Spatial and Temporal Patterns in Coevolving Plant and Pathogen Associations

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ABSTRACT: Spatial structuring is important in understanding the ecological and evolutionary dynamics of natural populations since local demes are rarely, if ever, completely isolated from neighboring demes. Plant host-pathogen interactions provide good examples of coevolutionary systems where both numerical and genetic dynamics have been explicitly investigated in a spatial context and where genes under selection can be unambiguously identified. In this article, we focus on long-term studies of several natural host-pathogen interactions that span a range of life histories and taxa. We use these studies to evaluate some predictions for numerical and genetic patterns at local and regional scales. Specifically, we examine the degree of among-population asynchrony in disease presence/absence and abundance, and the extent to which this is a function of isolation. For one host-pathogen interaction (*Linum-Melampsora*), we focus on whether there is local correspondence between resistance and virulence genes (as would be predicted by single-population coevolutionary models) or whether such correspondence occurs at larger spatial scales. Finally, we discuss the implications of these studies with respect to the impact of host and pathogen life-history variation on the spatial scale of coevolutionary interactions. Understanding coevolutionary interactions in nature requires a multidisciplinary approach, including long-term empirical studies of multiple populations and computer modeling.

Keywords: coevolution, disease, gene-for-gene, geographic mosaic, metapopulation, simulation modeling.

Spatial structuring has long been recognized as an important factor affecting demographic and genetic patterns in natural populations (Wright 1943; Hutchinson 1959). Major interest in this idea was stimulated by Levins's (1969, 1970) metapopulation theory, but it is only relatively recently, with the enunciation of the "geographic mosaic theory" of coevolution (Thompson 1994*a*, 1994*b*) with its clear recognition of the importance and distinction of different levels of spatial scale, that many of the implications of these ideas have been carried into the broad sweep of coevolutionary studies.

Understanding of coevolutionary processes in plant-pathogen associations has followed a broadly similar path. Despite Haldane's (1949) pioneering ideas, the field became rapidly dominated by an agricultural mind-set in which host and pathogen populations were largely seen as homogeneous entities in which spatial considerations played little role (Person 1966; Leonard 1977; Marshall and Pryor 1978). However, as interest in dissecting the structure of natural host-pathogen associations has grown, so too has recognition that different populations may show markedly different patterns of distribution of genetic variation for resistance and virulence (Burdon et al. 1983; Parker 1985; de Nooij and van Damme 1988; Jarosz and Burdon 1991; Bevan et al. 1993). In turn, this has helped focus attention on the importance of spatial aspects of host-pathogen associations and led to the recognition of a framework of different views of gene-for-gene coevolution—perhaps the simplest and genetically best understood basis for disease resistance and pathogen virulence. This hierarchy of views ranges from short-term interactions in human-dominated and relatively homogeneous agricultural systems through to a metapopulation view of gene-for-gene coevolution in natural host-pathogen associations (e.g., Thompson and Burdon 1992). Paralleling these developments has been a slowly increasing recognition that life-history traits of both host and pathogen may also influence the geographic scale of coevolutionary processes (Burdon et al. 1990; Thrall et al. 1993). This possibility was explored extensively in a series of heuristic and computer-simulation models (Thrall and Burdon 1997, 1999) that show the critically important impact that life-history characters may have on ecological and evolutionary trajectories, and the spatial scale of coevolutionary interactions.

Most biological systems in nature are characterized by the uneven distribution of individuals into a series of populations that show varying degrees of connectedness. This

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idea has been loosely formalized by the metapopulation concept (Levins 1969, 1970; Hanski and Gilpin 1991, 1997). Viewing populations in this way immediately shifts our viewpoint away from the largely theoretical convenience of single populations, while simultaneously recognizing that all ecological and evolutionary interactions have a strong spatial component. If such spatial structure is important, evolutionary processes in such metapopulations are likely to be quite different to those occurring in single populations. With respect to host-pathogen associations, Thompson and Burdon (1992) envisaged coevolution as a regional process in which different levels of gene flow, genetic drift, and various forms of natural selection within and among demes have profound effects on the development and direction of coevolutionary associations. Patterns occurring within individual populations are likely to be transitory and ephemeral, but when summed across the multiple demes of the metapopulation each contributes to longer-term, more permanent changes in both host and pathogen.

Because coevolutionary interactions commonly occur in spatially and temporally heterogeneous environments, it is important to know what patterns we might expect to find, and what consequences such heterogeneity might have for coevolutionary trajectories. The questions of scale, both relative and absolute, that considerations of migration and gene flow in hosts and pathogens imply, have enormous implications for the development of coevolving associations. These implications range from whether or not contact between a host and pathogen species will ultimately lead to the establishment of a long-term interaction through to questions of the geographic scale over which associations evolve.

Furthermore, given that much of the earlier theory on coevolutionary interactions in general, and host-pathogen associations in particular, has focused on a nonspatial view of the world (single-population models: Mode 1958; Person 1966; Leonard 1977) or has made unrealistic assumptions (Leonard 1997), it is also of importance to assess the ways in which a more explicit consideration of the impacts of spatial structure may alter expectations (Frank 1991; Thrall and Antonovics 1995; Gandon et al. 1996). From this, we can then determine whether observational and experimental data from real-world systems better match a spatial or nonspatial perspective.

To understand how, and at what spatial scale, host and pathogen associations evolve in response to each other, we must first understand the demographic framework of the interaction—its fluctuations and the spatial and temporal scale at which such dynamics occur. For many host-pathogen systems, these dynamics may be violent, leading to frequent extinctions, recolonization, genetic drift, and migration—all factors that have immediate consequences for genetic structure and hence real coevolutionary change (Burdon 1992). In other systems, such fluctuations are less apparent, but even there, marked changes may occur over time intervals that most evolutionary biologists would regard as luxuriously rapid. In order to illustrate this numerical dynamism in host-pathogen systems and its temporal and spatial unpredictability, we advance here a series of simple predictions of the likely demographic and genetic behavior of pathogen and host populations within a metapopulation compared with that expected from classical single-population models. We evaluate these predictions by drawing on results coming from studies of four separate extensive investigations of the interactions occurring within and among multiple host and pathogen populations of *Linum marginale–Melampsora lini*, *Silene alba–Ustilago violacea*, *Filipendula ulmaria–Triphragmium ulmariae*, and *Valeriana salina–Uromyces valerianae*. The host-pathogen systems represented in these interactions differ substantially in many aspects of their ecology (table 1; fig. 1), thereby allowing us to draw out some general patterns (although we recognize that these examples do not cover the full range of possible host-pathogen associations). From this, we progress to a consideration of the longer-term consequences of these patterns for the development of coevolutionary associations between host plants and their pathogens.

The Dynamic Nature of Interactions: Demographic Expectations and Evidence

Knowledge of demographic change in pathogen or host populations gives no direct assessment of coevolutionary patterns. However, following such changes provides a measure of the frequency of those demographic events and states—precipitous drops in population size, small population sizes, extinctions—that provide mechanisms whereby genetic change through drift, migration, and selection may be rapidly expressed. It is these genetic changes that are the building blocks of coevolution in which we are ultimately interested.

Studies of individual populations can provide detailed pictures of the fitness consequences of given levels of pathogen damage (Augspurger and Kelly 1984; Paul and Ayres 1986; Jarosz and Burdon 1992). However, from an evolutionary point of view, restriction of studies to such narrow spatial scales carry implicit assumptions of permanence of associations and a lack of extinction. In contrast, by following pathogen behavior in multiple populations within a single regional area, comparisons can easily be drawn between epidemiological patterns within and among demes, and hence an assessment can be made of their fit to the expectations of single-population versus metapopulation models. Thus, if dynamics and patterns

Table 1: Life-history features of four host-pathogen associations

Feature	*Filipendula ulmaria–Triphragmium ulmariae*	*Linum marginale–Melampsora lini*	*Silene alba–Ustilago violacea*	*Valeriana salina–Uromyces valerianae*
Host:				
Plant type	Herbaceous perennial	Herbaceous perennial	Herbaceous biennial	Herbaceous perennial
Dispersal	Water borne	Shaking	Shaking	Wind (pappus)
Pathogen:				
Type	Rust (nonsystemic)	Rust (nonsystemic)	Floral smut (systemic)	Rust (nonsystemic)
Dispersal	Wind/water	Wind	Insect vector	Wind
Dynamics	Epidemic (multiple cycles/year)	Epidemic (multiple cycles/year)	Endemic (one or two cycles/year)	Epidemic (multiple cycles/year)
Association:				
Relative dispersal	Host $\leq$ pathogen	Host $\ll$ pathogen	Host $\cong$ pathogen	Host $\leq$ pathogen
Length of association	Native	Native	Introduced	Native
Information available:				
Dynamics	Pathogen only	Pathogen and host (limited)	Pathogen and host	Pathogen only
Genetics	None	Extensive both pathogen and host	None	None
Number of populations	130+	20+	Several hundred	30
Years of data	6	12	11	13
References	Burdon et al. 1995	Burdon and Jarosz 1991; Burdon 1997	Antonovics et al. 1994; Alexander et al. 1996	Ericson et al. 1999

of disease are spatially and temporally synchronous among patches, then the system clearly approximates a single large population; if at the other extreme they are completely unconnected, then small isolated populations may be the rule. In either of these cases, a single-population model framework for coevolution may indeed be appropriate (table 2). However, a major overarching expectation for host-pathogen metapopulation dynamics is that patterns of disease prevalence will tend to be simultaneously both spatially and temporally asynchronous, although the degree to which this occurs will be at least partially a function of distance. Bearing these points in mind, it is possible to make the following set of predictions regarding the interaction of host and pathogen demes in a metapopulation framework.

