The Evolutionary Genetics of Plant-Pathogen Systems

Understanding the coevolution of hosts and parasites is key to understanding their ecology

Ellen L. Simms

In a host-parasite system the level of genetic variance in resistance and virulence can strongly influence the population dynamics and equilibrium of the interacting species.

The chestnut blight was first noticed in the New York Zoological Gardens in 1904 (Rice et al. 1980); within 50 years the disease had swept across the eastern deciduous forests, leaving 3.6 million hectares of American chestnut trees (Castanea dentata) dead or dying (Anagnostakis 1987). Once an economically, socially, and ecologically important component of the hardwood forests of the eastern United States (Anagnostakis 1987), American chestnuts persist today only as dwindling stump sprouts from rootstocks of these once magnificent trees (Griffin 1992). The loss of mature chestnut trees to the blight fungus, Cryphonectria parasitica, has reduced the carrying capacity of Appalachian forests for wild animals (Griffin 1992) and deprived humans and domesticated animals of an important source of food and income (Rice et al. 1980).

As the chestnut blight pandemic illustrates, infectious diseases can dramatically alter biological communities. However, coevolution between hosts and pathogens is likely to condition the states of traits, such as resistance and virulence, that are important to the host-pathogen interaction. Understanding how pathogens and their hosts coevolve is therefore critical to understanding how this interaction is likely to influence communities. In this article I briefly describe how pathogens may affect biological communities and then examine in more depth our understanding of the evolution of plants and their microbial pathogens.

Population ranges and community diversity. The outcome of competition between pairs of species may depend upon the presence or absence of disease-inducing parasites (Park 1948). In Maine and Nova Scotia, white-tailed deer (Odocoileus virginianus) have replaced moose (Alces alces) as the dominant cervid because deer are tolerant carriers of the meningeal worm, Parelaphostrongylus tenuis, which causes severe neurological damage to other cervids (Anderson 1972). After mosquitoes were introduced to Hawaii in 1826, avian malaria played an important role in the extinction of many Hawaiian land birds (Warner 1968) and significantly restricted the distributions of others (van Riper et al. 1986). Parasites may also hinder repopulation of ancestral ranges or migration into new areas (Price 1980). The meningeal worm may be blocking reintroduction of woodland caribou (Rangifer tarandus caribou) into habitats now occupied by white-tailed deer (Anderson and Prestwood 1979). In another example, the RNA virus that causes rinderpest eliminated certain artiodactyls from such large areas of Africa (May 1983) that lack of hosts led to the extermination of tsetse flies (Glossina) and the sleeping sickness-causing try-

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The terms parasite and pathogen are used interchangeably in this article.
Panama they carry (Stevenson-Hamilton 1957). With sleeping sickness eliminated, humans and domesticated animals invaded these regions, rendering them unavailable to repopulation by the original native artiodactyls (Stiling 1992).

Finally, disease-causing parasites may assume a keystone role, increasing species diversity by undermining the competitive superiority of their host and permitting persistence of an inferior competitor (Burdon and Chilvers 1977). This keystone function may even be important in ecological succession. For example, a soil-borne pathogen causes degradation of beach grass, *Ammophila arenaria*, thereby facilitating replacement of early successional species by later species on coastal foredunes in northern Europe (Van der Putten and Troestra 1990, Van der Putten et al. 1993).

**Population dynamics and classical biological control.** Success stories in the biological control literature offer ample evidence of the ability of parasites to control host population densities (DeBach 1974). A classic example is the use of myxoma virus to control European rabbits (*Oryctolagus cuniculus*) in Australia. This example is particularly valuable because, unlike many biocontrol efforts, it was closely monitored over the decades subsequent to the release of the pathogen (Fenner and Myers 1978, Fenner and Radcliffe 1965, Fenner et al. 1956, 1957). Initially, infections were fatal more than 99% of the time, but within a year after release this value had dropped to 90%. Mortality continued to decline in subsequent years (Fenner and Woodroffe 1965) because of the evolution of both increased resistance in the rabbit population and decreased viral virulence. Although the virus was still the major controlling agent of rabbits in Australia in the mid-1980s (Parrer et al. 1985), it remains unclear whether this situation is likely to persist. The system might reach an evolutionary equilibrium at which the disease can still control the host population. Alternatively, directional evolutionary change could result in extinction of the rabbit if disease virulence outruns host resistance. Then again, if host resistance evolves more quickly than viral virulence, the disease may cease to control the rabbit. Detailed modeling by Dwyer and colleagues (1990) suggests that the virus is likely to remain an effective control agent in the near future. However, predicting the longer term outcome of this coevolutionary interaction between rabbit and virus is likely to require greater knowledge of the genetic structure of the two populations.

