10):1245–1255.
- Lion, S. and Gandon, S. (2009). Habitat saturation and the spatial evolutionary ecology of altruism. *Journal of Evolutionary Biology*, 22(7):1487–1502.
- Lion, S. and van Baalen, M. (2008). Self-structuring in spatial evolutionary ecology. *Ecology Letters*, 11(3):277–295.
- Lipsitch, M. and Moxon, E. R. (1997). Virulence and transmissibility of pathogens: What is the relationship? *Trends in Microbiology*, 5(1):31–37.
- Loeuille, N. (2010). Influence of evolution on the stability of ecological communities. *Ecology Letters*, 13(12):1536–1545.
- Marland, G., Pielke, R. A., Apps, M., Avissar, R., Betts, R. A., Davis, K. J., Frumhoff, P. C., Jackson, S. T., Joyce, L. A., Kauppi, P., Katzenberger, J., MacDicken, K. G., Neilson, R. P., Niles, J. O., Niyogi, D. D. S., Norby, R. J., Pena, N., Sampson, N., and Xue, Y. K. (2003). The climatic impacts of land surface change and carbon management, and the implications for climate-change mitigation policy. *Climate Policy*, 3(2):149–157.
- Matsuda, H., Ogita, N., Sasaki, A., and Sato, K. (1992). Statistical mechanics of population: The lattice lotka-volterra model. *Progress of Theoretical Physics*, 88(6):1035–1049.

- May, R. M. (1971). Stability in multi-species community models. *Mathematical Biosciences*, 12:59–79.
- May, R. M. and Anderson, R. M. (1979). Population biology of infectious-diseases. 2. *Nature*, 280(5722):455–461.
- May, R. M. and Anderson, R. M. (1982). Parasite-host coevolution. In Futuyma, D. J. and Slatkin, M., editors, *Coevolution*, pages 186–206. Sinauer Associates, Inc., Sunderland, MA.
- McCann, K. (2000). The diversity-stability debate. *Nature*, 405(6783):228–233.
- Melian, C. J., Bascompte, J., Jordano, P., and Krivan, V. (2009). Diversity in a complex ecological network with two interaction types. *Oikos*, 118(1):12–130.
- Messenger, S. L., Molineux, I. J., and Bull, J. J. (1999). Virulence evolution in a virus obeys a trade-off. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 266(1417):397–404.
- Messinger, S. M. and Ostling, A. (2009). The consequences of spatial structure for the evolution of pathogen transmission rate and virulence. *American Naturalist*, 174(October).
- Messinger, S. M. and Ostling, A. (In Review). The influence of host demography, pathogen virulence, and tradeoffs with pathogen virulence on the evolution of pathogen transmission in a spatial context. *Evolutionary Ecology*.
- Meyers, L. A., Newman, M. E. J., and Pourbohloul, B. (2006). Predicting epidemics on directed contact networks. *Journal of Theoretical Biology*, 240(3):400–418.
- Mideo, N., Alizon, S., and Day, T. (2008). Linking within- and between-host dynamics in the evolutionary epidemiology of infectious diseases. *Trends in Ecology and Evolution*, 23(9):511–517.
- Mithen, S. J. and Lawton, J. H. (1986). Food-web models that generate constant predator-prey ratios. *Oecologia*, 69(4):542–550.
- Mollison, D. (1995). The structure of epidemic models. In Mollison, D., editor, *Epidemic models: Their structure and relation to data*, pages 17–33. Cambridge University Press.
- Moreno, A., Nebreda, M., Diaz, B. M., Garcia, M., Salas, F., and Fereres, A. (2007). Temporal and spatial spread of lettuce mosaic virus in lettuce crops in central Spain: factors involved in lettuce mosaic virus epidemics. *Annals of Applied Biology*, 150(3):351–360.
- Morris, A. J. (1997). *Representing spatial interactions in simple ecological models*. PhD thesis, University of Warwick.

