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MODELS AND DATA ON PLANT-ENEMY COEVOLUTION

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■ **Abstract** Although coevolution is complicated, in that the interacting species evolve in response to each other, such evolutionary dynamics are amenable to mathematical modeling. In this article, we briefly review models and data on coevolution between plants and the pathogens and herbivores that attack them. We focus on "arms races," in which trait values in the plant and its enemies escalate to more and more extreme values. Untested key assumptions in many of the models are the relationships between costs and benefits of resistance in the plant and the level of resistance, as well as how costs of virulence or detoxification ability in the enemy change with levels of these traits. A preliminary assessment of these assumptions finds only mixed support for the models. What is needed are models that are more closely tailored to particular plant-enemy interactions, as well as experiments that are expressly designed to test existing models.

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INTRODUCTION

In evolutionary biology, progress has historically been aided by the construction of mathematical models that describe how allele frequencies change within populations. Most such population-genetic models have concentrated on the evolution of traits that affect how a species is adapted to its physical environment (68), rather than how it interacts with other species. Understanding the evolution of traits that affect interactions between species, however, is complicated by the possibility of coevolution, in which each species evolves in response to the other. This complication has limited both the development and the application of coevolutionary models (60). Nevertheless, recent work has led to the development of promising new modeling approaches (1). Moreover, the advent of evolutionary genomics may soon allow us to test these models more thoroughly than before.

In this article, we consider the usefulness of mathematical models for understanding coevolution between plants and their natural enemies. By "natural enemies" we mean herbivores or pathogens, as opposed to competitors such as other plants, or mutualists, such as pollinators. Much of the interest in coevolutionary dynamics of victim-exploiter interactions has to do with the possibility of so-called arms races (25), or Red-Queen dynamics (18, 92). An arms race occurs when a trait in each species evolves toward ever more extreme values in response to the evolution of a corresponding trait in the other species. The simplest such example might be evolution toward increased host resistance to a pathogen, in response to increased virulence in the pathogen. Local adaptation is said to have occured either when a natural enemy strain has higher fitness when attacking a plant strain from the same area than when attacking a plant strain from a different area, or when a plant strain has higher fitness when being attacked by a natural enemy strain from the same area than when being attacked by a natural enemy from a different area. Because local adaptation has recently been reviewed elsewhere (13, 51, 84, 93), here we focus primarily on arms races.

An important feature of recent modeling work on coevolution is the proposed solution to a perceived problem in the usual definition of an arms race (77). Specifically, limitless escalation in trait values would naturally lead to infinite values, which is of course implausible. One possible solution to this problem is to have trait values cycle, so that victim and exploiter trait values rise for several generations, then fall to their previous values in a dynamic polymorphism (3, 28). It has been argued that this kind of coevolutionary dynamic is an arms race because trait values escalate at least some of the time. Our intent in this review is to show how arms race models have been developed out of classical population-genetic models, and to indicate one way that such models may be compared with data.

We first briefly review mathematical models that describe coevolution in victim-exploiter interactions, a category that includes predator-prey, host-parasite, host-pathogen, and plant-herbivore interactions. Second, we review data sets for plants and their enemies, focusing mostly on insect herbivores, in order to examine the extent to which basic assumptions of the models accurately describe real plant-enemy

interactions. Third, we assess models in terms of the accuracy of their predictions. And, finally, we highlight some interactions between plants and enemies that have thus far not been incorporated into models but that have the potential of generating interesting dynamics. Our goal is to foster a better connection between models and data in the study of plant-enemy coevolution.

MATHEMATICAL MODELS OF THE EVOLUTION OF VICTIM-EXPLOITER INTERACTIONS

For practical reasons, most empirical studies of victim-exploiter interactions focus on cases in which either the victim has a strong effect on the fitness of the exploiter or, conversely, the exploiter has a strong effect on the fitness of the victim. Most mathematical models of arms races in victim-exploiter interactions therefore focus on natural selection as the primary evolutionary force, often to the exclusion of mutation, genetic drift, or migration. In the absence of these other forces, the standard population-genetic model for selection acting on two alleles at a single locus is

$$p_{t+1} = \frac{p_t w_t}{\bar{w}_t}, \qquad 1.$$

where p_t is the frequency of the allele in generation t, w_t is the allele's fitness in generation t averaged over genotypes, and $\bar{w}_t$ is the average fitness of the entire population in generation t (68). If fitnesses are constant and unequal, then p_t will approach 1, unless the population is diploid and there is heterozygote overdominance. A basic feature of loci that affect species interactions, however, is that the fitnesses of different alleles are not constant. In particular, the fitness of an allele may depend on the frequency of the other alleles in the population. To see why this might be true, consider a haploid host in which allele *A* confers resistance to pathogen strain 1, and allele *a* confers resistance to pathogen strain 2. If allele *A* is at high frequency for several generations, it is likely that its fitness will decline as the density of pathogen 1 increases. High fitness of allele *a* may thus be associated with a high frequency of allele *A*.

One of the simplest ways to model this kind of interaction is to use a one-locus, two-allele model for the hosts, to assume that the pathogens are haploid, and then to assign fitnesses to each host and pathogen combination. For example, Levin (58) presents a generalization of several basic early models, according to which the host alleles *A* and *a* have frequencies p_t and $1 - p_t$, and the pathogen alleles *B* and *b* have frequencies q_t and $1 - q_t$. Pathogens of type *B* that attack hosts of genotype *AA* have fitness α, those that attack hosts of genotype *Aa* have fitness β, and those that attack genotype *aa* have fitness γ. The fitness of the alternative pathogen type *b* is antisymmetric, meaning that pathogens of type *b* that attack hosts of type *AA* have fitness γ, those that attack *Aa* have fitness β, and those that attack *aa* have fitness α. The probability that a particular pathogen genotype will

attack a particular host genotype is assumed to depend only on the frequency of the host genotype, so that the mean fitnesses of the two pathogen types in generation t are

$$v_B = p_t^2\alpha + 2p(1-p_t)\beta + (1-p_t)^2\gamma, \quad 2.$$

$$v_b = p_t^2\gamma + 2p_t(1-p_t)\beta + (1-p_t)^2\alpha. \quad 3.$$

Host fitnesses follow similar rules, in that the fitness of host genotype *AA* when attacked by pathogen type *B* is $1-\alpha$, the fitness of host genotype *Aa* when attacked by pathogen type *B* is $1-\beta$, etc. The usefulness of this type of model is that it can be used to understand the circumstances under which polymorphism is possible. It turns out that polymorphism in the host is maintained whenever

$$\beta < \frac{\alpha+\gamma}{2}. \quad 4.$$

In other words, the fitness of the pathogen that attacks the heterozygote host must be less than the fitness of the pathogen that attacks either homozygote. Polymorphism of both host and pathogen, however, requires the stronger condition,

$$\beta^2 < \left(\frac{\alpha+\gamma}{2}\right)^2 - \left(\frac{\alpha-\gamma}{2}\right)^2. \quad 5.$$

Because we shortly address the issue of whether polymorphisms are dynamic, here we point out that much of this early literature focuses strictly on conditions under which polymorphism occurs and apparently does not consider whether cycling in allele frequencies might also occur.

