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EVOLUTION OF HOST-PARASITE DIVERSITY

STEVEN A. FRANK
Department of Ecology and Evolutionary Biology, University of California, Irvine, California 92717

Abstract.—Hosts and parasites often have extensive genetic diversity for resistance and virulence (host range). Qualitative diversity occurs when the success of attack is an all-or-nothing response that varies according to the genotypes of the host and parasite. Quantitative diversity occurs when the success of attack is a graded response that depends on additive genetic variation in the host and parasite. Community diversity occurs when parasites vary in the success with which they can attack different host species, leading to a mixture of specialists and generalists. I developed a series of models that classify components of host-parasite interactions according to whether they cause stabilizing or disruptive selection for resistance and virulence. Stabilizing selection reduces diversity by favoring a single optimal phenotype. Disruptive selection creates diversity by favoring a mixture of widely separated phenotypes. The evolution of maximal resistance and virulence are opposed by one of three forces: metabolic costs, frequency dependence, or negative genetic correlations among beneficial traits. The models predict that qualitatively inherited resistance and virulence traits typically cause greater diversity than quantitatively inherited traits. However, each natural system is composed of many stabilizing factors that reduce diversity and disruptive factors that promote diversity. I advocate a style of modeling in which families of related assumptions are compared by their equilibrium properties, and general conclusions from equilibrium properties are tested by complete dynamical analysis. The comparison among models highlights the need for empirical studies that compare levels of diversity among related host-parasite systems.

Key words.—Community ecology, disease, genetic polymorphism, herbivory, specialist versus generalist.

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Genetic diversity often occurs in host-parasite interactions. Qualitative diversity occurs when the success of a parasitic attack tends to be an all-or-nothing response caused by relatively few genetic variants. For example, Burdon and Jarosz (1991) classified 67 wild flax plants into 10 distinct resistance genotypes when tested against six races of flax rust. One host genotype was completely resistant to all six pathogen races, whereas another genotype was susceptible to five of six races.

Quantitative diversity occurs when the resistance to attack is a graded response, and the variation in resistance has a genetic basis. For example, Simms and Rausher (1989) found additive genetic variation for seed number in the host plant *Ipomoea purpurea* when herbivores were present, but no variation when herbivores were excluded.

Community diversity occurs when parasites vary in the success with which they can attack different host species. For example, Via (1991) found genetic variation among pea aphid clones for their ability to attack alfalfa and red clover. Those clones most successful on one host tended to be least successful on the other host, suggesting a genetically based trade-off in performance. Specialization may evolve in response to this trade-off.

Many details of diversity remain unclear (e.g., Fritz and Simms 1992). I develop new models that clarify a variety of comparative questions: Are qualitatively inherited traits more or less diverse than quantitatively inherited traits? Are the benefits of resistance and virulence (host range) more commonly balanced by metabolic costs, frequency dependence, or negative genetic correlations among beneficial characters? What explains the fact that some parasites are highly specialized to attack only a single host species, whereas other parasites are generalists that can attack a wide array of hosts?

The processes that cause diversification can be studied by detailed models of dynamical systems. This approach requires assumptions about birth and death rates, epidemiology, patterns of inheritance, and the way in which host and parasite traits affect the success of an attack. Dynamical analysis, usually by computer simulation, establishes how numerous parameters interact to determine fluctuating patterns of disease, population size, and genetic diversity. Such analysis is crucial because nonequilibrium fluctuations and colonization-extinction dynamics

often play as great a role as the location of equilibria.

Dynamical analysis has certain drawbacks, however. Realism is achieved by time-consuming computer models, large parameter spaces with complex behavior, highly specific assumptions and, consequently, little generality.

I attempt a more general analysis of diversification. My primary method is equilibrium analysis of a dynamical system, but game theory proves to be a powerful supplementary method. My goal is to provide a framework for rational speculation about diversity, where the analysis is easier than a complete dynamical study but derives from a formal dynamical model. This approach provides hypotheses about diversity based on various biological assumptions. More detailed dynamical study can follow when interesting assumptions have been identified and stronger conclusions are needed. Extensive dynamical analyses for a qualitative model of plant-pathogen coevolution (Frank 1993) and a quantitative model of host-parasite coevolution (Frank 1994) show that my approach gives a very good first approximation for the evolution of diversity.

I develop several new models for host-parasite diversity that classify the components of interactions according to whether they cause stabilizing or disruptive selection. Stabilizing selection reduces diversity by favoring a single optimal type. Disruptive selection creates diversity by favoring a mixture of widely separated phenotypes. To give one example, the models predict that qualitatively inherited resistance and virulence traits typically cause greater diversity than quantitatively inherited traits. However, each natural system is composed of many stabilizing factors that reduce diversity and disruptive factors that promote diversity. I show how general predictions can be derived by the comparison of expected diversity among a variety of models.

Basic Model

The evolutionary dynamics of the host-parasite interaction follow a system of Lotka-Volterra equations (e.g., May 1974):

$$\Delta h_{\mathbf{i}} = h_{\mathbf{i}}\left[r_{\mathbf{i}} - \sum_{\mathbf{u}} r_{\mathbf{u}} h_{\mathbf{u}} - m \sum_{\mathbf{u}} \lambda_{\mathbf{iu}} p_{\mathbf{u}}\right]$$

$$\Delta p_{\mathbf{j}} = p_{\mathbf{j}}\left[-s + b_{\mathbf{j}} \sum_{\mathbf{u}} \lambda_{\mathbf{uj}} h_{\mathbf{u}}\right]. \qquad (1)$$

The values of $h_{\mathbf{i}}$ and $p_{\mathbf{j}}$ are the abundances of hosts of type **i** and parasites of type **j**. Each type is a haploid genotype of an asexual population when thought of in a genetical context and a species when thought of in an ecological context. Each host type has n resistance traits, $\mathbf{i} = \{i_1, i_2, \ldots, i_n\}$, and each parasite type has n matching virulence traits to counter host defense, $\mathbf{j} = \{j_1, j_2, \ldots, j_n\}$. All values of $\{i_k\}$ and $\{j_k\}$ range between zero and one. The sums are, depending on context, for **u** over all host types, **i**, or parasite types, **j**.

