Coevolution in Natural Pathosystems: Effects of Dominance on Host–Pathogen Interactions

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Accepted for publication 25 December 2002.

ABSTRACT

Ye, T. Z., Yang, R.-C., and Yeh, F. C. 2003. Coevolution in natural pathosystems: Effects of dominance on host–pathogen interactions. *Phytopathology* 93:633–639.

We have developed a new complementary model of gene interaction between diploid host and haploid pathogen by allowing for arbitrary levels of dominance in the host. This model enables us to assess the effects of overdominance, incomplete dominance, and underdominance on the equilibrium frequencies of resistance and virulence genes and on the stability of equilibria. Our model reduces to a gene-for-gene model when complete dominance of resistance is assumed. Computer simulations show that our model has two new features. First, when there is overdominance or underdominance of resistance, the internal equilibrium points

exist even when there is no cost of unnecessary virulence or when there is a cost of necessary virulence at the balance between cost of unnecessary virulence and effectiveness of resistance. Second, the occurrence of stable resistance and virulence polymorphism is strongly dependent on the level of dominance. These two features suggest the need for caution when using the gene-for-gene model, especially in the presence of overdominance or underdominance. Our model is particularly suitable for studying the coevolutionary dynamics between hybrid populations and their pathogens in natural pathosystems.

Additional keywords: balancing selection, heterozygous effect, population genetics.

Interspecific hybridization and introgression combine different species' genomes in hybrids and generate greater genetic variation than that found in the individual species. Because hybrid swarms harbor a great amount of genetic variability, they host unique arrays of ecological and evolutionary interactions. One such interaction is between host plants and their pathogens that have co-evolved in complementary genetic systems. The dynamics of natural host–pathogen systems is necessarily complex, but the gene-for-gene relationship proposed for agricultural crops and their pathogens (3) works in natural populations as well (4,18). Natural pathosystems may maintain high levels of polymorphism in both hosts and pathogens as a result of their adaptation to one another and in response to heterogeneous environments. Furthermore, gene exchange between host populations or taxa across their hybrid zones can disrupt the local dynamic balance between hosts and pathogens, thereby bringing endemic disease levels to epidemic outbreaks (4).

Population genetic analysis is essential for characterizing the properties of host–pathogen systems and for predicting magnitudes and trends of their coevolution. Several genetic models have been proposed to study the gene-for-gene relationships or complementary gene interactions between host and pathogen (4,6,8,11–13). Of these, Leonard's (8) model of selection in a natural host–pathogen system that conforms to the gene-to-gene relationship in identifying the conditions for maintaining resistance and virulence polymorphisms has received increasing attention. Although Leonard's model could predict the equilibrium frequencies of resistance and virulence genes, there was debate on the stability of equilibria attained from the model (2,10,14). Recently, Leonard

(9) carried out extensive computer simulations to investigate the stability of equilibria attained from the model and revealed the unstable limit cycles in which convergence to the equilibrium frequencies failed when initial allele frequencies were outside a critical cycle. This new analysis has since been extended to include the effects of mutation and migration (7) and human perturbations such as replacement of resistant genotypes to the host population every generation (16,17).

Despite these new analyses, one important feature that has been overlooked is the fitness differences between heterozygote and homozygote for the dominant allele because all these analyses of Leonard's model assume the complete dominance of resistance in host populations. In explaining varying hybrid responses to pest infestation, Strauss (15) identified four hypotheses in resistance between the two species: (i) hybrid intermediacy (additive hypothesis); (ii) hybrid > both parents (hybrid resistance hypothesis); (iii) hybrid < both parents (hybrid susceptibility hypothesis or hybrids-as-sinks hypothesis); and (iv) hybrid = one parent (dominance hypothesis). These four hypotheses signal the pivotal role that the dominance effect could play in host resistance: (i) no dominance in hypothesis, (ii) overdominance in hypothesis, (iii) underdominance in hypothesis, and (iv) complete dominance in hypothesis. There is evidence that these gene actions operate in hybrid populations for pest resistance (15,19,21). In this paper, we develop a new complementary model of gene interaction between host and pathogen by extending Leonard's (8,9) model to allow for arbitrary levels of dominance in a diploid host genotype. Our objective is to investigate how dominance could affect equilibrium frequencies and the stability of equilibria.