Although in this model the emphasis is on the assignment of fitnesses to particular host-pathogen combinations, it is important to remember that victim fitness is also affected by the probability of attack, and thus by the ecology of the victim and the exploiter. Because ecological theory emphasizes the importance of density for species interactions, an important next step in the development of coevolutionary models of victim-exploiter interactions was the incorporation of density effects. The simplest way to do this is to begin with host-pathogen interactions, focusing specifically on the classic epidemic model (22):

$$\frac{dS}{dt} = -\beta SI, \quad 6.$$

$$\frac{dI}{dt} = \beta SI - \alpha I. \quad 7.$$

Here, S and I are the densities of the uninfected and infected host populations, β is the rate of horizontal transmission, and α is the rate of disease-induced death. Because this model describes the progress of the epidemic, one can use it to assign fitnesses to different victim and exploiter genotypes. To see how this is done, we focus on the simplest case, in which the host is haploid and there is only one pathogen strain, so that allele A confers resistance, a confers susceptibility, and p_t

is the frequency of the *A* allele in generation *t*, following Gillespie (43). If we then allow $t \to \infty$ in Equations 6 and 7, the fraction of hosts that become infected, *i*, can be expressed by the implicit equation

$$1 - i = e^{-R_0 i(1-p_t)}. \quad 8.$$

Here, R_0 is defined as the absolute fitness of the pathogen, which can be derived from Equations 6 and 7 as

$$R_0 = \frac{\beta K}{\alpha}, \quad 9.$$

where *K* is the population density of the host, which is assumed to be fixed. From this expression, in the haploid case the fitnesses of the susceptible and resistant hosts are

$$W_a = (1 - i(p_t)) + i(p_t)(1 - t), \quad 10.$$

$$W_A = (1 - s), \quad 11.$$

where $(1 - t)$ is the fitness of susceptible hosts that have survived infection, and $(1 - s)$ is the fitness of resistant hosts. As in the simpler models, one can then consider the conditions under which host polymorphism occurs; specifically, polymorphism will be maintained if the ratio of selection coefficients is less than what the fraction infected, *i*, would be if the entire population were susceptible, so that $s/t \leqq i(p_t = 0)$. The key innovation, however, is that now polymorphism depends on host population density. For example, for high values of absolute pathogen fitness R_0, the equilibrium frequency of susceptibility p_t drops very rapidly with increasing population density *K*. Note that again there is no consideration of whether or not cycling will occur.

Although this model assumes that there is only one pathogen strain, it can be extended easily to allow for multiple pathogen strains by rewriting Equation 8 as

$$1 - i = e^{-R_j i f_{j,t}}, \quad 12.$$

where R_j is the basic reproductive rate for strain *j* ($j = 1$ for pathogen strain 1, 2 for pathogen strain 2), and $f_{j,t}$ is the frequency of the host strain that is susceptible to pathogen strain *j* in generation *t* (64). Note that by proper definition of $f_{j,t}$, one can use this model to describe either a haploid host or a diploid host with complete dominance. As with the earlier models, this model can be used to consider conditions under which polymorphism occurs. The interesting feature of the work by May & Anderson (64), however, was that they were able to show that for some parameter values the model produces fluctuations in the frequency of the two host alleles. In fact, in the case for which one host strain is completely resistant, and thus has no pathogen, the May & Anderson model reduces to the Gillespie model, showing that the Gillespie model can also show dynamic polymorphism.

A second simplifying assumption of the Gillespie model is that the annual epidemic is begun by an extremely small density of the pathogen. An additional

extension of this model is therefore to explicitly keep track of the density of overwintering spores or other infectious stages from generation to generation by replacing Equation 8 with

$$1 - i = e^{-K(R_0 i(1-p_t)+Kz_t)}, \qquad 13.$$

where z_t is the density of the infectious, possibly free-living stage of the pathogen (83). In addition to the usual equations for the frequency of host alleles, as in Equation 1, we have an additional equation for pathogen density,

$$z_{t+1} = \phi K p_t i(p_t, z_t) + \gamma z_t, \qquad 14.$$

where γ is the probability that the infectious stage of the pathogen will survive over the long term, and ϕ is the population growth of the pathogen between epidemics. Because this model assumes that there is only one pathogen strain, like the Gillespie model but unlike the May & Anderson model, it requires a cost of resistance to permit polymorphism. Also, like the May & Anderson model, it shows cycles in the frequency of resistance. An interesting difference between the dynamic polymorphisms in the two models, however, is that in the model of Stahl et al. (83) the pathogen can build up to high levels over several generations, leading to long-period fluctuations in the frequency of resistance. In contrast, fluctuations in the May & Anderson model invariably have a short period.

The models we have discussed all assume a single locus. Because in nature the traits in question are often affected by many loci, an important next step was to allow for several loci. Perhaps the most direct way to do this is to extend the epidemic model to include multiple genotypes of hosts and pathogens. For example, Frank (38) presented the model

$$\Delta h_i = h_i \left(r_i - \sum_{k=0}^{2^N-1} r_k h_k - m \sum_{k=0}^{2^N-1} \lambda_{ik} p_k \right), \qquad 15.$$

$$\Delta p_j = p_j \left(-s + b_j \sum_{k=0}^{2^N-1} \lambda_{kj} h_k \right). \qquad 16.$$

Here, h_i and p_j are the densities of hosts and pathogens of strain i and j, respectively, r_i is the host-strain–specific reproductive rate, N is the number of host and pathogen loci, m is the rate of disease transmission, s is the pathogen death rate, and b_j is the pathogen birth rate, the rate at which infected hosts produce pathogens of type j. Note that in Equations 15 and 16, infection will occur unless the host has a resistance allele and the pathogen has an avirulence allele at a particular locus, following the gene-for-gene interactions typical of many plants and their pathogens (reviewed in 44). This model is effectively a generalization of the earlier models we discussed in which there were two strains of the host and two strains of the pathogen. To allow for the additional complication of multiple genotypes, Equations 15 and 16 introduce the variable λ_{ik}, which is equal to zero if the host

has a resistance allele and the pathogen has a virulence allele, otherwise it is equal to one.

Although Equations 15 and 16 are more complicated than the earlier models we discussed, it turns out they are fundamentally similar to Equations 6 and 7. To see this, note first that Equations 15 and 16 assume a time step of one generation. If we instead allow for time steps of any number of generations, and we allow for only one strain of the host or the pathogen, we have,

$$\Delta h = (rh - rh^2 - mhp)\Delta t, \qquad 17.$$

$$\Delta p = (bhp - s)\Delta t. \qquad 18.$$

If we then set $r = 0$ in Equations 15 and 16, divide both sides by Δt and let $\Delta t \rightarrow 0$, we again have Equations 17 and 18. For $r \neq 0$, we have instead a discrete-generation version of the Lotka-Volterra predator-prey equations in which the prey experiences intraspecific competition for resources. An important difference, however, is that all the models we have discussed so far have assumed that host population sizes are constant. Equations 15 and 16 instead allow host population densities to fluctuate freely. An additional difference is that the Frank model allows for a full range of population genetic processes, although the earlier models can in general be extended to allow for some of these complexities [see, for example, Damgaard (23) for gene flow]. First, host genotypes that have fallen to 0.1% of their carrying capacity are set to a density of zero but are reintroduced randomly whether they are extinct or not. The overall effect is thus to allow for either mutation or immigration from outside the population. Also, a sexual version of the model assumes that there is a recombination fraction of 0.5 between adjacent loci.

Like the other models we have described, this model can show polymorphism in both victim and exploiter. For the earlier models, costs of resistance were assigned on a case-by-case basis, but for this model one instead specifies a function that describes how the cost of resistance increases with an increasing number of alleles for any host genotype. There is also a cost of virulence, in that pathogens with more virulence alleles have lower reproductive rates, which is again specified by a function rather than by case-by-case assignment. Both costs are thus quantitative functions of the number of alleles.

This model is substantially more complex than the earlier models we described, even though Frank restricted the model to eight loci. Because of this complexity, summarizing the model's behavior is more difficult. The major results first have to do with the probability that a randomly selected host genotype will be resistant to a randomly selected pathogen genotype. If host and pathogen densities are stable, this probability will be low, but if host and pathogen densities fluctuate, then this probability will fluctuate as well. Second, the average number of resistance alleles carried by a host strain increases with the slope of the relationship between the cost of virulence and the number of virulence alleles. This occurs because lower costs of virulence lead to a higher number of avirulence alleles, which in turn favors resistance alleles. The average number of virulence alleles carried by a

pathogen strain instead increases with 1 minus the rate at which resistance costs increase with increasing numbers of resistance alleles. This occurs because large costs of resistance lead to a reduction in the number of resistance alleles, which in turn favors avirulence alleles. Surprisingly, the number of resistance alleles is unaffected by the costs of resistance, and the number of virulence alleles is unaffected by the costs of virulence.

