Popul Ecol (2001) 43:3–14 

SPECIAL FEATURE: ORIGINAL ARTICLE

**Joel Kniskern · Mark D. Rausher**

# Two modes of host–enemy coevolution

Received: May 26, 2000 / Accepted: January 26, 2001

**Abstract** The process of coevolution between host and enemy has traditionally been viewed as an evolutionary arms race between resistance and counterresistance. The arms-race metaphor of coevolution is widely accepted because it explains the evolution of many characters in species involved in host–enemy interactions. However, molecular work in plant–pathogen systems suggests a coevolutionary interplay between plant recognition of an attacking pathogen and pathogen evasion from recognition. We refer to this process as information coevolution, and contrast this with arms race coevolution to show that these two processes result in very different patterns of host resistance and enemy virulence at the population level. First, information coevolution results in a lower proportion of hosts that are susceptible to enemy attack within a population. Second, information coevolution produces a pattern of local maladaptation of enemy on host, a naturally occurring phenomenon that is difficult to explain under arms race coevolution. We then conduct a literature review to survey the empirical support for either mode of coevolution using the predicted patterns of host resistance and enemy virulence. Evidence supports both modes of coevolution in plant–enemy interactions, whereas no support is found for information coevolution in vertebrate–parasite and invertebrate–parasite systems.

**Key words** Local adaptation · Resistance · Arms race · Information race

## Introduction

For more than three decades, coevolution has assumed a central role in biologists' explanations for diversity and adaptation. For example, coevolution has been invoked to explain the evolution of specialization in herbivorous insects (Dethier 1954; Krieger et al. 1971; Feeny 1975; Smiley 1978), the evolutionary elaboration of shells in marine mollusks (Vermeij 1987, 1993), and the generation of diversity in plant secondary chemistry (Ehrlich and Raven 1964; Berenbaum 1983) and morphology (Janzen 1969; Gilbert 1971, 1975; Rausher 1981; Janzen and Martin 1982). Examples of coevolution may be divided into two main groups reflecting the nature of the interaction between the coevolving species. One type of coevolution may be termed mutualistic coevolution. In this type, interactions are beneficial for all species involved and natural selection often leads to very tight mutualistic relationships. Familiar examples of this type of coevolution include specialized interactions among plants and their pollinators (Feinsinger 1983), maintenance of internal symbionts by insects and several marine phyla (Vermeij 1983; Moran and Telang 1998), and ant–plant mutualisms (Janzen 1966).

The second type of coevolution, which may be termed antagonistic coevolution, may be divided into two subtypes: competitive coevolution and trophic coevolution. Purported examples of the former include genetic specialization of plant populations to tolerate the suite of locally competing species (Turkington and Harper 1979) and character displacement in animals (Grant 1986; Schluter and McPhail 1992). Here we concentrate on trophic coevolution, which, in its broadest conception, is characterized by species interacting trophically. This category includes predator–prey coevolution, plant–pathogen coevolution, and plant–herbivore coevolution.

The traditional conceptualization of trophic coevolution is in terms of an arms race metaphor (Ehrlich and Raven 1964; Whittaker and Feeny 1971; Dawkins and Krebs 1979; Berenbaum and Zangerl 1988). Hosts (or prey) are visualized as being attacked by one or more species of natural enemy, which reduces individual host fitness. The first step in the coevolutionary arms race is the evolution of some type of resistance in the host. Genes (alleles) conferring resistance are favored by natural selection because by definition they reduce attack rates and thus increase host fitness. The reduction in attack rates is also envisioned to reduce the average fitness of the natural enemies, which sets

J. Kniskern (✉) · M.D. Rausher
Evolution, Ecology and Organismal Biology Group, Department of Zoology, Duke University, Durham, NC 27708-0325, USA
Tel. +1-919-684 2295; Fax +1-919-660 7293
e-mail: jmk8@acpub.duke.edu

the stage for the second step in the coevolutionary cycle: evolution of counterresistance in the natural enemies. Specifically, genes (alleles) that reduce the detrimental effects of host resistance, and thus increase enemy fitness, are favored by natural selection. Completion of this second step sets the stage once again for the evolution of resistance in the host, to be followed by the evolution of counterresistance in the enemy in repeated cycles.

The arms race conceptualization of enemy–host coevolution has been successful at accounting for many observed features of enemy–host interactions. For example, numerous examples of resistance characters in plants including secondary metabolites (Whittaker and Feeny 1971), hairs and trichomes (Mauricio and Rausher 1997), egg mimics (Williams and Gilbert 1981), and tough, nutrient-poor leaves (Feeny 1975; Rausher 1981) are readily interpretable as defensive adaptations arising from coevolutionary interactions. Similarly, it is clear that many plant natural enemies have adapted to overcome resistance factors in their host plants (Edmunds and Alstad 1978; Berenbaum and Zangerl 1998). Insects are known to have enzymes that detoxify secondary compounds that plants produce to deter herbivory (Rosenthal et al. 1977; Brattsten 1980); fungal pathogens have been reported to detoxify plant phytoalexins, a class of products that is highly fugitoxic (see references in Vidhyasekaran 1997); and some predators are resistant to harmful compounds produced by their prey (Brodie and Brodie 1990). Additional support for the operation of arms-race coevolution is provided by phylogenetic comparisons of related host species and their associated natural enemies (Ehrlich and Raven 1964; Berenbaum 1983).

A final type of evidence pointing toward the occurrence of arms-race coevolution was recently provided by Bishop et al. (2000), who examined evolution of antifungal chitinases in several species of the crucifer *Arabis*. In addition to detecting positive selection favoring amino acid substitutions in these chitinases, the authors showed that this protein exhibited the greatest number of substitutions in the region that interacts with chitin. These observations suggest repeated coevolutionary change in which the fungus produces an altered chitinase inhibitor that inhibits the ability of the chitinase to digest the fungal cell wall, while the plant produces an altered chitinase that is not subject to inhibition.

Despite these successes, there remain aspects of evolutionary interactions among hosts and enemies that are difficult to reconcile with the arms race view of coevolution. One particular aspect that has received much recent attention is the nature of the local adaptation of enemy to host. Because at least in plant–pathogen and plant–herbivore interactions the generation time of the natural enemies is often much shorter than that of the host plant, it has been argued repeatedly that natural enemies will be able to adapt more rapidly than their host plants, and therefore enemies should characteristically exhibit local adaptation to their hosts (Ebert 1994; Lively 1996; Morand et al. 1996; Gandon and Van Zandt 1998; Mopper and Strauss 1998; Kaltz and Shykoff 1998). Such local adaptation can be revealed experimentally by transplant experiments, in which natural enemies are transplanted among populations and at each site susceptibility to attack by natural enemies is measured. Local enemy adaptation is indicated by greater susceptibility to home-site enemies than to transplanted (away-site) enemies.

Although a number of investigations have demonstrated local enemy adaptation, a number of others have failed to do so. Some have even demonstrated local enemy maladaptation: home-site natural enemies are less successful at attacking hosts than away-site enemies (see following references). Attempts to reconcile these empirical results with the naïve expectation of local enemy adaptation have focused almost exclusively on elaborating the arms race conceptualization of coevolution by examining how factors such as relative generation time of enemies and hosts, gene flow, and population spatial structure influence predictions about local enemy adaptation versus maladaptation (Kaltz and Shykoff 1998). To date, however, there is little empirical evidence bearing on the validity of these theoretical explanations.

Although these attempts to explain patterns of adaptation may ultimately prove successful, recent advances in the molecular biology of host–enemy interactions suggest that an entirely different explanation should be considered. As is described here in detail, recent studies have made clear that there are two basic types of molecular interaction that determine whether an attack by a natural enemy is successful and reduces host fitness. The first type is that assumed by the arms race conceptualization: resistant host genotypes produce some substance that is either toxic or growth inhibitory, and counterresistant enemy genotypes produce some substance or feature that reduces or eliminates the effects of the toxin. We term this a toxin–detoxifier (T-D) type interaction.