Prediction 1: Patterns of Disease Prevalence Will Be Spatially and Temporally Asynchronous

The importance of spatial structure in the dynamics of natural host-pathogen systems is exemplified by long-term studies of the natural host-pathogen systems described in table 1. While all these studies incorporate multiple populations and/or time series of data, the linear roadside *Silene-Ustilago* interaction in Virginia (see Alexander et al. 1996 for an overview and references) provides a particularly clear picture of dynamic change in both host and pathogen numbers within and among individual populations through time. In any given year, sites can be healthy and occupied, diseased and occupied, or unoccupied, while through time all transitions are possible. Some host and/or pathogen populations become extinct, some sites become newly colonized, while in yet others, populations simply grow or shrink in size (fig. 2).

At the level of the individual population there is significant turnover, as shown by estimates of colonization and extinction rates over a 4-yr period (table 3). However, despite this frequent occurrence of local extinctions, long-term averages of colonization and extinction rates suggest that these processes are roughly in balance across the metapopulation as a whole (table 3; Antonovics et al. 1994). This indicates that disease persistence in this system is likely to be dependent on the ability of the pathogen to disperse among host populations and on the ability of the host to colonize vacant sites—a point further supported by experimental and theoretical studies showing that long-term persistence within single populations is unlikely (Thrall and Jarosz 1994*a*, 1994*b*).

Results from long-term studies of the *Valeriana-Uromyces* and *Filipendula-Triphragmium* associations (figs. 3 and 4, respectively) also show marked fluctuations in local pathogen populations such that extinction and re-

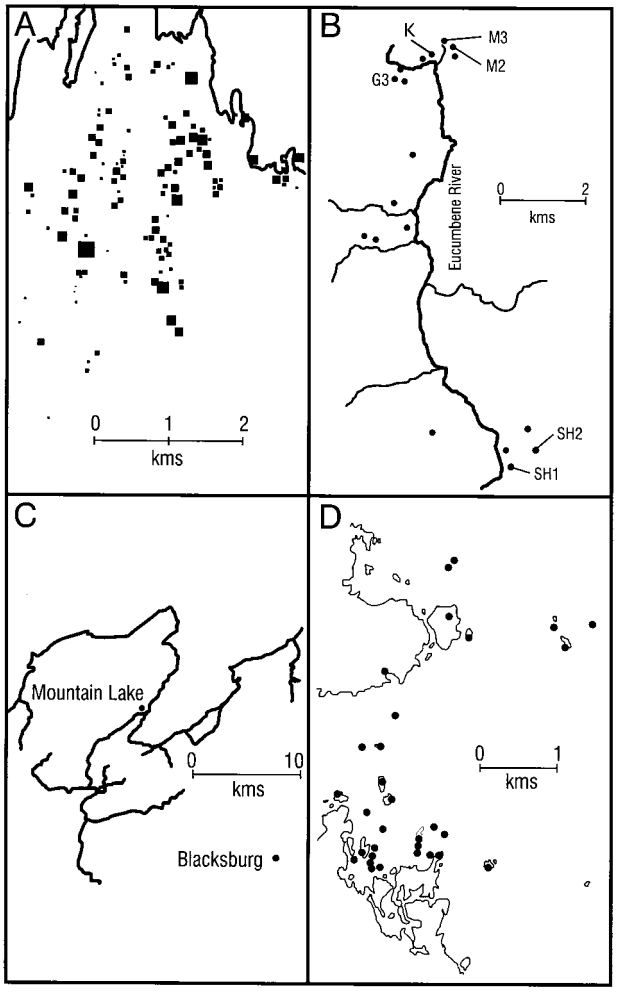

Figure 1: Maps of the spatial distribution of (*A*) *Filipendula ulmaria–Triphragmium ulmariae*, (*B*) *Linum marginale–Melampsora lini*, (*C*) *Silene alba–Ustilago violacea*, and (*D*) *Valeriana salina–Uromyces valerianae* host-pathogen metapopulations. *A*, *D*, Distribution of populations in two archipelagoes of islands in Sweden; *B*, two-dimensional distribution of populations on the Kiandra Plain, New South Wales; *C*, linear system of roads along which censuses are carried out in Virginia, U.S.A, where sites are defined as 40-m segments of roadside.

colonization again occur at significant levels. Moreover, when the temporal dynamics of disease in individual *Valeriana* populations in the archipelago are compared, it is clear that these patterns are generally asynchronous, with populations experiencing disease epidemics and extinctions at very different times. However, this asynchrony occurred against a backdrop of a general tendency for increasing similarity of pathogen dynamics with increasing population proximity. Indeed, over the 13 yr of the study, there were even times when all populations within the archipelago were more or less in synchrony (most likely indicating larger-scale environmental influences).

Despite major differences in important life-history attributes of these host-pathogen systems (table 1), all these interactions are characterized by the contrasting features of high fluctuations in disease levels within individual populations and a relative constancy of disease prevalence on a regional scale (figs. 2–4). Clearly, persistence of disease in these systems is dependent on the ability of the pathogen to disperse to new host populations.

Overall, these well-studied host-pathogen interactions highlight a general pattern, where, regardless of the temporal nature of the disease dynamics (endemic vs. epidemic), local colonizations and extinctions play a significant role in the dynamics of the system. This has enormous implications for the most likely spatial scale at which coevolutionary interactions will develop. If local patches are unconnected, then coevolution between host and pathogen is simply not possible because the pathogen in each interaction deme would ultimately be lost. Equally, if systems are completely connected, then all populations would be expected to show general synchrony in disease dynamics and presence/absence. Neither of these scenarios fit with observed patterns. Rather, these census data lend strong support to the notion that it is the regional disposition of hosts and pathogens in multiple semi-independent populations that provides the basic framework that allows species to continue to interact and coevolve. Our expectation therefore is that colonization and extinction processes will play a major role in the ecological and evolutionary dynamics of host-pathogen interactions.

A particularly important potential consequence of asynchrony of individual demes is that the intensity of selection may differ markedly between neighboring host and pathogen populations. The degree to which this occurs is likely to depend on specific features of host and pathogen life history (e.g., dispersal ability, whether infection is localized vs. systemic, host longevity) and on the relative spatial scales at which hosts and pathogens interact (e.g., ranging from soil host-pathogen interactions to vector-mediated disease dispersal through to aerially dispersed pathogens; Thrall and Burdon 1997, 1999). However, together, these forces are predicted to have a major impact on the type of resistance and virulence structures that coevolve in nature (i.e., quantitative vs. gene-for-gene; see Thrall and Burdon 1997; and "Interactions of Host and Pathogen: Longer-Term Consequences").

Prediction 2: The Amplitude of Pathogen Population Fluctuations Will Vary between Host Populations

For aerially dispersed rusts that form local lesions and often have a large number of reproductive cycles per host growing season, the normal sequence of within-season epidemic buildup eventually comes to an end as the physical

Table 2: Expected changes in pathogen virulence and host resistance as a function of the spatial scale at which hosts and pathogens interact

	Spatial structure		
Expectation	Single large population	Partially connected patches	Isolated local patches
Pathogen virulence	Initial virulence structure maintained through time; frequent between-population movement overwhelms local extinction events.	Apparently chaotic changes in local pathogen populations; both stochastic extinctions and relatively frequent migration events occur.	In most cases, one pathogen type will come to predominate in local patches because of the overwhelming importance of stochastic extinctions.
Host resistance	No change in host resistance structure; all patches are predicted to track each other in unison because of continual recolonization by all host and pathogen types; coevolutionary dynamics will be similar at both local and regional scales.	Coevolutionary dynamics not predictable in single patches but will be present at larger spatial scales; any directional change will be slow relative to more isolated situations since some genetic migration of host and pathogen will occur.	Directional changes in host resistance structure; each population is predicted to follow a different trajectory depending on which pathogen types come to predominate; fits coevolutionary expectations from classical single-population models.