This model begins to make clear some of the difficulties of constructing coevolutionary models. To begin with, all multilocus population genetic models that attempt to assign fitnesses to each genotype face the problem that the number of possible genotypes increases rapidly with the number of loci. For example, if there are two alternative loci at each of n loci, the number of possible genotypes is 2^n. As we have discussed, however, much of the interest in coevolutionary models of victim-exploiter interactions focuses on evaluating the possibility of "arms races" (25), or "Red-Queen dynamics" (18, 92). Understanding such an evolutionary dynamic clearly requires that there be no a priori limit on the number of possible genotypes. At the same time, however, plausibility requires that arms races do not lead to infinitely large trait values or to infinite numbers of genotypes (77). Much recent work has therefore focussed on modeling approaches that can show arms races without putting arbitrary limits on the number of possible genotypes, yet without leading to infinite trait values.

The basic approach taken in most of these models is first to assume that victim and exploiter traits are quantitative rather than all- or-none, so that at the population level phenotypes can be described by continuous probability distributions. Second, various simplifying assumptions are made about the genetics of the relevant traits. For example, one recent approach known as "adaptive dynamics" assumes that both victims and exploiters are asexual and haploid, and that offspring are identical to their parents unless a mutation occurs (27, 28). The distribution of phenotypes is identical to the distribution of genotypes, and it changes only because of differential net reproduction, or mutation. Mutations are assumed to be of small effect, in the sense that the probability that the offspring trait is greatly different from the parent's trait is small. Fitnesses are described by an ecological model, typically a predator-prey model that is similar to Equations 17 and 18, except with completely overlapping generations.

Although the resulting model is complex, it turns out its dynamics can be closely approximated by a deterministic model in which victim and exploiter are monomorphic, but for which the phenotype of each species can change from generation to generation (62). To understand the full model, we can therefore focus on the simpler approximate model. To derive the equations of change for the approximate model, one begins with a predator-prey model with overlapping generations:

$$\frac{dh}{dt} = h(r - \alpha(s_h) - \beta(s_h, s_p)p), \qquad 19.$$

$$\frac{dp}{dt} = p(\gamma(s_h, s_p)h - s). \qquad 20.$$

Here, s_h and s_p are the victim and exploiter phenotypes, so the density-dependence in the victim reproductive rate $\alpha(s_h)$ is a function of victim phenotype, and the rates of victim deaths, $\beta(s_h, s_p)$, and exploiter births, $\gamma(s_h, s_p)$, are functions of both host and pathogen phenotypes. It turns out that for fixed phenotypes, allowing for continuous time ensures that host and pathogen densities will be constant, a feature that simplifies the model results and permits a focus on the evolutionary dynamics rather than the ecological dynamics. The specific functions used assume that fitness is highest at intermediate trait values. To begin with, the density-dependence term $\alpha(s_h)$ is assumed to be parabolic, so that in the absence of predation, the optimal victim trait is at an intermediate value of the victim phenotype. Next, one assumes that $\gamma(s_h, s_p) = k\beta(s_h, s_p)$, where k is a constant of proportionality, and that β (and thus γ) is a bivariate Gaussian distribution (normal curve) with respect to the host and pathogen phenotypes s_h and s_p. In the context of predator-prey interactions, s_h and s_p are often taken to be equivalent to prey and predator body sizes. Predator fitness is then maximized when the predator has the same body size as the prey. The prey, however, faces a trade-off because its birth rate is maximized at an intermediate size, through the density-dependence term $\alpha(s_h)$, but its death rate is maximized when it is the same size as the predator. These trade-offs cause the model to show an interesting array of behaviors. Specifically, if h, the constant of proportionality between victim and exploiter body sizes, is such that $0.05 < k < 0.098$, victim and exploiter phenotypes will reach a stable equilibrium, but for $0.098 < k < 0.148$ and for sufficiently large values of r, the model shows cycles in host and pathogen phenotypes. If k is increased still further, the model will again reach equilibrium. In this range of k, however, there are two alternative equilibria, and the one that is reached depends on the starting values of the host and pathogen phenotypes.

As described above, Dieckmann and coauthors (27, 28) have argued that the dynamic in this model, in which trait values cycle, represents a plausible arms race because trait values sometimes escalate without reaching infinite values. Clearly, however, the assumptions of simple genetics and of trait-matching in the predator at least superficially appear to be restrictive, which suggests that the models may not be widely applicable. It turns out, however, that neither assumption is quite as restrictive as it seems. For example, Sasaki & Godfray (80) used an adaptive-dynamics approach to modeling the evolution of the interactions between a host insect and its parasitoid. In their model, host resistance (x) and parasitoid virulence (y) are quantitative characters, and the probability that a host is able to encapsulate an attacking parasitoid, which allows the host to survive but kills the parasitoid, is described by the function

$$\eta(x - y) = \frac{1}{1 + e^{-2A(x-y)}}. \qquad 21.$$

If the resistance trait and the virulence trait are equal, so that $x = y$, the probability of encapsulation is 0.5. If resistance is greater than virulence, so that $x > y$, the host has a better chance than the parasitoid of surviving, whereas if $x < y$ the reverse is true. As with the previous models, this model also assumes that there

is a cost to resistance, in that the number of hosts produced by a surviving host declines with increasing resistance x, so that the total fecundity of surviving hosts is $a(x) = G\exp(-c_h x)$. Similarly, there is a cost of virulence, in that the fraction of emerging parasitoids that survive to reproduce is $b(y) = \exp(-c_p y)$. The full model is then

$$N_{t+1}(x) = a(x)N_t(x)\left(F_t + (1 - F_t)\int_0^\infty \eta(x - y)Q_t(y)dy\right), \qquad 22.$$

$$P_{t+1}(y) = b(y)\int_0^\infty N_t(x)(1 - \eta(x - y))(1 - F_t)Q_t(y)\,dx. \qquad 23.$$

Here, $N_t(x)$ and $P_t(x)$ are the densities of hosts and parasitoids that have resistance level x or virulence level y, respectively, in generation t. $Q_t(y)$ is the fraction of parasitoids that have virulence level y, so that $Q_t(y) = P_t(y)/\bar{P}_t$, where $\bar{P}_t$ is the total parasitoid density in generation t. F_t is the fraction of hosts that become parasitized in generation t, which can be described by standard host-parasitoid population-dynamic models. Equation 22 thus says that of the fraction F_t of hosts that become parasitized, a fraction $Q_t(y)$ are parasitized by parasitoids of virulence level y, and so a fraction $\eta(x - y)$ survive parasitization.

Like the work of Dieckmann and coworkers (27, 28), this model assumes that victim and exploiter are haploid and asexual, and that mutations are of small effect. An additional similarity to the models of Dieckmann and coworkers is that this model can also show coevolutionarily cycling, in which resistance and virulence oscillate between low levels and high levels. The important difference, however, is that this arms-race dynamic occurs without the assumption that selection favors exploiters that match the trait value of the victim. It thus appears that the key ecological assumption governing the dynamics of this class of models is not the assumption of trait matching. Instead, the key assumption is that victim and exploiter traits can be expressed in the same currency, thus permitting the construction of a function such as Equation 21, that relates differences in victim and exploiter trait values to their respective fitnesses. Although it remains to be seen whether one could define a virulence or resistance metric that would permit parameterization of such a function, the approach nevertheless may be generally useful.

Whether or not one can relax the second restrictive assumption of adaptive dynamic models, that the genetics of victim and exploiter are simple, is less clear. An alternative method of simplifying the genetics that allows for diploidy is to use a quantitative genetic model (1, 2). As with adaptive dynamic models, quantitative genetic models generally assume that there is some continuous distribution of phenotypes, except that the distribution of phenotypes is normal with fixed variance (but see 29, 30). Quantitative genetic models also allow for the possibility that offspring are not identical to their parents, although the ratio of additive genetic to phenotypic variance is assumed to be constant over time (4). Because of these simplifying assumptions, these models need keep track only of changes in the mean phenotype. For such models, it turns out that the rate of change in the mean

phenotype is proportional to the derivative of fitness with respect to the phenotype value evaluated at the mean phenotype of all interacting populations, according to

$$\Delta\bar{z} = \frac{V_a}{\bar{W}}\left(\left.\frac{\partial W}{\partial z}\right|_{\bar{z}}\right), \qquad 24.$$

where $\Delta\bar{z}$ is the rate of change of the mean phenotype $\bar{z}$, V_a is the additive genetic variance of the distribution of phenotypes, W is the fitness function, and $\bar{W}$ is the mean fitness. Using this result, one can construct a full coevolutionary model by again expressing victim and exploiter fitnesses in terms of a predator-prey model. For example, Abrams and coauthors (3, 4) used a continuous-generation quantitative-genetic model defined according to

