9 Kelly, M. *et al.* (1988) *EMBO J.* 7, 1537–1547
10 Klar, A.J.S. and Miglio, L.M. (1986) *Cell* 46, 725–731
11 Nielsen, O. and Egel, R. (1989) *EMBO J.* 8, 269–276
12 Egel, R., Beach, D.H. and Klar, A.J.S. (1984) *Proc. Natl Acad. Sci. USA* 81, 3481–3485
13 Schmidt, H., Kapitza, P. and Gutz, H. (1987) *Curr. Genet.* 11, 303–308
14 Schmidt, H., Kapitza-Fecke, P., Stephen, E.R. and Gutz, H. (1989) *Curr. Genet.* 16, 89–94
15 Klar, A.J.S., Bonaduce, M.J. and Cafferkey, R. (1991) *Genetics* 127, 489–496
16 Arcangioli, B. and Klar, A.J.S. (1991) *EMBO J.* 10, 3025–3033
17 Miyata, H. and Miyata, M. (1981) *J. Gen. Appl. Microbiol.* 27, 365–371
18 Egel, R. and Eie, B. (1987) *Curr. Genet.* 12, 429–433
19 Klar, A.J.S. (1990) *EMBO J.* 9, 1407–1415
20 Egel, R. (1984) *Curr. Genet.* 8, 205–210
21 Klar, A.J.S. (1987) *Nature* 326, 466–470
22 Klar, A.J.S. and Bonaduce, M.J. (1991) *Genetics* 129, 1033–1042
23 Egel, R., Willer, M. and Nielsen, O. (1989) *Curr. Genet.* 15, 407–410
24 Thon, G. and Klar, A.J.S. *Genetics* (in press)
25 Strathern, J.N. *et al.* (1982) *Cell* 31, 183–192
26 Hicks, J.B. and Herskowitz, I. (1976) *Genetics* 83, 245–258
27 Strathern, J.N. and Herskowitz, I. (1979) *Cell* 17, 371–381
28 Nasmyth, K.A. (1983) *Nature* 302, 670–676
29 Kostriken, R. *et al.* (1982) *Cell* 35, 167–174
30 Nasmyth, K.A., Seddon, A. and Ammerer, G. (1987) *Cell* 49, 549–559
31 Sternberg, P.W., Stern, M.J., Clar, I. and Herskowitz, I. (1987) *Cell* 48, 567–577
32 Moll, T. *et al.* (1991) *Cell* 66, 743–758
33 Klar, A.J.S., Hicks, J.B. and Strathern, J.N. (1982) *Cell* 28, 551–561

A.J.S. Klar is in the NCI-Frederick Cancer Research and Development Center, ABL-Basic Research Program, PO Box B, Bldg 539, Frederick, MD 21702-1201, USA.

Models of plant–pathogen coevolution

S.A. FRANK

Plant populations are often genetically polymorphic for resistance to pathogens. The effectiveness of this resistance is limited because the pathogens are, in turn, polymorphic for virulence genes that can evade plant resistance. Theoretical models and intriguing preliminary data suggest that these plant–pathogen polymorphisms are maintained by continual cycles of coevolution within populations, combined with occasional immigration of new virulence and resistance genes from distant populations.

Plant defense against pathogens often involves a single-gene resistance factor. Pathogens can escape this resistance if they carry a matching single-gene virulence factor. This gene-for-gene interaction between a host and a pathogen can occur at more than 20 separate loci, leading to genetic battles between host and pathogen populations and to extensive genetic polymorphisms for resistance and virulence[1].

The extensive polymorphisms are, at first glance, rather puzzling. Why should a plant population maintain variability for disease resistance? The resistance is presumably advantageous and should therefore spread to fixation. Likewise, why should pathogens be polymorphic for the ability to overcome host defenses? An avirulent pathogen cannot attack a host, cannot reproduce, and does not contribute genes to future generations.

To make matters more complex – and more interesting – preliminary data suggest that the frequency of each resistance gene varies widely over space: it may be absent in one place, fixed in another, and polymorphic in a third[2,3]. The pathogens vary in a similar way. These observations, and some related theories, lead to an intriguing conjecture: disease polymorphisms are the result of continual cycles of coevolution woven through time and space[3–5].

Against this idea of shifting polymorphisms, nearly all authors suggest that the distribution of disease in wild populations is a fragile equilibrium between hosts and pathogens – a delicate balance of nature. According to this view the frequencies of polymorphic genes are held nearly constant in most situations. Epidemics and fluctuating gene frequencies result from environmental disturbances caused, more often than not, by human infraction[6].

This review summarizes the complex polymorphisms in gene-for-gene systems and the theories that attempt to explain these polymorphisms.

Observations

Plant defense against pathogens includes specific major-gene resistance, which is effective against certain genetic races of pathogens, and general polygenic resistance, which is effective against a broader range of pathogens[1,7]. This review focuses on the major-gene factors. In this section I condense the vast literature on plant–pathogen genetics to a few general observations that any theory of disease polymorphism must explain.