The second type of molecular interaction between enemies and hosts involves not a toxin–detoxification interplay but rather information exchange. In many plant–enemy interactions, an induced defensive response (including the accumulation of toxins and growth inhibitors) is triggered by the plant "sensing" the presence of a natural enemy. Sensing is accomplished by one or more types of cellular receptors that are triggered by elicitor substances or other signals produced by the natural enemy. In many interactions, it is known that "virulent" enemy genotypes have elicitors that are not recognized by the host plant receptors. Metaphorically, these enemy genotypes have reduced or eliminated the information needed by the host plant to detect the enemy presence.

Just as coevolution may proceed by successive alterations of toxins and detoxification mechanisms, it may also proceed by successive modifications of receptors and elicitors. Starting with a host attacked by natural enemies (which do not trigger the host's induced defenses), natural selection will favor any alteration of host receptors that allows recognition of enemy attack. In turn, once hosts have evolved to recognize the signals given off by their enemies, selection will favor genes (alleles) in the natural enemy that alter the elicitor so as to be no longer recognizable by the host. This cycle, which can presumably be repeated indefi-

nitely, we term information coevolution to distinguish it from arms-race coevolution. We term this type of molecular interaction an elicitor–receptor (E-R) interaction.

Recognition of this new type of coevolution is important only insofar as it helps us understand ecological or evolutionary patterns that the arms-race conceptualization does not adequately explain. In this article, we show that these two types of coevolution result in different patterns of variation in resistance and virulence at the population level. We also argue that the distinction between these two types of coevolution may help explain why some natural enemies are locally adapted to their hosts, while others appear to be locally maladapted, as already described.

## The molecular basis of information–race coevolution

Since the early work by Flor (1956, 1971), it has become clear that many interactions between plants and pathogens are mediated by fairly simple genetic interactions. In particular, in many systems, each resistance allele identified in the host plant interacts with a single, specific avirulence allele in the pathogen to induce a resistance response. Such a response can be a "hypersensitive response," in which cells in the neighborhood of the initial infection undergo programmed death, or a "systemic response," which involves an induced accumulation of toxins and other antibacterial or antifungal substances (Hammond-Kosack and Jones 1996; Ryals et al. 1996; Hutchenson 1998).

Either of two types of genetic interactions determine whether a plant's resistance response is activated. Under a "gene-for-gene" system, there are multiple loci in both the plant and the pathogen that interact in pairs (Flor 1956, 1971; Lamb et al. 1989; Hammond-Kosack and Jones 1997) (Fig. 1A). For each locus in the plant, there is a corresponding locus in the pathogen that may induce resistance, depending on which alleles are present. Typically, at the pathogen locus, there is a "virulent" allele (*avr*) and an "avirulent" allele (*Avr*), while at the host locus there is a "resistance" allele (*R*) and a "susceptible" allele (*r*). When the host is *R*− and the pathogen is *Avr*−, resistance is induced and the plant is protected from the pathogen. With any other combination of genotypes, the pathogen is potentially able to successfully invade its host. Whether it actually can do so depends on host and pathogen genotypes at the other loci that influence susceptibility. If, for any pair of loci, the host and pathogen genotypes are *R*− and *Avr*−, respectively, the host's resistance response is triggered and the pathogen is checked. If these genotypes are not obtained for any of the pairs of loci, however, the pathogen is able to invade.

In the second genetic system, a "matching-allele" system, there is one locus in both the host and pathogen that mediates the outcome of the host–pathogen interaction (Nee 1989; Frank 1993) (Fig. 1B). At each locus there are multiple resistance alleles, $R_1$, $R_2$, $R_3$, ... , in the host, and multiple virulence alleles, $V_1$, $V_2$, $V_3$, ... , in the pathogen. Each allele in the host "matches" one of the alleles in the pathogen, in the sense that resistance is induced if the pathogen carries an allele that matches one of the resistance alleles carried by the host (i.e., if the host is $R_1 R_2$, resistance will be induced if the pathogen carries $V_1$ or $V_2$).

A.

| Enemy genotype | Host genotype | | | |
|---|---|---|---|---|
| | $R_1$- $R_2$- | $R_1$- $r_2r_2$ | $r_1r_1$ $R_2$- | $r_1r_1r_2r_2$ |
| $V_1$- $V_2$- | - | - | - | + |
| $V_1$- $v_2v_2$ | - | - | + | + |
| $v_1v_1$ $V_2$- | - | + | - | + |
| $v_1v_1v_2v_2$ | + | + | + | + |

B.

| Enemy genotype | Host genotype | | |
|---|---|---|---|
| | $R_1$ $R_1$ | $R_1$ $R_2$ | $R_2$ $R_2$ |
| $V_1$ $V_1$ | - | - | + |
| $V_1$ $V_2$ | - | - | - |
| $V_2$ $V_2$ | + | - | - |

**Fig. 1.** Patterns of resistance and virulence under the elicitor–receptor model for two-locus gene-for-gene interaction and single-locus matching-alleles systems. Host and enemy are both diploids. **A** Gene-for-gene system. **B** Matching-alleles system. Symbols: +, host susceptible, enemy virulent; −, host resistant, enemy avirulent

One hypothesis consistent with these two patterns is that induction of resistance is initiated when the host "recognizes" the presence of the pathogen (Parker and Coleman 1997). Recognition could be accomplished, for example, by a cellular receptor in the host that is stimulated by some type of "elicitor" molecule produced by the pathogen, such that the precise molecular configurations of the receptor and elicitor are specified by the host and pathogen genotype, respectively. Only when pathogens produce a "matching" elicitor with the precise molecular configuration that allows it to fit into the receptor would the host be able to recognize the presence of the pathogen and mount resistance. This hypothesis then explains why host resistance alleles tend to be dominant whereas pathogen avirulence alleles tend to be recessive: only one copy of the resistance allele is needed to produce a particular type of receptor for recognition, but to prevent recognition, no copies of the matching allele can be present in the pathogen.

This hypothesis appears to be supported by recent work that has examined the molecular basis of the genetic interactions between hosts and pathogens (Hammond-Kosack and Jones 1997; De Wit 1997; Parker and Coleman 1997). In several plant species, including tomato, rice, tobacco, and

*Arabidopsis*, and their associated pathogens, resistance gene–virulence gene pairs have been cloned and characterized. Pathogen virulence genes from different pathogens have little in common structurally, as would be expected if plants target pathogen proteins opportunistically as signal for induction. By contrast, resistance genes from different plants show some remarkable similarities to known signal transduction proteins (Staskawicz et al. 1995; Michelmore 1995; De Wit 1997). Most contain leucine-rich repeat regions that are believed to interact with the pathogen elicitor; those which are believed to be located cytoplasmically also tend to contain a nucleotide-binding site, suggesting that these receptors bind ATP or GTP in initiating the signal cascade that produces induced resistance. Finally, one study has demonstrated that the *Pto* resistance gene of tomato interacts physically with the avirulence gene *AvrPto* in the pathogen *Pseudomonas syringae*, as would be expected if the products of these two genes constitute a receptor–ligand system (Tang et al. 1996).

The general model that has emerged from these investigations is depicted in Fig. 2. The pathogen produces some sort of elicitor molecule, which may either be secreted into a host cell, or, in the case of fungal pathogens that do not invade host cells, into the intercellular space. Within the host cell cytoplasm or on the cell surface resides a receptor protein, a product of a specific resistance gene. If that protein is able to bind the elicitor molecule, one or more signal cascades are initiated that ultimately trigger the hypersensitive response, as well as the onset of systemic resistance as reflected in the accumulation of pathogenesis-related defensive proteins. If the protein is not able to bind the elicitor, as could occur if the pathogen carries mutant copies of the gene specifying the elicitor, the signal transduction pathway is not initiated and resistance responses are not induced.