Note: Changes in spatial scale are presumed to be determined both by physical structure (e.g., average distance between patches) and life history (e.g., dispersal mode).

environment becomes unfavorable and host numbers (or susceptible host tissue) decline to critically low levels. Figures 3 and 4 clearly show not only that pathogen populations are temporally and spatially asynchronous, but that within particular years the severity of epidemics varies considerably among populations, while across years the recovery of pathogen populations is unpredictable. As a consequence, rapid and massive declines in pathogen population size may occur, generating possibilities of genetic drift among the survivors, total extinction, and/or marked effects of migration/recolonization (Burdon 1992). However, we note that both the tendency to exhibit cyclical dynamics and the severity of such fluctuations are likely to be a function of pathogen life history (Thrall and Burdon 1999). For example, in the *Silene-Ustilago* system, the pathogen is systemic and typically has only one to two cycles per growing season; thus changes in population size are much slower than would be expected for aerially dispersed rusts.

In the context of paired associations in which one partner is dependent more or less exclusively on the other for survival (e.g., a pathogen and its host), these factors may rapidly lead to shifts in the direction of selective pressures exerted by pathogens on the resistance structure of individual host populations—shifts that are not directly related to the current structure of those host populations. The consequences of these changes for the spatial scale of coevolution is discussed in "Prediction 4."

Prediction 3: Disease Levels in Neighboring Host Populations Will Affect the Probability of Disease

As demonstrated abundantly by data from natural systems, even over relatively short distances, spatially separated populations often exhibit a considerable degree of asynchrony. At the same time, colonization of new host populations by pathogens clearly plays a significant role in determining dynamics and long-term disease persistence. Taken together, these observations suggest that gene flow and migration patterns will be a function of distances between neighboring populations. Data from both the *Silene-Ustilago* interaction as well as the *Filipendula-Triphragmium* system show that the probability of colonization by the pathogen is highly distance dependent (Antonovics et al. 1994; Burdon et al. 1995), with most new colonization events occurring within 160 m for *Ustilago*, and within 500 m for *Triphragmium*. (It is tempting here to speculate that these differences in colonization distance reflect the basic life-history differences in transmission mode that occur between *Ustilago* and *Triphragmium* [see table 1].)

One consequence of the local nature of among-population disease movement is that we should expect a degree of similarity in local population behavior analogous to neighborhood effects observed in plants. Thus near-neighboring populations, while still showing some asynchrony, should show higher levels of correlated pathogen dynamics (and for that matter, genetic structure) than more distantly placed ones (Burdon et al. 1990). Evidence for this can be

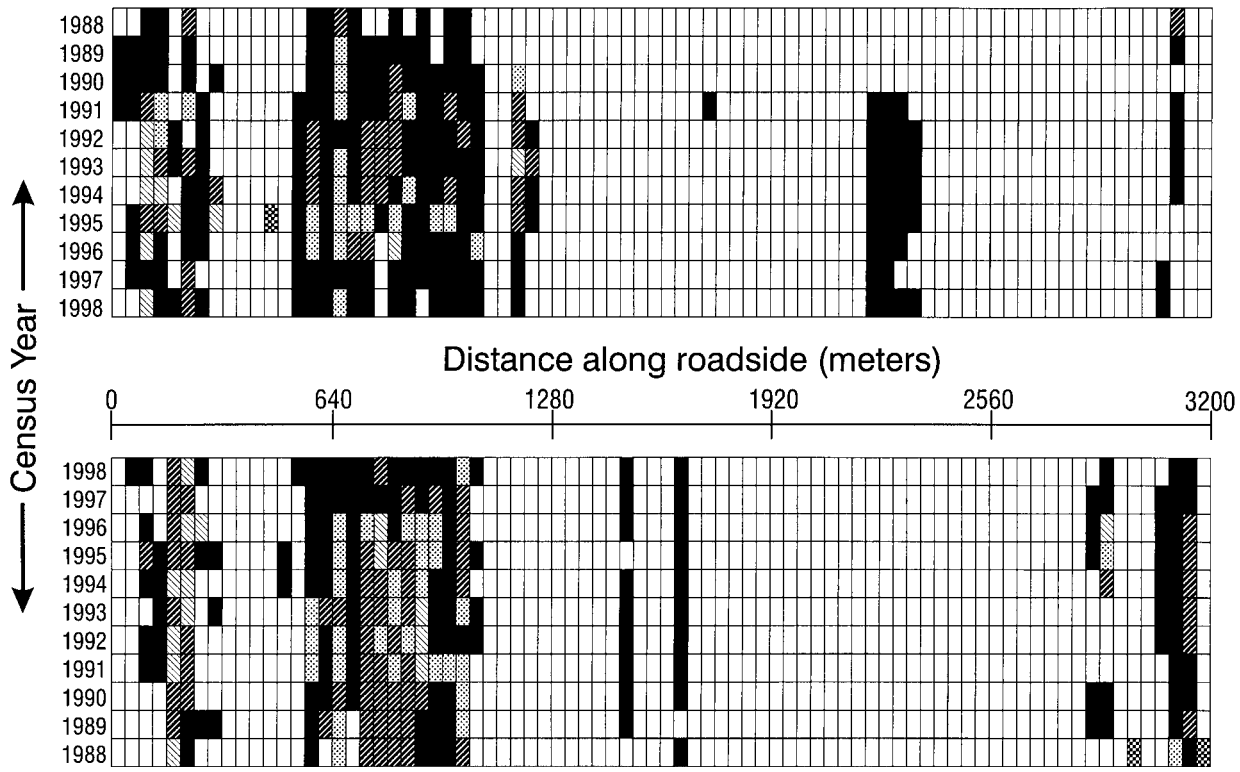

Figure 2: Spatial and temporal patterns in the distribution of populations of *Silene alba* and the incidence of the floral smut *Ustilago violacea* along a 2-mile section of roadside in Virginia, U.S.A. The two graphs show data for opposite sides of the road, and each square represents a 40-m segment. Open squares = unoccupied sites; black squares = sites with plants but no disease; lightly stippled squares = sites with 1%–10% disease prevalence; lightly cross-hatched squares = 11%–30% disease prevalence; heavily cross-hatched squares = 31%–70% prevalence; heavily stippled squares = 90%–100% disease prevalence.

gleaned from the *Filipendula-Triphragmium* system, where in two of four years, populations whose nearest neighbor was diseased had a higher probability of being infected than ones where the nearest neighbor was disease free (Burdon et al. 1995).

At the demographic level, data from the natural host-pathogen interactions discussed above provide strong corroborative support for the geographic mosaic theory of coevolution (Thompson 1999, in this issue). The asynchrony of pathogen population dynamics, relationship between population proximity and the probability of disease occurrence, and frequent reductions in population size to critically low levels (and even local extinction) together provide solid evidence for demographic change and fluctuation. When imposed on the genetic structure of host and pathogen, this dictates the geographic scale of coevolutionary accommodation that occurs within the broad framework set by the interaction of host and pathogen life-history characters.

The Dynamic Nature of Interactions: Genetic Expectations and Evidence

The essential messages from the previous discussion of host-pathogen dynamics in a range of real-world systems are that situations in which ecological and evolutionary interactions are played out in spatial arenas are likely to be the rule, rather than the exception, and therefore local drift, colonization, extinction, and migration will also be significant. In this section, we therefore apply these messages to a consideration of the genetic structure of host and pathogen populations. This illustrates the complexity of these interactions across a range of spatial scales and further develops the notion of coevolution occurring among the populations present in a regional area. We conclude by considering the long-term implications of coevolutionary patterns, their scale, and the all-pervading complexities introduced by differences in life-history characters.