$$\frac{dx}{dt} = V_x \left.\frac{\partial W_h}{\partial x}\right|_{\bar{x}}, \qquad 25.$$

$$\frac{dy}{dt} = V_y \left.\frac{\partial W_p}{\partial y}\right|_{\bar{y}}, \qquad 26.$$

where x and y are the prey and predator trait values, respectively, and V_x, V_y, W_x, and W_y are the respective additive genetic variances (V) and fitnesses (W) of prey and predator. The fitness function W_x is then derived from a generalized form of the right-hand side of the prey Equation 19, divided by prey density h, whereas predator fitness W_y is derived similarly from the predator Equation 20. As in the adaptive dynamic models, a key step is the expression that translates differences in the victim and exploiter traits into victim and exploiter fitnesses. Abrams & Matsuda (3) used trait matching as expressed by a bivariate Gaussian distribution, and like the adaptive dynamic models, the resulting model shows coevolutionary cycling for some range of parameter values. It turns out, however, that cycling is also achieved when one drops the bivariate Gaussian assumption and instead uses the function

$$M(x, y) = M_{\max}\left(0.5 + \frac{1}{\pi}\arctan[k(x - y)]\right). \qquad 27.$$

Here, $M_{\max}$ is the maximum rate at which predators capture prey, and k is a constant. This function approaches zero as $x - y$ becomes larger and more negative, and it approaches $M_{\max}$ as $x - y$ approaches larger positive values. Exploiter fitness thus increases as the exploiter's trait value becomes larger relative to the victim's value.

The fact that this model also shows coevolutionary cycling suggests that the genetic assumptions of the adaptive dynamics approach are not as restrictive as they seem, at least in that the approach ostensibly allows for diploidy and for environmental influences on offspring phenotypes. Abrams et al. (2) showed that the genetic assumptions of adaptive dynamics models and quantitative genetic models are mathematically almost identical. It is probably the case that neither model is terribly realistic in this regard. Indeed, the basic assumption of quantitative

genetic models, that the distribution of phenotypes is unchanging from generation to generation, has been shown to be only a rough approximation under strong truncating selection (90). Perhaps what is needed is an exploration of the extent to which more genetically explicit models can show arms race dynamics, which might be accomplished through an extension of the Frank model to allow for more loci. An important point, however, is that the behavior of the Frank model can, for the most part, only be analyzed using computer simulations, whereas adaptive dynamic and quantitative genetic models can be analyzed mathematically. Although this issue might seem arcane, in fact it is very important because mathematical analyses permit a much deeper understanding of the models.

The models we have discussed so far have emphasized how natural selection will affect the possibility of polymorphism, including the possibility of cycles in trait values or allele frequencies. An additional way to extend coevolutionary models is to allow for gene flow among populations. It turns out that models that allow for metapopulation structure make interesting testable predictions about the degree to which victim and exploiter are adapted to each other. For example, Gandon et al. (41) added metapopulation structure to Equations 15 and 16, such that a varying number of populations were linked via stepping stone migration. The authors then showed that when the ratio of host migration to parasite migration is <1, and when host migration is relatively small, then parasites tend to be locally adapted, and when the ratio is >1, then the hosts are locally adapted. A potential explanation for this observation is that relatively high migration introduces genetic variation at a rate sufficient to allow rapid adaptation to a wide array of antagonist genotypes. That is, migration acts as a proxy for gene flow in these models. One twist to the prediction that elevated migration rates (or gene flow) enhance local adaptation has been proposed in a model by Nuismer et al. (69). In this model, communities selecting for antagonism and for mutualism are linked by migration. By using simple population genetics recursion relations for allele frequencies with spatially varying allele fitnesses, the authors observe a wide variety of behavior. Notably, though, they find that local trait mismatching can commonly result when selection differs markedly between communities (such as the difference between selection for antagonism and mutualism assumed in this model) and when migration is high. The extent to which varying levels of selection for antagonism among communities linked by migration can similarly generate local maladaptation remains to be explored.

ASSESSING THE ASSUMPTIONS OF VICTIM-EXPLOITER COEVOLUTION MODELS

Our brief review of mathematical models of victim-exploiter interactions is intended to show the range of modeling techniques applied to the problem of understanding coevolutionary dynamics. An important additional issue is that most of the models in question have had little connection to data. This lack of connection has occurred for two reasons. First, a primary goal of some coevolutionary modeling

has been to show simply that arms race dynamics can occur without infinite trait values. In these cases, there is little motivation to tailor a model to a particular system. Second, traits involved in coevolutionary interactions are likely to be multilocus with many alternative alleles and the organisms in question are likely to be diploid, thereby violating the assumptions of many of the models that we have described. Frank's work has shown that computer simulations of modest numbers of loci can give some insight into coevolutionary problems, but it is clear that truly realistic models will be very hard to understand. Nevertheless, such models should increase in importance as genomic level characterization of resistance alleles becomes feasible. Such models may be useful in statistical analyses of genomic data, but the general goal of most modeling in ecological genetics and population genetics is understanding, and so we may ultimately be faced with a trade-off between models that are realistic and models that can be understood.

This trade-off between realism and comprehensibility does not necessarily mean that simple models cannot be usefully applied to data. That is, in spite of their simplifying assumptions, coevolutionary models may provide useful descriptions of the dynamics of real coevolutionary interactions. Indeed, in spite of the fact that his models include only eight loci, Frank (38, 39) argues quite effectively that his models nevertheless provide accurate descriptions of important features of the interactions between plants and their pathogens. In that spirit, here we show some examples of data that could be used to parameterize some of the coevolutionary models that we have discussed. Although the application of simple models to complex data sets is in general a challenging statistical topic (16), here our intent is to simply rough out some basic ways in which these models may be compared with data.

Costs of Plant Resistance

With few exceptions (but see 23, 29, 30), most models of plant-enemy coevolution assume a cost of resistance; that is, they assume that resistant individuals are less fit than are susceptible individuals in the absence of attack. As we have described, the occurrence of costs is generally essential for maintaining polymorphisms, and thus for achieving intermediate, rather than maximal, levels of resistance. Given that resistance is generally neither ubiquitous nor absolute, the ability to mimic these patterns under a wide range of parameter values is a desirable attribute of any coevolutionary model. It is therefore not surprising that there is substantial evidence that many resistance characters can be costly. In a review of published studies, Bergelson & Purrington (11) found that 56% and 29% of published studies detected a statistically significant reduction in the fitness of plants resistant to pathogens and herbivores, respectively, relative to their susceptible counterparts. Many more studies showed costs but did not reach statistical significance. For the subset of studies in which costs occurred, magnitudes were variable, ranging from no cost to a 20% reduction in the fitness of resistant plants relative to nonresistant plants.

Although empiricists have been acutely aware that most coevolutionary models assume the presence of a cost of resistance, they have not always appreciated that

TABLE 1 Summary of representative victim-exploiter coevolutionary models[a]

Type	Citation	Damage	Victim costs	Model behavior
Single-locus	58	Genotype specific	Genotype specific	Polymorphism
	43	Genotype specific	Genotype specific	Polymorphism
	64	Genotype specific	Genotype specific	Host cyclic polymorphism, short period
	83	Genotype specific	Genotype specific	Host cyclic polymorphism, pathogen density fluctuations
Multilocus	39	Gene-for-gene	Multiplicative (≈exponential)	Cycles in host & pathogen density & frequencies
AD	28	$\exp(-a(x-y)^2/\sigma^2)$	$a-bx+cx^2$	Cycles in traits
	80	$1/(1+\exp(-2a(x-y)))$	$\exp(ax)$	Cycles in traits & densities
QG	3	$a/(b+(x-y)^2)$	fitness $=\exp(-ax)$	Cycles in traits & densities
	3	$a(0.5+\frac{1}{\pi}\arctan(x-y))$	ax^3	Cycles in traits & densities
	42	$\exp(-a(x-y)^2/\sigma^2)$	$\exp(-a(x-b)^4)$	Cycles in traits
	30	$\exp(-a(x-y)^2/\sigma^2)$	ax	Cycles in traits & densities

[a]AD, adaptive dynamic models; QG, quantitative genetic models. Among the latter two groups of models, x is the value of the victim trait, and y is the value of the enemy trait.

the models assume a particular shape to the cost function. Table 1 summarizes the shapes of the cost functions assumed in a variety of published models, including the models described above. These functions take one of two forms. First, several assume a monotonic decrease in fitness, measured in the absence of attack, as resistance increases. Within this group, some functions can be additionally distinguished according to whether they assume a positive (38, 80) or negative (3) second derivative at low costs. A positive second derivative, for example, is found with an exponential decline, whereas a negative second derivative leads to a more gradual decline. The other set of models (3, 27, 29, 30, 42, 62) assumes that fitness is greatest at an intermediate level of resistance, even though natural enemies are absent. Although not an obviously sensible assumption, we show below that several datasets actually seem to have an intermediate optimum.