In a host-parasite system the level of genetic variance in resistance and virulence can strongly influence the population dynamics and equilibrium of the interacting species (Frank 1993, Seger 1992). Ecologically unstable systems can be stabilized by the presence of sufficient genetic variance in virulence and resistance (Salonen 1993). Thus, predicting the population dynamics and possible equilibrium states of a host-parasite system depends on knowing whether genetic diversity for resistance and virulence is likely to persist in the system.

**Genetic models of host-parasite coevolution.**

The mutually antagonistic interaction between host and parasite is often called an arms race (van Valen 1973). Several models have been developed to examine how negative effects of disease on host fitness select for the evolution of resistance and how negative effects of resistance on parasite fitness select for the evolution of virulence (Burdon 1987, Seger 1992, Thompson 1994). In this article I describe the assumptions and predictions of these models.

The earliest models of host-parasite coevolution (e.g., Leonard 1977, Mode 1958, 1961) were inspired by Flor's (1956) discovery that individual dominant resistance alleles in flax (*Linum usitatissimum*) are complemented by specific recessive virulence alleles in the fungal parasite that causes flax rust (*Melampsora lini*; Table 1). These relatively simple models all assume that resistance and virulence are beneficial to the organisms possessing each trait. Most models also assume that these traits involve fitness costs, or trade-offs. A trade-off is defined as the fitness decrement experienced by an individual possessing a trait, either virulence or resistance, as measured in an environment where it is not needed (Simms 1992). Costs of virulence are incorporated in these models as reduced fitness of the virulent pathogen relative to that of the avirulent strain when each infects a susceptible host. Resistance costs are depicted as reduced fitness of the resistant host relative to that of the susceptible host in a disease-free environment (Table 2). When costs are absent, these models predict that

![Table 1. Phenotypic outcome of interaction between host and pathogen predicted by the gene-for-gene complementation system. When the avirulent (V) pathogen matches the appropriate host resistance allele (R), a hypersensitive response by the host is likely to prevent infection (+). In all other cases (susceptible host (V), virulent pathogen (V)), or both), a compatible reaction is likely to result in successful infection (-).](https://academic.oup.com/bioscience/article-abstract/46/2/136/252437)

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![Table 2. Host and pathogen fitnesses in the model developed by Leonard (1977).](https://academic.oup.com/bioscience/article-abstract/46/2/136/252437)

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the virulence allele will become fixed in the pathogen population, rendering the resistance allele selectively neutral. Because neutral alleles may be lost or fixed by genetic drift (Kimura 1983), genetic variance is not likely to be maintained. Selection is likely to then favor any new host allele that confers resistance to the new virulence allele in the pathogen. Because new resistance alleles are constantly needed by the host to avoid infection and new virulence alleles are required by the pathogen to overcome these defenses, van Valen (1973) named this process for the Red Queen encountered by Alice in Wonderland. The Red Queen complained that in Wonderland, one must always be running just to stay in place.

When virulence and resistance are both costly, these simple genetic models predict cycling of host and pathogen allele frequencies around a locally unstable equilibrium point (Burdon 1987, Seger 1992). Cycling occurs because negative frequency-dependent selection on resistance and virulence is indirect and time-delayed (Seger 1992). Alleles common in the current generation are less fit in a future generation; hence the time delay. Frequency dependence is indirect because the fitness of each host genotype depends on the frequency of virulence alleles in the pathogen population, and the fitness of each pathogen genotype depends on the frequency of resistance alleles in the host population. For example, a newly mutated resistance allele confers high fitness because virulence to that allele is initially rare (or absent) in the pathogen population. Initially, the new host gene is also rare and has little selective influence on the pathogen population. However, as the novel resistance trait spreads in the host population, any pathogens possessing virulence to that gene are likely to obtain a fitness advantage via access to an unused resource. Pathogen virulence is likely to then spread, reducing the fitness advantage of the once-novel resistance allele.

Even a slight increase in the complexity of the transmission genetics underlying resistance and virulence causes the behavior of these models to become extraordinarily complex.