Theoretical studies have shown that disease resistance

Table 3: Host and pathogen colonization and extinction rates calculated from the census of roadside populations of *Silene alba* and *Ustilago violacea*

	1989–1990	1990–1991	1991–1992	1992–1993	Mean
Host:					
Colonization	.20	.29	.15	.17	.20
Extinction	.20	.14	.21	.22	.19
Pathogen:					
Colonization	.45	.25	.25	.23	.30
Extinction	.27	.23	.36	.29	.29

Note: Sites are defined as 40-m linear segments along roadsides (Antonovics et al. 1994; Thrall and Antonovics 1995).

is no different from other genetically based characters in that variation is much more likely to persist in a spatially heterogeneous environment than in a nonspatial interaction (Thrall and Antonovics 1995; Antonovics et al. 1997). However, corroborative empirical data assessing any aspect of the genetic structure of host-pathogen associations are scarce. Possibly this paucity of data results from perceived difficulties associated with such studies. Indeed, as Price pointed out some time ago, pathogens are insidious creatures (Price 1980), and it is in the "hidden" genetic effects that this is particularly the case. Despite this, detailed long-term studies of the *Linum marginale–Melampsora lini* association have provided insight into at least one type of interaction (table 1).

Prediction 4

In line with the numerical fluctuations predicted to occur in the pathogen, and the potential consequences of rapid, substantial crashes in population size ("Prediction 3"), in host-pathogen systems dominated by gene-for-gene interactions, **the virulence and resistance structures of pathogen and host populations, respectively, are likely to show spatial and temporal diversity**. This then also argues strongly for the importance of considering both genetic and numerical dynamics simultaneously.

Host Populations. The general idea of spatial diversity in host populations at a geographic scale has been documented for some time, with many studies of patterns of resistance to rusts and mildews in wild relatives of cereals (*Avena*, *Hordeum*, *Triticum*) in the Fertile Crescent of the Middle East showing differences in the frequency of resistances between areas (Dinoor 1970; Fischbeck et al. 1976; Nevo et al. 1984). The geographic scale of these broad differences is such that more than one climatic and epidemiological zone is covered with areas of high coevolutionary activity (Thompson's "hot spots"; Thompson 1999, in this issue) contrasting with others in which pathogen occurrence is more unpredictable and ephemeral, and hence genetic interplay between the partners is more limited. In Israel, coevolutionary hot spots for interactions between *Avena fatua* and *Puccinia coronata* and between *Hordeum spontaneum* and *Rhynchosporium secalis* in the northern Galilee and Golan Heights area are marked by a high diversity of disease resistance. This compares with the coevolutionary cold spot of the Negev Desert, where resistance is very uncommon (Dinoor 1970).

Over the past decade or so, evidence has been accumulating to indicate that similar discontinuities in resistance may occur abruptly between populations that occur within just a few hundred meters of each other. In some instances, these patterns are linked to obvious environmental differences that have a direct impact on the frequency and severity of pathogen epidemics (e.g., differences in shade, moisture, and soil nutrient status affecting *Erysiphe cichoracearum* on *Phlox* sp. [Jarosz 1984] and *R. secalis* on *Hordeum leporinum* [Jarosz and Burdon 1988]). In other cases, genetic and environmental factors may interact (e.g., different genetically based ecotypes of *L. marginale*), while in yet others, no obvious environmental differences are apparent, with differences in resistance between closely adjacent populations being manifest in the number, frequency, and identity of different resistance phenotypes.

The most detailed examples of assessments of the genetic structure of host resistance in multiple populations are found in an ongoing study of *L. marginale* inhabiting the Kiandra Plain in southern Australia. There, host populations just a few hundred meters apart show both similarities and differences. When challenged with either local or more distantly derived pathogen isolates, pairs of adjacent populations varied widely in their resistance response to individual pathotypes (fig. 5). However, in general, a greater divergence in resistance structure was apparent among groups of populations from different parts of the Kiandra region (M2, M3 vs. SH1, SH2; see fig. 1) than within either group. The greater similarity of the resistance structure of neighboring populations provides at least circumstantial evidence for varying levels of

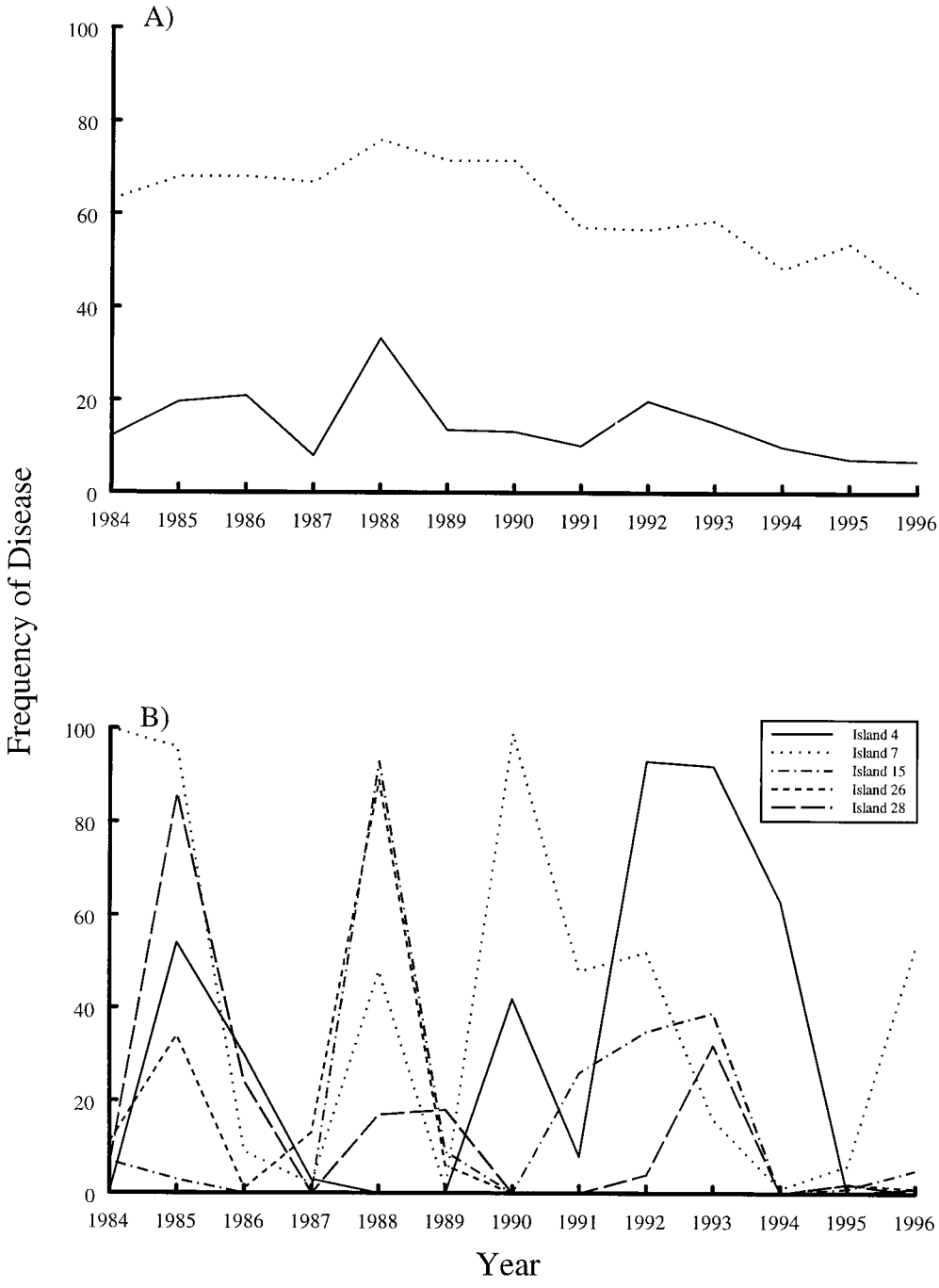

Figure 3: Patterns in the epidemiology of the rust fungus *Uromyces valerianae* occurring on island populations of the host plant *Valeriana salina* in the Bothnian Gulf, central Sweden (Ericson et al. 1999). *A*, Mean incidence (presence/absence; *dotted line*) and prevalence of disease (percentage of plants infected; *solid line*) across the 30 islands of the metapopulation as a whole. *B*, Year-to-year fluctuations in the prevalence of individuals infected with *U. valerianae* in five representative populations occurring on five islands within a 1-km radius of each other.