The terms $r_{\mathbf{i}}$, $\Sigma\, r_{\mathbf{u}} h_{\mathbf{u}}$, s, and $b_{\mathbf{j}}$ have their usual meanings in Lotka-Volterra systems: these are, respectively, host **i**'s intrinsic rate of increase, density dependent competition among hosts with carrying capacity normalized to one, parasite death rate, and parasite **j**'s intrinsic birth rate. The $\lambda_{\mathbf{ij}}$ are the success of parasite **j** when attacking host **i**.

Two types of assumption determine the general properties of genetic diversity and community evolution. First, how do host and parasite traits interact to determine the success of a parasitic attack? Second, what constrains the evolution of universally resistant hosts or universally successful parasites?

Success of Attack

All models assume a one-to-one correspondence between the n traits in the hosts and parasites. In the *sequential* defense models an attacking parasite must get past all n host defense traits. A parasite's success is the product of its successes at handling each of the n barriers. In symbols, $\lambda_{\mathbf{ij}} = \Pi_\alpha f(i_\alpha, j_\alpha)$, where f determines the interaction between the matching pairs of host-parasite traits. Multiplicative interaction means that a parasite's failure against any single defense trait, $f(i_k, j_k) = 0$, implies total failure, $\lambda_{\mathbf{ij}} = 0$.

In the *simultaneous* defense models, a parasite succeeds according to how well the host can defend each of several points of attack. In this case, it is natural to take the sum of the successes at each point, $\lambda_{\mathbf{ij}} = \Sigma_\alpha f(i_\alpha, j_\alpha)$.

Costs and Constraints

Three different assumptions are used that prevent hosts or parasites from always evolving to a maximally resistant or virulent type.

1. The effectiveness of resistance may depend on the *phenotypic match* between host and parasite traits. For example, suppose $\lambda_{\mathbf{ij}} = \Pi_\alpha |j_\alpha - i_\alpha|$. The advantage for a phenotype depends on

distance between host and parasite phenotypes. No inherent advantage to large or small trait values exists in the absence of antagonists. This assumption is similar to traditional models of frequency dependence. In those models, the relative resistance value of different host traits depends on the frequency distribution of parasite traits (Clarke 1979; Slatkin and Maynard Smith 1979).

2. Hosts and parasites may pay *metabolic costs* for traits that increase success (Leonard and Czochor 1980; Simms 1992). For example, suppose an increase in a host trait i_k improves resistance with respect to pathogen trait j_k. This host benefit in interactions with parasites is associated with a cost that applies to fecundity or viability independently of interactions with parasites. This metabolic cost for host **i** will typically be a reduction in the intrinsic rate of increase such that $r_i = r \Pi_\alpha (1 - ai_\alpha)$, where the cost of resistance per trait is a multiplied by the trait level, i_k. Similarly, cost for parasites is given by $b_j = b \Pi_\alpha (1 - vj_\alpha)$.

3. There may be *negative trade-offs* (genetic correlations) between the resistance or virulence contribution of one trait and the effectiveness of other traits (Gould 1983; Mitter and Futuyma 1983). In the simplest form for hosts, $\Sigma_\alpha i_\alpha = n\bar{\imath}$, where the average trait value, $\bar{\imath}$, is a constant, such that increased resistance for one trait causes lower resistance in other traits. The analogous constraint for parasites is $\Sigma_\alpha j_\alpha = n\bar{\jmath}$.

I refer to traits as "directional" if selection favors higher trait values when costs or trade-offs are ignored.

Methods of Solution

Ideally one would like to know the equilibria and the dynamics for equation (1). An equilibrium point occurs for a set of abundances for host genotypes, h_i, and for parasite genotypes, p_j, such that no further change in abundances will follow because $\Delta h_i = \Delta p_j = 0$ in equation (1) for all genotypes **i** and **j**. Dynamical analysis provides information about the local stability of equilibria and the global behavior of the system. An equilibrium is locally stable if, when genotypic abundances are perturbed by a small amount from an equilibrium point, the abundances return to that nearby equilibrium. Global analysis describes whether a system attains a stable equilibrium given any initial starting condition, or whether nonequilibrium changes in genotypic abundances occur indefinitely.

Analysis of equation (1) requires attention to the specific structure of the biological interaction. For example, when there are no metabolic costs then host and parasite traits affect equation (1) only through λ_{ij}, where host resistance is proportional to $-\lambda_{ij}$ and parasite virulence is proportional to λ_{ij}. In this case we can analyze equation (1) in two stages.

First, an equilibrium genotype frequency distribution can be found for hosts and parasites. This stage can be analyzed independently of the total abundance of the hosts and parasites when traits affect only λ_{ij}. In this case, the direction of selection on the frequency distribution of host genotypes depends only on the frequency distribution of parasite genotypes, and the direction of selection on the frequency distribution of parasite genotypes depends only on the frequency distribution of host genotypes. Thus, the direction of the global dynamics for genotype frequencies can be analyzed by focusing solely on λ_{ij}.

Second, given equilibrium distributions for genotype frequencies, equation (1) can be solved for $\Delta h_i = \Delta p_j = 0$ to obtain the equilibrium abundances of hosts and parasites. In particular, $\lambda_{ij} = \lambda$ is a constant for all **i** and **j** at genotypic equilibrium, thus the total equilibrium abundances of hosts and parasites that solve equation (1) are $H^* = s/b\lambda$ and $P^* = r(1 - H^*)/m\lambda$.