For example, treating the host as diploid with several alleles at a single resistance locus and incorporating multiple alleles at a haploid pathogen virulence locus are likely to produce patterns resembling chaos (Seger 1992). On the other hand, quantitative inheritance may reduce the complexity of evolutionary dynamics. When resistance is modeled independent of virulence and treated as a continuously variable trait determined by small contributions of many alleles at a large number of loci, the trade-off between costs and benefits can produce stabilizing selection for an intermediate optimal value of resistance (Simms 1992, Simms and Rausher 1987). In the absence of any other evolutionary force, stabilizing selection on a quantitative trait is likely to erode genetic variance at the loci affecting the trait (Scharloo 1964, Wright 1969). Seger (1992) provides a lucidly intuitive description of why this is so.

Frank (1995) published a quantitative genetic model that considers coevolution of both host and pathogen simultaneously. This model corroborates the conclusions of previous evolutionary models of resistance: In the presence of a sufficiently large pathogen population, stabilizing selection can produce an intermediate level of resistance with little genetic variance. However, the evolutionary outcome depends on the shape of the benefit function. Earlier models assumed that the benefit of resistance increases at a decelerating rate with increasing allocation to resistance (Fagerstrom et al. 1987, Simms and Rausher 1987). If benefits instead increase at an accelerating rate, selection on resistance is likely to be disruptive, producing a bimodal distribution of host phenotypes. In this case, under certain ecological circumstances, genetic variance can be maintained in the host population (Frank 1993).

In the quantitative genetic model, evolution of virulence in the pathogen is influenced by the interaction of two factors. As in hosts, decelerating benefits of virulence are likely to produce stabilizing selection and little genetic variance, whereas accelerating benefits are likely to produce disruptive selection and potentially large amounts of genetic variance. However, the distribution of host genotypes also influences equilibrium genetic variance in virulence. A bimodal distribution of resistance phenotypes, due to disruptive selection on the host population, is likely to produce bimodality in pathogen phenotypes. As was true for resistance, a bimodal distribution of virulence phenotypes may maintain substantial levels of genetic variance in the pathogen population (Frank 1993).

Three major messages arise from antagonistic models of host-pathogen coevolution. First, the specific modes of genetic transmission of resistance and virulence are important factors determining the evolutionary behaviors and equilibria of host-parasite systems. A second determining factor is the array of trade-offs, or costs, associated with resistance in the host and virulence in the parasite. Some trade-offs can arise from the costs of maintaining relevant biochemical pathways or allocating resources to resistance or virulence (Simms 1992). Furthermore, if resistance and virulence traits are specifically targeted in a one-to-one complementary fashion, another trade-off can occur when, for example, virulence to one form of resistance makes a pathogen relatively less fit on hosts lacking that resistance trait (Parker 1992). Thus the specificity of resistance and virulence is a third important factor that influences evolutionary outcome in a host-pathogen system.

To understand how pathogens influence host ecology, we must assess the validity of the assumption that virulence and resistance involve fitness trade-offs as well as determine the nature of genetic transmission of these traits in particular host-pathogen systems. The first and arguably some of the best understood systems of genetically controlled disease compatibility are found in plants. Consequently, this article focuses on the genetics of resistance and virulence in phytopathogenic systems.

Biology of phytopathogenic organisms

Although infectious diseases of plants may be caused by many kinds
Successful infection of a host is a complex multistep process. The pathogen must find and recognize its host, invade host tissues, withstand any defenses, and proliferate within the host. Finally, progeny or propagules must be disseminated to an environment in which new hosts can be encountered.

For microbial disease agents, finding the host is generally a nonspecific process. Most microbes have little control over their movements, being instead dependent on air or water currents, or on the movements of hosts and/or vectors. Host resistance at this stage generally takes the form of disease avoidance (Thrall et al. 1993); for example, a host may be dormant when the parasite is present (Burdon 1987).

After a potential host has been located, its suitability for infection becomes an issue. Most organisms are resistant to most pathogens; only particular combinations of host genotype, microbe genotype, and environment produce a compatible interaction leading to disease. Some pathogens may require specific surface characteristics, such as hardness or hydrophobicity, or topographic features, such as ridges or grooves, as germination stimulants or to direct growth of germ tubes (Gow 1993, Kolattukudy et al. 1993). The pathogen must also penetrate mechanical barriers to infection. Such characteristics are important features of plant resistance but are generally not involved in determining specific resistance or susceptibility of cultivars or species (Bailey 1991). Furthermore, much of the research on the molecular genetic basis of plant resistance bypasses host barriers by vacuum infiltrating microbes directly into host tissue.

Once it enters host tissue, the pathogen must run a gauntlet of both induced and constitutive defenses. It is at this point that the specificity of plant-pathogen interactions is determined. The pathogen must possess metabolic pathways that allow it to live in and feed on host tissue (termed pathogenicity) as well as to avoid ringing the alarm bells of the plant. These alarms often summon the host's rapidly induced defenses to the infection site.