- Mosquera, J. and Adler, F. R. (1998). Evolution of virulence: a unified framework for coinfection and superinfection. *Journal of Theoretical Biology*, 195(3):293–313.
- Mougi, A. (2010). Coevolution in a one predator-two prey system. *Plos One*, 5(11).
- Mougi, A. and Nishimura, K. (2009). Species invasion history influences community evolution in a tri-trophic food web model. *Plos One*, 4(8).
- Murase, Y., Shimada, T., Ito, N., and Rikvold, P. A. (2010). Effects of demographic stochasticity on biological community assembly on evolutionary time scales. *Physical Review E*, 81(4).
- North, A., Cornell, S., and Ovaskainen, O. (2011). Evolutionary responses of dispersal distance to landscape structure and habitat loss. *Evolution*, 65(6):1739–1751.
- Nowak, M. and Sigmund, K. (1990). The evolution of stochastic strategies in the prisoner’s dilemma. *Acta Applicandae Mathematicae*, 20(3):247–265.
- Nowak, M. A. and May, R. M. (1992). Evolutionary games and spatial chaos. *Nature*, 359(6398):826–829.
- Nowak, M. A. and Sigmund, K. (2002). Super- and coinfection: The two extremes. In Dieckmann, U., Metz, J. A. J., Sabelis, M. W., and Sigmund, K., editors, *Adaptive dynamics of infectious diseases: In pursuit of virulence management*, pages 124–149. Cambridge University Press, Cambridge.
- Ohtsuka, K., Konno, N., Masuda, N., and Aihara, K. (2006). Phase diagrams and correlation inequalities of a three-state stochastic epidemic model on the square lattice. *International Journal of Bifurcation and Chaos*, 16(12):3687–3693.
- Osnas, E. E. and Dobson, A. P. (2010). Evolution of virulence when transmission occurs before disease. *Biology Letters*, 6(4):505–508.
- Palkovacs, E. P. and Post, D. M. (2008). Eco-evolutionary interactions between predators and prey: can predator-induced changes to prey communities feed back to shape predator foraging traits? *Evolutionary Ecology Research*, 10(5):699–720.
- Parvinen, K. (2005). Evolutionary suicide. *Acta Biotheoretica*, 53(3):241–264.
- Peak, D., West, J. D., Messinger, S. M., and Mott, K. A. (2004). Evidence for complex, collective dynamics and emergent, distributed computation in plants. *Proceedings of the National Academy of Sciences*, 101(4):918–922.
- Pech, R. P. and Hone, J. (1988). A model of the dynamics and control of an outbreak of foot and mouth disease in feral pigs in australia. *Journal of Applied Ecology*, 25:63–77.
- Pelletier, F., Garant, D., and Hendry, A. P. (2009). Eco-evolutionary dynamics. *Philosophical Transactions of the Royal Society B-Biological Sciences*, 364(1523):1483–1489.

- Pels, B., de Roos, A. M., and Sabelis, M. W. (2002). Evolutionary dynamics of prey exploitation in a metapopulation of predators. *The American Naturalist*, 159(2):172–189.
- Pervez, A. and Omkar (2005). Functional responses of coccinellid predators: An illustration of a logistic approach. *Journal of Insect Science*, 5(5).
- Peyrard, N., Dieckmann, U., and Franc, A. (2008). Long-range correlations improve understanding of the influence of network structure on contact dynamics. *Theoretical Population Biology*, 73(3):383–394.
- Pianka, E. (2000). *Evolutionary Ecology*. Benjamin Cummings, sixth edition.
- Pielke, R. A., Marland, G., Betts, R. A., Chase, T. N., Eastman, J. L., Niles, J. O., Niyogi, D. D. S., and Running, S. W. (2002). The influence of land-use change and landscape dynamics on the climate system: relevance to climate-change policy beyond the radiative effect of greenhouse gases. *Philosophical Transactions of the Royal Society of London Series a-Mathematical Physical and Engineering Sciences*, 360(1797):1705–1719.