Game theory can be used to obtain the genotype frequency distributions for the first stage of the analysis. The interaction between host and parasite forms a zero-sum game because, with respect to genotype distribution, host resistance is proportional to $-\lambda_{ij}$, and parasite virulence is proportional to λ_{ij}. Stable equilibria for this game can be obtained from the minimax solution, which provides powerful analytical (von Neumann and Morgenstern 1953, ch. 3; Luce and Raiffa 1957, ch. 4) and numerical techniques (Luce and Raiffa 1957, Appendix A6.5; Fryer 1978, ch. 8; Press et al. 1986, sec. 10.8). The minimax solution occurs at the point where a player's probability distribution of strategies (genotypes) minimizes the opponent's maximum gain. Stable strategy distributions in a zero-sum game satisfy the minimax criterion.

The equilibria obtained by this two-step process are solutions to $\Delta h_i = \Delta p_j = 0$ in the full dynamical system given in equation (1). The dynamical stability properties of the minimax solution are, in principle, easy to evaluate in the context of equation (1), but in practice this may

TABLE 1. Framework for classifying models of host-parasite interaction and types of analysis that have been completed.

Kind of trait	Cost or trade-off	Equilibrium analysis	Stability analysis
Match distance			
Quantitative	none	solution of eq. (1)*	game th.†
	trade-off	solution of eq. (1)*	game th.†
Directional			
Qualitative	trade-off	solution of eq. (1)*	game th.†
	cost	solution of eq. (1)	global‡
Quantitative	trade-off	shape of fitness function	game th.§
	cost ($n = 1$)	solution of eq. (1)	global‖
	cost ($n > 1$)	shape of fitness function	none

* Uses minimax solution as intermediate step. See Methods of Solution section.

† Refers to game-theoretic stability. See Methods of Solution section.

‡ Global dynamic analysis by computer iteration of system in equation (1). The analysis is presented in Frank (1993).

§ Numerical analysis of minimax solution supports the predicted pattern of stabilizing and disruptive selection shown in table 3.

‖ Local stability analysis by algebraic study and global dynamic analysis by computer iteration of equation (1). These analyses are presented in Frank (1994).

be difficult. I do not address this problem, but instead analyze the stability of minimax solutions only in the game-theoretic sense—that is, whether a minimax solution is a stable solution to the zero-sum game determined by interaction between host and parasite genotype frequencies.

Table 1 summarizes the assumptions and methods of solution for each of the models in the following sections. Further details are provided below. I have focused in this section on the use of game-theory techniques because the approach is unusual but, as shown in table 1, this approach is used in only one-half of the cases. For example, when resistance or virulence traits have pleiotropic metabolic costs that affect growth parameters r_i and b_j, the analysis focuses simultaneously on abundance and frequency.

MATCH DISTANCE

Suppose that a close match between host and parasite traits allows a host to resist attack. A parasite's success is therefore a function of distance between the n matching host-parasite traits: if traits are used sequentially in an attack, $\lambda_{ij} = \Pi_\alpha |j_\alpha - i_\alpha|^z$, and if traits are used simultaneously, $\lambda_{ij} = \Sigma_\alpha |j_\alpha - i_\alpha|^z$. The parameter z describes whether attack success increases in an accelerating ($z > 1$) or decelerating ($z < 1$) manner with increasing match distance. In this model, traits do not have metabolic costs, that is, $r_i = r$ and $b_j = b$. Defense and attack traits affect fitness only through λ_{ij}, thus the analysis follows the minimax approach outlined in the Methods of Solution section.

No Constraints

If there are no constraints that force an association among characters, then each character is optimized independently. The minimax problem can therefore use the payoff $|j - i|^z$ for both simultaneous and sequential models.

The solution for $z > 1$ is all hosts adopting the middle trait value, $i = \frac{1}{2}$, and parasites splitting equally between the extreme values, that is, half of the individuals of the parasite community have $j = 0$ and other half have $j = 1$. The solution can be understood by recalling that hosts are favored to be as close as possible to the distribution of parasites, and parasites are favored to be as far as possible from the distribution of hosts. With $z > 1$, attack success accelerates with increasing distance, thus the hosts can do no better than stick to the middle and force the parasites to the extremes. The contribution to λ_{ij} for each trait is $(\frac{1}{2})^z$ at the equilibrium.

For n traits, and $z > 1$, the parasites are spread equally among the 2^n vertices of an n-dimensional hypercube, and all hosts are at the center of the cube. Thus, the parasite community is highly diversified but each parasite is equally a generalist on the monotypic hosts. This joint distribution of hosts and parasites is the unique minimax solution, and therefore is globally stable in a game-theoretic sense. I have not analyzed stability in the context of the dynamical system in equation (1).