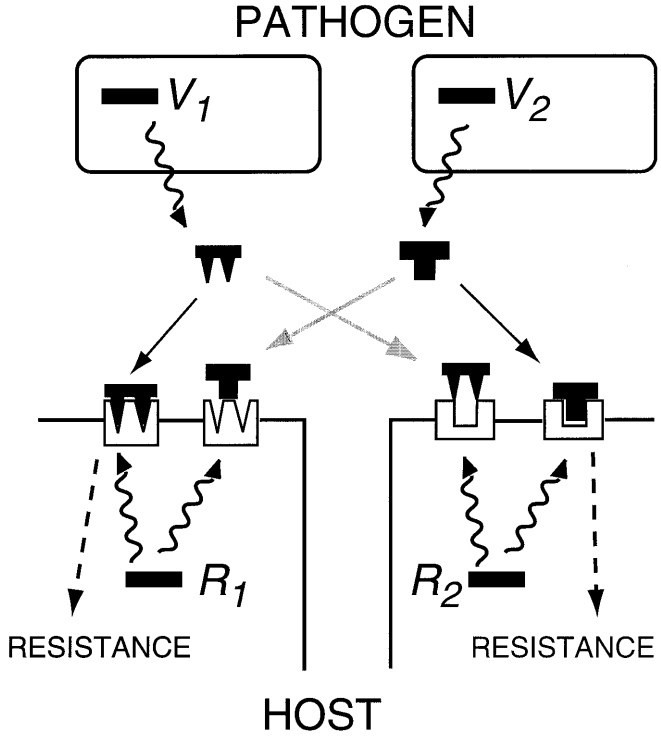


**Fig. 2.** Schematic illustration of elicitor–receptor interaction between host and pathogen cells, showing specificity of the interaction in a matching-alleles system. *Vi* and *Ri* are genes for pathogen elicitor and host receptor, respectively. *Wavy arrows* indicate production of elicitor (*solid figures*) and receptor (*open figures*) proteins, respectively. *Solid black arrows* indicate a fit between receptor and elicitor proteins, which triggers an induced resistance response (*broken arrows*). *Gray arrows* indicate lack of fit between elicitor produced by pathogen gene *Vi* and receptor produced by host gene $R_j$ ($i$ not equal $j$), which fails to trigger induced resistance

Examination of within- and between-species variation in the structure of *R* genes have provided evidence that these receptors and elicitors are involved in coevolutionary interactions between hosts and pathogens. In particular, several recent studies have demonstrated rapid evolution of *R* genes (Parniske et al. 1997; Wang et al. 1998; Meyers et al. 1998; McDowell et al. 1998). In addition, the rate of nonsynonymous substitutions is often higher than the rate of synonymous substitutions, indicating that much of the observed evolutionary change is adaptive (Wang et al. 1998; Meyers et al. 1998). Finally, amino acid substitution tends to be concentrated in the regions of the receptor proteins that are thought to interact with the elicitor, as would be expected if these regions were changing in response to evolutionary changes in those elicitors. It thus appears that many host–pathogen systems are engaged in information race coevolution, in which the pathogen is selected to minimize the information it reveals about its presence, while the host is selected to detect information the pathogen is unable to hide. Although most of the evidence for this type of coevolution has been supplied by investigations of plant–pathogen interactions, it is also known that feeding by herbivores can trigger induced defensive responses, through a signal transduction system that is now beginning to be understood (Karban and Baldwin 1997). Consequently, there is reason to anticipate the operation of information race coevolution between plants and herbivores as well [Rhoades' (1985) notion of "stealthy" herbivores presages this idea to some extent].

## Contrasting information-race coevolution and arms-race coevolution: patterns of variation within and between species

The molecular details of host–enemy interactions are of interest to evolutionary biologists insofar as variation in those details leads to different evolutionary patterns. In this section, we present a verbal model that contrasts arms-race and information-race modes of coevolution. This model indicates that both the pattern of variation in resistance within populations, and whether enemies appear locally adapted to their host plants in between-population comparisons, differ depending on the mode of coevolution.

### Within-population variation in resistance

Consider first a situation in which interactions between plant and enemy are controlled by a matching-alleles

system, in which there is one locus controlling resistance in the plant and one locus controlling virulence in the enemy. Several authors have demonstrated that frequency-dependent selection can maintain polymorphisms at both loci for extended periods, often with the frequencies of the different alleles oscillating (Nee 1989; Frank 1992, 1993; Seger 1992).

In such polymorphic populations, interactions between host and enemy individuals may result in either resistance or susceptibility of the host, depending on the particular genotypes that interact. It is thus of interest to ask whether the proportions of interactions among individuals that result in susceptibility differ under arms-race versus information-race coevolution. The simplest situation, in which the host is diploid and the enemy is haploid, is portrayed in Fig. 3 for a matching-allele system in which three alleles are maintained in both the host and enemy. This figure shows that there are fewer combinations of genotypes that result in resistance for an E-R (information-race) system than for a T-D (arms-race) system.

More generally, for polymorphisms in a matching-alleles system with $n$ alleles, the numbers of host–enemy genotype combinations that result in susceptibility and resistance are given in Table 1, for both haploid and diploid enemies. The numbers in this table indicate that, except for the case of $n = 2$ for haploid enemies and $n = 3$ for diploid enemies, the number of host–enemy genotype combinations that result in resistance differ for the E-R and T-D systems. More specifically, with $n > 2$ for haploid enemies and $n > 3$ for diploid enemies, a smaller proportion of genotype combinations result in resistance for an E-R system than for a T-D system. This result suggests that, in general, genetically variable populations of hosts will be more susceptible to attack by natural enemies if the host–enemy interaction is mediated by an E-R system than if it is mediated by a T-D system. In this sense, toxins are more effective defenses than induced responses in polymorphic populations.

This analysis is admittedly crude because it does not take into account the relative frequencies of the different host and enemy genotypes. However, because the frequencies of alleles associated with polymorphisms involving resistance and virulence tend to oscillate (Nee 1989; Frank 1992, 1993; Seger 1992), we anticipate that on average the corresponding allele frequencies in E-R and T-D systems will tend to be roughly equal. If more detailed analyses prove this conjecture to be the case, the inferences drawn from our current analyses should be valid.

A similar result is obtained under a gene-for-gene system. Resistance and susceptibility for genotypic combinations in such a system with two loci, each with two alleles in both the host and enemy, are portrayed in Fig. 4. To construct this matrix, we assumed that under the E-R system, resistance is induced if either $R_1$ and $V_1$ or $Q_1$ and $X_1$ alleles occur together (i.e., if a functional receptor is present as well as the elicitor it detects); otherwise, resistance is not induced. In this model, $R_2$ and $Q_2$ are nonfunctional resistance alleles that produce a receptor that is not capable of recognizing any elicitors. For the T-D model, we assume that for the plant to be susceptible, the enemy must be able to detoxify all toxins produced by the host and that $V_i$ and $X_i$ produce enzymes that are capable of detoxifying the toxins produced by $R_i$ and $Q_i$, respectively. The latter assumption is conservative, in that the alternate assumption that $V_2$ and $X_2$ are null alleles that are incapable of detoxification produces more genotype combinations that are resistant.

Once again, fewer combinations of genotypes result in resistance under an E-R system than under a T-D system (see Fig. 4), indicating that overall level of resistance would be higher under a toxin–detoxification (T-D) system of resistance. Examination of a limited number of cases suggests that this result also holds for gene-for-gene systems with more than two loci and if the enemy is diploid, though we have not yet obtained a general proof for all cases.