Gene-for-gene systems

During the 1940s and 1950s, H.H. Flor studied the inheritance of specific resistance and virulence factors in flax and its fungal pathogen flax rust[8]. The interaction between host and pathogen genotypes turned out to have simple properties that Flor referred to as a 'gene-for-gene' system. In an idealized gene-for-gene system, each pair of resistance and susceptibility alleles in the host has a matching pair of virulence and avirulence alleles in the pathogen. Tables 1 and 2

TABLE 1. One-factor gene-for-gene interaction

Classification	Pathogen genotype	Host genotype		
Genotypic		*RR*	*Rr*	*rr*
	VV	–	–	+
	Vv	–	–	+
	vv	+	+	+
Phenotypic		*R–*	*rr*	
	V–	–	+	
	vv	+	+	

TABLE 2. Two-factor gene-for-gene interaction

Pathogen genotype	Host genotype			
	R1–R2–	*R1–r2r2*	*r1r1R2–*	*r1r1r2r2*
V1–V2–	–	–	–	+
V1–v2v2	–	–	+	+
v1v1V2–	–	+	–	+
v1v1v2v2	+	+	+	+

Box 1. Gene-for-gene interactions and underlying molecular mechanisms

Table 1 shows the interaction between one locus in the host and one locus in the pathogen. The host alleles *R* and *r* are for resistance and susceptibility, respectively, and the pathogen alleles *V* and *v* are for avirulence and virulence, respectively. The result of an inoculation is + for susceptible and – for resistant. Resistance (*R*) is usually dominant to susceptibility (*r*) in the host, and virulence (*v*) is usually recessive to avirulence (*V*) in the pathogen. The top part of Table 1 shows the full array of host and pathogen genotypes; the lower part uses the dominance relationships to reduce the array to distinct phenotypes. Table 2 shows a two-factor interaction with hosts and pathogens classified by distinct phenotypes. In a multifactor interaction, if a resistance allele and an avirulence allele occur at any one of the matching host and pathogen loci, then the host is resistant to the pathogen.

Resistance in gene-for-gene interactions often causes a hypersensitive response – the accumulation of defensive compounds in the tissue surrounding the point of invasion and an associated confinement of pathogen proliferation[9]. Susceptible hosts and virulent pathogens, differing by as little as a single allele from resistant interactions, do not elicit the hypersensitive response.

The specificity of the hypersensitive response, the dominance relationships within loci, and the interactions among loci suggest the following mechanism underlying the gene-for-gene phenomenon[9,10]. An avirulence pathogen allele is recognized by a resistance host allele, and the recognition induces the expression and accumulation of host defense compounds. Lack of an avirulence allele prevents recognition by the host, so avirulence corresponds to a particular molecular product and is dominant to virulence. On the host side, the resistance allele is required for recognizing an avirulence allele, so resistance corresponds to a particular molecular product and is dominant to susceptibility. Recognition and induction of the hypersensitive response occurs if the host matches the pathogen at any single locus among the many that may be involved, explaining the observed multilocus pattern summarized in Table 2. Although many authors support this model, few data are available.

Tables 1 and 2 are redrawn from Tables 4.3 and 4.4 of Ref. 1.

show this gene-for-gene interaction; Box 1 describes the Tables and a model for the underlying molecular mechanism of the specificity.

Although the relationship between specific factors is simple in a gene-for-gene system, the total interaction between a host and its pathogen is complex. Flor and others have identified 29 separate host resistance factors in flax, each with a complementary virulence factor in flax rust[8,11]. Similar gene-for-gene interactions are now known or suspected for over 25 different host–pathogen pairs[1]. These systems do not conform exactly to the idealized gene-for-gene assumptions[7], but they do have complementary major-gene interactions between hosts and pathogens.

Amount of polymorphism in nature

Only a few studies of natural populations have been published. Most of these studies, although quite limited in scope, have shown an astonishing amount of genetic polymorphism for host resistance and pathogen virulence[1]. The available data can be summarized by two tentatively drawn conclusions, each of which suggests unresolved theoretical problems and focal questions for future empirical research.

(1) Each host carries few resistance factors; each pathogen carries many virulence factors. Figure 1 shows that in groundsel, a weedy plant, each individual carries a relatively small number of resistance factors, even though many factors occur in the population and many different genotypes can be found[12]. By contrast, analyses of the fungal pathogen that attacks groundsel show that each individual pathogen carries nearly the maximum number of virulence factors detectable, although each of the 33 pathogen isolates tested carried its own unique combination of factors[2].

A more extensive analysis of a pathogen population has been conducted on the powdery mildew fungus that attacks wild barley in Israel[13]. This wild pathogen population was screened for virulence genes by scoring reactions on cultivated barley lines of known resistance genotypes. The data confirm the pattern found in the mildew population attacking groundsel: each pathogen isolate carries most or all detectable virulence factors (Fig. 2).