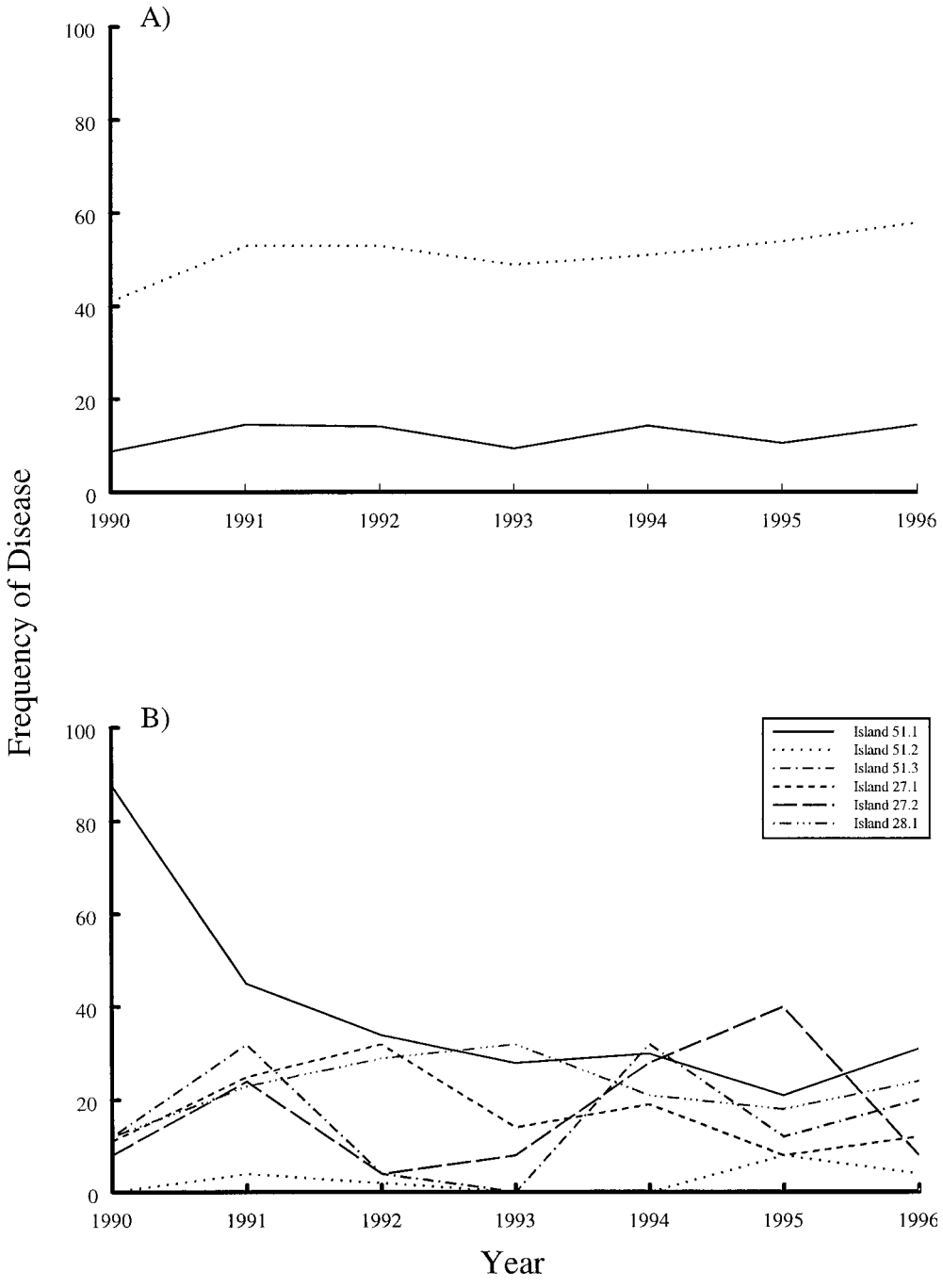

Figure 4: Patterns in the epidemiology of the rust fungus *Triphragmium ulmariae* occurring on island populations of the host plant *Filipendula ulmaria* in the Bothnian Gulf, northern Sweden (L. Ericson and J. J. Burdon, unpublished data). *A*, Mean incidence (presence/absence; *dotted line*) and prevalence of disease (percentage of plants infected; *solid line*) across the 130 demes of the metapopulation as a whole. *B*, Year-to-year fluctuations in the prevalence of individuals infected with *T. ulmariae* in six representative populations occurring on three islands within 1 km of each other.

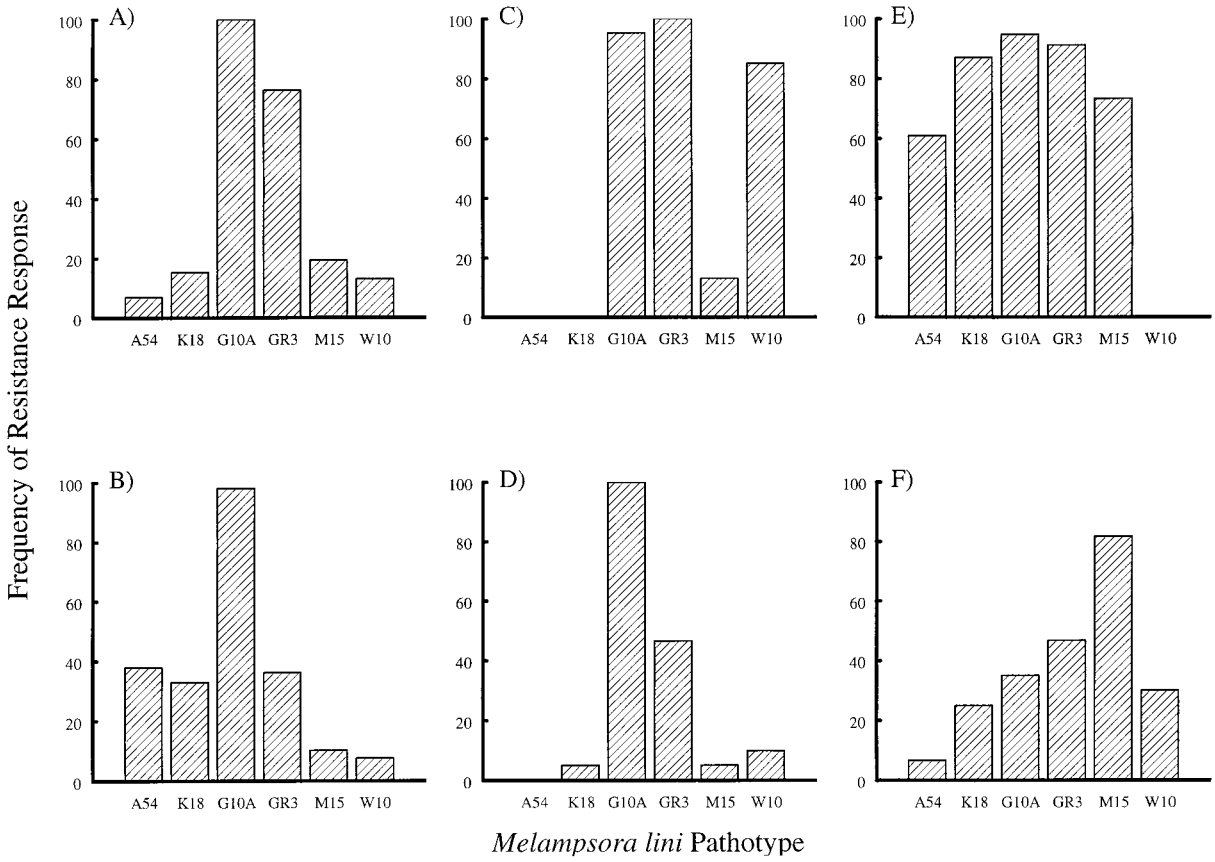

Figure 5: Patterns of distribution of resistance shown by six demes of a metapopulation of *Linum marginale* ($n = 20$ per population) to six different pathotypes of *Melampsora lini* collected both locally (A54, K18) and more distantly (G10A, GR3, M15, W10). *Linum* populations are grouped in pairs according to proximity (see fig. 1). *A*, Kiandra; *B*, G3; *C*, M2; *D*, M3; *E*, SH1; *F*, SH2.

connectedness among neighboring demes in the region as a whole.