To assess the appropriateness of these model assumptions, we examined how damage, assumed to be correlated with fitness in the presence of the enemy, changes with the level of resistance for published and unpublished data made available to us by personal communication (45, 63, 79, 81). We restricted our

attention to natural rather than agricultural systems so that the levels of resistance would not be the result of artificial selection. The results are illustrated in Figure 1, where fitness, or some proxy for fitness, is plotted against level of resistance for nine characters, and in each a best-fit polynomial is drawn. Note, first, that the fit of these relationships is often poor. With this in mind, we find general consistency in that fitness decreases with increasing levels of resistance. When relationships are monotonically decreasing, it appears that most data are more consistent with a negative second derivative than a positive second derivative (Figure 1*B–E*). And somewhat surprisingly, we find several examples more or less consistent with an intermediate optimum (Figure 1*F–H*) (although some of the cases that we have classified as showing a monotonic decline in fact sometimes show very slight humps or are flat at low trait values). Only one curve (Figure 1*I*) appears superficially inconsistent with assumed functional forms, but this is

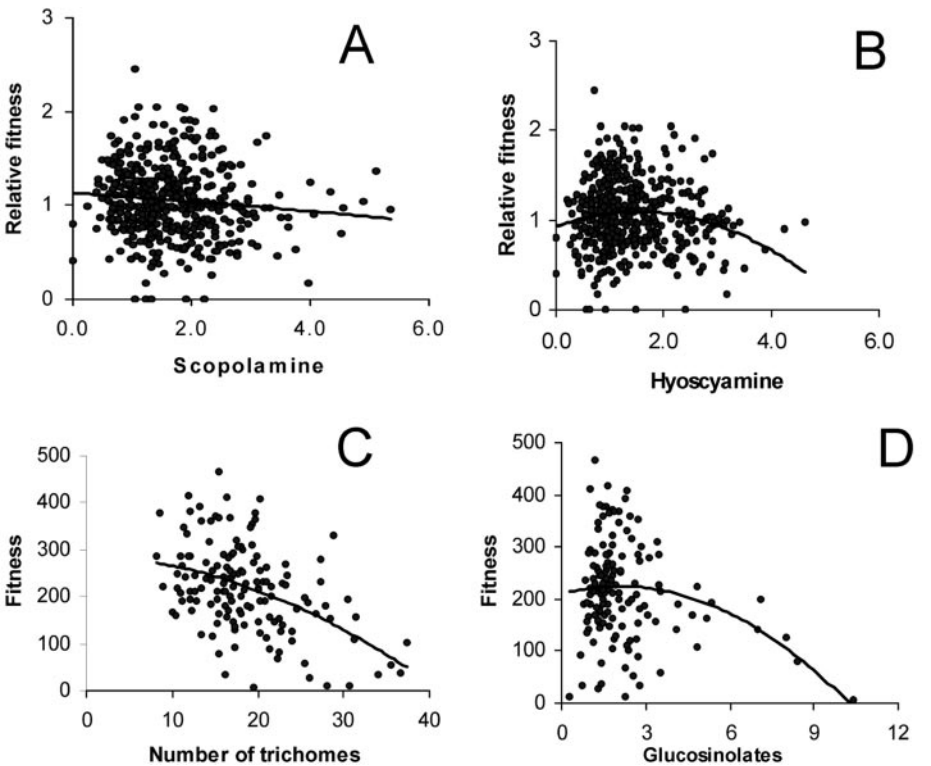


Figure 1 Plots of host plant fitness versus resistance in the absence of natural enemies. (*A*, *B*) *Datura stramonium* [from Shonle & Bergelson (81)]; (*C*, *D*) *Arabidopsis thaliana* [from Mauricio (63)]; (*E*) *Diplaucus aurantiacus* [from Han & Lincoln (45)]; (*F*) *Silene alba* [from Biere & Antonovics (12)]; (*G*, *H*) *Psychotria horizontalis* [from Sagers & Coley (79)]. Curves were fit in MS Excel, assuming a polynomial functional form.

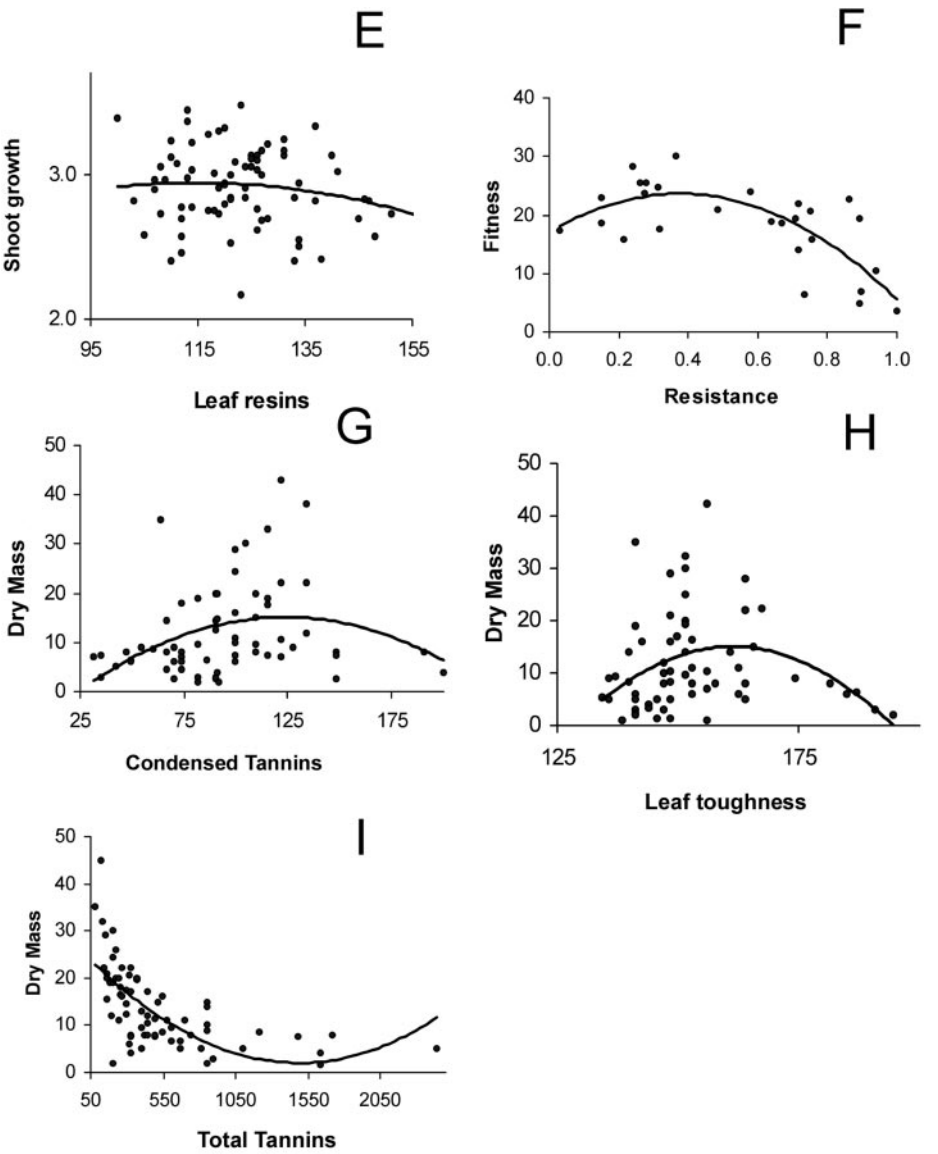


Figure 1 (*Continued*)

certainly the result of poor model fit. In short, the existing data are roughly in agreement with the assumptions of many of the models. This suggests that for the systems for which we have data, there is at least the potential for arms races to occur.