One reaction, termed the hypersensitive response, frequently involves death of cells in and around the infected area, production and accumulation of hydrogen peroxide during an oxidative burst (Tenhaken et al. 1993), and the subsequent accumulation of phenolics, phytoalexins, chitinases, and other pathogenesis-related proteins in cells surrounding the infected tissue (Bailey and O'Connell 1989). The hypersensitive response is triggered when the plant recognizes particular compounds produced by the invading pathogen. Pathogen genotypes that produce these compounds are termed avirulent or incompatible, because their invasion of the plant is checked by the hypersensitive response they elicit. Pathogen genotypes that do not produce these compounds are termed virulent or compatible, because they can evade detection by the plant. To successfully infect a resistant plant, a microbe must be both virulent and pathogenic.

The invading pathogen may also induce a systemic response that decreases the probability of subsequent infection of existing sites elsewhere in the host (Ryals et al. 1991, 1995). Large-scale tissue loss may even stimulate a developmental response involving the production of new tissue that is more resistant than older tissue (Bryant et al. 1988).

Genetics of resistance and virulence

As described previously, mathematical models of host-pathogen interactions indicate that the ecological and evolutionary outcomes of these interactions depend in part on the mode of inheritance of resistance and virulence. Although there is a great variety of mechanisms by which these traits are inherited, much of the current research centers on resistance and virulence involved in gene-for-gene systems of host-pathogen interaction.

Gene-for-gene interactions. The dominant genetic paradigm of plant-pathogen interaction derives from Flor's (1956) pioneering work describing the complementary gene-for-gene system of flax and its obligately biotrophic fungal pathogen, flax rust. This type of interaction has since been described for a number of phytopathogenic systems (Day 1974, Thompson 1994, Thompson and Burdon 1992). Usually, plant resistance genes are dominant and pathogen virulence genes are recessive. When the host possesses the
dominant resistance allele (R), infection by the avirulent (V) pathogen provokes a hypersensitive response in the plant. All other combinations of alleles at the resistance and virulence loci are compatible and result in successful infection (Table 1).

The molecular model proposed to explain this pattern invokes the action of chemical signaling between plant and pathogen (de Wit 1992, Keen 1990). The model posits that an incompatible reaction occurs because resistant plants can recognize and respond to a gene product of the avirulent pathogen genotype. Pathogens evade host detection and acquire virulence (v) by ceasing to produce the recognizable gene product.

Although gene-for-gene interactions between plants and biotrophic fungi provided the first and most widely recognized paradigm of specific host-pathogen resistance, the obligate biotrophy of these fungi has hampered detailed molecular genetic work on them. However, other types of phytopathogenic organisms, ranging from hemibiotrophic fungi to bacteria and viruses, can also induce a hypersensitive response (Keen 1993) and often conform to the gene-for-gene model. Consequently, most research on the genetics of virulence and resistance involving the hypersensitive response has focused on these more tractable organisms.

This research has revealed that induction of the hypersensitive host response is conditioned by avirulence (avr) and hypersensitive reaction and pathogenicity (hrp) genes in the pathogen. Avirulence genes produce a pattern of dominant resistance and recessive virulence reminiscent of that found by Flor (1955) in flax and flax rust. As predicted, avr genes encode products that are positive factors in the generation of a resistance response in the host (Lindsay et al. 1993). These products are called elicitors (Keen 1975) because they interact directly with the plant to elicit the host hypersensitive response. A pathogen that is "wild type" at an avr gene produces the elicitor and is therefore avirulent (V), incapable of infecting a resistant host. A mutation in an avr gene deactivates its elicitor, which prevents the elicitor from inducing the host hypersensitive response. Thus avr mutants are virulent (v) and can infect a resistant host. Unlike avr genes, hrp genes are essential to growth inside a plant. The hrp mutants cannot cause disease, even on a susceptible host. Moreover, they generally do not elicit a hypersensitive response on nonhost or resistant host genotypes (Long and Staskawicz 1993).