If, in general, each host carries few resistance factors effective against the local pathogens, and each pathogen carries many virulence factors effective against the local hosts, then the frequency of resistance per inoculation would be low. Indeed, three intensively studied wild plant populations support this conclusion[2,14,15].

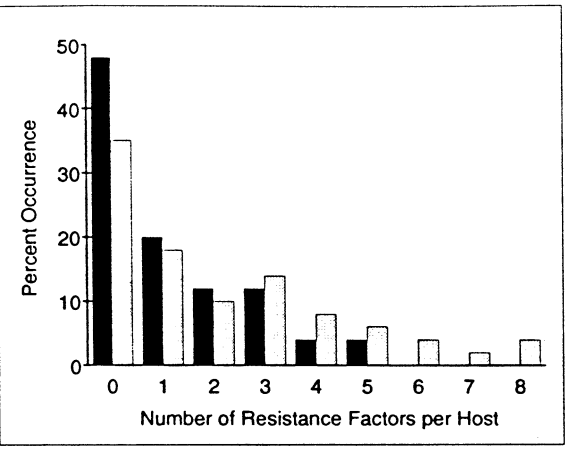

FIG **1**

Distribution of the number of resistance factors per plant. The host is groundsel (*Senecio vulgaris*), a naturally occurring weedy species, and the pathogen is a powdery mildew (*Erysiphe fischeri*). The number of factors was inferred from the 28 distinct resistance phenotypes observed in 250 plant lines tested against five pathogen strains (solid bars); the maximum number of detectable phenotypes under a gene-for-gene system with five test strains is $2^5 = 32$. Of these 250 lines, 51 were tested against the original five pathogen strains plus three additional strains (stippled bars), yielding 29 distinct resistance phenotypes. The different distributions result mainly from the different number of test strains rather than different genotypes of the plants. Limited genetic analysis supports the hypothesis that each factor is a single locus of a gene-for-gene interaction between host and pathogen[2]. The host lines were collected from 20 locations in Scotland and five other locations in the British Isles. Sixteen of the 250 plant lines were derived from primarily outcrossing populations; the rest were derived from populations that reproduce almost entirely by self-fertilization. Data from Ref. 12.

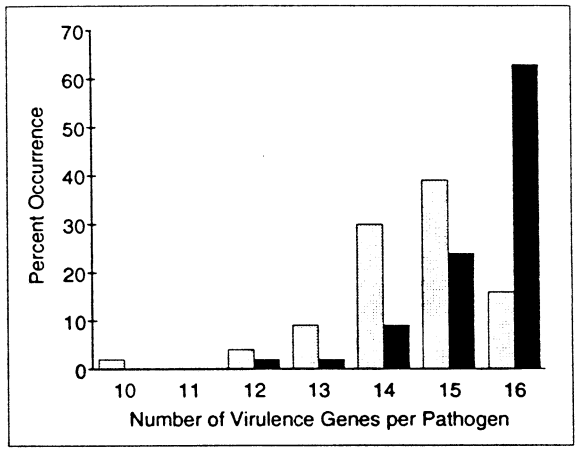

FIG **2**

Distribution of the number of virulence genes per pathogen. The powdery mildew pathogens (*Erysiphe graminis*) were isolated from populations of wild barley (*Hordeum spontaneum*). The pathogen isolates were tested against barley cultivars of known resistance genotype. Pathogens were obtained from five separate locations in Israel: among these five locations, the most skewed distribution (black bars, 63 isolates) and the least skewed distribution (stippled bars, 57 isolates) are shown. Data from Ref. 13. Two caveats: no data are available for the distribution of resistance genes in the wild barley population, and the pathogen population may be influenced by the use of resistant cultivars and migration between pathogen populations that attack cultivated and wild hosts.

(2) Genetic diversity among spatially separated populations may be as high as diversity within populations. Figure 3 demonstrates striking differences in the genotypic composition of wild flax plants and their fungal pathogens over distances of a few kilometers[16]. The frequency of resistance phenotypes of groundsel (Fig. 1) also varied considerably over space[2].

Theories

Theoreticians have analysed several processes that can influence disease polymorphisms, such as negative side-effects of resistance and virulence genes or repeated epidemics and fluctuating population sizes. Many authors have commented on the need to integrate different processes into a general theory, but little synthetic work has been accomplished. Some of the observations and concepts that must be incorporated into a general theory are summarized in Box 2. In the following sections I describe theoretical work on four ecological and genetic attributes of host–pathogen coevolution.

Polymorphism and the costs of resistance and virulence

Resistance alleles have an obvious advantage over susceptibility alleles. Why do intermediate frequencies of alternative resistance and susceptibility alleles occur? Likewise, why do intermediate frequencies of alternative virulence and avirulence alleles occur?