Benefits of Resistance

A second assumption made in models of coevolution is that plant defenses are beneficial to plants and that, in some cases, a particular function describes the relationship between damage and plant resistance. These functions are given in Table 1. Here, *x* designates a trait in the enemy that makes particular genotypes more or less tolerant of a defensive trait, and *y* designates the level of that defense in a particular plant. With only minor deviation, these functions, when plotted for a particular value of *x*, all describe a monotonically decreasing curve with a positive second derivative for the relationship between damage (dependent variable) and the level of defense (independent variable). However, in all these cases, the data were collected without reference to the herbivore's genotype. This is important because in the models, the functions relating damage to levels of resistance are invariably expressed in terms of the difference between the plant's trait and the enemy's trait. It is therefore difficult to assess how well these functions fit field data, as we could find no cases in which the damage imposed by one genotype of an herbivore species was measured for plants that vary in their levels of defense. When variation in levels of tolerance among enemy genotypes is small, however, one would expect that damage imposed by a population of enemies would follow the same functional forms as those indicated.

We obtained data from four studies that enabled us to begin to explore the shape of the relationship between damage and plant resistance (12, 63, 81; T.E. Juenger, unpublished data). We restrict attention to those studies that distinguished types of damage, at least according to general classes of herbivores (e.g., flea beetles, leaf beetles), or to studies that reported that the vast majority of damage was inflicted by one type of enemy species. We were able to find data for the damage associated with only one disease (12). As is apparent in Figure 2, we found, first, that these data are tremendously messy and provide a poor fit to virtually any function. One plot, Figure 2*A*, shows an increasing relationship between resistance and damage, a nonsensical pattern that presumably results from noisy data. Of the remaining plots, three patterns are apparent: a more or less flat relationship (Figure 2*B–E*), a monotonically decreasing curve with a negative second derivative (Figure 2*F*, *G*), and a curve with an intermediate optimum (Figure 2*H*). Notably, none of these plots match the functional form assumed in most models. Whether this is because the model assumptions are incorrect, because the experiments did not control for the genotype of the natural enemy, or because the data are simply messy is unclear.

Costs of Virulence

In addition to costs of resistance for the victim, several of the models described incorporate costs for the exploiter. In the context of host-pathogen interactions, these

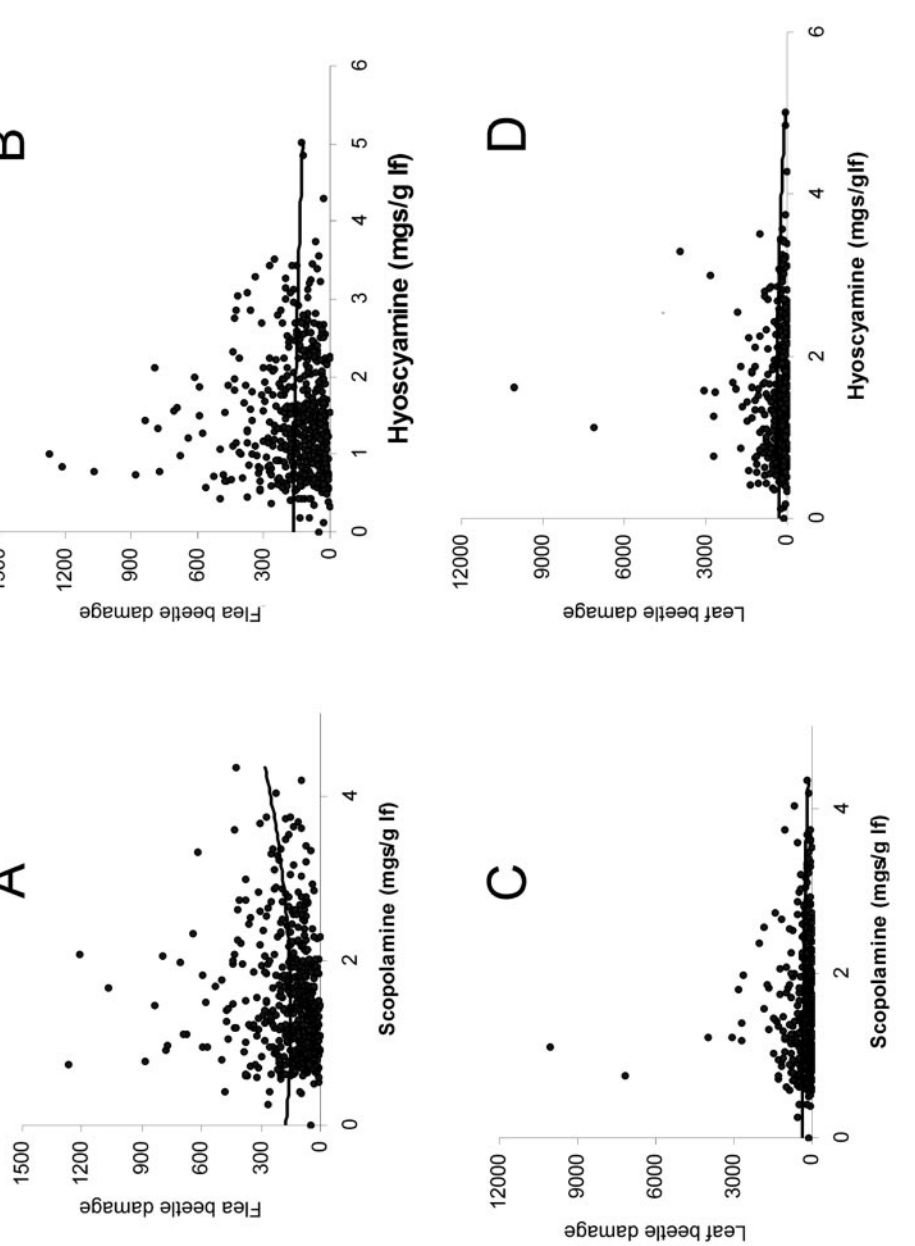
costs typically consist of trade-offs between virulence and transmissibility (40, 64). Within plants in particular, the best-studied host-pathogen systems are gene-for-gene interactions. As is well known, in gene-for-gene interactions, pathogen avirulence is conferred by a particular allele that, among other things, alerts the plant to the growth of the pathogen in the plant's tissues. Because pathogen strains that lack this allele can infect a wider range of host strains, the allele is said to confer avirulence and, hence, is known as an *avirulence* allele, or an *avr*. Clearly *avr* alleles must confer a fitness advantage under some circumstances, otherwise their frequency would decline to zero. Nevertheless, little is known about the fitness benefit of these alleles, and hence about the costs of virulence. What is known is that many *avr*'s are turned on by the so-called type III secretion system, the genes for which are homologous to genes in animal pathogens that play a key role in allowing bacterial growth and hence pathogenicity (48). The few *avr*'s that have been shown to confer fitness benefits do indeed enhance either bacterial growth, disease symptoms, or both (55, 61, 75, 88, 95). Notably, though, none of these studies has been completed under field conditions, and thus the magnitude of the benefit is unknown.

In short, to our knowledge there is generally too little data on plant-pathogen systems to allow model assumptions about costs of virulence to be compared with data. Moreover, the best-known host-pathogen systems appear to lead to qualitative resistance and, thus, would appear to be unsuitable for the quantitative models we have described. Ultimately, it may be the case that the possession of multiple *avr*'s leads to fitness that is higher under some circumstances than others, which would therefore allow for direct application of at least the Frank model, and possibly modified versions of some other models. Currently, however, not enough is known to permit such an application.