Plant resistance genes: receptors? It is presumed by Keen (1993) and others that some types of plant resistance involve genes encoding receptors for pathogen-produced elicitors, and a major goal of recent research has been to identify these postulated receptors. After decades of work, resistance genes complementary to known avirulence genes are being identified and sequenced (Ausubel et al. 1995, Dinesh-Kumar et al. 1995, Martin et al. 1993, Moffat 1994). Because the products of these genes have not yet been identified, their mode of function remains a matter of speculation. For example, the amino acid sequence of RPS2, which confers resistance to the bacterial pathogen Pseudomonas syringae in the mouse-eared cress, Arabidopsis thaliana, suggests that it may have a membrane-spanning domain (Bent et al. 1994). Such a protein could be exposed on the cell surface and might act as a receptor of extracellular signals.

However, resistance does not necessarily involve only receptors. For example, it may be that the ability to produce glucanase is in part responsible for the general resistance of soybeans (Glycine max) to Phytophthora. When glucanase activity is increased, soybeans become more resistant to infection (Yoshikawa et al. 1990), and expression of the cloned soybean glucanase gene in transgenic tobacco confers general resistance to several pathogens, including Phytophthora. Thus, glucanases, which are enzymes that degrade glucans, may play a general role in resistance by releasing elicitor-active molecules from pathogens (Yoshikawa cited in Keen 1993).

The potential number of resistance mechanisms in a host is large, as demonstrated by studies of tomato (Lycopersicon esculentum) resistance to Cladosporium fulvum (Hammond-Kosack and Jones 1994). A large number of Cf (C. fulvum resistance) genes have been bred into tomato from close wild relatives. All of these genes confer dominant resistance, but in a detailed study on the relative efficiencies of these and two other Cf genes, Hammond-Kosack and Jones (1994) demonstrated that dominance is not complete at most of these resistance loci. Instead, heterozygotes at each gene exhibited a delayed resistance reaction relative to that of homozygotes. Interestingly, resistance conditioned by different genes acted at different times during the infection process. Genes that acted earlier in infection restricted hyphal ingress into the mesophyll more than those acting later. Furthermore, resistance conditioned by earlier acting genes made resistance at later acting genes irrelevant. Finally, in comparison to resistance expressed in the parental L. esculentum genome, each Cf gene was less effective when expressed against a hybrid L. esculentum × Lycopersicon pennellii F1 background, indicating that interaction with other components of the genome also influences resistance phenotype. Of course, tomato cultivars evolve primarily in response to artificial selection. However, the level of complexity involved in the transmission of Cf resistance suggests that simple single gene models would be insufficient to accurately predict the evolution of this trait in wild relatives of tomato.

Mechanisms to increase mutation rates. Coevolutionary models predict that rare host genotypes should be resistant to common pathogen genotypes. By similar reasoning, novel pathogen genotypes should escape detection by common host genotypes. Thus selection should favor resistance and virulence genes with structures that promote high mutation rates. Studies in barley (Hordeum vulgare) and flax suggest that resistance against specific biotrophic fungi may involve complex genes within which unequal
crossing-over or some other mechanism of gene rearrangement can produce unusually high levels of mutation (Pyror 1987). A similar mechanism produces high levels of genetic variation for mating types in yeast (Saccharomyces cerevisiae) and surface antigens in trypanosomes (Borst and Greaves 1987), both systems in which rapid production of genetic variants is advantageous. The structure of the avrBs3 gene in the bacterial pathogen Xanthomonas campestris pv. vesicatoria exhibits another mechanism for enhanced rates of evolution. This gene encodes a large protein with 17 repeated amino acid motifs in its central region (Bonas et al. 1989), and different deletion mutants exhibit different host specificities (Conrads-Strauch et al. 1993, Herbers et al. 1991).

Quantitative resistance. The breeding of resistance into crop plants has focused almost exclusively on resistance genes of major effect (Nass et al. 1981). Major resistance genes frequently produce dramatic levels of resistance to specific fungal genotypes, but evolutionary change in pathogenic fungi often defeats this resistance quickly. This phenomenon has led some plant breeders to look to polygenic resistance as a potential source of durable crop protection. Whereas major gene resistance produces categorical differences in resistance among individuals, polygenic resistance results in continuously distributed variation in resistance level.

Polygenic traits, also called quantitative traits, are generally assumed to be conditioned by the small additive effects of many alleles at many loci (Falconer 1981). There are many examples of polygenic resistance to phytopathogens (reviewed in Thompson and Burdon 1992). Recent efforts to estimate the number of genes involved in polygenic resistance have produced variable results. Pe and colleagues (1993) found at least five loci involved in resistance to Gibberella zeae infection in maize (Zea mays). In barley, variation in adult plant resistance to powdery mildew (Erysiphe graminis) has been attributed to additive and dominant effects of as many as five independent genes (Heun 1987). In oats (Avena sativa), four to nine genes have been postulated to be responsible for this trait (Jones 1986), while differences between winter wheat (Triticum aestivum) cultivars have been ascribed to as few as two or three genes (Das and Griffey 1994) or as many as 14 different chromosomes (Chae and Fischbeck 1979). Virtually nothing is known about the numbers of genes underlying quantitative resistance in natural plant populations. Moreover, there is little or no discussion in the literature of polygenic virulence in phytopathogens.