Vanderplank[22] argued that 'unnecessary' virulence alleles – those not needed for successful infection of the local host genotypes – reduce the fitness of a pathogen: there is a 'cost' of virulence. Pathogen polymorphism is maintained because virulence alleles are favored when challenged with specific resistance, and avirulence alleles are favored in the absence of specific resistance. Similarly, susceptibility alleles in the host may have a higher fitness than resistance alleles in the absence of attack by a matching pathogen race[23,24] – there is a cost of resistance.

Several mathematical models have analysed the role of costs in the maintenance of polymorphism[23–27]. The models derive two predictions about the equilibrium of the system that, at first, seem rather surprising: the frequency of a particular resistance allele in the host increases as the cost increases for the matching virulence allele in the pathogen, and the frequency of a particular virulence allele increases as the cost decreases for the matching resistance allele. The frequencies of virulence and resistance alleles are often independent of their own fitness costs.

Host–pathogen genetics are intertwined in this way because a costly virulence allele increases the frequency of the avirulence allele, which in turn increases the value of resistance alleles in the host [because an avirulent pathogen genotype can attack a host unless the host carries the corresponding resistance allele (see Box 1 and Table 1)]. The increased frequency of resistance alleles in the host in turn increases the value

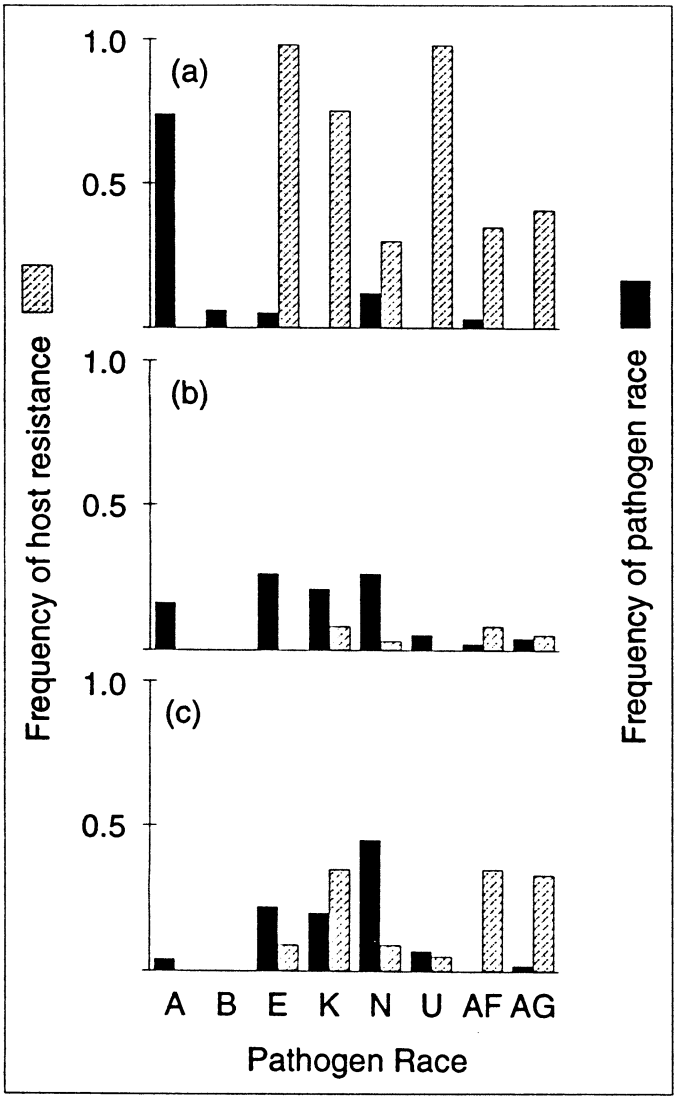

FIG 3

Spatial variation in pathogen genotypes and host resistance among wild populations of flax (*Linum marginale*) and flax rust (*Melampsora lini*). Both host and pathogen isolates were obtained from several different sites. Each panel shows the racial composition of the pathogen population and the frequency of host resistance to each pathogen race when summarized over a different geographic scale. (a) Data from a one-hectare plot for 67 host lines and 94 pathogen isolates. (b) Combined data for 40 host lines and 37 pathogen isolates from two populations 300 m and 2.7 km away from the plot summarized in (a). (c) Combined data for 108 host lines and 80 pathogen isolates from six populations 13.8–75 km away from the plot summarized in (a). Redrawn from Ref. 16.

of the virulence allele in the pathogen. A balance of these forces may occur when the difference in fitness between virulence and avirulence alleles – the cost of virulence – is exactly balanced by the frequency of susceptible and resistant host genotypes that each allele can attack. A similar argument applies to the cost of resistance (see Fig. 4).