Pathogen Populations. Information on spatial and temporal changes in the structure of pathogen populations is even more limited than equivalent data for host populations. Some evidence is available that compares differences in vegetative compatibility alleles (e.g., *Cryphonectria parasitica*; Anagnostakis and Kranz 1987), RNA sequences (e.g., kennedya yellow mosaic tymovirus; Skotnicki et al. 1996), and even pathogenicity (e.g., *Erysiphe fischeri*; Bevan et al. 1993). However, these studies are based on such limited numbers of distantly separated populations that it is impossible to obtain any real concept of the extent of coevolutionary interaction. In contrast, a comparison of the distribution of diversity in the rust pathogens *Puccinia coronata* and *Puccinia graminis* attacking *Avena* species in New South Wales, Australia, showed clear evidence for broad geographic regions of high and low coevolutionary activity. In this example, both host and pathogen diversity was assessed with distinct differences being apparent between a southern cold spot and a northern region of high coevolutionary interaction (Burdon et al. 1983; Oates et al. 1983).

For more detailed analysis of multiple populations where available evidence indicates we are dealing with coevolutionary patterns within a single metapopulation, we must again turn to the *L. marginale–M. lini* association. Detailed assessments of the structure of *M. lini* populations occurring in two *L. marginale* populations within 300 m of each other paint a picture of variable pathogen populations typically dominated by just a few pathotypes, although many others may be present in any given growing season. In one of the pathogen demes, the identity of the dominant pathotype fluctuates from year to year, while in the other population a single pathotype has remained dominant over more than 10 yr (fig. 6; J. J. Burdon, unpublished data). The link between demographic patterns and genetic consequences in pathogen demes, and the need to consider these simultaneously to develop an under-

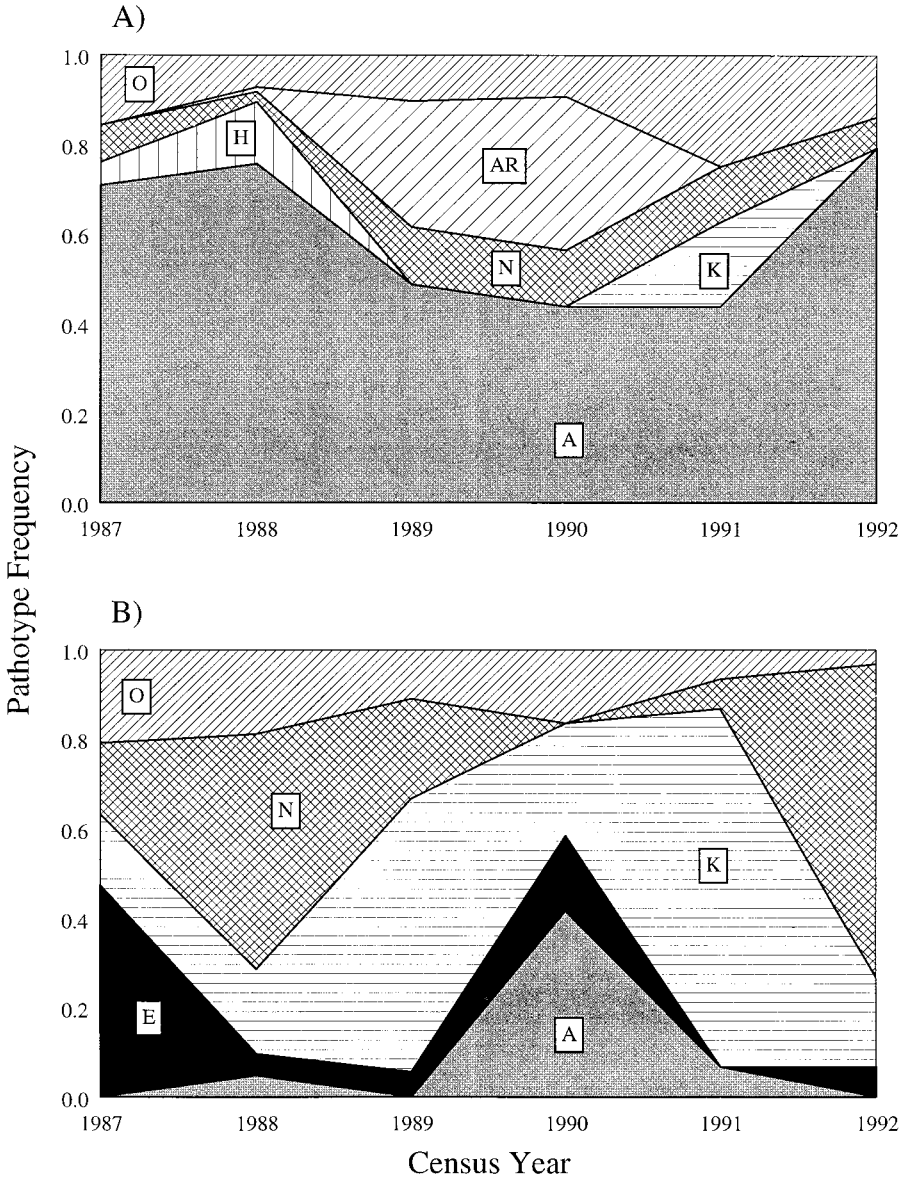

Figure 6: Variation in the structure of two *Melampsora lini* populations occurring 300 m apart on the Kiandra Plain, New South Wales, Australia

standing of evolutionary trajectories in host-pathogen associations (May and Anderson 1983; Antonovics 1994), is particularly evident in these populations. Thus the intermittent presence of some pathotypes reflects the almost inevitable consequences of temporary loss of particular genotypes through drift in an association in which the pathogen undergoes abrupt collapses in population size. Similarly, their reappearance in subsequent years is suggestive of immigration from other populations in the local vicinity, while the dominance of different pathotypes in different populations in the same year provides further evidence of the asynchrony that increases the general inertia countering loss of particular genotypes from the metapopulation as a whole. At the other end of the dispersal scale, the sudden appearance, rapid rise, and equally sudden disappearance of the unique pathotype AR at Kiandra proves strong evidence of occasional longer-distance migration.

In line with predictions of the geographic mosaic theory of coevolution (Thompson 1994*a*, 1994*b*, 1999, in this issue), diversity in host resistance and pathogen virulence structures clearly occurs over a variety of spatial and tem-

poral scales ranging from broad geographic patterns down to sharp differences among adjacent populations that might reasonably be expected to exchange genes. At broad geographic scales, differences in diversity may broadly equate with past and potentially present coevolutionary activity that frequently results from physical environmental patterns that favor (hot spots) or disadvantage (cold spots) pathogen development.

At the more local scale represented by a single metapopulation, the available evidence provides strong support for the concept of a fluctuating mosaic of host and pathogen genotypes (Frank 1997) generated by a complex interaction between colonization-extinction processes and asynchronous dynamics. It has been suggested (Wright 1940, 1943) that in such situations, chance effects caused by drift, extinction, recolonization, or migration in individual, semi-isolated demes will permit characters to move from one adaptive state to another through intermediate states of lower fitness, and in doing so should ensure that evolution is more rapid than in single all-embracing populations. This idea has gained support recently from a series of spatially explicit simulations of the *Silene-Ustilago* system (Antonovics et al. 1997). Moreover, because such populations often undergo rapid increases and decreases in size, conditions fluctuate between expanding populations in which new, advantageous genes may be rapidly incorporated (here, deleterious genes have virtually no chance of fixing) and shrinking populations in which deleterious mutants have an enhanced chance of establishment (Otto and Whitlock 1997; Phillips 1997). Clearly then, studies focused solely on only one such deme could easily be misinterpreted without the context of patterns in adjacent populations.

Even within this constantly shifting mosaic, though, it may be possible to identify warmer and cooler hot spots of coevolutionary interplay. Thus, depending on a range of factors including the rate of gene flow and the extent of genetic variation available in a neighborhood area, local host populations founded by a single susceptible individual may be little more than passive receptors of pathogen attack. However, populations at the center of local interspecific (Le Brun et al. 1992; Whitham et al. 1994) or intraspecific (U. Carlsson-Granér, J. J. Burdon, and P. H. Thrall, unpublished manuscript) hybridization zones may provide an evolutionary "testing ground" for novel combinations of resistance or pathogenicity.

Prediction 5

Given the diversity of patterns of resistance and virulence in individual populations and the occurrence of drift, extinction, and migration, **the virulence and resistance structures of individual pathogen and host populations, respectively, will not necessarily be correlated**.

Change in the genetic structure of host populations in response to pathogen pressure is the rationale that lies behind most disease-resistance breeding programs in agriculture. As a pathogen evolves to overcome current varieties, new varieties that incorporate novel resistances are deployed to thwart further pathogen development. In turn, these resistances act as a selective pressure on the pathogen, "guiding" the development of a pattern in which the pathogen tracks (human-induced) changes in the host population (Wolfe 1984). Such agricultural systems are clearly highly artificial but have a parallel in early models of the coevolution of host-pathogen associations in which frequency-dependent interactions without mutation, drift, or migration lead to a predictable tracking of the genetic structure of individual host populations by that of the pathogen (Person 1966).