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Publication no. P-2003-0320-01R
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THEORY AND APPROACHES

Leonard's model. Before developing our model, we present a brief overview of Leonard's model (8,9). In essence, Leonard's

model is a single-locus population genetic model for a gene-for-gene interaction between a diploid plant host and its haploid pathogen, both with discrete generation intervals. There are two alleles at the host locus, one for resistance (R) and one for susceptibility (r), and similarly there are two alleles at the pathogen locus, one for virulence (V) and one for avirulence (v). The allele for resistance in the host is assumed to be dominant, but dominance is ignored in the haploid pathogen. Thus, there are two host phenotypes, resistant (RR or Rr) and susceptible (rr), and two pathogen phenotypes, virulent (V) and avirulent (v). The gene-for-gene interaction stipulates that the resistant host is resistant to the avirulent pathogen but susceptible to the virulent pathogen, whereas the susceptible host is susceptible to both pathogen phenotypes. Thus, the relative fitnesses of host or pathogen phenotypes differ depending on the counterpart's phenotypes. This model further assumes that there are fitness costs associated with unnecessary resistance or virulence. This will ensure that the coevolutionary process does not reach an unstable state in which all hosts are resistant and all pathogens are virulent.

The fitnesses of pathogen and host phenotypes for Leonard's model can be obtained from Table 1 by letting $h = 1$ (complete dominance) so that the fitnesses for genotypes Rr and RR are the same. Frequencies of gene for virulence and avirulence in the pathogen population at the i th generation are n_i and m_i with $n_i + m_i = 1$. Frequencies of gene for resistance and susceptibility in the host population at the i th generation are p_i and q_i with $p_i + q_i = 1$. Leonard's model assumes that the host population undergoes random mating so Hardy-Weinberg equilibrium is achieved in each generation. Thus, frequencies of three genotypes, RR , Rr , and rr , at the i th generation are p_i^2 , $2p_iq_i$, and q_i^2 , and the frequency of host phenotype for the dominant resistance gene (RR or Rr) is $1 - q_i^2$. During the i th generation, selection changes the frequency of virulence gene in the pathogen population from n_i to n_{i+1} ,

$$n_{i+1} = g(p_i, n_{i+1}) = \frac{n_i[1 - k + (1 - q_i^2)a]}{1 - (1 - q_i^2)t + n_i[(1 - q_i^2)(a + t) - k]} \quad (1)$$

The selection induced by the pathogen infection on reproduction of resistant and susceptible host phenotypes at the i th generation determines the frequency of resistance gene in the host population at the $(i + 1)$ th generation,

$$p_{i+1} = f(p_i, n_{i+1}) = \frac{p_i[1 - c - s(1 - t) + n_{i+1}s(k - a - t)]}{1 - s + n_{i+1}ks + 1(1 - q_i^2)[ts - c - n_{i+1}s(a + t)]} \quad (2)$$

It is evident that genetic feedback between host and pathogen populations is delayed rather than immediate. In other words, the composition of pathogen population may change in response to selection during the current generation, but the impact of the changed pathogen population on the relative fitness of the host population is not shown until the next generation.

When equilibrium is reached between selection pressures exerted by host resistance and pathogen virulence (i.e., there is no

change in gene frequencies for resistance in host [$p_{i+1} = p_i = p_e$] and for virulence in pathogen [$n_{i+1} = n_i = n_e$]), the equilibrium frequencies for the resistance gene in host and for the virulence gene in pathogen are functions of fitness parameters as defined in Table 1,

$$p_e = 1 - q_e = 1 - \sqrt{1 - \frac{k}{a + t}} \quad (3)$$

and

$$n_e = \frac{ts - c}{s(a + t)} \quad (4)$$

Mathematical analysis of the model showed that the equilibrium point was not locally stable. Extensive computer simulations by Leonard (9) revealed the presence of an unstable limit cycle for each combination of parameter values, i.e., gene frequency starting inside the limit cycle spiraled inward toward an internal equilibrium point; those starting outside the limit cycle spiraled outward toward fixation or extinction. Leonard (9) concluded that the internal equilibrium point was stable in a biological sense, although it may not meet mathematical criteria for the stability.