Data on the costs of resistance and virulence are inconclusive: some studies report a measurable cost[25,28], whereas others do not[29]. Negative evidence is difficult to interpret because small costs are difficult to measure and because there are so many different ways for a cost to be expressed; any study examines only a few of the possibilities.

In addition to the cost theory, three other factors can influence polymorphism[26]. Unnecessary resistance and virulence may be maintained by: linkage with favorably selected loci; immigration from a nearby region where the resistance or virulence is advantageous; or transience, where observed polymorphisms may be the transient phase during which recently introduced advantageous mutations are steadily increasing in frequency.

One way to test the cost theory is to compare its predictions about the frequencies of resistance and virulence alleles with those observed in natural populations[26]. According to the costs model, a small cost of resistance implies a high frequency of virulence, and a small cost of virulence implies a low frequency of resistance. Studies of a few wild populations show the frequencies of resistance (Fig. 1) and virulence (Fig. 2) expected for small costs, but do not report estimates for these costs.

Epidemiology and ecology

There is a pervasive myth that diseases evolve to a relatively benign state. This peaceful outcome is characterized by reduced aggressiveness of the pathogen and a low but steady endemic frequency of disease. There is, however, little evidence to support this view[30], and mathematical models show that benign disease is a possible but not particularly commonly expected outcome of natural selection[19,27,31]. This epidemiological theory emphasizes that the simplest coevolutionary interactions may be characterized by complex cycles or chaotic fluctuations of disease and of the associated frequencies of virulence and resistance genes[32].

The epidemiological theory is more in the tradition of ecology than genetics: the theory emphasizes fluctuating population sizes caused by disease but generally ignores genetic changes within populations. By contrast, the models of host–pathogen coevolution described in the previous section typically analyse changing gene frequencies but ignore epidemiology: those models assume that population sizes of both hosts and pathogens are held constant in spite of changing amounts of disease. Apart from a few preliminary attempts[18–20,24], the theories of epidemiology and coevolutionary genetics remain separate. This separation is not caused by lack of interest but by the difficulty of incorporating so many fluctuating quantities – population sizes of host and pathogen, morbidity and mortality, and gene

Box 2. Challenges for a theory of disease polymorphism

This is a tentative list of the range of observations and processes that a comprehensive theory must ultimately encompass. Some items are based on clear patterns in the data, some on the barest hint of a pattern in a limited set of observations, and others on intrinsic processes that are likely to occur in coevolutionary interactions.

General aspects of plant resistance

(1) Resistance is based on a combination of factors: single-gene factors, polygenic traits, inducible defenses, physiological stress and environmental factors. This list focuses on single-gene factors, although general processes such as migration and epidemiology apply to any genetic system.

(2) Many separate host–pathogen genetic interactions are involved in each resistance–virulence response. In a gene-for-gene system, each interaction is probably a host recognition mechanism that is associated with a particular locus (Box 1).

Observed polymorphism in gene-for-gene systems

(3) There is often extensive polymorphism for resistance and virulence[1], although polymorphism is low in some cases[17].

(4) Each individual plant carries few resistance factors (Fig. 1); each individual pathogen carries many virulence factors (Fig. 2).

(5) Resistance to locally occurring pathogens tends to be rare[2,14,15].

(6) Polymorphism and genotypic composition vary spatially[2,16].

Theoretical aspects of polymorphism

(7) Epidemics and the resulting fluctuations in population sizes can, in theory, affect genetic polymorphism[18–20]. For example, a highly virulent pathogen race may spread rapidly, temporarily reducing the host population to a few resistant genotypes and a small size which, in turn, temporarily reduces the diversity and size of the pathogen population.

(8) There is no evidence that population sizes and genotypic compositions of hosts and pathogens are in equilibrium. A balance of nature is, *a priori*, no more likely than an endless flux of genotypic composition.

(9) If populations are in flux, then no particular conclusion will hold for every population. Populations that are usually diverse may be caught at a rare moment when diversity is low. Spatial samples of systems in flux may provide information on temporal dynamics[3,5,21].