Empirical evidence to date concerning the potential interplay of the genetic structure of host and pathogen associations is very limited, although host genetic factors clearly play a role in determining the numerical dynamics of the pathogen in the *Silene-Ustilago* system (Thrall and Jarosz 1994*a*, 1994*b*) and the incidence and severity of the pathogen *Synchytrium decipiens* attacking the annual legume *Amphicarpaea bracteata* (Parker 1985). But again, with the exception of the *Linum-Melampsora* system, insufficient information is available to permit direct comparisons to be drawn between the resistance structure of host populations and the pathotypic structure of associated pathogen demes. At one long-term site used in the *Linum-Melampsora* study, the genetic structure of both host and pathogen was monitored over a number of years, including one in which there was a major disease outbreak. At the time of the epidemic, the host population was composed of a large number of resistance phenotypes, all of which were susceptible to the dominant pathotype present but were differentially resistant to other pathotypes that together constituted 50% of the population. Although the pathogen epidemic resulted in the death of 85% of the host population (Burdon and Thompson 1995; J. J. Burdon, unpublished data) and substantial changes in the frequency of four of five common resistance types occurred, none of these changes were related to the structure of the co-occurring pathogen population (or any other obvious traits). Indeed, the pattern of change often ran counter to that which would have been expected under a frequency-dependent host-pathogen model. Thus, a common host phenotype that was resistant to 40% of the pathogen population declined more than 10-fold across the epidemic period, while two other host lines that were susceptible to all pathotypes present increased between four-

and sevenfold in frequency (fig. 7; Burdon and Thompson 1995; J. J. Burdon, unpublished data).

Clearly, at the level of the individual interaction deme, while the structure of pathogen and host populations must be broadly adapted genetically (i.e., only pathotypes that are capable of infecting at least some host individuals will be present), any tighter relationship is likely to be heavily affected by a wide range of ecological and life-history factors. Thus the prevalence of particular pathogen lines will depend on a range of factors, including the frequency of migration from, and the resistance structure of, adjacent host populations. On the host side of the equation, linkage between resistance genes and other traits in the host's genome may provide a very powerful brake to adaptive change (Hedrick 1980), as has been previously argued to explain similar nonadaptive changes in resistance in the *Amphicarpaea bracteata–Synchytrium decipiens* association (Parker 1991).

If a coevolutionary association between the virulence and resistance structures of individual populations is unlikely in many host-pathogen interactions, what pattern might be expected at a broader spatial scale? Simulation modeling suggests that such interactions may for all intents and purposes be frequency dependent when viewed in terms of the occurrence of host resistance genes and pathogen virulence across an entire metapopulation (Thrall and Burdon 1999). Empirical evidence is very limited. However, in a study of the occurrence of the rust fungus *Puccinia chondrillina* in 16 clonal populations of its host *Chondrilla juncea*, the first or second most common host clone was infected in all populations, with the most common clone being the only clone infected in 10 of those demes (Chaboudez and Burdon 1995). While the coincidence of common clone and infection is not particularly remarkable on an individual population basis, the repeated nature of this pattern in population after population supports the hypothesis that the pathogen may be imposing frequency-dependent selection on host genotypes across a broader geographic scale.

Interactions of Host and Pathogen: Longer-Term Consequences

Spatial structuring at the local, regional, and continental scale has enormous implications for the coevolutionary dynamics of host-pathogen associations. However, as we have already seen in comparisons of the *Silene-Ustilago* interaction with those involving *Linum*, *Filipendula*, and *Valeriana* with their rusts, the spatial scale at which hosts and pathogens coevolve may be magnified or ameliorated by life-history characters as apparently simple as whether or not the pathogen is vector transmitted.

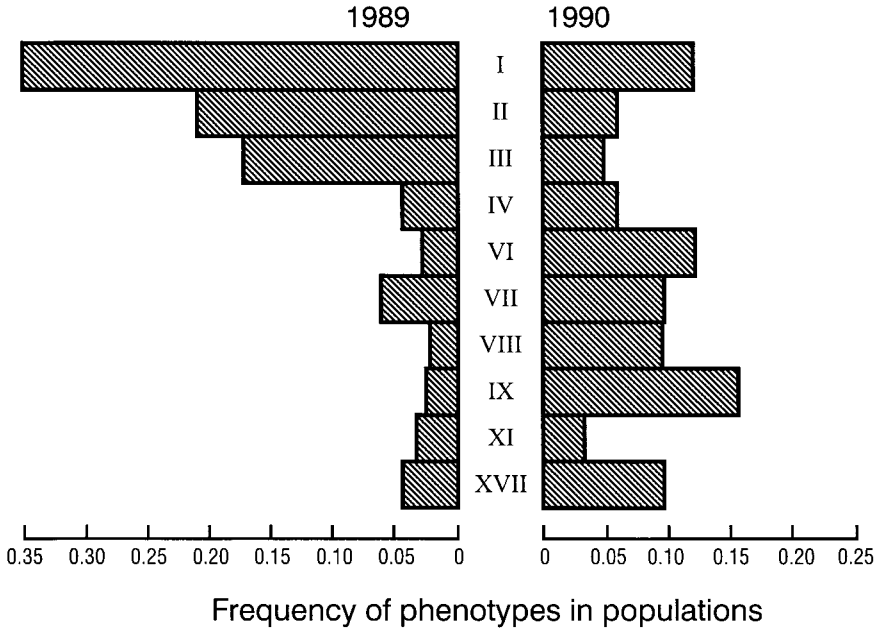

Figure 7: Change in the frequency of 10 resistance phenotypes in a single population of *Linum marginale* following an epidemic of the pathogen *Melampsora lini*. *1989*, Population structure in the epidemic year; *1990*, population structure in immediate following year (data from Burdon and Thompson 1995).

Interactions between Life-History Character and Spatial Subdivision

The range of life-history characters that potentially may affect the dynamics of host-pathogen associations is enormous and effectively permeates virtually every interaction. These may be features of the host or the pathogen, or they may result from an interaction of the two; they may be obvious (e.g., transmission modes) or subtle (e.g., ephemerality of susceptible tissues) and are likely to particularly reflect features that determine disease transmission rates, dispersal distances, survival capabilities, host range, and mechanisms of genetic recombination. Ultimately, these different life-history characters all influence encounter rates and contact times between host and pathogen genotypes (=transmission opportunities). In turn, this will further shape the spatial scale of interaction metapopulations and lead to differences in evolutionary trajectories that may differ not only between different associations but also between the same association in different metapopulations. As noted later, differences between two adjoining *Linum* metapopulations are substantially affected by differences in host mating system and the yearly timing of growth of both host and pathogen (Burdon et al. 1999).

A recent comparative study of life-history features associated with sexually transmitted diseases of animals showed the importance of such characters in molding the coevolutionary association between host and pathogen (Lockhart et al. 1996). A similar comprehensive comparison is yet to be done for plant pathogens. However, preliminary steps in this direction involving the subdivision of pathogens into "killers," "debilitators," and "castrators" (Burdon 1993), comparison between associations involving systemic diseases of plants with varying degrees of vegetative reproduction (Wennström and Ericson 1992), and comparison between sporulation and infection characteristics in airborne pathogens (Sache and de Vallavielle Pope 1995) all illustrate interesting life-history differences that are likely to have consequences for coevolutionary dynamics.

Thrall and Burdon (1997) have taken this a further step by developing an extensive framework to illustrate three realistic scenarios of simple host and pathogen life-history combinations. These were predicted to have substantial effects on the spatial scale of particular host-pathogen associations, their temporal predictability within given populations, and, through these processes, the long-term evolutionary trajectory of the association. In essence, this recognized the existence of associations in which the scale of pathogen dispersal was likely to be substantially less than that of its host (e.g., soil-borne pathogens such as *Pythium* or *Fusarium* parasitizing a host with aerially dispersed seeds); interactions where dispersal distances of both host and pathogen are comparable (e.g., seed-borne viruses, vector-borne floral smuts—cf. *Silene-Ustilago*); and situations in which the scale of pathogen dispersal far exceeded that of its host (e.g., wind-dispersed rusts—cf. *Linum-Melampsora*). Thus, to the extent that these three scenarios represent increasingly epidemic dynamics, we have predicted an increasing tendency toward resistance being qualitatively based (gene-for-gene). As with all broad-brush approaches, a range of other life-history characters may modify these basic scenarios. Nevertheless, these scenarios further serve to illustrate the importance of spatial scale and the occurrence of multiple demes showing varying degrees of interconnectedness in the longer-term dynamics of hosts and their parasites.