ASSESSING THE PREDICTIONS OF VICTIM-EXPLOITER COEVOLUTION MODELS

Our treatment of coevolutionary models focuses on their prediction of escalating arms races, at least under defined parameter ranges. The fact that this dynamic occurs in many different models is not surprising because, as we described, several

Figure 2 Plots of damage versus putative resistance characters. (*A–D*) From Shonle & Bergelson (81); (*E*) from T. Juenger & J. Bergelson, unpublished data; (*F–G*) from Mauricio (63); (*H*) from Biere & Antonovics (12). The enemies inflicting damage are indicated on the *Y* axis label for *A–F*. (*F, G*) Damage was measured as the number of holes in the leaves. Most of this damage was caused by two species of flea beetles, although other minor herbivores were present. (*H*) Damage was measured as the loss in fitness between damaged and undamaged plants. This damage was caused by anther smut. Curves were fit in Exel, assuming a polynomial functional form.



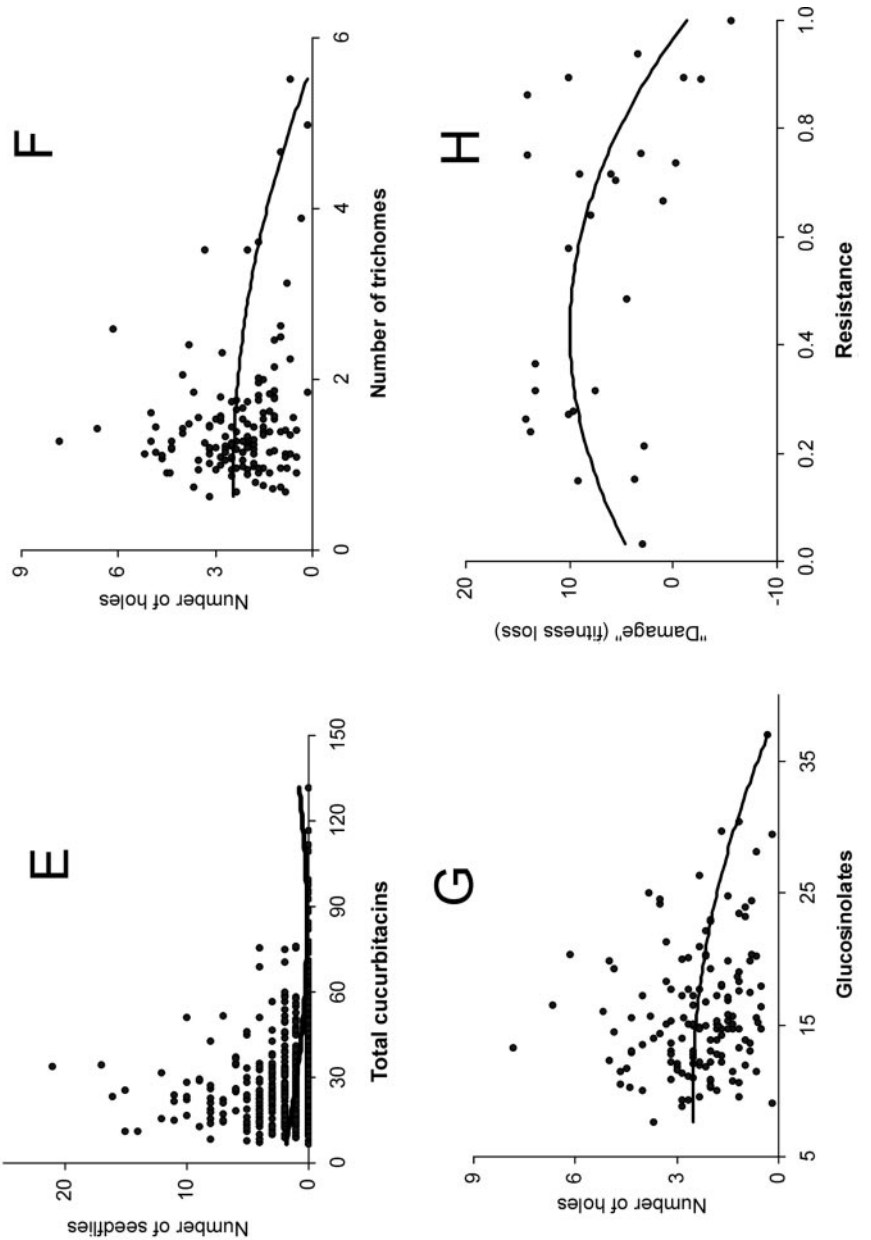


Figure 2 (*Continued*)

of these models were designed with the intent of demonstrating that arms race dynamics are plausible. Despite the widespread interest in arms races that motivates these models, it is surprising that there is little in the way of evidence that arms races actually occur in plant-enemy systems. Perhaps the most widely cited example of an arms race involves Berenbaum's hypothesis that the sequence of evolution of the coumarins, from p-coumaric acid to hydroxycoumarins, to linear furanocoumarins, to angular furanocoumarins, entails a progression in levels of defense (6). There are additional, less-celebrated examples of escalation that have also involved comparisons of plant taxa to demonstrate that derived host plant species are more toxic than are less-derived species (21, 34). These examples occur, however, on an evolutionary timescale that is not particularly relevant to extant victim-exploiter coevolutionary models that focus on the dynamics of single host species.

Within species, there is little evidence for an arms race between plants and their enemies. One suggestive example is the report that levels of sphondin are found at higher concentrations in contemporary Pastinaceae than in roughly 100-year-old herbarium specimens (7). Because sphondin, a furanocoumarin, is known to confer resistance to webworms, this pattern suggests an escalation in defense since the first reported occurrence of webworms in 1883. The other primary form of evidence involving species-level comparisons is molecular evolutionary data. There are now several examples of accelerated rates of adaptive evolution in plant resistance genes, which is suggestive of an arms race (reviewed in 10). However, as Bergelson et al. (10) discussed, it is important to note that other aspects of these data are inconsistent with a classical arms race model of a continual turnover of resistance specificity.

A much more restrictive prediction of coevolutionary models is that of local adaptation. A great number of studies find local adaptation (Table 2) (reviewed recently in 13, 51, 84, 93), although this outcome is by no means universal. For example, a meta-analysis by Van Zandt & Mopper (93) concludes that breeding mode (which affects rates of recombination) and feeding mode strongly influence the extent of local adaptation, whereas dispersal does not. In particular, these authors find that local adaptation occurs most frequently for parthenogenic and haplodiploid pathogens, and for endophagous insects that interact in a relatively pairwise manner with their host. The review by Kaltz & Shykoff (51) finds a more significant role for migration (a proxy for gene flow) but nonetheless concludes that local adaptation is an average consequence of metapopulation dynamics, migration, and variable selection pressure. Thus, the collection of studies examined does not support strongly a pivotal role of dispersal in determining local adaptation. Before rejecting the conclusion of coevolutionary models, however, it is important to note that in few systems was gene flow, or even migration, measured directly. In addition, it is not clear at what scale definitions of dispersal (or gene flow) should be applied. Thus, more comprehensive data are necessary before model predictions can be tested rigorously.

TABLE 2 Empirical studies of local adaptation[a]

Plant host species	Enemy species	Local adaptation[b]	Exploitation type	Relative dispersal rates (plant/enemy)	Relative generation time (plant/enemy)	Host breadth of enemy	Trait	Experiment type	References
Perennial herb	Anther smut fungus	E	Anther fungal infection	>1	~1	Family-species	Infectivity	Cross inoculation	17
Sand-live oak and myrtle oak	Mobile leaf miner	E	Leafmining	<1	>1	Species	Insect survival	Egg transfer	66
Annual vine	Fungal pathogen	E	Fungal infection	Not measured	~1	Genus	Infectivity	Transplant	70
Ponderosa pine	Black pineleaf scale insect	E	Folivory	>1	>>1	11 host species	Insect survival	Egg transfer	74
Sea daisy	Gall-forming midge	E	Gall formation	Not measured	>1	Not measured	Gall abundance, gall size	Reciprocal transplant	84
Beech	Beech scale	E	Exophagus needle herbivory	>1	>1	Not measured	Larval survival and adult fecundity of insects	Larvae transfer	94
Herbaceous perennial	Rust fungus	E	Fungal infection	<<1	>1	Species	Infectivity	Reciprocal cross inoculation	15, 49
White mulberry	Armored scale insect	E	Exophagus needle herbivory	>1	>1	55 families	Insect survival	Egg transfer	46, 47
Seaside daisy	Thrips	E	Folivory	>1	>1	Unclear	Insect survival	Immature insect transplanting across clones	52–54