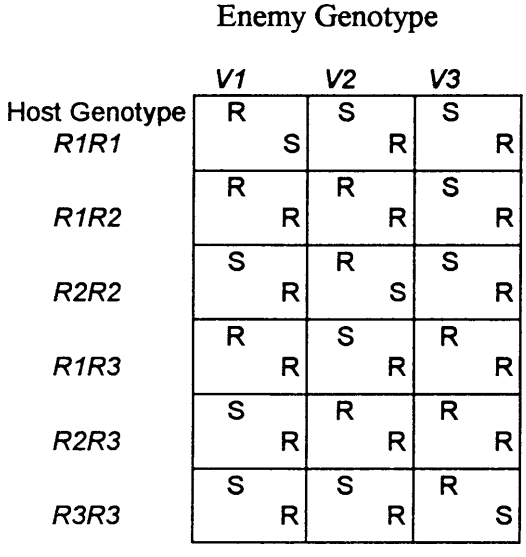


**Fig. 3.** Outcome of interaction between host and enemy genotypes for matching-alleles system with three alleles and with enemy haploid: *R*, host is resistant; *S*, host is susceptible. *Upper left entry* in each square is for elicitor–receptor system; *lower right entry* in each square is for toxin–detoxifier system

## Between-population effects

In addition to the within-population effects documented here, whether coevolution is primarily of the arms-race or

**Table 1.** Number of host–enemy matching-alleles genotype combinations that result in either resistance or susceptibility under elicitor–receptor (E-R) and toxin–detoxifier (T-D) models

| Host | Elicitor–receptor | | Toxin–detoxifier | |
|---|---|---|---|---|
| genotype | Resistant | susceptible | Resistant | susceptible |
| A. Diploid host and haploid enemy: | | | | |
| *ii* | 1 | $n - 1$ | $n - 1$ | 1 |
| *ij* | 2 | $n - 2$ | $n$ | 0 |
| B. Diploid host and diploid enemy: | | | | |
| *ii* | $n$ | $n(n - 1)2$ | $n(n - 1)/2$ | $n$ |
| *ij* | $2n - 1$ | $1 + n(n - 3)/2$ | $[n(n + 1)/2] - 1$ | 1 |

Entries are numbers of combinations for either a homozygous host genotype (*ii*) or a heterozygous (*ij*) host genotype; $n$ is number of alleles

| Host Genotype | Enemy Genotype V1 X1 | Enemy Genotype V1 X2 | Enemy Genotype V2 X1 | Enemy Genotype V2 X2 |
|---|---|---|---|---|
| *R1R1Q1Q1* | R / S | R / R | R / R | S / R |
| *R1R2Q1Q1* | R / R | R / R | R / R | S / R |
| *R2R2Q1Q1* | R / R | S / R | R / R | S / R |
| *R1R1Q1Q2* | R / R | R / R | R / R | S / R |
| *R1R2Q1Q2* | R / R | R / R | R / R | S / R |
| *R2R2Q1Q2* | R / R | S / R | R / R | S / R |
| *R1R1Q2Q2* | R / R | R / R | S / R | S / R |
| *R1R2Q2Q2* | R / R | R / R | S / R | S / R |
| *R2R2Q2Q2* | S / R | S / R | S / R | S / S |

**Fig. 4.** Outcome of interaction between host and enemy genotypes for gene-for-gene system with two loci and with enemy haploid: *R*, host is resistant; *S*, host is susceptible. *Upper left entry* in each square is for elicitor–receptor system; *lower right entry* in each square is for toxin–detoxifier system

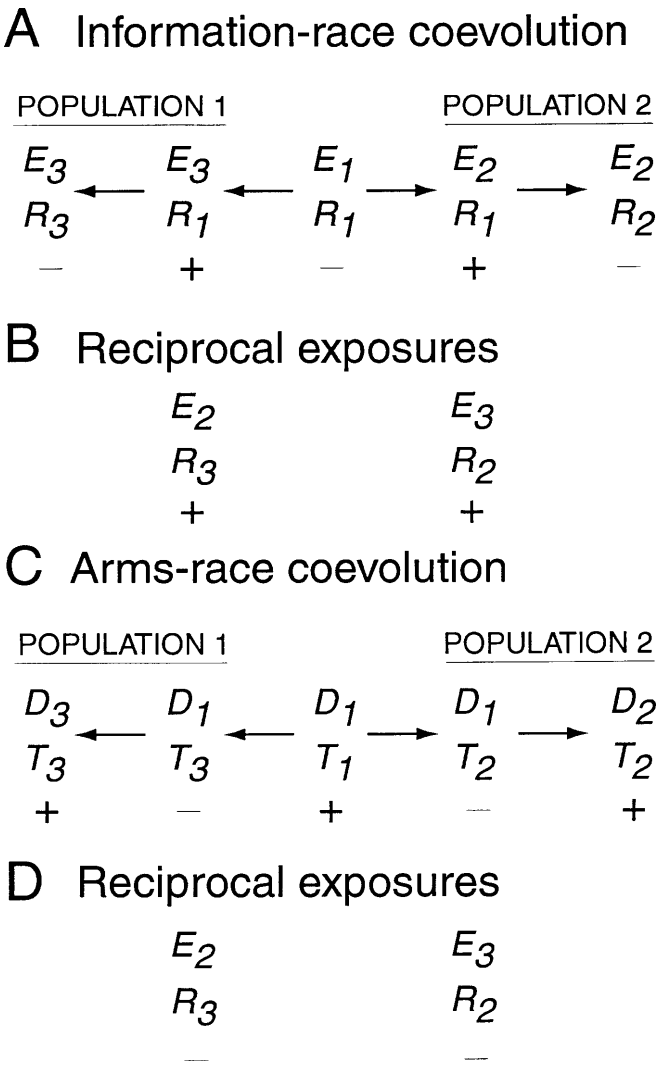


**Fig. 5.** Schematic portrayal of successive allele substitutions during divergent coevolution. **A** Two pairs of daughter host–enemy populations diverging via information–race coevolution. $E_i$ and $R_j$ represent fixed elicitor and receptor alleles of the enemy and host, respectively. When $i = j$, the receptor recognizes the elicitor and the plant is resistant (indicated by the *minus sign* below the genotype combination). When $i$ is not equal to $j$, receptor does not recognize elicitor, and plant is susceptible (indicated by *plus sign*). Common ancestral population is represented by the elicitor–receptor allele combination $E_1R_1$. **B** Outcome of reciprocal exposure of enemy from one population to host of other population after one round of allele substitutions in each population by the process in **A**. Receptors do not recognize "foreign" elicitors, resulting in host susceptibility. **C** Two pairs of daughter populations diverging via arms race coevolution. $D_i$ and $T_j$ represent fixed detoxifier and toxin alleles of the enemy and host, respectively. When $i = j$, the enemy neutralizes the host toxin and the plant is susceptible (indicated by the *plus sign*). When $i$ is not equal to $j$, enemy does not neutralize the host toxin, and plant is resistant (indicated by the *minus sign*). The common ancestral population is represented by detoxifier–toxin allele combination $D_1T_1$ . **D** Outcome of reciprocal exposure after one round of allele substitutions by the process in **C**. Toxins are not neutralized, and host is resistant

information-race type is also likely to influence whether enemies exhibit local adaptation to their hosts. To see why this is the case, first consider how coevolutionary divergence under the arms-race model is likely to affect the outcome of the typical reciprocal transplant experiment that is used to assess local adaptation. In particular, imagine two pairs of host–enemy populations that are diverging from a common ancestor in genes affecting resistance and virulence (Fig. 5). For simplicity of exposition, we consider a matching-alleles scenario, although similar patterns result from a gene-for-gene interaction.

Arms-race coevolution is most easily envisioned as involving host resistance genes that produce toxins and enemy virulence genes which produce detoxifiers of those toxins. If we assume there are a large number of potential alleles at the host toxin and enemy detoxification loci, then as each pair of interacting populations takes its own coevolutionary trajectory, different toxin and detoxifying alleles sequentially appear and become fixed in each population (Fig. 5C). After one complete round of coevolution in each pair of populations, each host population will produce one or more toxins for which enemies from the other population lack effective detoxifiers. Consequently, in a transplant experiment, when a host is exposed to an enemy with which it has not coevolved, the host will be resistant (Fig. 5D). By contrast, whether the same host is resistant to enemies from its own population depends on the exact state of the coevolutionary process. If the host has recently evolved a novel toxin, then it will generally be resistant to its associated enemy; however, if the enemy has recently evolved a novel detoxifier, the host will generally be susceptible. In either case, however, resistance to the "local" enemy population is

less than or equal to resistance to the "foreign" enemy population. Another way of saying this is that the enemy appears to be, on average, locally adapted to its host.