Empirical testing of the causal relationships between, and polarity of, particular life-history attributes and the structure of host and pathogen populations is always going to be very difficult. The accumulation of knowledge from many different systems showing a range of life-history combinations will, over time, lead to the emergence of meaningful correlations between these and particular patterns of host and pathogen dynamics. On the other hand, direct assessments of the effects of life-history attributes are likely to be restricted to two quite distinct situations. The first of these approaches to assessing the interactive effect of life-history attributes and spatial scale on coevolutionary patterns is achieved through comparisons across different regional groupings or metapopulations of the same interaction. In developing the geographic mosaic theory of coevolution, Thompson (1994*a*, 1994*b*) drew attention to the different levels of scale at which interactions could occur. Much of the earlier discussion in this article of dynamic and genetic differences among host and pathogen populations confirms the potential for different evolutionary trajectories occurring at the level of different populations (Hanski and Gilpin 1991; Hastings and Harrison 1994; Harrison and Hastings 1996). Equally, though, viewing coevolution across the entire spatial scale of distribution of a species (Thompson 1997) also emphasizes the possibility that differences in evolutionary trajectories may occur between the different metapopulations that together constitute the species as a whole. If these metapopulations differ in ways other than simple physical separation, then direct comparisons should provide a clearer picture of the consequences of particular life-history character combinations and through this the limits of evolutionary flexibility of the host-pathogen association.

To date, examples of such complementary host-pathogen metapopulations appear to be restricted to a comparison involving the *Linum-Melampsora* association, where populations occurring in the Kiandra Plain region of the Snowy Mountains are part of a metapopulation that is quite distinct in terms of the timing of yearly host and

pathogen development, and the breeding system of the host, to another metapopulation occurring on the drier and warmer Plains. Differences in host outcrossing rates between the two metapopulations are reflected in marked differences in the overall level of resistance, its partitioning within and among populations, the number and distribution of resistance phenotypes in the two areas, and the level of polymorphism for specific virulence factors in the pathogen (Burdon et al. 1999).

The second situation in which the interaction between spatial scale and life-history attributes is likely to be apparent is in the mix of resistance mechanisms hosts adopt and virulence/aggressiveness traits that pathogens evolve. Thus, while some combinations of attributes and environments may favor the development of gene-for-gene host-pathogen interactions, other combinations may favor host resistance–pathogen virulence and aggressiveness patterns that are characterized by the interaction of multiple genes. A very powerful way to explore these possibilities is through the investigation of situations in which one host species is parasitized by more than one pathogen species. Such situations are very common but unfortunately to date have not been exploited in this way. However, the potential of this approach can be seen in a simple comparison of the interactions occurring between the deciduous tree *Populus* sp. and two of its fungal pathogens that possess quite distinct life histories—the leaf rust pathogen *Melampsora* sp. and the stem canker fungus *Hypoxylon* sp. (Burdon et al. 1996). In the *Populus-Melampsora* interaction, race-specific resistance genes and corresponding avirulence genes have been detected in host and pathogen, respectively (Prakash and Thielges 1987; Hsiang and Chastagner 1993). This interaction is one involving an annual host target (leaves) and hence in this deciduous system, one in which the pathogen tends to cycle through massive amplitudes in population size over short periods of time. Because the pathogen cannot survive on this host during the winter season, it is repeatedly forced to reestablish through migration. Under these circumstances, resistance genes that thwart initial entry may provide adequate long-term resistance for the host. In contrast, once the canker fungus *Hypoxylon* gains entry to the trunk of a poplar host, it is protected from environmental vicissitudes, and progress through the tree is primarily determined by characters that are controlled through the combined action of multiple genes (French and Manion 1975).

A particularly intriguing twist to this interaction is the marked change in the genetic basis for resistance that occurs between *Populus* and *Melampsora* populations to the east and west of the Rocky Mountains. The pattern described above with major gene resistance is typical of the interaction occurring in the dry interior of western Canada. West of the Rockies, in contrast, the winter environment is more benign and the pathogen is constantly present. In these areas only multigenic race-nonspecific resistance is known (Hsiang and Chastagner 1993).

Comparisons of this nature, in which at least some features of the life history of at least one player in the association can be held constant, provide powerful clues to the interactive effects of life-history characters and host spatial heterogeneity in the long-term development of coevolutionary trajectories of specific associations.

Role of Models

As shown by the range of long-term studies described in this article, a number of aspects of the ecological and coevolutionary dynamics of host-pathogen systems are amenable to descriptive and experimental approaches. Nevertheless, the spatial nature of coevolutionary interactions also suggests that models, both analytical and computer simulation, must play a significant role if we are to advance our understanding of such processes in nature. For example, we have earlier hypothesized (Thrall and Burdon 1997) that the central role taken by dispersal scale and distance in determining the "metapopulation" nature of host-pathogen associations will itself be a major determinant of whether host resistance and pathogen virulence evolves toward a gene-for-gene system versus a more quantitative structure. While it will clearly be important to relate such ideas to natural systems (e.g., through comparative studies of many different systems), it is equally the case that testing the feasibility of such ideas will be facilitated by investigation of model systems where one can explicitly address how different parameter combinations (e.g., dispersal scale, severity of pathogen effects on host fitness) influence ecological and evolutionary outcomes. Thus, the advantage of simulation models, beyond the ability to incorporate explicitly various spatial structures, is that we are able to conduct experiments that would never be possible in the real world. Such simulation approaches can provide specific hypotheses that are testable in real-world situations.

In recent years, there have been a number of studies of host-pathogen metapopulation dynamics based on simulation models with varying degrees of complexity and biological realism (e.g., Frank 1993; Thrall and Antonovics 1995; Gandon et al. 1996). Thus, Frank (1991, 1993, 1997) explored a series of pseudospatial models that explicitly incorporated host and pathogen variation in resistance and virulence. He concluded that increasing severity of disease epidemics would result in a lower number of virulence factors per pathogen genotype, a higher number of resistance factors per host, and lower overall genetic diversity in both host and pathogen. Gandon et al. (1996) used an explicitly spatial model to investigate how the degree of

correlation between host resistance and pathogen virulence genes at the local scale depends on relative rates of host and pathogen migration. Realistic spatial models centered around the *Silene-Ustilago* interaction (Thrall and Antonovics 1995; Antonovics et al. 1997) have focused primarily on numerical dynamics but have also made specific predictions about correlations between disease presence and levels of resistance (these were later confirmed through field experiments; Thrall and Antonovics 1995). More generally, Antonovics et al. (1997) have shown that conditions for maintenance of resistance polymorphisms and disease persistence are drastically altered in a regional context. Most recently, Thrall and Burdon (1999) have used spatial simulations to investigate how the relative scales of host and pathogen dispersal interact to influence the degree to which dynamics are epidemic, as well as the scale at which there are correlations between host and pathogen genotype frequencies, one of the signatures of coevolution (see discussion above where we suggest that the meaningful scale at which we see coevolutionary patterns is likely to depend on host and pathogen life histories). These model results highlight this possibility as well as making specific predictions about factors that are likely to determine relevant ecological and coevolutionary scales. While some model predictions may be difficult to assess experimentally, clearly such approaches will be invaluable in guiding future empirical studies, as well as focusing on critical issues.

Conclusions

If there is a single overriding message from the long-term studies presented in this article, it is that the numerical and coevolutionary dynamics of host-pathogen interactions cannot be understood on the basis of investigations of single populations. Clearly, local history (e.g., where colonists arrive from, genetic drift) as well as larger-scale colonization and extinction processes play major roles in determining observed patterns of disease prevalence. In general, it is unlikely that expectations based on classical single-population models will be met in the real world. Certainly, in the case of the *Linum-Melampsora* system, where detailed spatial information on the genetic structure of virulence and resistance is available, there is no indication of a tight correspondence between host and pathogen at the within-population level. Theoretical studies also suggest that the spatial scale at which coevolution is likely to occur will depend heavily on specific features of host and pathogen life history, such as dispersal mode, and whether disease dynamics are epidemic or endemic. Understanding the complexities of real-world coevolutionary systems will require integrating computer modeling with long-term empirical studies of multiple populations. The empirical studies highlighted in this article serve to demonstrate that such approaches not only are possible but can be highly instructive.

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