For $z < 1$, the minimax solution is an identical probability distribution of host and parasite traits, where the shape of the distribution depends on

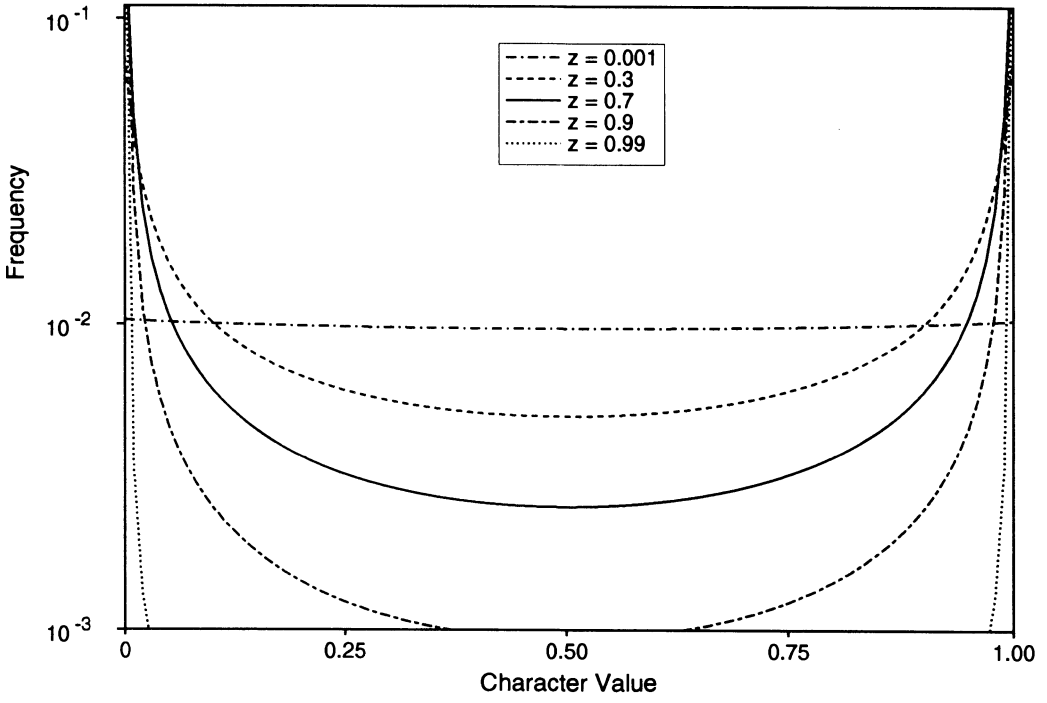

FIG. 1. Frequency distribution of character values under match distance model. No genetic constraints exist and $z < 1$.

z (fig. 1). This solution was obtained numerically by the techniques listed in the Methods of Solution section. Numerical convergence suggests local and probably global stability in a game-theoretic sense.

The hosts and parasites are spread equally near the 2^n vertices of the unit hypercube when z is less than one and not close to zero. For the sequential (multiplicative) model, this creates a community with many highly specialized host-parasite pairs, where each parasite can attack the hosts only at the opposite vertex. For the simultaneous (additive) model, the community has the same degree of phenotypic diversification but, from each parasite's point of view, the hosts are split into n groups with resistance increasing linearly with the number of matching traits. The general patterns of stabilizing and disruptive selection are summarized in table 2. If increasing distance caused greater resistance rather than greater virulence, then the roles of the host and parasite would be reversed in each entry.

Genetic Correlation among Traits

Traits may be genetically correlated within hosts or parasites. I analyze the case with two traits, $n = 2$, and $\Sigma_\alpha j_\alpha = 1$, such that $\bar{j} = 0.5$. The average trait value for hosts, $\bar{\imath}$, varies between zero and one. The results are based primarily on numerical studies backed up with supporting analysis.

The minimax equilibrium for the sequential attack model (multiplicative fitness), $\lambda_{ij} = \Pi_\alpha |j_\alpha - i_\alpha|^z$, has two forms depending on the average value of host traits, $\bar{\imath}$. In essence, when hosts are narrowly constrained then hosts diverge over a narrow range, and parasites evolve to be monomorphic generalists. When hosts can vary over a wide range, then hosts evolve to an intermediate monomorphism and parasites diverge but remain equal generalists on the single host type.

TABLE 2. Effects on host and parasite diversification caused by accelerating ($z > 1$) or decelerating ($z < 1$) virulence with increasing distance in a match distance model with no constraints: S, stabilizing; D, disruptive. Ordered pairs of S and D are for host and parasite, respectively.

	$\lambda_{ij} = \Pi F$	$\lambda_{ij} = \Sigma F$
$z > 1$	S, D	S, D
$z < 1$	D, D	D, D

Specifically, for $1 - \sqrt{3}/2 < \bar{\imath} < \sqrt{3}/2$, the parasites are split equally near the two vertices that satisfy the constraint $(j_1, j_2) = (1, 0)$ or $(0, 1)$, and the hosts are monomorphic at $i_k = \bar{\imath}$ for all k. For small and large values of $\bar{\imath}$, the parasites are monomorphic at the midpoint, $(j_1, j_2) = (0.5, 0.5)$, and the hosts are split evenly between $(i_1, i_2) = (0, 2\bar{\imath})$ and $(2\bar{\imath}, 0)$ for $\bar{\imath} < \frac{1}{2}$, and $(i_1, i_2) = (1, 2\bar{\imath} - 1)$ and $(2\bar{\imath} - 1, 1)$ for $\bar{\imath} > \frac{1}{2}$.

These results can be obtained by noting that when parasites take the midpoint, the hosts use the split strategy, yielding parasite fitness $[(\frac{1}{2})|\frac{1}{2} - 2\bar{\imath}|]^z$, and when parasites play the split strategy and hosts play the monomorphic strategy, parasite fitness is $[\bar{\imath}(1 - \bar{\imath})]^z$. The fitnesses of these two strategies are equal when $\bar{\imath} = 1 - \sqrt{3}/2$. In effect, because fitness is multiplicative, parasites attempt to maximize the average and minimize the variability in success for each trait, whereas hosts attempt the reverse.