Extension of Leonard's model. To extend Leonard's model and allow for an arbitrary degree of dominance in the diploid host population, we introduce a new parameter (h) called the heterozygous effect (5) to measure the fitness of the heterozygote relative to the selective difference between the two homozygotes (Table 1). If resistance is completely dominant ($h = 1$), the fitness for the heterozygote (Rr) is the same as that for the resistant homozygote (RR) (i.e., Leonard's original model as described in the previous section). If susceptibility is completely dominant ($h = 0$), the fitness for the heterozygote (Rr) is the same as that for the susceptible homozygote (rr). Incomplete dominance ($0 < h < 1$) indicates that the fitness for heterozygote (Rr) lies between those for the two homozygotes (RR and rr). In particular, with $h = 0.5$, there is no dominance and the fitness for the heterozygote is the average fitness of those for the two homozygotes. Finally, heterozygote inferiority (underdominance) or superiority (overdominance) needs to be described with respect to the type of pathogens. In the presence of avirulent pathogens, underdominance of resistance is indicated by $h < 0$ because heterozygote Rr is more susceptible to the pathogen than recessive homozygote rr , whereas overdominance is indicated by $h > 1$ because heterozygote Rr is more resistant to the pathogen than dominant homozygote RR . In the presence of virulent pathogens, however, the reverse is true provided that there is advantage of virulent pathogen on resistant hosts (i.e., $a > 0$); underdominance and overdominance of resistance are indicated by $h > 1$ and $h < 0$, respectively. Thus, to avoid any confusion in using h as a measure of dominance, we will hereafter refer to $h < 0$ as underdominance of resistance and $h > 1$ as overdominance of resistance.

When two pathogen phenotypes, V and v , attack three genotypes (RR , Rr , and rr) in the host population whose frequencies

TABLE 1. Relative fitnesses of haploid pathogen and diploid host genotypes in a complementary gene interaction model^a

Genotype	Frequency	rr	Rr	RR
		q_i^2	$2p_iq_i$	p_i^2
Fitness of two pathogen genotypes on three host genotypes				
v (avirulent)	m_i	1	$1 - ht$	$1 - t$
V (virulent)	n_i	$1 - k$	$1 - k + ha$	$1 - k + a$
Fitness of three host genotypes on two pathogen genotypes				
v (avirulent)	m_i	$1 - s$	$1 - ch - s(1 - ht)$	$1 - c - s(1 - t)$
V (virulent)	n_i	$1 - s(1 - k)$	$1 - ch - s(1 - k + ha)$	$1 - c - s(1 - k + a)$

^a Three host genotypes respond differently to attacks by either avirulent or virulent pathogens and their responses are measured by the respective fitness values. The genotypic frequencies are those for the i th generation. h = heterozygous effect in the diploid host; k = cost of virulence in the parasite; t = effectiveness of the resistance in the host; a = advantage of virulent pathogen on hosts with corresponding gene for resistance; s = severity of disease; and c = cost of resistance in the host.

are p_i^2 , $2p_iq_i$, and q_i^2 at the i th generation, their relative fitnesses change according to the composition of host population and the parameters given in Table 1,

$$W_v = q_i^2 + 2p_iq_i(1-ht) + p_i^2(1-t) = 1 - p_i^2t - 2p_iq_iht$$

and

$$W_V = q_i^2 + (1-k) + 2p_iq_i(1-k+ha) + p_i^2(1-k+a) = 1 - k + p_i^2a + 2p_iq_iha$$

The frequency of V after one generation of selection is

$$\begin{aligned} n_{i+1} &= g(p_i, n_i) = \frac{n_i W_V}{n_i W_V + m_i W_v} \\ &= \frac{n_i(1-k + p_i^2a + 2p_iq_iha)}{n_i(1-k + p_i^2a + 2p_iq_iha) + m_i(1-p_i^2t - 2p_iq_iht)} \end{aligned} \quad (5)$$

which reduces to equation 1 if $h = 1$ (Leonard's model). The change in frequency of V due to selection is

$$\Delta n = n_{i+1} - n_i = \frac{m_i n_i (W_V - W_v)}{W_v + n_i (W_V - W_v)} \quad (6)$$

where $W_V - W_v = (1-2h)p_i^2 + 2hp_i - k/(a+t)$. Obviously, the change in frequency of V causes the change in fitnesses of host genotypes and the frequency of resistance gene (R). The fitnesses of the three host genotypes are

$$\begin{aligned} W_{RR} &= m_{i+1}[1-c-s(1-t)] + n_{i+1}[1-c-s(1-k+a)] \\ &= 1-c-s(1-m_{i+1}t-n_{i+1}k+n_{i+1}a) \end{aligned}$$