Rockcress	Rust fungi	P	Fungal infection	<1	~1	Species	Infectivity and general herbivory	Reciprocal transplant	78
Northern red oak	General herbivores: all herbivory	P	Folivory	<1	>1	Not measured	Percent leaf damage	Transplant	82
Weedy perennial	Anther smut fungus	P	Fungal infection	>1	~1	Family-species	Infectivity	Cross inoculation	14, 26, 50
Stinging nettle	Holoparisitc plant	Varies	Xylem and phloem parasitized with haustoria	Not measured	>1	Generalist	Parasite infectivity and biomass & host biomass	Reciprocal cross infection	57
Pinyon pine	Pinyon needle scale	None	Exophagus needle herbivory	>1	>>1	Not measured	Scale survival and abundance	Egg transfer	19
Prarie cordgrass	Two rust fungi	None	Fungal infection	Not measured	>1	Generalists	Infectivity and plant survival	Reciprocal transplant	24
Scots pine	Fungal canker pathogen	None	Invasion of phloem, cambium, and xylem by mycelium	~1	>1	Genus	Selective value (in relation to other genotypes)	Reciprocal transfer of mixed inocula	33
Canyon grape	Leaf galling insect	None	Folivory and root herbivory	>1	>1	Genus	Insect survival and fecundity	Insects choose host	56
Mexican cypress	Aphid	None	Herbirvory	<1	>1	Not measured	Insect survival	Nymph aphid transfer	65

(*Continued*)

TABLE 2 (*Continued*)

Plant host species	Enemy species	Local adaptation[b]	Exploitation type	Relative dispersal rates (plant/enemy)	Relative generation time (plant/enemy)	Host breadth of enemy	Trait	Experiment type	References
Long-lived perennial grass	Root hemi-parasitic plant	None	Root parasitism	Not measured	>1	Not measured	Host and parasite performance and reproduction and infectivity	Reciprocal cross infection	67
Mayapple	Rust fungus	None	Nonsystemic rust infection	<1	>1	Species	Infectivity	Reciprocal transplant	71
Rhus glabra	Mobile herbivorous beetle	None	Herbivory	<1	>1	Genus	Insect survival and weight	Reciprocal egg transfer	86
Pinyon pine	Scale insect	None	Exophagus needle herbivory	>1	>1	Not measured	Insect survival	Egg transfer	91
Ponderosa pine and other pine	Black pineleaf scale insect	None[c]	Exophagus needle herbivory	<1	>1	11 conifer species	Insect survival	Scale transfer	5, 31
Herbaceous perennial herb	Rust pathogen	None	Rust fungus infection	≪1	>1	Species	Resistance and virulence	Reciprocal cross inoculation	T&B[d]

[a]Adapted from a compilation of local adaptation studies treated elsewhere (51, 93), as well as some located subsequent to publication of (51, 93). Personal communication supplements that data found in the references when necessary.

[b]E, enemy species; P, plant species. ''None'' signifies no strong pattern for either.

[c]Note: Edmunds & Alstad (31) found local adaptation, but this conclusion is reversed in Alstad (5).

[d]T&B, P.H. Thrall & J.J. Burdon, submitted for publication.

CONCLUSIONS AND SUGGESTIONS FOR FURTHER MODELING

In the interests of brevity, our review of mathematical models of coevolutionary dynamics has only skimmed the surface of the relevant literature; for example, we have not touched at all on how arms races may favor the evolution of sexual recombination (72). Nevertheless, we hope to have shown that the relevant models have moved far beyond the classical single-locus, two-allele approach. As we have described, in some cases, the cost of particular innovations has been a superficial description of the genetic basis of the traits of interest. The conclusion that arms races are possible through coevolutionary cycling is certainly of basic interest, but given the simple genetics that are typically assumed, it remains to be seen whether these models will be of more practical use in the future. By comparing the models to data sets for particular plant-herbivore interactions, we further hope to have shown one way to relate coevolutionary models to data. Our preliminary conclusion is that the data provide only scanty support for the models, but there are two important caveats. First, almost none of the articles in question considers alternative functional forms for damage functions, so it is hard to know what it means when data do not support an assumption of a model. Second, the data we reviewed were produced by experimental designs that had little or no ties to any models. We therefore argue that what is needed is a closer tie between theoretical and experimental work.

An additional issue is that consideration of natural plant-enemy interactions makes clear that many systems do not fit into existing modeling frameworks. Here, we briefly describe four phenomena that to our knowledge have not been incorporated into coevolutionary models. First, resistance is often more complex than is assumed in typical models, particularly in terms of costs. Alternatively, many plants show tolerance, meaning they are able to maintain high reproductive output in the face of enemy attack. Trade-offs between resistance (the ability to fend off attack) and tolerance may substitute for costs of resistance (36, 85; but see 89). The coevolutionary dynamics of plants capable of both tolerance and resistance are likely to be different from the dynamics of plants that show resistance or tolerance alone. Tolerance traits thus present important opportunities for coevolutionary modelers.

Second, most models assume two-way interactions between a plant and its enemy, but in some cases a third species, which is not necessarily an enemy, can modify the two-species interaction in a complex way. For example, pollinators of *Brassica rapa* discriminate between individual plants according to levels of resistance (87). Specifically, the pollinators avoid plants from lines that have been selected for high resistance, as measured by myrosinase concentrations, because such plants have less attractive floral displays. Pollinators, however, also discriminate against plants that have been selected for low resistance but that have experienced damage by herbivores. Similarly, attacks by a fungal pathogen against the wildflower *Silene alba* interact with pollination in complex ways (12). Male flowers,

but not females, show a significant cost of resistance that appears to be mediated through late onset of flowering. More generally, levels of nutrient and competition stress in the environment can strongly affect costs of resistance (8, 9), and there can be large effects of genetic background on the magnitude and demonstration of costs (reviewed in 11). These complex effects, especially those changing mating behavior, have not to our knowledge been incorporated into existing theoretical frameworks.

Third, an alternative to the usual fitness cost of resistance is an ecological trade-off among resistance characters. For example, at the *Arabidopsis thaliana Rpp8* (resistance to *Peronospora parasitica* 8) locus, one allele confers resistance to a fungal disease, whereas an alternative allele confers resistance to a virus disease (20). Other trade-offs in the ability of plants to defend against multiple enemies have been observed, although these are not allelic variants. For example, it has been demonstrated that the interaction between a resistance (*R*) gene in *A. thaliana* and its corresponding pathogen avirulence (*avr*) gene interferes with the interaction of another *avr-R* gene pair (73, 76). This interaction appears to result from competition for a common element of the signal transduction pathway, so that plants carrying both *R* genes are fully resistant to each pathogen, provided the two pathogen isolates do not attack the plant at the same time. More generally, signal cross-talk (reviewed in 35) between two pathways involved in defense against pathogens and herbivores has been demonstrated. In a variety of systems, induction of defense through one pathway reciprocally alters induction of defense through the other pathway. This improved understanding of the molecular biology of plant-pathogen interactions will, we hope, lead to new and exciting interactions between empiricists and modelers in their efforts to understand plant-enemy coevolution.

Fourth, many insect-herbivore interactions involve multiple defenses on the part of the host; indeed, the poor fit of the lines in Figures 2*A* and *B* occurs partly because of an interaction between the production of scopolamine and hyoscyamine (81). To date, however, little modeling work has been done on coevolution between herbivores and multiple plant defenses. Clearly there is much room for additional work, and Levin et al. (59) suggest some promising lines of attack.

A final point is that in fact there are many interesting coevolutionary interactions between plants and their natural enemies that fall more naturally into the kind of qualitative framework provided by classical single- or possibly two-locus models. For example, the plant *Datura wrightii* has two phenotypes, one known as sticky and the other as velvety, that differ in the relative proportions of two types of glandular trichomes. Although the interactions between this plant and its herbivores have been studied extensively from the perspectives of costs as well as damage (32, 37), as yet we are unaware of the application of coevolutionary models to predict the future evolutionary dynamics of the system. Indeed, the specifics of this system echo our underlying argument that future modeling efforts would benefit by the construction of models tailored to particular systems but based on existing general models.

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