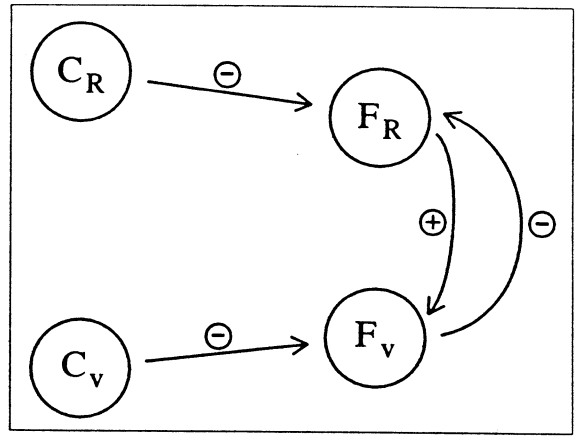

FIG 4

The forces acting on resistance and virulence frequencies in the cost model of a gene-for-gene system. The frequencies of virulence and resistance alleles are often independent of their own fitness costs because of two frequency-dependent components of the interaction. (1) An increase in the frequency of resistance (F_R) in the host causes an increase in the frequency of virulence (F_V) in the pathogen. These changes are linked because virulent genotypes can attack resistant host genotypes, whereas avirulent genotypes cannot attack resistant hosts. This interaction is shown by the '+' arrow from F_R to F_V. A positive arrow means that cause and effect change in the same direction: either both increasing or both decreasing. A negative arrow means that cause and effect change in opposite directions: one increasing and the other decreasing. (2) An increase in the frequency of virulence (F_V) in the pathogen causes a decrease in the frequency of resistance (F_R) in the host. These changes are linked because resistant host genotypes are only effective against the avirulent fraction of pathogen genotypes. The frequency of resistance declines when resistance is ineffective, because of the cost of resistance. This coupling between the frequencies of resistance and virulence is shown by the '–' arrow from F_V to F_R. The effect of an increased cost of resistance can now be traced through the diagram. An increased cost of resistance (C_R) causes (1) a decrease in the frequency of resistance (F_R) which in turn causes (2) a decrease in the frequency of virulence (F_V) which feeds back and causes (3) an increase in the frequency of resistance. Mathematical analyses show that the net effect of the opposing forces in (1) and (3) cancel, so the only overall change caused by an increased cost of resistance is a decrease in the frequency of virulence. A similar chain of causes applies when the cost of virulence (C_V) is increased. The net effect is an increase in the frequency of resistance and almost no change in the frequency of virulence.

frequencies of resistance and virulence – into a single model.

A brief example demonstrates the importance of epidemiology for genetic polymorphisms of resistance and virulence[20]. Suppose epidemics occur occasionally, causing a decline in the host population and, in turn, a crash in the population of pathogens, which no longer have hosts to attack. Recolonization by the hosts will occur by a few genotypes, and the population will develop into one that is genetically impoverished for resistance/susceptibility polymorphisms. Reinvasion by pathogens will eventually follow, but the pioneers will be only one or a few races, and the subsequent explosive proliferation of pathogens will lead to a population with very limited genetic diversity. By contrast, coexisting host and pathogen populations can slowly accumulate and maintain polymorphisms over time.

The main factor controlling epidemics appears to be the capacity of the pathogen population for rapid multiplication and transmission relative to the passage of host generations[19]. Thus, rapidly multiplying pathogens are predicted to be less diverse genetically than slowly multiplying pathogens, and their hosts are also predicted to be relatively less diverse[20]. This prediction is independent of the costs of virulence and resistance and the relative fitnesses of host and pathogen genotypes – the parameters that determine polymorphism

in purely genetic models that ignore ecological aspects of disease.

Spatial variation and migration

Recurring epidemics deplete polymorphism within the diseased area. The pathogen races that spread and the resistant plant genotypes that are spared may differ from one disease episode to the next. Suppose, for example, that a plant population is recovering from a recent epidemic, and a few resistant genotypes are increasing in abundance. The population density will build quickly, but the genetic diversity will be low. The next epidemic is likely to be caused by pathogen races virulent on the dominant host genotypes. The survivors of the second epidemic will be host genotypes that are resistant to the second wave of pathogen attack; these hosts will be different genetically from the survivors of the first epidemic. Two epidemic cycles therefore cause radical changes in the genotypic compositions of host and pathogen populations[20]. Less extreme fluctuations in gene frequencies can occur without epidemics and radical changes in population sizes.

Consider now variation over space rather than time. Two patches of plants that rarely exchange migrants are likely to pass through genetic shifts in an independent, uncoupled way. Thus, although genetic diversity may be low within each patch, diversity may be high among patches[3,5].

It is difficult to obtain long temporal sequences of data to test the idea that the distribution of genotypes is changing continually within each patch. Data on spatial variation may, however, provide some insight into temporal dynamics[5,33,34]. If the dynamics of spatially separated patches are uncoupled, then spatial variation observed at one point in time provides a snapshot of the temporal variation that is likely to occur within a patch over time. The main difficulty with this method is that spatial variation can also be maintained by environmental variation. For example, plants in wetter patches may be more susceptible to disease than those in drier patches, and the temporal dynamics of these two patches may differ considerably.

The temporal cycles described here may depend on the occasional introduction into a patch of locally absent virulence and resistance alleles. Spatial variation suggests that migration is a likely mechanism for the influx of genetic novelty. The combined picture is one of spatial variation, introduction of genetic variants by migration, local spread of new genotypes at the expense of dominant genotypes, and then a newly arrived genetic variant to begin the cycle again[5,34]. The polymorphisms are locally transient but are maintained globally. The costs of resistance and virulence still play a key role because cost-free resistance and virulence are likely to spread to fixation globally. Thus cost and transience models of polymorphism are likely to be complementary.