$$\begin{aligned} W_{Rr} &= m_{i+1}[1-ch-s(1-ht)] + n_{i+1}[1-ch-s(1-k+ha)] \\ &= 1-ch-s(1-m_{i+1}th-n_{i+1}k+n_{i+1}ah) \end{aligned}$$

$$W_{rr} = m_{i+1}(1-s) + n_{i+1}[1-s(1-k)] = 1-s + n_{i+1}ks$$

The frequency of R after one generation of selection is

$$\begin{aligned} p_{i+1} &= f(p_i, n_{i+1}) = \frac{p_i^2 W_{RR} + p_i q_i W_{Rr}}{p_i^2 W_{RR} + 2p_i q_i W_{Rr} + q_i^2 W_{rr}} \\ &= \frac{p_i \left(n_{i+1} s \{ k - [h + (1-h)p_i] a - [h + (1-h)p_i] t \} \right)}{1-s + n_{i+1}ks + (1-q_i)(1-q_i + 2hq_i)[ts-c-n_{i+1}s(a+t)]} \end{aligned} \quad (7)$$

which reduces to equation 2 if $h = 1$ (Leonard's model). The change in frequency of R due to selection is

$$\begin{aligned} \Delta p &= p_{i+1} - p_i = \frac{p_i q_i [p_i(W_{RR} - W_{Rr}) + q_i(W_{Rr} - W_{rr})]}{p_i^2 W_{RR} + 2p_i q_i W_{Rr} + q_i^2 W_{rr}} \\ &= \frac{p_i q_i^2 [ts-c-n_{i+1}s(a+t)](2h-1)}{1-s + n_{i+1}ks + (1-q_i)(1-q_i + 2hq_i)[ts-c-n_{i+1}s(a+t)]} \end{aligned} \quad (8)$$

When the equilibrium is reached between selection pressures from the resistant hosts and virulent pathogens, there is no change in the frequencies of resistance and virulence genes over generations, $n_i = n_{i+1} = n_e$ and $p_i = p_{i+1} = p_e$. The equilibrium frequency of

resistance gene (p_e) can be obtained by solving the following equation (setting $\Delta n = 0$):

$$(1-2h)p_e^2 + 2hp_e - \frac{k}{a+t} = 0 \quad (9)$$

In the special case in which there is no dominance (i.e., $h = 0.5$), equation 9 reduces to $p_e - k/(a+t) = 0$, and thus, the equilibrium frequency is

$$p_e = \frac{k}{a+t} \quad (10a)$$

In all other cases, the equilibrium frequency is affected by the dominance as measured by the heterozygous effect (h),

$$p_e = \frac{h - \sqrt{h^2 - \frac{(2h-1)k}{a+t}}}{2h-1} \quad (10b)$$

In the case of complete dominance for resistance ($h = 1$; Leonard's model), equation 10b reduces to equation 3. Similarly, the equilibrium frequency of virulence gene (n_e) is obtained by setting $\Delta p = 0$ in equation 8. In other words, we need to solve for n_e in the following equation given that the equilibrium frequency of resistance gene is nonboundary ($0 < p_e < 1$), $ts - c - n_e s(t+a) = z$, where constant z is zero if there is dominance ($h \neq 0.5$), but z may be nonzero if there is no dominance ($h = 0.5$). Thus,

$$n_e = \frac{ts-c-z}{s(a+t)} \quad (11)$$

which is the same as equation 4 when $h \neq 0.5$. In general, dominance does not affect the equilibrium frequency of the virulent gene in a haploid pathogen population as expected. In addition to the internal equilibrium points (p_e, n_e), there are four trivial equilibrium points, (0, 0), (0, 1), (1, 0), and (1, 1).

Fig. 1. Equilibrium frequencies of resistance gene (p_e) over the range of heterozygous effects ($-1 \leq h \leq 2$) for three sets of fitness parameters: (▲) $a = k = 0.0$, $t = 0.5$, $s = 0.5$, and $c = 0.03$; (●) $a = k = t = 0.5$, $s = 0.5$, and $c = 0.03$; and (■) $a = 0.0$, $k = t = 0.5$, $s = 0.5$, and $c = 0.03$, where k is cost of virulence, t is effectiveness of the resistance, a is advantage of virulent pathogen on hosts with corresponding gene for resistance, s is severity of disease, and c is cost of resistance in the host. The parameter h takes values ranging from -1 to 2 to cover underdominance ($-1 \leq h < 0$), complete recessiveness for resistance ($h = 0$), incomplete dominance ($0 < h < 1$) including no dominance ($h = 0.5$), complete dominance for resistance ($h = 1$), and overdominance ($1 < h \leq 2$).