Instead of viewing polygenic resistance as a panacea for crop breeders, Nelson (1979) and others suggested that oligogenic resistance (conditioned by few genes of major effect) and polygenic resistance actually involve the same genes, but that the level of resistance that these genes produce is conditional on the internal and external genetic environment in which they are expressed. In particular, Nelson (1979) and others (Abdalla and Hermsen 1971, Arnold and Brown 1968) proposed that so-called defeated major resistance genes might still condition minor levels of resistance against virulent pathogen genotypes and that the cumulative effects of many archaic resistance genes are responsible for observed quantitative resistance.

Using methods developed to identify and map quantitative trait loci, several laboratories have sought empirical evidence with which to test this hypothesis. Some studies have produced corroborating evidence. For example, some major resistance genes in winter wheat that have been defeated by virulence genes in powdery mildew (E. graminis f. sp. tritici) still have a measurable ability to restrict the increase and severity of disease (Nass et al. 1981). Other studies have found correlations between major gene loci and quantitative resistance but have also revealed quantitative trait loci unlinked to known major genes (Freymark et al. 1993, Heun 1992). Apparently, defeated genes may contribute to polygenic resistance but do not completely explain all the variance in these traits.

Costs and benefits of resistance and virulence

In addition to being influenced by the mode of inheritance of resistance and virulence, the ecological and evolutionary outcome of host-pathogen coevolution is also likely to depend on whether these traits are involved in fitness trade-offs.

Durability of nonhost resistance and fitness costs of virulence. The degree of specificity of the complementary interaction between host and pathogen has been used to categorize resistance into two types: nonhost and race-specific. Nonhost resistance protects an entire plant species from infection by all members of a pathogenic taxon, whereas race-specific resistance protects only some members of a host species from only certain members of the pathogenic taxon. This distinction is of considerable economic significance because race-specific resistance is more easily overcome through pathogen evolution than is nonhost resistance. Breeding new resistant crop varieties is a costly and time-consuming task. Consequently, the length of time it takes the pathogen population to evolve virulence to the new resistance allele, commonly referred to as the durability of the allele, determines in part the economic value of the new variety.

Until recently, it was assumed that the genetic mechanisms underlying differential resistance among host species are distinct from those underlying resistance differences among genotypes within a species. However, recent work suggests that the dichotomy is artificial. Many aspects of the host responses of race-specific and nonhost resistance are similar, especially with respect to the mRNAs and protein products that accumulate as disease resistance is expressed (Hadwigter and Culley 1993). These results have led to a more general paradigm of the chemical signaling that conditions incompatibility in both nonhost and race-specific interactions. Within this framework, elicitors are categorized as either general or specific, depending on the taxonomic range of compatibility they condition. However, the general mechanisms by which
they elicit host resistance are assumed to be similar.

General elicitors are produced by an entire pathogen species or genus and induce resistance reactions in entire species of hosts. For example, all members of the fungal species *Phytophthora megasperma* produce glucans in their cell walls (Sharp et al. 1984). These glucans are potent elicitors of the hypersensitive response in all varieties of soybeans, but they are ineffective in parsley (*Petroselinum crispum*; Parker et al. 1991). In contrast to general elicitors, specific elicitors are found only in particular pathogen genotypes and function only in some plant cultivars within a host species (Keen 1993). For example, the *avr*9 gene of the hemibiotrophic fungus *C. fulvum* encodes a small peptide that elicits the hypersensitive response in tomato plants possessing the complementary disease resistance gene, *Cf9* (Van den Ackerveken et al. 1992). Strains of the fungus without *avr*9 successfully infect hosts with the *Cf9* resistance gene (Van den Ackerveken et al. 1992), raising an interesting question that pertains to all pathogen elicitors: Why do pathogens continue to produce compounds that stimulate host reactions that prevent or limit infection and thereby reduce pathogen fitness?