- Pielke, R. A., Pitman, A., Niyogi, D., Mahmood, R., McAlpine, C., Hossain, F., Goldewijk, K. K., Nair, U., Betts, R., Fall, S., Reichstein, M., Kabat, P., and de Noblet, N. (2011). Land use/land cover changes and climate: modeling analysis and observational evidence. *Wiley Interdisciplinary Reviews-Climate Change*, 2(6):828–850.
- Pillai, P., Gonzalez, A., and Loreau, M. (2011). Metacommunity theory explains the emergence of food web complexity. *Proceedings of the National Academy of Sciences*, 108(48):19293–19298.
- Pimm, S. L. and Lawton, J. H. (1977). Number of trophic levels in ecological communities. *Nature*, 268(5618):329–331.
- Platt, W. J., Evans, G. W., and Rathbun, S. L. (1988). The population dynamics of a long-lived conifer (*pinus palustris*). *The American Naturalist*, 131(4):491–525.
- Post, W. M. and Pimm, S. L. (1983). Community assembly and food web stability. *Mathematical Biosciences*, 64(2):169–192.
- Prado, F. and Kerr, B. (2008). The evolution of restraint in bacterial biofilms under nontransitive competition. *Evolution*, 62(3):538–548.
- Pugliese, A. (2002). On the evolutionary coexistence of parasite strains. *Mathematical Biosciences*, 177 and 178:355–375.
- Rachid, R., Djebar-Berrebah, H., and Djebar, M. R. (2008). Growth, chitin, and respiratory metabolism of *tetraymena pyriformis* exposed to the insecticide novaluron. *American-Eurasian Journal of Agriculture and Environmental Science*, 3(6):873–881.

- Rankin, D. J., Bargum, K., and Kokko, H. (2007). The tragedy of the commons in evolutionary biology. *Trends in Ecology and Evolution*, 22(12):643–651.
- Rankin, D. J. and Lopez-Sepulcre, A. (2005). Can adaptation lead to extinction? *Oikos*, 111(3):616–619.
- Rauch, E. M. and Bar-Yam, Y. (2006). Long-range interactions and evolutionary stability in a predator-prey system. *Physical Review E*, 73(2):4.
- Rauch, E. M., Sayama, H., and Bar-Yam, Y. (2002). Relationship between measures of fitness and time scale in evolution. *Physical Review Letters*, 88(22).
- Rauch, E. M., Sayama, H., and Bar-Yam, Y. (2003). Dynamics and genealogy of strains in spatially extended host-pathogen models. *Journal of Theoretical Biology*, 221(4):655–664.
- Read, J. M. and Keeling, M. J. (2003). Disease evolution on networks: the role of contact structure. *Proceedings of the Royal Society of London Series B-Biological Sciences*, 270(1516):699–708.
- Read, J. M. and Keeling, M. J. (2006). Disease evolution across a range of spatio-temporal scales. *Theoretical Population Biology*, 70(2):201–213.
- Read, J. M. and Keeling, M. J. (2007). Stochasticity generates an evolutionary instability for infectious disease. *Ecology Letters*, 10:818–827.
- Ricciardi, A. (2007). Are modern biological invasions an unprecedented form of global change? *Conservation Biology*, 21(2):329–336.
- Rice, S. H. (2004). *Evolutionary theory: mathematical and conceptual foundations*. Sinauer Associates, Inc., Sunderland, MA.
- Richards, S. A., Wilson, W. G., and Socolar, J. E. S. (1999). Selection for intermediate mortality and reproduction rates in a spatially structured population. *Proceedings of the Royal Society of London B*, 266:2383–2388.
- Rietkerk, M., Dekker, S. C., de Ruiter, P. C., and van de Koppel, J. (2004). Self-organized patchiness and catastrophic shifts in ecosystems. *Science*, 305(5692):1926–1929.