RESULTS

Effect of dominance on equilibrium frequency. It is evident from equations 10b and 11 that only the equilibrium frequency for resistance (p_e) in the diploid host population is affected by dominance, whereas the equilibrium frequency for virulence (n_e) in the haploid pathogen population is not affected. However, p_e is also affected by the fitness-related factors (a , k , and t) as given in Table 1 (8). Thus, we now examine the effect of dominance along with a series of values of the fitness-related parameters.

For our numerical analysis, h takes values ranging from -1 to 2 to cover underdominance ($-1 \leq h < 0$), complete recessiveness for resistance ($h = 0$), incomplete dominance ($0 < h < 1$) including no dominance ($h = 0.5$), complete dominance for resistance ($h = 1$), and overdominance ($1 < h \leq 2$). Leonard (8,9) described in detail the possible ranges for a , k , and t . Here, we use the following ranges for our numerical evaluation: $0 \leq a \leq 0.5$, $0 \leq k \leq 0.5$, and $0.5 \leq t \leq 1$. Although our ranges for a and k are consistent with Leonard's, our range for t is much greater. Leonard (8) determined his t values based on the disease data from annual crop plants in which "pure" lines with major resistance genes were grown to overcome the attack by prevalent virulent pathogens and thus his t values were equal to or very close to 1 as expected. In natural

pathosystems on which our study is focused, however, t may be appreciably less than 1 because a host population is likely to be genetically heterogeneous with a mixture of resistant and susceptible genotypes and their hybrids. Furthermore, genes with partial resistance may be prevalent in natural populations but rare in cultivated crops because detection and introgression of these genes with small effects are difficult for most crop improvement programs. To calculate the equilibrium frequency for virulence gene (n_e), the range of the two other fitness-related parameters (c and s) need to be determined. We calculate n_e using c values in the range of 0.0 to 0.1 and s values in the range of 0.2 to 0.8. These values are within the ranges proposed by Leonard (8).

The numerical results show an interesting pattern on the equilibrium frequencies for resistance gene (p_e). Across the range of $0 \leq h \leq 1$, p_e can take values from 0 to 1. However, the value for p_e with underdominance of resistance is proportional to the degree of underdominance, but the value for p_e with overdominance of resistance is inversely proportional to the degree of overdominance. Figure 1 shows plots of p_e against h ($-1 \leq h \leq 2$) for three cases of a , k , and t : (i) $a = 0.0$, $k = 0.0$, and $t = 0.5$; (ii) $a = 0.5$, $k = 0.5$, and $t = 0.5$; and (iii) $a = 0.0$, $k = 0.5$, and $t = 0.5$. Cases one and three display the constrained minimum and maximum p_e values for underdominance ($h < 0$) and overdominance ($h > 1$), respectively.

Fig. 2. Phase planes from simulations of a host-parasite coevolution model with four levels of dominance effect: **A**, $h = 1.2$; **B**, $h = 1.0$; **C**, $h = 0.5$; and **D**, $h = -0.2$. In each plot, p is the frequency of gene for resistance in the diploid host and n is the frequency of gene for virulence in the haploid pathogen. Fitness parameters used are $a = k = 0.2$, $s = 0.8$, $t = 1.0$, and $c = 0.03$. Simulations start with the same initial frequencies ($n_0 = 0.3$, $p_0 = 0.2$) at the 0th generation and continue until the 30,000th generation. The dots indicate the internal equilibrium points.

It is evident from equation 10b that p_e in case one, and in other cases in which $k = 0$, is determined by

$$p_e = \frac{h - |h|}{2h - 1} = \begin{cases} 2h/(2h - 1), & \text{if } h < 0 \\ 0, & \text{if } h \geq 0 \end{cases} \quad (12a)$$

where $|h|$ is the absolute value of h . Similarly, p_e in case three, and in other cases in which $a = 0$ and $k = t$, is determined by

$$p_e = \frac{h - |h - 1|}{2h - 1} = \begin{cases} 1/(2h - 1), & \text{if } h > 0 \\ 1, & \text{if } h \leq 0 \end{cases} \quad (12b)$$

Case two is an example with nonboundary p_e values.