The outcome under information-race coevolution is quite different. Again we assume that there are a large number of potential alleles at the host receptor and enemy elicitor loci, which again means that the two pairs of populations undergo different coevolutionary trajectories. As before, different elicitor and receptor alleles will become fixed in each population (Fig. 5A). In this case, however, after one complete round of coevolution in each pair of populations, each enemy population will produce elicitors that are not recognized by hosts from the other population. Therefore, in a transplant experiment, when a host is exposed to an enemy with which it has not coevolved, the host will be susceptible because it does not recognize that enemy's elicitor(s) (Fig. 5B). By contrast, whether the "local" host is resistant to the same enemy will again depend on the exact state of the coevolutionary process: if the host has recently evolved an effective receptor, and is thus able to recognize the enemy and mount an induced defense, the host will be resistant; however, if the enemy has recently evolved an altered elicitor that is no longer recognized by the local host, that host will be susceptible. In either case, however, resistance to the local enemy population is greater than or equal to resistance to the foreign enemy population. Another way of saying this is that the enemy appears to be, on average, locally maladapted to its host (Gandon and Van Zandt 1998; Kaltz and Shykoff 1998; Kaltz et al. 1999).

These considerations indicate that arms-race coevolution and information-race coevolution are expected to produce very different spatial patterns of resistance and virulence. Arms-race coevolution produces a pattern of apparent local adaptation whereas information-race coevolution produces a pattern of apparent local maladaptation. Both these patterns have been documented for different plant–enemy associations (see following). We suggest that some of these differences among host–enemy species pairs may result from differences in whether arms-race coevolution or information-race coevolution has dominated their interactions.

One additional comment is in order: although greater susceptibility of a host to enemies from foreign populations (or, equivalently, greater virulence of foreign than local enemy populations) has typically been termed maladaptation in the literature (Gandon and Van Zandt 1998; Kaltz et al. 1999), information race coevolution does not result at any point in maladaptive evolution by natural enemies. Within each pair of coevolving populations, every genetic change in the enemy population is adaptive; i.e., every new elicitor allele is positively selected because it increases virulence and hence enemy reproductive success. The pattern of between-population "maladaptation" arises as a by-product of divergence between reproductively isolated populations, much in the same way that reproductive isolation is thought to arise in isolated populations as a result of independent divergence (Dobzhansky 1970). In essence, an enemy population is more successful on a foreign host simply because that foreign host has never previously been "challenged" by the enemy's elicitors, and thus has not, unlike the local host, had the opportunity to evolve receptors that recognize that elicitor.

## Distinguishing empirically between modes of coevolution

The analysis in the preceding sections indicates that arms-race coevolution may be distinguished from information-race coevolution empirically by examining patterns of variation in resistance and virulence both within and between populations. In practice, however, using within-population patterns of variation in this way is likely to be difficult for at least two reasons:

1. *Populations may not be genetically variable for resistance or virulence*. Although some models (e.g., Burdon 1987; Nee 1989; Frank 1992, 1993; Seger 1992) of host–enemy coevolution indicate that frequency-dependent selection can maintain fluctuating polymorphisms for both resistance and virulence, these models are all deterministic and do not allow for the elimination of alleles by genetic drift when they reach low frequencies in their cycles. Consequently, even moderately sized populations may fail to harbor sufficient genetic variation for analysis.
2. *Documenting the pattern of resistance–susceptibility interactions among genotypes within a population requires extensive genetic crosses and large sample sizes.* Although our analysis suggests that under the T-D mode of coevolution a greater proportion of randomly paired hosts and enemies should result in induction of host resistance, it does not establish a critical proportion that can always be used to distinguish T-D systems from E-R systems. In fact, as illustrated by Table 1, the proportion of resistant interactions varies with the number of alleles in the matching-alleles case; in the gene-for-gene case, it varies with the number of loci. Consequently, only by characterizing, for each host–enemy genotype combination, whether an interaction results in host resistance or susceptibility can the E-R pattern be distinguished from the T-D pattern. Naturally, this approach requires that all resistance and virulence genotypes be identified, a prerequisite that will often be very difficult for investigators wishing to study coevolution in natural systems.

Although these problems make distinguishing between arms race and information race coevolution using patterns of variation within populations difficult, it is likely to be much easier to distinguish between these two modes of coevolution using between-population comparisons. For such comparisons, standard reciprocal transplant experiments may be employed. In these experiments, it is not necessary to characterize the individual genes or genotypes involved. Instead, all one need ascertain is whether on average hosts are more (or less) resistant to local enemies than to enemies from another population, i.e., whether there is a pattern of local enemy adaptation or maladaptation.

Because of the relative ease with which such transplant experiments can be performed, a relatively large number of investigations have examined whether specific host–enemy systems exhibit local adaptation or maladaptation. Although many of these experiments have been reviewed previously in other contexts (Kaltz and Shykoff 1998), the potential implications of these investigations for understanding the relative importance of arms-race versus information-race coevolution in natural systems have not previously been explored. It is thus instructive to examine what these investigations may tell us about these two modes of coevolution. We therefore have conducted our own literature survey with the goal of addressing two issues: (1) among all host–enemy associations that have been examined, is there evidence that either of the two modes of coevolution predominates; and (2) does the predominant mode differ among different types of interactions (e.g., plant–pathogen versus plant–herbivore versus invertebrate–parasite versus vertebrate–parasite interactions).

## Literature survey

We have attempted to examine all published investigations of natural host–enemy associations in which between-site (population) reciprocal transplant experiments involving hosts and either one or more of their natural enemies have been performed. In these studies, host resistance and enemy virulence were estimated in a variety of ways, as necessitated by the differences in basic biology of the organisms examined. To be included in this analysis, an investigation had to satisfy two criteria:

1. *Transplant localities had to plausibly represent separate populations for both hosts and enemies*. This requirement was imposed to be reasonably confident that divergent coevolution could have occurred between the localities examined. This criterion eliminated several studies involving intertree transfer of insect herbivores among trees at the same site (Edmunds and Alstad 1978; Cobb and Whitham 1993; Sork et al. 1993; Hanks and Denno 1994). Although it is conceivable that in these studies insect colonies on different trees represent reproductively isolated demes, it is virtually certain that the trees employed represented individuals from a single population.
2. *Inference of local adaptation or maladaptation had to be supported by an appropriate statistical analysis.* Acceptable statistical analyses included examination of host site × enemy site interaction and home versus away contrasts, as well as other more idiosyncratic analyses adapted to the specifics of the experimental design used.

We located 18 investigations of natural populations that satisfied these two criteria. Of these, 8 involved plant–pathogen interactions, 5 involved plant–herbivore interactions, 5 involved invertebrate–parasite interactions, and 1 involved vertebrate–parasite interactions. This sample is admittedly small, but serves to illustrate some preliminary patterns that should be viewed as tentative, pending additional investigations. Table 2 lists the relevant characteristics of these investigations.

Considering all types of plant–enemy interactions together, there is not a marked preponderance of one mode of coevolution. Eight investigations revealed some form of local adaptation by the enemy, consistent with the expectations of arms-race coevolution, while four exhibited local maladaptation, consistent with information-race coevolution (Table 3). Six investigations were ambiguous, exhibiting neither local adaptation nor local maladaptation. It is unclear whether these six studies indicate lack of coevolutionary divergence between the populations examined or a joint, compensatory operation of both modes of coevolution. Overall, this small sample of studies suggests that information-race coevolution may be slightly, though not substantially, less common in nature than arms-race coevolution.