- Rikvold, P. A. (2007). Self-optimization, community stability, and fluctuations in two individual-based models of biological coevolution. *Journal of Mathematical Biology*, 55(5-6):653–677.
- Rikvold, P. A. and Sevim, V. (2007). Individual-based predator-prey model for biological coevolution: Fluctuations, stability, and community structure. *Physical Review E*, 75(051920):1–17.

- Rikvold, P. A. and Zia, R. K. P. (2003). Punctuated equilibria and $1/f$ noise in a biological coevolution model with individual-based dynamics. *Physical Review E*, 68(031913):1–16.
- Roberts, M. G. (2007). The pluses and minuses of $r=0$. *Journal of the Royal Society Interface*, 4(16):949–961.
- Roche, B., Drake, J. M., and Rohani, P. (2011). The curse of the pharaoh revisited: Evolutionary bi-stability in environmentally transmitted pathogens. *Ecology Letters*, 14(4):569–575.
- Rohani, P., May, R., and Hassell, M. P. (1996). Metapopulations and equilibrium stability: The effects of spatial structure. *Journal of Theoretical Biology*, 181:97–109.
- Roumagnac, P., Pruvost, O., Chiroleu, F., and Hughes, G. (2004). Spatial and temporal analyses of bacterial blight of onion caused by *Xanthomonas axonopodis* pv. *allii*. *Phytopathology*, 94(2):138–146.
- Santini, G., Ramsay, P. M., Tucci, L., Ottonetti, L., and Frizzi, F. (2011). Spatial patterns of the ant *crematogaster scutellaris* in a model ecosystem. *Ecological Entomology*, 36(5):625–634.
- Sarukhan, J. and Harper, J. L. (1973). Studies on plant demography: *Ranunculus repens* L., *R. bulbosus* L., and *R. acris* L. i. population flux and survivorship. *Journal of Ecology*, 61:675–716.
- Sato, K., Matsuda, H., and Sasaki, A. (1994). Pathogen invasion and host extinction in lattice structured populations. *Journal of Mathematical Biology*, 32(3):251–268.
- Schwaegerle, K. E. (1983). Population growth of the pitcher plant, *Sarracenia purpurea* L., at cranberry bog, Licking county, Ohio. *Ohio Journal of Science*, 83(1):19–22.
- Silvertown, J., Franco, M., Pisanty, I., and Mendoza, A. (1993). Comparative plant demography—relative importance of life-cycle components to the finite rate of increase in woody and herbaceous perennials. *Journal of Ecology*, 81(3):465–476.
- Slobodkin, L. B. (1974). Prudent predation does not require group selection. *The American Naturalist*, 108(963):665–678.
- Stewart, A. D., Logsdon, Jr., J. M., and Kelley, S. E. (2005). An empirical study of the evolution of virulence under both horizontal and vertical transmission. *Evolution*, 59(4):730–739.
- Szathmari, E. (2001). Biological information, kin selection, and evolutionary transitions. *Theoretical Population Biology*, 59(1):11–14.

- Taylor, A. D. (1998). Environmental variability and the persistence of parasitoid-host metapopulation models. *Theoretical Population Biology*, 53:98–107.
- Thomas, C. D., Cameron, A., Green, R. E., Bakkenes, M., Beaumont, L. J., Collingham, Y. C., Erasmus, B. F. N., de Siqueira, M. F., Grainger, A., Hannah, L., Hughes, L., Huntley, B., van Jaarsveld, A. S., Midgley, G. F., Miles, L., Ortega-Huerta, M. A., Peterson, A. T., Phillips, O. L., and Williams, S. E. (2004). Extinction risk from climate change. *Nature*, 427(6970):145–148.
- Thompson, J. N. (1998). Rapid evolution as an ecological process. *Trends in Ecology and Evolution*, 13(8):329–332.
- Thompson, J. N. (2005). *The Geographic Mosaic of Coevolution*. University of Chicago Press, Chicago.