When interactions follow the simultaneous attack model (additive fitness across traits), the outcome depends on whether parasites gain accelerating ($z > 1$) or decelerating ($z < 1$) success with increasing distance. For $z > 1$ and $\bar{\jmath} = 1/n$, parasites spread uniformly over the n vertices at which one trait has value one and the others have value zero; hosts are monomorphic at $i_k = \bar{\imath}$. The results for $z < 1$ and $n = 2$ are similar to the multiplicative model because, in this case, parasites again seek to maximize average success per trait while minimizing the variability across traits. The results can be given as the transition values, x, for which $\bar{\imath}$ satisfying $x < \bar{\imath} < 1 - x$ yield monomorphic hosts at $\bar{\imath}$ and parasites spread near the vertices where traits sum to one. For small and large values of $\bar{\imath}$, hosts split between the two strategies given above and parasites are monomorphic at the midpoint. The transition values for $z = 0.1, 0.5, 0.9$ are, respectively, $x = 0.14, 0.10, 0.03$.

Qualitative Traits

Many interactions are governed by matching major-gene factors in hosts and parasites (Burdon 1987; Frank 1992; Thompson and Burdon 1992). Each matching pair contributes either a fixed level of resistance or provides no defense. For example, in the gene-for-gene interactions between plants and their fungal parasites (Flor 1956, 1971), the host has several loci each of which provides either a resistant or susceptible phenotype. For each host locus, the parasite carries a matching locus with either a virulent or avirulent phenotype. A resistant phenotype at a host locus matched with an avirulent phenotype at the parasite locus confers a fixed level of resistance (usually complete); the other three combinations of host and parasite phenotype at this matching pair do not affect the success of attack.

The host phenotype at the kth locus is set to one for resistance and zero for susceptibility. The parasite phenotype is set to one for avirulence and zero for virulence. The success of attack depends on the number of matching ones. For additive effects over n loci, $\lambda_{ij} = f(M)$, where M is the number of matches, $\Sigma_\alpha\, i_\alpha j_\alpha$, and f is a decreasing function of M. For multiplicative effects, $\lambda_{ij} = \Pi_\alpha(1 - i_\alpha j_\alpha)$, which is one for no matches and zero for one or more matches.

Genetic Correlation among Traits

There may be a limit to the number of resistance and virulence factors that hosts and parasites can carry. Suppose that a host can carry x resistance alleles and a parasite can carry y virulence alleles. Thus, $\binom{n}{x}$ host and $\binom{n}{y}$ parasite phenotypes exist. Clearly an equal frequency of each host phenotype is favored because any concentration would be countered by avoidance by the parasites and a reduction in the number of matches. Likewise an equal frequency of each parasite phenotype is favored because any concentration causes a shift in hosts toward the concentration and an increased probability of a match. The uniform host and parasite distributions are favored for either additive or multiplicative interactions. These uniform distributions are the minimax solution.

Given uniform distributions, the probability of M matches between randomly chosen hosts and parasites is

$$\text{Prob}(M \text{ matches}) = \binom{y}{x - M} \Big/ K$$

$$K = \sum_{i=\beta_1}^{\beta_2} \binom{y}{x - i}$$

$$\beta_1 = \max(0, x - y)$$

$$\beta_2 = \min(n - y, x), \qquad (2)$$

where M ranges from β_1 to β_2. Some examples of this probability distribution are shown in figure 2. For each fixed number of resistance alleles, the associated contour shows the probability distribution for the number of matches. The distributions in figure 2 show, for an additive mod-

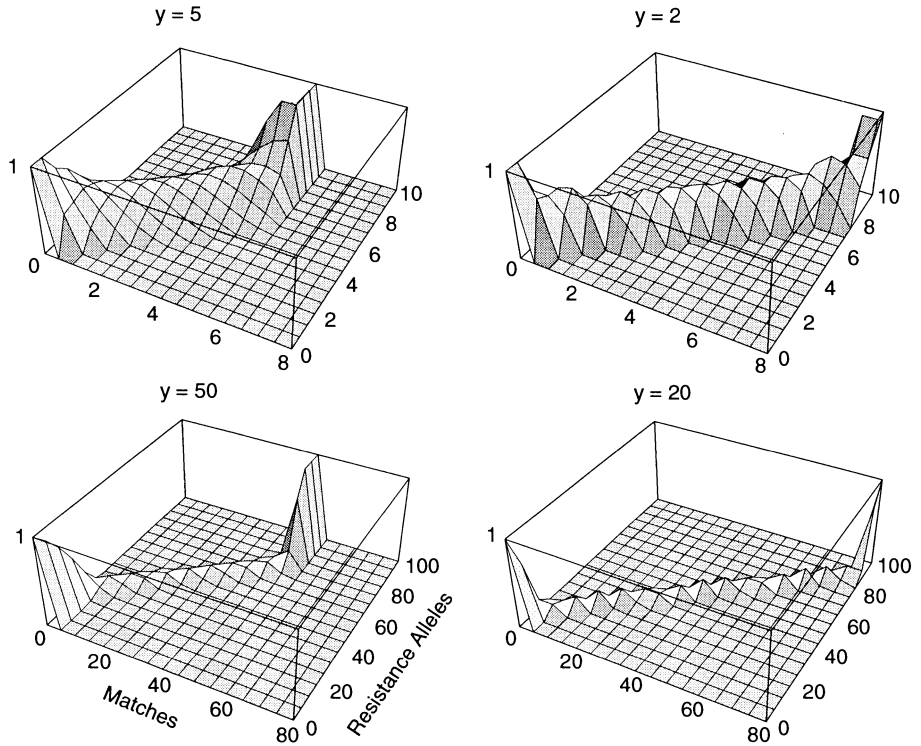

FIG. 2. Probability distribution for the number of matches between host resistance and parasite avirulence. The number of resistance and virulence alleles per individual is fixed by constraint; the distribution of phenotypes evolves under these constraints. The top row is for $n = 10$ loci, the bottom for 100 loci. The number of virulence alleles, y, is shown for each panel. In an additive model more matches corresponds to greater resistance. The graphs were obtained from equation (2).

el, how each parasite has a range of hosts that it can attack with decreasing success as the number of matches increases.