Multiple loci and breeding system

Gene-for-gene systems are characterized by multilocus interactions, whereas most coevolutionary models analyse systems with only one or two loci. A few models have analysed coevolutionary genetics when the amount of genetic diversity is not limited by assumption[20,34–36]. In these models, an increasing number of loci or alleles per locus enhances the transient nature of fluctuating gene frequencies because the host–pathogen chase occurs over a much larger set of possible genotypes.

The breeding system imposes two contrasting pressures on the dynamics of disease genotypes. Inbred and asexual systems maintain higher levels of genic (per locus) diversity than outbred sexual systems because, in asexual systems, only the genotype as a whole can respond to long-term selection, and selection is much weaker on individual loci[1]. Put another way, unnecessary and costly resistance and virulence alleles are lost much more quickly from outcrossed than inbred populations. By contrast, outcrossed systems support higher levels of genotypic diversity than inbred systems for a given level of genic diversity because recombination causes greater evenness in the distribution of genotypes.

Few comparative data are available on genotypic diversity and breeding system. A wild, inbred species of *Glycine* (soybean) apparently maintains much higher levels of genic diversity for resistance to soybean rust than a related, outcrossed species of soybean[17]. Comparison among cereal rust populations found on crops showed that sexual populations had a more even distribution of genotypes than asexual populations[37].

Models and tests

Burdon and Jarosz have conducted field studies to test the dynamic model of ever-changing genotypic composition within patches, spatial variation among patches, and the importance of occasional immigrant genotypes[15,16]. Their approach included sampling intensively within selected patches and sampling widely at different spatial scales. This type of spatial analysis is essential if the basic model is correct because any single population at a single time represents only a small part of the global polymorphism and dynamics[3,5,21,34].

Some models suggest that the growth rate of the pathogen population is the key variable controlling epidemiology[19] and patterns of genetic polymorphism in both hosts and pathogens[20]. These models predict that slowly growing pathogens will typically have higher genotypic diversity within patches and less spatial variation than those with greater potential for rapid growth[20]. Although this prediction, which depends heavily on 'all else being equal', may be difficult to evaluate, these models do focus attention on contrasting pathogen demography rather than on host demography or on the costs of resistance and virulence. Such models are perhaps best viewed as tentative directions for future research rather than as firm predictions.

Many interesting types of disease will not follow the simple epidemiology and genetics of the preliminary models currently available. For example, the dioecious, perennial herb *Silene alba* is attacked by the anther-smut fungus *Ustilago violacea*, which causes both male and female plants to produce anthers that carry fungal spores instead of pollen[38]. The spores are transmitted mainly by insect pollinators; the system thus has the epidemiological characteristics of venereal

diseases. Male plants with relatively many flowers have a greater incidence of disease than those plants with fewer flowers, perhaps because larger floral displays attract more pollinators and thus increase the likelihood of infection[39,40]. If flower number has a genetic component, then there is a positive genetic correlation between potential fecundity and loss of fitness by disease: in effect, genes for low fecundity enhance resistance. This example shows that costs of resistance can be quite complex in natural populations[38], and highlights the fact that complementary major-gene systems are only one of many possible genetic interactions[41].

Any study designed to test models of disease dynamics requires wide sampling of genotypes. This is, at present, very difficult because genotype identification is a laborious process based on comparing each isolate against a series of test strains. Molecular probes are now being developed that can be used to screen samples much more efficiently[42]. These molecular methods will provide a new window onto the diversity of natural populations.

Acknowledgements

I thank J.J. Burdon, A.M. Jarosz and R. Bush for helpful comments on the manuscript. My research is supported by NSF grant BSR-9057331 and NIH grants GM42403 and BRSG-S07-RR07008.