- Tilman, D. (1994). Competition and biodiversity in spatially structured habitats. *Ecology*, 75(1):2–16.
- Todar, K. (2008). The growth of bacterial populations. online textbook of bacteriology. <http://www.textbookofbacteriology.net>.
- Urban, M. C. and Skelly, D. K. (2006). Evolving metacommunities: Toward an evolutionary perspective on metacommunities. *Ecology*, 87(7):1616–1626.
- van Baalen, M. and Rand, D. A. (1998). The unit of selection in viscous populations and the evolution of altruism. *Journal of Theoretical Biology*, 193(4):631–648.
- van Baalen, M. and Sabelis, M. W. (1995). The milker-killer dilemma in spatially structured predator-prey interactions. *Oikos*, 74:391–400.
- van der Heide, T., Bouma, T. J., van Nes, E. H., van de Koppel, J., Scheffer, M., Roelofs, J. G. M., van Katwijk, M. M., and Smolders, A. J. P. (2010). Spatial self-organized patterning in seagrasses along a depth gradient of an intertidal ecosystem. *Ecology*, 91(2):362–369.
- Virol, J. A., Mahoney, S. P., and Mawhinney, K. (2003). Phenotypic variation in skull size and shape between newfoundland and mainland populations of north american black bears, *ursus americanus*. *Canadian Field-Naturalist*, 117(2):236–244.
- Volz, E. and Meyers, L. A. (2007). Susceptible-infected-recovered epidemics in dynamic contact networks. *Proceedings of the Royal Society B-Biological Sciences*, 274(1628):2925–2933.
- Walther, B. A. and Ewald, P. W. (2004). Pathogen survival in the external environment and the evolution of virulence. *Biological Reviews*, 79(4):849–869.
- Waxman, D. and Gavrillets, S. (2005). 20 questions on adaptive dynamics. *Journal of Evolutionary Biology*, 18:1139–1154.

- Webb, S. D., Keeling, M. J., and Boots, M. (2007a). Host-parasite interactions between the local and the mean-field: How and when does spatial population structure matter? *Journal of Theoretical Biology*, 249(1):140–152.
- Webb, S. D., Keeling, M. J., and Boots, M. (2007b). Spatially extended host-parasite interactions: The role of recovery and immunity. *Theoretical Population Biology*, 71(2):251–266.
- Weitz, J. S. and Levin, S. A. (2006). Size and scaling of predator-prey dynamics. *Ecology Letters*, 9:548–557.
- Werner, E. E. and Peacor, S. D. (2003). A review of trait-mediated indirect interactions in ecological communities. *Ecology*, 84(5):1083–1100.
- White, E. P., Ernest, S. K. M., Kerkhoff, A. J., and Enquist, B. J. (2007). Relationships between body size and abundance in ecology. *Trends in Ecology and Evolution*, 22(6):323–330.
- White, P. J., Norman, R. A., and Hudson, P. J. (2002). Epidemiological consequences of a pathogen having both virulent and avirulent modes of transmission: the case of rabbit haemorrhagic disease virus. *Epidemiology and Infection*, 129(3):665–677.
- Wild, G., Gardner, A., and West, S. A. (2009). Adaptation and the evolution of parasite virulence in a connected world. *Nature*, 459(7249):983–986.
- Wong, M. C. and Barbeau, M. A. (2006). Rock crab predation of juvenile sea scallops: the functional response and its implications for bottom culture. *Aquaculture International*, 14:355–376.
- Woolhouse, M. E. J., Webster, J. P., Domingo, E., Charlesworth, B., and Levin, B. R. (2002). Biological and biomedical implications of the co-evolution of pathogens and their hosts. *Nature Genetics*, 32(4):569–577.
- Yodzis, P. and Innes, S. (1992). Body size and consumer-resource dynamics. *American Naturalist*, 139(6):1151–1175.