When the interaction is multiplicative, a parasite succeeds if there are zero matches or fails if there are one or more matches. The probability of successful attack (zero matches) between randomly chosen pairs of hosts and parasites is shown in figure 3. A high probability means that parasites are generalists and can attack most hosts; a low probability means that each parasite phenotype is specially adapted to attack a small fraction of hosts.

Both the additive and multiplicative models support heritable variation for resistance and virulence at equilibrium. For example, one would typically observe a strong response of hosts to selection for resistance against a single parasite phenotype, and likewise a strong response of parasites to selection for virulence against a single host phenotype. In the additive model, the response is quantitative because resistance is based on the number of matches between qualitative traits. In the multiplicative model, the response is in the frequency of all or none resistance. The genetic variability is maintained by the tendency for hosts and parasites to diversify in response to each other.

Metabolic Costs

The previous section showed the consequences of genetic constraints for polymorphism and degree of specialization. In this section, no fixed limits are assumed for numbers of resistance and virulence alleles per individual. Instead, metabolic costs of resistance and virulence alleles maintain polymorphism in qualitative traits. The model presented here is based on results given in Frank (1993).

Hosts pay a cost by reduction in intrinsic rate of increase for each resistance allele carried, $r_x = r(1 - a)^x$, where x is the total number of resistance alleles in the host, and a is the cost per resistance allele. Similarly, parasites pay a cost

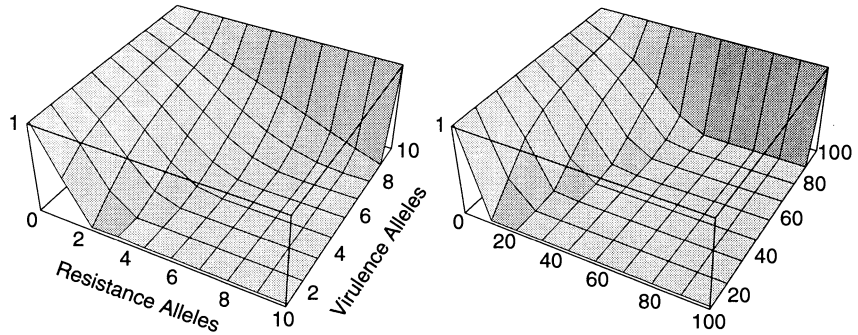

FIG. 3. The probability of successful attack (zero matches) between randomly chosen hosts and parasites in a multiplicative model. The number of resistance and virulence alleles per individual is constrained. A high probability of successful attack corresponds to generalist parasites; a low probability corresponds to specialist parasites. The left panel is for $n = 10$ loci, the right panel is for 100 loci. The graphs were obtained from equation (2) with $M = 0$.

by reduction in birth rate for each virulence allele carried, $b_y = b(1 - v)^y$, where y is the total number of virulence alleles in the parasite and v is the cost per virulence allele.

The equilibrium of the system cannot be obtained by simple game theory analysis because fitness now depends on an interaction between benefits in the λ_{ij} term of equation (1) and the metabolic costs. Instead the system of equations must be solved directly for the point at which no changes occur. When the equilibrium is expressed as the probability distribution of hosts carrying x resistance alleles and parasites carrying y virulence alleles, the result is nearly independent of the birth and death rates and depends almost entirely on the number of loci, n, and the costs of resistance and virulence, a, and v (Frank 1993):

$$\hat{h}_x^* = \binom{n}{x} v^x (1 - v)^{n-x} \tag{3}$$

$$\gamma_y = \binom{n}{y} (1 - a)^y a^{n-y}$$

$$y = 0, 1, \ldots, n - 1 \tag{4}$$

$$\gamma_y = (1 - a)^y (1 - H^*) \quad y = n \tag{5}$$

$$\hat{p}_y^* = \gamma_y \Big/ \sum_{y=0}^{n} \gamma_y, \tag{6}$$

$$H^* = \frac{s}{b(1 - v)^n}, \tag{7}$$

where $\hat{h}_x^*$, the probability of hosts with x resistance alleles, follows a binomial distribution with parameters (n, v), and $\hat{p}_y^*$, the probability of parasites with y virulence alleles, approximately follows a binomial distribution with parameters $(n, 1 - a)$. The probability $\hat{h}_x^*$ is spread equally among the $\binom{n}{x}$ different ways in which a host can carry x resistance alleles, and the probability $\hat{p}_y^*$ is spread equally among the $\binom{n}{y}$ different ways in which a parasite can carry y virulence alleles.

The system can maintain extensive host and parasite polymorphism at equilibrium. Associated with this polymorphism is a high heritability for resistance of hosts to particular parasite genotypes and high heritability for virulence of parasites to particular host genotypes. The global dynamics of the system were analyzed elsewhere (Frank 1993) and will not be discussed except to note that extensive polymorphism is often maintained when the system fluctuates over time.

The probability that a parasite can attack a randomly encountered host is a measure of generalization, G, and is given by (Frank 1993)

$$G = \frac{(1 - av)^n (1 - H^*)}{1 - H^*(1 - av)^n}, \tag{8}$$

where H^* is given in equation (7). Figure 4 shows the effects of cost per locus and number of loci in equilibrium systems. An increase in the number of traits (loci) causes a decrease in generalization even when costs of resistance and virulence are low. This result also appears to hold in nonequilibrium systems. Fluctuating allele frequencies and abundances also appear to reduce generalization below the equilibrium level predicted in figure 4.

TABLE 3. Effects on host and parasite diversification caused by accelerating (Acc) or decelerating (Dec) benefits in a quantitative model with constraints: S, stabilizing; D, disruptive. Ordered pairs of S and D are for host and parasite, respectively.