Considering different types of plant–enemy interactions separately, some tantalizing hints of patterns are evident. For example, within invertebrate–parasite and vertebrate–parasite interactions there are no cases of local maladaptation. Although little is known about the molecular basis of resistance and virulence in these organisms, these limited results suggest T-D systems may form the basis for coevolution in these interactions. In contrast, for plant–pathogen interactions, local adaptation and local maladaptation appear equally common. Although most recent discussions of plant–pathogen coevolution either explicitly or implicitly assume interactions based on elicitors and receptors, this result is consistent with what is known about the defenses of plants against pathogens. On the one hand, recent elaboration of the molecular basis of gene-for-gene systems clearly implicates the potential for the type of coevolution of elicitor–receptor interactions characteristic of information-race coevolution (Hammond-Kosack and Jones 1997; De Wit 1997; Parker and Coleman 1997). On the other hand, plants are also defended from their pathogens by various toxin-like factors (Dixon 1986; Ebel 1986; Bishop et al. 2000), which can give rise to arms race coevolution.

Although the sample size is very small, plant–herbivore associations exhibit the same number of cases of local maladaptation, indicative of information race coevolution, and of local adaptation. This result is surprising because, in contrast with plant–pathogen coevolution, the toxin–detoxifier arms-race metaphor is closely identified with plant–herbivore coevolution (Rosenthal et al. 1977; Berenbaum 1983; Bowers 1988). Plants produce numerous types of toxins, growth inhibitors, and other traits that confer active resistance of the type involved in arms-race coevolution, and it is largely these traits that have been the focus of discussions of plant–herbivore coevolution. Over the past two decades, however, it has become clear that in many plants, chemical resistance factors may be induced by herbivore damage (Ryan 1983; Karban and Carey 1984; Baldwin 1988a,b). Such induction requires a signal–re-

**Table 2.** Characteristics of host–enemy associations examined

| Host species | Enemy species | Transplant distance | Measure of resistance/virulence | Outcome | Reference |
|---|---|---|---|---|---|
| **Plant–pathogen associations** | | | | | |
| *Triticum aestivum* | *Septoria tricici* | Between CA and OR | Percent leaf area infected | + | Ahmed et al. 1995 |
| *Silene dioica* | *Microbotryum violaceum* | 2 km | Percent infection | + | Carlsson-Graner 1997 |
| *Spartina pectinata* | *Puccinia* spp. | 4.5 km | Percent leaf area infected | 0 | Davelos et al. 1996 |
| *Silene latifolia* | *Microbotryum violaceum* | 10–170 km | Percent infection | − | Kaltz et al. 1999 |
| *Stipa leucotricha* | *Atkinsonella hypoxylon* | Between counties | Percent infection | 0 | Leuchtmann and Clay 1989 |
| *Amphicarpaea bracteata* | *Synchytrium decipiens* | 1 km | Percent infection | + | Parker 1985 |
| *Podophyllum peltatum* | *Puccinia podophylli* | 48 km | Percent infection | − | Parker 1989 |
| *Arabis holboellii* | *Puccinia* spp. | Between mountain valleys | Percent infection | − | Roy 1998 |
| **Plant–herbivore associations** | | | | | |
| *Erigeron glaucus* | *Apterothrips secticornis* | 500 m | Number of thrips per plant | + | Karban 1989 |
| *Arabis holboelli* | *Pieris* sp. | Between mountain valleys | Percent attacked | − | Roy 1998 |
| *Rhus glabra* | *Blepharida rhois* | >10.9 km | Larval survival, weight | 0 | Strauss 1997 |
| *Pinus monophylla* | *Matsucoccus acalyptus* | Between counties | Larval survival | 0 | Unruh and Luck 1987 |
| **Invertebrate–parasite associations** | | | | | |
| *Daphnia magna* | *Pleistophora intestinalis* | 0.5–1.5 km | Spore load, host reproduction | + | Ebert 1994 |
| *Bombus terrestris* | *Crithidia bombi* | >20 km | Percent infection, host survival | 0 | Imhoof and Schmid-Hempel 1998 |
| *Potamopyrgus antipodarum* | *Microphallus* spp. | 10–85 km | Percent infection | + | Lively 1989 |
| *Bulinus globosus* | *Schistosoma* spp. | 60 km | Percent infection | + | Manning et al. 1995 |
| *Bulinus truncatus* | *Schistosoma haematobium* | 500 km | Percent infection | 0 | Vera et al. 1990 |
| **Vertebrate–parasite association** | | | | | |
| *Phoxinus phoxinus* | *Diplostomum phoxini* | 35 km | Host size | + | Ballabeni and Ward 1993 |

CA, California; OR, Oregon
+, local adaptation; −, local maladaptation; 0, neither

**Table 3.** Number of studies reporting local adaptation, local maladaptation, and neither, categorized by type of host–enemy association

| Type of host–enemy association | Local adaptation | Neither | Local maladaptation |
|---|---|---|---|
| Plant–pathogen | 3 | 2 | 3 |
| Plant–herbivore | 1 | 2 | 1 |
| Invertebrate–parasite | 3 | 2 | 0 |
| Vertebrate–parasite | 1 | 0 | 0 |
| Totals | 8 | 6 | 4 |

sponse system that triggers induction and that could serve as a focus for coevolution between the elicitors and receptors that mediate the signaling. Moreover, the molecular details of this signal–response system are beginning to be elucidated (Karban and Baldwin 1997). It might thus be expected that coevolution between plants and herbivores would sometimes occur in the information race mode. In fact, our preliminary analysis suggests (weakly) that information-race coevolution may be roughly as common as arms-race coevolution in plant–herbivore associations. If this pattern is confirmed by additional analyses, evolutionary biologists will be led to conclude that coevolution in plant–herbivore and plant–pathogen systems is more similar than currently appreciated.

## Conclusions and caveats

We have argued that host–enemy antagonistic coevolution can occur in two fundamentally different modes. We have also argued that these modes are expected to produce different ecological patterns both within and between populations. In particular, information race coevolution naturally gives rise to heretofore puzzling instances of apparent local enemy maladaptation. Finally, utilizing the assumption that local enemy adaptation reflects the arms-race mode and local maladaptation reflects the information-race mode of coevolution, we have shown that a literature review of reciprocal transplant experiments suggests some interesting patterns in the relative prevalence of these two modes of coevolution that deserve further examination.

We recognize that few of our suggestions are supported by definitive proof. For example, although the operation of information-race coevolution *can* explain cases of apparent local enemy maladaptation, other explanations are also fea-

sible. Extinction, migration, and genetic drift may prevent any correlation between host resistance and pathogen virulence alleles within a single population (Burdon and Thrall 1999). This possibility supports the notion that transient local maladaptation may sometimes arise when coevolving traits are temporarily mismatched within a population that exists in a complex geographic landscape with variable demographics (Thompson 1999).

Other authors have also argued that gene flow among populations within a metapopulation, differing spatial structure of host and enemy populations, and long enemy generation times can, under some circumstances, produce at least transiently a pattern of apparent local maladaptation (Gandon et al. 1996; Lively 1996; Mopper and Strauss 1998; Kaltz and Shykoff 1999). The existence of examples of local maladaptation clearly cannot be used to distinguish among these alternative hypotheses. Rather, the intent of our arguments is to present a conceptually novel explanation for this phenomenon and to illustrate the kinds of inferences that might be drawn if this explanation is correct.

We offer this explanation in part to suggest an alternative to the conclusion of some authors that local maladaptation indicates that enemy-imposed selection for host resistance is more effective than host-imposed selection for virulence in enemies (Kaltz et al. 1999). We also offer this explanation in the belief that it will be easier to distinguish empirically between these two classes of alternative explanations – information-race coevolution versus complicated demographics – than among the existing hypotheses in the demographics category. Establishing a definitive causal connection between, for example, gene flow or enemy generation time and the pattern of local adaptation in natural host–enemy associations, may well be impossible both because these demographic characteristics often cannot be manipulated; also, even if they can be manipulated, the time scales necessary for observing subsequent evolutionary divergence of populations will likely be prohibitive.