References

1 Burdon, J.J. (1987) *Diseases and Plant Population Biology*, Cambridge University Press
2 Clarke, D.D., Campbell, F.S. and Bevan, J.R. (1990) in *Pests, Pathogens and Plant Communities* (Burdon, J.J. and Leather, S.R., eds), pp. 189–201, Blackwell Scientific
3 Burdon, J.J., Brown, A.H.D. and Jarosz, A.M. (1990) in *Pests, Pathogens and Plant Communities* (Burdon, J.J. and Leather, S.R., eds), pp. 233–247, Blackwell Scientific
4 Hamilton, W.D. (1982) in *Population Biology of Infectious Diseases* (Anderson, R.M. and May, R.M., eds), pp. 269–296, Springer-Verlag
5 Frank, S.A. (1991) *Evolutionary Ecology* 5, 193–217
6 Harlan, J.R. (1976) *Annu. Rev. Phytopathol.* 14, 31–51
7 Christ, B.J., Person, C.O. and Pope, D.D. (1987) in *Populations of Plant Pathogens* (Wolfe, M.S. and Caten, C.E., eds), pp. 75–88, Blackwell Scientific
8 Flor, H.H. (1971) *Annu. Rev. Phytopathol.* 9, 275–296
9 Gabriel, D.W. and Rolfe, B.G. (1990) *Annu. Rev. Phytopathol.* 28, 365–391
10 Callow, J.A. (1987) in *Genetics and Plant Pathogenesis* (Day, P.R. and Jellis, G.J., eds), pp. 283–295, Blackwell Scientific
11 Lawrence, G.J., Mayo, G.M.E. and Shepherd, K.W. (1981) *Phytopathology* 71, 12–19
12 Harry, I.B. and Clarke, D.D. (1986) *New Phytol.* 103, 167–175
13 Dinoor, A. and Eshed, N. (1987) in *Populations of Plant Pathogens* (Wolfe, M.S. and Caten, C.E., eds), pp. 75–88, Blackwell Scientific
14 Parker, M.A. (1985) *Evolution* 39, 713–723
15 Burdon, J.J. and Jarosz, A.M. (1991) *Evolution* 45, 205–217
16 Jarosz, A.M. and Burdon, J.J. (1991) *Evolution* 45, 1618–1627
17 Jarosz, A.M. and Burdon, J.J. (1990) *Heredity* 64, 347–353
18 Gillespie, J.H. (1975) *Ecology* 56, 493–495
19 May, R.M. and Anderson, R.M. (1983) *Proc. R. Soc. London Ser. B* 219, 281–313
20 Frank, S.A. (1991) *Heredity* 67, 73–83
21 Thompson, J.N. (1990) in *Pests, Pathogens and Plant Communities* (Burdon, J.J. and Leather, S.R., eds), pp. 249–271, Blackwell Scientific
22 Vanderplank, J.E. (1982) *Host–Pathogen Interactions in Plant Disease*, Academic Press
23 Mode, C.J. (1958) *Evolution* 12, 158–165
24 Mode, C.J. (1961) *Biometrics* 17, 386–404
25 Leonard, K.J. (1977) *Ann. NY Acad. Sci.* 287, 207–222
26 Leonard, K.J. and Czochor, R.J. (1980) *Annu. Rev. Phytopathol.* 18, 237–258
27 Levin, S.A. (1983) in *Coevolution* (Nitecki, M.H., ed.), pp. 21–65, University of Chicago Press
28 Webster, R.K., Saghai-Moroof, M.A. and Allard, R.W. (1986) *Phytopathology* 76, 661–668
29 Parker, M.A. (1990) *Evolution* 44, 1872–1875
30 Ewald, P.W. (1983) *Annu. Rev. Ecol. Syst.* 14, 465–485
31 Levin, S.A. and Pimental, D. (1981) *Am. Nat.* 117, 308–315
32 May, R.M. (1990) in *Pests, Pathogens and Plant Communities* (Burdon, J.J. and Leather, S.R., eds), pp. 309–325, Blackwell Scientific
33 Burdon, J.J., Jarosz, A.M. and Kirby, G.C. (1989) *Annu. Rev. Ecol. Syst.* 20, 119–136
34 Frank, S.A. (1989) *Am. Nat.* 133, 345–376
35 Seger, J. (1988) *Phil. Trans. R. Soc. London Ser. B* 319, 541–555
36 Hamilton, W.D., Axelrod, R. and Tanese, R. (1990) *Proc. Natl Acad. Sci. USA* 87, 3566–3573
37 Groth, J.V. and Roelfs, A.P. (1982) *Phytopathology* 72, 1503–1507
38 Alexander, H.M. (1990) in *Pests, Pathogens and Plant Communities* (Burdon, J.J. and Leather, S.R., eds), pp. 31–45, Blackwell Scientific
39 Alexander, H.M. and Antonovics, J. (1988) *J. Ecol.* 76, 91–104
40 Alexander, H.M. (1989) *Evolution* 43, 835–847
41 Barrett, J.A. (1985) in *Ecology and Genetics of Host–Parasite Interactions* (Rollinson, D. and Anderson, R.M., eds), pp. 215–225, Academic Press
42 Hamer, J.E. (1991) *Science* 252, 632–633

S.A. Frank is in the Department of Ecology and Evolutionary Biology, University of California, Irvine, CA 92717, USA.

Any Technical Tips?

Technical Tips is a place where readers can exchange information about useful lab techniques. Technical Tips should be either new methods, or significant new modifications or applications of existing techniques. If you have developed a handy new method, why not share it with other *TIG* readers? Your article should be as brief as possible, but should give enough information to enable others to repeat the method. If any part of the method involves published procedures, you can refer to the appropriate paper(s) rather than repeating those details. All Technical Tips are peer-reviewed.

Please send three copies of your double-spaced typescript, plus three copies of any figures (including at least one set of originals) to:

Dr Alison Stewart, *Trends in Genetics*, Elsevier Trends Journals, 68 Hills Road, Cambridge, UK CB2 1LA.