It is clear from Figure 1 that when there is underdominance ($h < 0$), the internal equilibrium points (p_e, n_e) exist even when there is no cost of unnecessary virulence ($k = 0$). This is in contrast to Leonard's (9) conclusion that there could be no internal equilibrium point when $k = 0$. Leonard's conclusion was based on the assumption of complete dominance of resistance gene ($h = 1$). Thus, when $k = 0$ the whole population becomes susceptible to the pathogen (i.e., $p_e = 0$). Similarly, when there is overdominance ($h > 1$), the internal equilibrium points (p_e, n_e) exist even when there is a cost of necessary virulence ($a = 0$) at the balance between the cost of unnecessary virulence and effectiveness of resistance (i.e., $k = t$). Although such balance is needed to obtain equation 12b, it must be viewed as an extreme case in which the fitnesses of avirulent and virulent pathogens on the resistant (RR) plant are identical. In general, the condition of $k < t$ is required for an unequivocal definition of resistance. With $a = 0$ and $k = t$, Leonard's model ($h = 1$) would lead to the fixation of resistance gene (i.e., $p_e = 1$) at equilibrium.

Stability of equilibria. To examine the effect of dominance on the stability of internal equilibrium points (p_e, n_e), we identified unstable limit cycles for all combinations of fitness parameters and dominance effect (h) that generate the internal equilibrium points. Our results are in close agreement with Leonard's (9) three observations: (i) gene frequencies starting on an unstable limit cycle would continue in its closed trajectory; (ii) gene frequencies outside the unstable limit cycle would spiral outward toward fixation or loss of virulence and resistance genes; and (iii) gene frequencies inside the unstable limit cycle would spiral inward toward the internal equilibrium point. As an example, Figure 2 shows plots of the frequencies of resistance and virulence genes (p_i, n_i) using equations 5 and 7 for four levels of dominance ($h = 1.2, 1.0, 0.5$, and -0.2). The fitness parameters are $a = k = 0.2$, $s = 0.8$, $t = 1.0$, and $c = 0.03$. Initial frequencies are $n_0 = 0.3$ for virulence and $p_0 = 0.2$ for resistance. The frequencies (p_i, n_i) for 30,000 generations are plotted in a phase plane. In all four plots, the frequencies of genes spiral inward toward their internal equilibrium point but never reach that point even after 200,000 generations (data not shown). It is also evident from these plots that the rate at which the frequencies of resistance and virulent genes are approaching the internal equilibrium point (p_e, n_e) increases with decreasing h values. Thus, the level of dominance greatly affects the path and pace of host–pathogen coevolution.

Simulations were carried out to determine the position of the limit cycle for each combination of parameter values over the following ranges: $s = 0.2, 0.5$, or 0.8 ; $t = 0.5, 0.8$, or 1.0 ; $c = 0.00, 0.01, 0.02, 0.03, 0.05, 0.07, 0.10, 0.15$, and 0.30 ; $k = 0, 0.1, 0.2, 0.3, 0.4$, or 0.5 ; $a = 0$ or k ; and $h = -0.9, -0.75, -0.50, -0.25, 0, 0.25, 0.50, 0.75, 1.0, 1.25, 1.50, 1.75$, or 1.90 . We tested all combinations of parameter values that produced an internal equilibrium point. In addition, the two sets of parameter values that gave rise to the lower and upper boundaries for internal equilibrium points in Figure 1 are included. The initial frequency of the resistance gene, p_0 , in the test simulations is fixed to its equilibrium frequency. The choice of the initial frequency of virulence, n_0 , required a trial-and-error approach. When the initial run

produces an inward spiral, then the value of n_0 is increased in each consecutive run until the gene frequencies would spiral outward. The size of unstable limit cycle is measured by the value of $-\log(n)$, where n is the frequency of virulence at its lowest point on the limit cycle. As Leonard (9) pointed out, the stability of equilibrium or frequency polymorphism in a pathosystem increases with the size of limit cycle and thus with high values of $-\log(n)$. There is no stable polymorphism when $-\log(n)$ is zero and stability increases with increasing value of $-\log(n)$.