By contrast, establishing or refuting the importance of information-race coevolution in creating patterns of local maladaptation should require "only" performing the detailed molecular characterization of resistance–virulence genes that have diverged between populations. Without attempting to minimize the effort and funding that would be required for such a project, we suggest that recent progress in characterizing E-R (Hammond-Kosack and Jones 1997; De Wit 1997; Parker and Coleman 1997) and T-D (Hung et al. 1996; Bishop et al. 2000) systems at the molecular level indicates that it is technologically feasible. By applying this technology to a few well-chosen examples of both local adaptation and local maladaptation, it should be straightforward to determine whether these two patterns are strongly associated with changes in toxin–detoxifier interactions and elicitor–receptor interactions, respectively. Such an association would constitute, in our view, effectively definitive proof of the operation of information-race coevolution. Conversely, lack of a strong association would indicate the prevalence of demographic characteristics in causing apparent local maladaptation.

## References


Ahmed HU, Mundt CC, Coakley SM (1995) Host-pathogen relationship of geographically diverse isolates of *Septoria tritici* and wheat cultivars. Plant Pathol 44:838–847

Baldwin IT (1988a) The alkaloidal responses of wild tobacco to real and simulated herbivory. Oecologia (Berl) 77:378–381

Baldwin IT (1988b) Short-term damage-induced increases in tobacco alkaloids protect plants. Oecologia (Berl) 75:367–370

Ballabeni P, Ward PI (1993) Local adaptation of the trematode *Diplostomum phoxini* to the European minnow *Phoxinus phoxinus*, its second intermediate host. Funct Ecol 7:84–90

Berenbaum M (1983) Coumarins and caterpillars: a case for coevolution. Evolution 37:163–179

Berenbaum MR, Zangerl AR (1988) Stalemates in the coevolutionary arms race: syntheses, synergisms, and sundry other sins. In: Spencer KC (ed) Chemical mediation of coevolution. Academic Press, New York, pp 113–132

Berenbaum MR, Zangerl AR (1998) Chemical phenotype matching between a plant and its insect herbivore. Proc Natl Acad Sci USA 95:13743–13748

Bishop JG, Dean AM, Mitchell-Olds T (2000) Rapid evolution in plant chitinases: molecular targets of selection in plant-pathogen coevolution. Proc Natl Acad Sci USA 97:5322–5327

Bowers MD (1988) Chemistry and coevolution: iridoid blycosides, plants, and herbivorous insects. In: Spencer KC (ed) Chemical mediation of coevolution. Academic Press, New York, pp 133–165

Brattsten LB (1980) Biochemical defense mechanisms in herbivores against plant allelochemicals. In: Rosenthal GA, Janzen DH (eds) Herbivores. Their interaction with secondary plant metabolites. Academic Press, New York, pp 199–270

Brodie ED III, Brodie ED Jr (1990) Tetrodotoxin resistance in garter snakes: an evolutionary response of predators to dangerous prey. Evolution 44:651–659

Burdon JJ (1987) Diseases and plant population biology. Cambridge University Press, Cambridge

Burdon JJ, Thrall PH (1999) Spatial and temporal patterns in coevolving plant and pathogen associations. Am Nat 153:S15–S33

Carlsson-Graner U (1997) Anther-smut disease in *Silene dioica*: variation in susceptibility among genotypes and populations, and patterns of disease within populations. Evolution 51:1416–1426

Cobb NS, Whitham TG (1993) Herbivore deme formation on individual trees: a test case. Oecologia (Berl) 94:496–502

Davelos AL, Alexander HM, Slade NA (1996) Ecological genetic interactions between a clonal host plant (*Spartina pectinata*) and associated rust fungi (*Puccinia seymouriana* and *Puccinia sparganioides*). Oecologia (Berl) 105:205–213

Dawkins R, Krebs JR (1979) Arms race between and within species. Proc R Soc Lond B 205:489–511

De Wit PJGM (1997) Pathogen avirulence and plant resistance: a key role for recognition. Trends Plant Sci 2:452–458

Dethier VG (1954) Evolution of feeding preferences in phytophagous insects. Evolution 8:33–54

Dixon RA (1986) The phytoalexin response: elicitation, signalling and control of gene expression. Biol Rev (Camb) 61:239–291

Dobzhansky T (1970) Genetics and the evolutionary process. Columbia University Press, New York

Ebel J (1986) Phytoalexin synthesis: the biochemical analysis of the induction process. Annu Rev Phytopathol 24:235–264

Ebert D (1994) Virulence and local adaptation of a horizontally transmitted parasite. Science 265:1084–1086

Ehrlich PR, Raven PH (1964) Butterflies and plants: a study in coevolution. Evolution 18:586–608

Edmunds GF, Alstad DN (1978) Coevolution in insect herbivores and conifers. Science 199:941–945

Feeny P (1975) Biochemical coevolution between plants and their insect herbivores. In: Glibert LE, Raven PH (eds) Coevolution of animals and plants. University of Texas Press, Austin pp 3–19

Feinsinger P (1983) Coevolution and pollination. In: Futuyma DJ, Slatkin M (eds) Coevolution. Sinauer, Sunderland, MA pp 282–310

Flor HH (1956) The complementary genic systems in flax and flax rust. Adv Genet 8:29–54

Flor HH (1971) Current status of the gene-for-gene concept. Annu Rev Phytopathol 9:275–296