Host	Parasite	$\lambda_{ij} = \Pi F$	$\lambda_{ij} = \Sigma F$
Acc	Dec	D, S	D, S
Dec	Acc	?, ?	S, D

QUANTITATIVE TRAITS

In this section, I consider n continuously varying traits in the host and parasite with directional selection on each trait. Without an opposing force, hosts evolve to maximal resistance, and parasites evolve to maximal virulence. The following sections examine patterns of divergence under constraints or metabolic costs.

Genetic Correlation among Traits

Correlations are caused here by constraints of the form $\Sigma i_\alpha = n\bar{\imath}$ and $\Sigma j_\alpha = n\bar{\jmath}$, where overbars denote average trait values. A conjecture, given below, provides a general overview of host and parasite divergence according to the minimax solution for interactions given by λ_{ij}. The interactions λ_{ij} are the sum or product of terms of the form $F = (1 + j_k - i_k)^z$ or $F = 1 - [i_k(1 - j_k)]^z$ (this second form is equivalent to the gene-for-gene model in the qualitative section if i_k and j_k are constrained to be either zero or one).

Here is some background needed for the conjecture. First, classify the interaction function λ_{ij} according to whether hosts gain an accelerating or decelerating resistance benefit for increases in any trait, i_k, or, put another way, whether $\partial^2(-\lambda_{ij})/\partial i_k^2$ is greater or less than zero. For the terms of λ_{ij} given above, accelerating host benefits imply decelerating virulence benefits for the parasite ($\partial^2\lambda_{ij}/\partial j_k^2 < 0$), and decelerating host benefits imply accelerating parasite benefits. This antagonistic relationship is the outcome of combining pairwise trait interactions in a zero-sum game. Second, classify λ_{ij} according to whether terms are added ($\lambda_{ij} = \Sigma F$) or multiplied ($\lambda_{ij} = \Pi F$).

The conjecture is given by the general patterns of divergence for these assumptions as summarized in table 3. The *Acc* labels indicate accelerating gains and the *Dec* labels indicate decelerating gains. Each entry in the table shows an ordered pair of letters for hosts and parasites, respectively, that denote stabilizing selection (S) to a monomorphic state or disruptive selection (D) to numerous widely separated phenotypes.

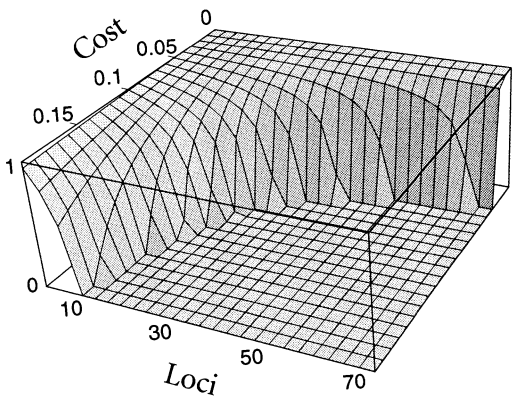

FIG. 4. The probability of successful parasite attack on a randomly chosen host in a qualitative model with metabolic costs. The figure is obtained from equation (8) with equal cost for hosts and parasites, $a = v$, and with $s = 0.5$ and $b = 4$ to obtain H^* from equation (7). An increase in s or a decrease in b lowers the surface. A probability of zero corresponds to the case where parasites are absent at equilibrium. The change between each contour line for cost is 0.01; the change between each contour line for loci is 3.

For example, if hosts diverge and parasites converge, (D, S), and $n\bar{\imath}$ is an integer, then hosts are spread with uniform probability among the vertices of the hypercube with $n\bar{\imath}$ ones and $n(1 - \bar{\imath})$ zeroes, and all parasites have $j_k = \bar{\jmath}$ for each trait.

I do not have a general proof of this conjecture, but the logic is straightforward. Decelerating gains cause stabilizing selection and accelerating gains cause disruptive selection. These properties are sufficient if traits combine additively, but traits that combine multiplicatively impose additional selection pressures. The additional pressure on hosts is disruptive because a product (in this case susceptibility, λ_{ij}) is reduced when its terms vary. The additional pressure on parasites is stabilizing because the product λ_{ij} (virulence) is increased when variation among terms is reduced. An entry in table 3 with a question mark means that opposing tendencies will be resolved according to the particular form of λ_{ij} and the specific parameters.

Numerical analysis supported the conjecture. I conducted a limited test by analysis of both $\lambda_{ij} = \Sigma F$ and $\lambda_{ij} = \Pi F$ for each of the two forms of F given in the first paragraph of this section. I used the numerical techniques described in the references on minimax problems listed in the Methods of Solution section. The test was a 2^4 factorial design with two characters ($n = 2$) and varying parameters $\bar{\imath} = 0.3, 0.7$, $\bar{\jmath} = 0.3, 0.7$, $z =$

TABLE 4. Predicted effects on host and parasite diversification caused by components of the interaction in a quantitative model with metabolic costs: S, stabilizing; D, disruptive; N, neutral; Dec, decelerating benefits; Acc, accelerating benefits.

Host factor	Effect	Parasite factor	Effect
$\Pi(1 - ai_\alpha)$	S	$\Pi(1 - vj_\alpha)$	S
Dec	S	Acc	D
Acc	D	Dec	S
$\lambda_{ij} = \Pi F$	D	$\lambda_{ij} = \Pi F$	S
$\lambda_{ij} = \Sigma F$	N	$\lambda_{ij} = \Sigma F$	N
		$\Pi(1 - vj_\alpha) \times \lambda_{ij}$	S

0.5, 2.0, and either additive or multiplicative effects across traits.