Figure 3 shows the plots of $-\log(n)$ against the h values for three sets of parameters used to produce Figure 1 and with $s = 0.5$ and $c = 0.03$. For all three sets of parameters, there is little stability with $0 \leq h \leq 1$ and when the values of $-\log(n)$ are close to or equal to zero. However, the nonzero values of $-\log(n)$ occur at $1 < h \leq 2$ for the cases of $a = 0.0, k = t = 0.5, s = 0.5$, and $c = 0.03$; and $a = k = t = 0.5, s = 0.5$, and $c = 0.03$, and at $-1 \leq h < 0$ for the cases of $a = k = 0.0, t = 0.5, s = 0.5$, and $c = 0.03$; and $a = k = t = 0.5, s = 0.5$, and $c = 0.03$. There are also many cases in which the stability of polymorphism is increased at $0 \leq h \leq 1$ (data not shown). Thus, the occurrence of stable polymorphism is strongly dependent on the level of dominance.

DISCUSSION

This study has extended Leonard's (8,9) model of host–pathogen interactions in natural pathosystems to assess the effects of overdominance, incomplete dominance, and underdominance on the equilibrium frequencies of resistance gene in a diploid host population and on the stability of equilibria. Our model reduces to Leonard's original model when complete dominance of resistance is assumed. Two new features of our model emerge from our numerical analyses. First, when there is underdominance or overdominance of resistance ($h < 0$ or $h > 1$), the internal equilibrium points exist even when $k = 0$ or when there is a cost of necessary virulence ($a = 0$) at the balance between cost of unnecessary

Fig. 3. Effect of dominance (h) on the stability of polymorphisms as measured by the position of the unstable limit cycle [$-\log(n)$] in a host–parasite coevolution model, where n is the frequency of gene for virulence at its lowest point on the limit cycle. Three sets of fitness parameters are used: (▲) $a = k = 0.0, t = 0.5, s = 0.5$, and $c = 0.03$; (●) $a = k = t = 0.5, s = 0.5$, and $c = 0.03$; and (■) $a = 0.0, k = t = 0.5, s = 0.5$, and $c = 0.03$, where k is cost of virulence, t is effectiveness of the resistance, a is advantage of virulent pathogen on hosts with corresponding gene for resistance, s is severity of disease, and c is cost of resistance in the host. The parameter h takes values ranging from -1 to 2 to cover underdominance ($-1 \leq h < 0$), complete recessiveness for resistance ($h = 0$), incomplete dominance ($0 < h < 1$) including no dominance ($h = 0.5$), complete dominance for resistance ($h = 1$), and overdominance ($1 < h \leq 2$).

virulence and effectiveness of resistance (i.e., $k = t$). In contrast, with $0 \leq h \leq 1$, the resistant gene is either lost ($p_e = 0$) or fixed ($p_e = 1$) and there is no internal equilibrium point in these two cases (cf. Fig. 1). This is the conclusion from the analysis of Leonard's model for the special case of complete dominance (8,9). Second, it is evident from Figure 3 that the occurrence of stable polymorphism is strongly dependent on the level of dominance (h). Even in the case where there is no cost of unnecessary virulence ($k = 0$), some level of stability is possible with underdominance ($h < 0$), confirming a well-known result from population genetic analysis of balancing selection (5). In contrast, Leonard (8,9) concluded from the analysis of his model of complete dominance that no stable polymorphism would be possible when $k = 0$. These two new features from our model suggest that care must be exercised in using Leonard's model particularly when there is evidence of overdominance or underdominance.

It is evident from equation 12a and Figure 1 that if $k = 0$, $p_e > 0$ only if $h < 0$, which signifies underdominance of resistance. In this case, the fitness of the avirulent pathogen type would be greater on the Rr host than on either homozygote host, implying that the heterozygous host is actually more susceptible to the avirulent pathogen than the homozygous susceptible host. To the

best of our knowledge, this "heterozygote susceptibility" phenomenon has not yet been documented in plant pathology literature. However, similar phenomena have been observed in many plant-herbivore interaction systems (15,19). For example, Whitham et al. (19) found that cottonwood hybrids between *Populus angustifolia* and *Populus fremontii* attracted more gall-forming aphids (*Pemphigus betae*) than did either resistant or susceptible parental species. Unfortunately, because most of these studies are conducted on unknown genotypes of hybrid plants in natural habitats, the genetic and environmental causes of the observed patterns remain to be investigated.