Frank SA (1992) Models of plant-pathogen coevolution. Trends Genet 8:213–219
Frank SA (1993) Specificity versus detectable polymorphism in host-parasite genetics. Proc R Soc Lond B 254:191–197
Gandon S, Van Zandt PA (1998) Local adaptation and host-parasite interactions. Trends Ecol Evol 13:214–216
Gandon S, Capowiez Y, Dubios Y, Michalakis Y, Olivieri I (1996) Local adaptation and gene-for-gene coevolution in a metapopulation model. Proc R Soc Lond Series B 263:1003–1009
Gilbert LE (1971) Butterfly-plant coevolution: has *Passiflora adenopoda* won the selection race with heliconiine butterflies? Science 172:585–586
Gilbert LE (1975) Ecological consequences of a coevolved mutualism between butterflies and plants. In: Gilbert LE, Raven PH (eds) Coevolution of animals and plants. University of Texas Press, Austin, pp 210–240
Grant PR (1986) Ecology and evolution of Darwin's finches. Princeton University Press, Princeton
Hammond-Kosack KE, Jones JDG (1996) Resistance gene-dependent plant defense responses. Plant Cell 8:1773–1791
Hammond-Kosack KE, Jones JDG (1997) Plant disease resistance genes. Annu Rev Plant Physiol Plant Mol Biol 48:575–607
Hanks LM, Denno RF (1994) Local adaptation in the armored scale insect *Pseudaulcaspis pentagona*. Ecology 75:2301–2310
Hung C-H, Holzmacher R, Connolly E, Berenbaum M, Schuler M (1996) Conserved promoter elements in the *CYP6B* genes suggest comon ancestry for cytochrome P450 monooxygenases mediating furanocoumarin detoxification. Proc Natl Acad Sci USA 93:12200–12205
Hutchenson SW (1998) Current concepts of active defense in plants. Ann Rev Phytopathol 36:59–90
Imhoof B, Schmid-Hempel P (1998) Patterns of local adaptation of a protozoan parasite to its bumblebee host. Oikos 82:59–65
Janzen DH (1966) Coevolution of mutualism between ants and acacias in Central America. Evolution 20:249–275
Janzen DH (1969) Seed-eaters versus seed size, number, toxicity and dispersal. Evolution 23:1–27
Janzen DH, Martin PS (1982) Neotropical anachronisms: the fruits the gomphotheres left behind. Science 215:19–27
Kaltz O, Shykoff JA (1998) Local adaptation in host-parasite systems. Heredity 81:361–370
Kaltz O, Gandon S, Michalakis Y, Shykoff JA (1999) Local maladaptation in the anther-smut fungus *Microbotryum violaceum* to its host plant *Silene lagifolia*: evidence from a cross-inoculation experiment. Evolution 53:395–407
Karban R (1989) Fine-scale adaptation of herbivorous thrips to individual host plants. Nature (Lond) 340:60–61
Karban R, Baldwin IT (1997) Induced responses to heribivory. University of Chicago Press, Chicago
Karban R, Karey JR (1984) Induced resistance of cotton seedlings to mites. Science 225:53–54
Krieger RI, Feeny PP, Wilkinson CF (1971) Detoxication enzymes in the guts of caterpillars: an evolutionary answer to plant defenses? Science 172:579–581
Lamb CJ, Lawton MA, Dron M, Dixon RA (1989) Signals and transduction mechanisms for activation of plant defenses against microbial attack. Cell 56:215–224
Leuchtmann A, Clay K (1989) Experimental evidence for genetic variation in compatibility between the fungus *Atkinsonella hypoxylon* and its three host grasses. Evolution 43:825–834
Lively CM (1989) Adaptation by a parasitic trematode to local populations of its snail host. Evolution 43:1663–1671
Lively CM (1996) Host-parasite coevolution and sex. Bioscience 46:107–114
Manning SD, Woolhouse MEJ, Ndamba J (1995) Geographic compatibility of the freshwater snail *Bulinus globosus* and schistosomes from the Zimbabwe highveld. Int J Parasitol 25:37–42
Mauricio R, Rausher MD (1997) Experimental manipulation of putative selective agents provides evidence for the role of natural enemies in the evolution of plant defenses. Evolution 51:1435–1444
McDowell JM, Dhandaydham M, Long TA, Aarts MGM, Goff S, Holub EB, Dangl JL (1998) Intragenic recombination and diversifying selection contribute to the evolution of downy mildew resistance at the RPP8 locus of *Arabidopsis*. Plant Cell 10:1861–1874
Meyers BC, Shen KA, Rohani P, Gaut BS, Michelmore RW (1998) Receptor-like genes in the major resistance locus of lettuce are subject to divergent selection. Plant Cell 11:1833–1846
Michelmore R (1995) Molecular approaches to manipulation of disease resistance genes. Annu Rev Phytopathol 15:393–427
Mopper S, Strauss SY (1998) Genetic structure and local adaptation in natural insect populations: effects of ecology, life history, and behavior. Chapman and Hall, New York
Moran NA, Telang A (1998) The evolution of bacteriocyte-associated endosymbionts in insects. Bioscience 48:295–304
Morand S, Manning SD, Woolhouse MEJ (1996) Parasite-host coevolution and geographic patterns of parasite infectivity and host susceptibility. Proc R Soc Lond B 263:119–128
Nee S (1989) Antagonistic coevolution and the evolution of genotypic randomization. J Theor Biol 140:499–518
Parker JE, Coleman MJ (1997) Molecular intimacy between proteins specifying plant-pathogen recognition. Trends Biochem Sci 22:291–296
Parker MA (1985) Local population differentiation for compatibility in an annual legume and its host-specific fungal pathogen. Evolution 39:713–723
Parker MA (1989) Disease impact and local genetic diversity in the clonal plant *Podophyllum peltatum*. Evolution 43:540–547
Parniske M, Hammond-Kosack KE, Holtstein C, Thomas CM, Harrison DA, Wulff BBH, Jones JDG (1997) Novel disease resistance specificities result from sequence exchange between tandemly repeated genes at the *Cf-4/9* locus of tomato. Cell 91:821–832
Rausher MD (1981) Host plant selection by *Battus philenor* butterflies: the roles of predation, nutrition, and plant chemistry. Ecol Monogr 51:1–20
Rhoades DF (1985) Offensive-defensive interactions between herbivores and plants: their relevance in herbivore population dynamics and ecological theory. Am Nat 125:205–238
Rosenthal GA, Dahlman DL, Janzen DH (1977) Degredation and detoxification of canaline by a specialized seed predator. Science 202:528–529
Roy BA (1998) Differentiating the effects of origin and frequency in reciprocal transplant experiments used to test negative frequency-dependent selection hypotheses. Oecologia (Berl) 115:75–83
Ryals JA, Neuenschwander UH, Willitis MG, Molina A, Steine H-Y, Hunt MD (1996) Systemic acquired resistance. Plant Cell 8:1089–1819
Ryan CA (1983) Insect-induced chemical signals regulating natural plant protection responses. In: Denno RF, McClure MS (eds) Variable plants and herbivores in natural and managed systems. Academic Press, New York, pp 43–60
Schluter D, McPhail JD (1992) Ecological character displacement and speciation in sticklebacks. Am Nat 140:85–108
Seger J (1992) Evolution of exploiter-victim relationships. In: Crawley MJ (ed) Natural enemies: the population biology of predators, parasites, and disease. Blackwell, Oxford, pp 3–25
Smiley J (1978) Plant chemistry and the evolution of host specificity: new evidence from *Heliconius* and *Passiflora*. Science 201:745–747
Sork VL, Stowe KA, Hochwender C (1993) Evidence for local adaptation in closely adjacent subpopulations of northern red oak (*Quercus rubra* L.) expressed as resistance to leaf herbivores. Am Nat 142:928–936
Staskawicz BJ, Ausubel FM, Baker BJ, Ellis JG, Jones JDG (1995) Molecular genetics of plant disease resistance. Science 268:661–667
Strauss SY (1997) Lack of evidence for local adaptation to individual plant clones or site by a mobile specialist herbivore. Oecologia (Berl) 110:77–85
Tang X, Frederick RD, Zhou J, Halterman DA, Jia Y, Martin GB (1996) Initiation of plant disease resistance by physical interaction of avrPto and Pto kinase. Science 274:2060–2063
Thompson JN (1999) Specific hypotheses on the geographic mosaic of coevolution. Am Nat 153:S1–S14
Turkington R, Harper JL (1979) The growth, distribution and neighbour relationships of *Trifolium repens* in a permanent pasture. IV. Fine scale biotic differentiation. J Ecol 67:245–254
Unruh TR, Luck RF (1987) Deme formation in scale insects: a test with the pinyon needle scale and a review of other evidence. Ecol Entomol 12:439–449
Vera C, Jourdane J, Sellin B, Bombes C (1990) Genetic variability in the compatibility between *Schistosoma haematobium* and its po-

tential vectors in Niger. Epidemiological implications. Trop Med Parasitol 41:143–148
Vermeij GJ (1983) Intimate associations and coevolution in the sea. In: Futuyma DJ, Slatkin M (eds) Coevolution. Sinauer, Sunderland, MA, pp 311–327
Vermeij GJ (1987) Evolution and escalation: an ecological history of life. Princeton University Press, Princeton
Vermeij GJ (1993) A natural history of shells. Princeton University Press, Princeton
Vidhyasekaran P (1997) Fungal pathogenesis in plants and crops: molecular biology and host defense mechanisms. Dekker, New York
Wang G-L, Ruan D-L, Song W-Y, Sideris S, Chen L, Pi L-Y, Zhang S, Zhang Z, Fauquet C, Gaut BS, Whalen MC, Ronald PC (1998) *Xa21D* encodes a receptor-like molecule with a leucine-rich repeat domain that determines race-specific recognition and is subject to adaptive evolution. Plant Cell 10:765–779
Williams KS, Gilbert LE (1981) Insects as selective agents on plant vegetative morphology: egg mimicry reduces egg laying by butterflies. Science 212:467–469
Whittaker RH, Feeny PP (1971) Allelochemics: chemical interactions between species. Science 171:757–770