This question is important because it suggests that focusing on the interaction of elicitors with the host may be the wrong approach to understanding the relative durabilities of host and nonhost resistances. In fact, the term elicitor is an unfortunate historical artifact of this focus. The pathogen does not produce an elicitor to alert the host of its presence. Instead, an elicitor is some substance needed by the pathogen for normal metabolism (Thompson 1994). The function of these compounds in avirulence is a secondary development occasioned by the evolution in hosts of mechanisms that detect and respond to the pathogen. By readjusting our perspective, we can see that the taxonomic breadth of general elicitors may provide an important clue as to why resistance to them (nonhost resistance) is more durable. These insights can also be helpful in evaluating the potential for fitness costs of virulence.

In general, genes producing products fundamental to organismal fitness tend to be highly conserved among taxa (Kimura 1983). General elicitors are, by definition, shared by a wider taxonomic range of organisms than are specific elicitors. For example, oligosaccharide elicitors, such as glucans, which serve as general elicitors of soybean resistance against *Phytophthora*, are conserved across a wide taxonomic range and have even been purified from commercial yeast extract (Hahn 1981). Such a general distribution of oligosaccharide elicitors, even in nonpathogenic fungi, suggests that they make some essential contribution to fungal fitness. If general elicitors perform more essential functions (or their specific conformation is more critical to their function) in the pathogen than do specific elicitors, then host resistance genes that detect and respond to general elicitors should be more durable than those that complement more specific elicitors. Resistance genes that recognize general elicitors are likely to be more durable because mutations in the pathogen to halt production of these compounds would be more detrimental to microbial fitness. Thus, although various elicitors may function similarly in provoking the host hypersensitive response, the observation that resistance to general elicitors is more durable seems to have a plausible evolutionary explanation. This argument also suggests that virulence acquired by losing general elicitor function should involve substantial fitness costs.

There is, however, an alternative explanation for elicitor homology among taxa. Specifically, gene homology may arise from a common recent origin followed by lateral gene transfer. For example, several different variations on the *avrBs2* gene in *X. campestris* pv. *vesicatoria* have virulence activity in tomato and pepper (*Capsicum annuum*). Because of their sequence homology, and because in some cases they are flanked by long inverted repeat sequences, there has been speculation that the *avrBs3* genes evolved recently and have spread among bacterial taxa via lateral transmission (Bonas et al. 1993). If so, then the expectation that resistance to elicitors conserved across taxa should be more durable may mislead plant breeders and produce erroneous expectations about virulence costs.

The hypothesis that elicitors produced by *avr* genes make essential contributions to pathogen fitness was tested by Kearney and Staskawicz (1990), who demonstrated that the *avrBs2* avirulence gene plays an important role in fitness of the bacterial pathogen *X. campestris* pv. *vesicatoria*. Like the genes producing glucans in *Phytophthora*, *avrBs2* is highly conserved among several other *X. campestris* pathogen varieties (Kearney and Staskawicz 1990). These researchers found that when grown on a susceptible host, *avrBs2* mutant (virulent) strains had lower fitness than the avirulent wild-type strain. Furthermore, when avirulence was restored to the mutant strain by complementing it with a plasmid-borne copy of the wild-type avirulence gene, fitness was restored to near wild-type levels. Thus the product of the *avrBs2* gene makes a significant contribution to pathogen fitness, and loss of that product to achieve virulence involves a detectable fitness cost to the pathogen. However, this cost can be detected only when the pathogen is grown in culture or infects a susceptible host—a host lacking the ability to detect the *avrBs2* gene product.

Other studies have also found evidence that virulence is costly. Rouse and colleagues (1980) found that *E. graminis* forms virulent to wheat cultivars with one resistance gene exhibited reduced fitness relative to avirulent forms on cultivars lacking that resistance gene. In survey studies, a decline in the frequencies of particular virulence genes following reductions in the frequencies of the corresponding resistance genes may indicate that virulence is costly. Grant and Archer (1983) found an approximately 5% cost for possessing unnecessary virulence at the Sr6 locus in *Puccinia graminis tritici* (wheat stem rust) and a similar cost of unnecessary virulence at the *Mla6* locus in *E. graminis*.

How do avirulence gene products contribute to pathogen fitness? Un-
fortunately, except for viral coat proteins, we do not know the function of avirulence gene products in the pathogens that produce them (Keen 1993). Nonetheless, it is interesting to speculate. Several proteinaceous elicitors have been characterized since the gene product of avr9 was described in Phytophthora; all are small, cysteine-rich proteins (reviewed in Templeton et al. 1994). Templeton and colleagues (1994) reviewed the functions of similar proteins in both fungal and nonfungal species and used this information to speculate upon the possible function of the avr gene products in fungi. For instance, small, cysteine-rich proteins are important in the self-recognition necessary for sporophytic pollen self-incompatibility in Brassica napus (Dzelzkalns et al. 1992), suggesting that they might also be important in fungal self-recognition (Templeton et al. 1994). This hypothesis is particularly intriguing because it would also explain the intraspecific diversity of elicitors produced by the avr9 gene. Self-recognition genes must have many loci so as to avoid false identification of conspecifics with the same self-recognition genotype as self.