The assumption of complete dominance in Leonard's model of gene-for-gene coevolution is reasonable in an agricultural pathosystem where a major dominant gene for resistance to a disease is usually found. In natural pathosystems, however, several modes of gene action for resistance may exist including complete dominance, overdominance, and underdominance. For example, there are numerous responses of natural hybrids to attacks by pests, including hybrid susceptibility (underdominance of resistance), hybrid dominance (complete dominance), and hybrid intermediacy (no dominance) (15). Our model allows for an arbitrary level of dominance and thus may be particularly useful for studying the coevolutionary dynamics between hybrid populations and their

Fig. 4. Phase planes from simulations to examine the joint effects of mutation (μ_h and μ_p) and dominance (h) using fitness values $a = k = 0.05$, $t = 1$, $c = 0.03$, and $s = 0.8$. The initial points are $n_0 = 0.00001$ and $p_0 = 0.2$. Results of 30,000 generations are shown in the case of **A**, no mutation ($\mu_h = \mu_p = 0.0$) for $h = 1.0$ and for three cases **B**, **C**, and **D**, where the mutation rate is low ($\mu_h = \mu_p = 10^{-10}$) for $h = 1.2$, 1.0 , and -0.2 , respectively. The dots indicate the internal equilibrium points.

pathogens. In the past, the effect of dominance on the equilibrium of resistance and its stability has been examined using simpler models (literature citation 1 is a review). For example, Levin (11) considered a symmetric fitness model in which the host genotypes, RR , Rr , and rr , have respective fitnesses of α , β , and γ in the presence of avirulent pathogens, but have respective fitnesses of γ , β , and α in the presence of virulent pathogens. Even with this simplified model, a linearization approximation is required to find the necessary and sufficient condition for stable polymorphism in the host, which is $\beta < (\alpha + \gamma)/2$. The condition

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

is required to maintain stable polymorphisms in both the host and pathogen. Thus, Levin's (11) model concurs with our model that stable polymorphisms are possible with overdominance or underdominance (heterozygote nonintermediacy) in the host.

The effects of mutation and population subdivision studied by Kirby and Burdon (7) on Leonard's model can also be incorporated into our model. With the mutation rates in forward or backward direction being μ_p for pathogen and μ_h for host, the recursion equations for frequencies of resistant and virulent genes in equations 5 and 7 become $n_{i+1} = g(p_i, n_i) + \mu_p[1 - 2g(p_i, n_i)]$ and $p_{i+1} = f(p_i, n_{i+1}) + \mu_h[1 - 2f(p_i, n_{i+1})]$. To illustrate the joint effects of dominance and mutation, we calculated the frequencies of resistance and virulence for 30,000 generations using the fitness values of Kirby and Burdon (7): $a = k = 0.05$, $t = 1$, $c = 0.03$, and $s = 0.8$. The initial point of $n_0 = 0.00001$ and $p_0 = 0.2$ is chosen because it is well outside the limit cycle for all h values examined. Figure 4 shows the results of 30,000 generations when there is no mutation ($\mu_h = \mu_p = 0.0$) for $h = 1.0$ and when the mutation rate is low ($\mu_h = \mu_p = 10^{-10}$) for three levels of dominance ($h = 1.2, 1.0$, and -0.2). As was found by Kirby and Burdon (7), in the absence of mutation, the virulence gene is fixed rapidly (in the 8th to 12th generation) regardless of the dominance effect. The addition of a tiny amount of mutation allows for converging cycles, and dominance affects the sizes of the limit cycles in the same way as found in Figure 2.

The effect of population subdivision can be considered for different models of population structure (20), from the simplest island model to the complex stepping stone model. Kirby and Burdon (7) used the island model to study the effect of population subdivision on the behaviors of Leonard's model. Under the island model, a large population is split into geographic subpopulations and a proportion of migrants is exchanged among them every generation. With subpopulations of finite size, the effect of random drift will balance the effect of migration at equilibrium. The net result at equilibrium is the increased homozygosity and decreased heterozygosity in the whole population. It is likely that population subdivision would diminish the effect of dominance in our model.

ACKNOWLEDGMENTS

This research represents a portion of a dissertation submitted by T. Z. Ye to the University of Alberta in partial fulfillment of the requirements for his Doctor of Philosophy degree. We thank two anonymous reviewers for insightful reviews, the University of Alberta for a dissertation scholarship to T. Z. Ye, and the Natural Sciences and Engineering Research Council of Canada for grants to R.-C. Yang (A3983) and F. Yeh (A2282).

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