I classify an outcome as disruptive if genotypes are spread equally among the most distant possibilities and stabilizing if the genotypic distribution is monomorphic. For example, if $\bar{\imath} = 0.7$, $\bar{\jmath} = 0.3$, $z = 0.5$, and traits are additive, then the prediction from table 3 is disruptive selection on hosts and stabilizing selection on parasites (upper-right cell in the table). Thus, hosts are expected to split equally between (0.4, 1.0) and (1.0, 0.4), where ordered pairs are trait values for the first and second traits, respectively. Parasites are expected to be monomorphic for (0.3, 0.3).

Results for all 16 cases in the factorial design matched the predictions in table 3. In the four cases for which $z = 2$ and traits combined multiplicatively, no prediction was made (?,?) in table 3. The outcomes were disruptive for hosts and stabilizing for parasites (D,S) for all four of these cases.

Metabolic Costs

Metabolic or structural costs may prevent the evolution of maximal resistance or virulence when there are no genetic or developmental constraints. Specifically, each host trait i_k is free to vary independently of the other $n - 1$ traits, but increasing resistance benefit for this trait carries a cost. The cost over all traits is imposed on the intrinsic rate of increase such that $r_i = r\Pi_\alpha(1 - ai_\alpha)$, where a provides a scaling for the cost per unit benefit. Similarly for parasites, each virulence trait j_k varies independently of other traits but carries a cost such that the birth rate is $b_j = b\Pi_\alpha(1 - vj_\alpha)$, where v provides a scaling for the cost per unit benefit.

The host-parasite interaction is no longer a zero-sum game with this combination of costs of benefits. A direct analysis of the dynamical system given by equation (1) is needed. Such an analysis is, in general, very difficult because of the nonlinearity and high dimensionality. Elsewhere I have given a detailed study of this system for a single trait in the host and parasite ($n = 1$) and a form of λ_{ij} proportional to $F = (1 + j_k - i_k)^z$ (Frank 1994). Here I give a set of qualitative conjectures about how various components of the interaction cause stabilizing or disruptive selection on host and parasite traits. These conjectures are based on the detailed analysis for $n = 1$ and on the results given in the previous section.

Table 4 shows the ways in which different components of the host-parasite interaction affect diversity. The first line shows that costs, by accumulating multiplicatively, impose stabilizing selection on resistance and virulence traits. This occurs because minimum variation among traits maximizes the products shown in the first line. These products are proportional to growth rates, thus maximum values are favored.

The second and third lines of table 4 show that decelerating benefits stabilize trait values, and accelerating benefits diversify trait values. On each line, host and parasite are paired with opposing tendency. This opposing tendency is true for the two explicit forms of interaction mentioned above, $F = (1 + j_k - i_k)^z$ and $F = 1 - [i_k(1 - j_k)]^z$, and is also true for many plausible forms of interaction. It is possible to construct F such that these tendencies in host and parasite are concordant rather than discordant, but such cases appear to have reduced pairwise interaction between traits, for example, $F = 1 + j_k^w - i_k^z$, where the contribution of host and parasite traits is independent.

The fourth and fifth lines of table 4 show that the way in which interactions accumulate over traits influences patterns of diversification. In the multiplicative (sequential) model, variation in the contribution of each trait reduces λ_{ij}. This causes hosts to diversify, because $-\lambda_{ij}$ is proportional to the resistance of the hosts. Parasites, however, are stabilized by this factor because they favor an increase in λ_{ij}, which is proportional to virulence. In the additive (simultaneous) model, variation among terms has no effect.

The bottom line of table 4 shows an additional stabilizing factor that applies only to parasites. The interaction between costs and benefits is multiplicative in parasites because the parasites give birth only when successful in interacting with

hosts (Frank 1994). This multiplicative interaction favors a reduction in variation among parasite traits to reduce the product shown in the table, which is proportional to the actual birth rate of the parasites.

Looking over table 4, it appears that parasites will most often be monomorphic unless benefits accelerate rapidly enough to overcome several stabilizing effects. On the host side, several opposing tendencies exist, such that either monomorphism or divergence appear to be possible equilibrium states. These general tendencies of parasite monomorphism and the host's sensitivity to particular assumptions were observed in a detailed study of a single trait (Frank 1994).

Conclusions

The results show many ways by which polymorphism and specialization can evolve. The different components of host-parasite interactions can be arranged by their tendency to cause diversity (tables 1–4). For example, multiplicative pleiotropic costs of resistance and virulence cause stabilizing selection (table 4, row 1). Disruptive selection occurs in hosts when resistance benefits accumulate multiplicatively across traits, whereas multiplicative virulence benefits cause stabilizing selection in parasites (table 4, row 4).

A host-parasite interaction has many components. Thus, a theory cannot predict with certainty that, for example, qualitatively inherited traits will be more diverse than quantitatively inherited traits, even though there is a tendency in that direction. Instead, the approach I advocate for both theoretical and empirical study is a family of related comparisons. For example, if a particular host-parasite interaction involves both qualitative traits and quantitative, directional traits, the qualitative ones are likely to be more diverse. Comparison is the key: only for relative predictions can one obtain the required data. Isolated estimates of diversity and heritability are always difficult to interpret.

Studies of nonequilibrium dynamics also emphasize the need for comparison. Temporal dynamics will often be difficult to measure, whereas comparison of diversity patterns across space can differentiate between an attracting equilibrium and fluctuating polymorphisms (Thompson 1988; Burdon et al. 1989, 1990; Frank 1989, 1991). Similarly, the role of particular demographic or genetic properties in nonequilibrium dynamics cannot be assessed within a single system. Instead, comparison among systems that differ in a few parameters must be used to test specific predictions.

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Corresponding Editor: J. B. Walsh