**Costs of resistance.** Although introduction of resistance alleles into crop varieties is only rarely accompanied by yield penalties (Burdon 1987), some exceptions have been reported. For example, genes for resistance to crown rust that were introduced into cultivated oats (Avena sativa) from the wild red oat (Avena sterilis) were found to reduce grain yields (Simons 1979). Yield reductions were also observed in tobacco lines resistant to tobacco mosaic virus and Fusarium wilt (Chaplin 1970), although this study used conventional methods of tobacco culture, including removal of flowers and basal branches, which may extrapola­tion of fitness from leaf yield questionable. Bergelson (1994) found that when protected from herbivores and fungi by pesticides, two lettuce cultivars resistant to leaf root aphid and downy mildew produced fewer flower buds than near-isogenic lines that lacked such resistance. Moreover, the magnitude of this cost differed between cultivars, indicating that the resistance trade-off is contingent on genetic background.

Some studies found increases in yields of cultivars with resistance alleles, even in the absence of disease. For example, two different genes for resistance to crown rust were each associated with increased yield in cultivated oats (Frey and Browning 1971). The effects of resistance on yield may vary with both the physical and the genetic environment. The magnitude by which resistance genes increased oat yield depended on the genetic background into which a gene was placed. In another study, temperature influenced the costs of resistance in the wild oat Avena fatua (Burdon and Müller 1987). In a warm greenhouse, genotypes susceptible to crown rust performed better than resistant genotypes; in a cold greenhouse the relationship was reversed. Bergelson and Purrington (in press) found that disease resistance involved fitness costs in 34% of 46 studies, 4 of which were mentioned above.

**Summary on costs.** The evidence suggests that costs of virulence are more common and perhaps of larger magnitude than costs of resistance. The reasons for this pattern seem clear: to become virulent, pathogens must often lose the function of conserved genes that are important to fitness. In contrast, specific resistance in the host plant is likely to involve the acquisition of function, such as production of receptors to detect pathogen growth. Such traits may involve allocation costs or entail deleterious alterations of previously functioning biochemical pathways (Simms 1992), but the magnitudes of such costs are likely to be less than those incurred by virulent pathogens. I would predict a different pattern, however, for cases in which virulence involves a gain of function, such as the production of toxins (Panaccione 1993). In this situation virulence might be less costly than resistance, especially when resistance involves modification and consequent loss or reduction of function of the molecular targets of microbial toxins.

**Coevolution in natural plant populations.** It has been suggested that gene-for-gene relationships between phytopathogens and crop hosts are an artifact of plant breeding procedures (Day et al. 1983) and may not be typical of interactions of pathogens with natural plant populations (Parker 1992). Several studies of natural plant populations have identified gene-for-gene relationships with pathogens (reviewed in Parker 1994), but so few studies have been done on natural populations that generalization is difficult.

Studies of natural plant populations have produced little evidence that disease resistance involves fitness trade-offs. In experiments designed to minimize the potential for bias due to genetic background in the hog peanut, Amphicarpaea bracteata, Parker and colleagues (Parker 1992, Parker and Wilkins 1990) found no evidence that genes for disease resistance were harmful in a disease-free environment. In fact, in the absence of disease, resistant hog peanuts had higher mean seed biomass than did susceptible plants. In the tall morning glory, Ipomoea purpurea, resistance to the hemibiotrophic fungal pathogen Colletotrichum dematium was not associated with any reduction in survival or flower or fruit production (Simms and Triplett 1994). This pattern is similar to that found for costs of resistance to insect herbivores in this species (Simms and Rausher 1987, 1989). Costs of resistance to herbivores do occur in natural populations of this plant, but they are often small in magnitude and are by no means ubiquitous (Simms 1992).

These results have motivated Parker (1992) to argue that high levels of genetic variation for pathogen resistance that are observed in natural plant populations may frequently be due to historical effects in nonequilibrial systems. However, because so few studies have been done on natural plant populations (e.g., we have no evidence regarding costs of virulence in pathogens on natural plant populations), it is too early to determine how often Parker’s argument is correct.

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