SUMMARY

For the past decade, the attention given to genetic variation of pathogens by plant pathologists has increased dramatically, while interest in epidemiology appears to have declined. This increase in interest in genetic variation is clearly evident in the profusion of recent publications, and by conferences such as EFPP 2000, whose theme is biodiversity. Valuable advances in our understanding of plant diseases and their management can potentially be made by exploiting genetic variation. However, the bold – and sometimes simplistic – claims for the potential of these contributions to disease management have been too often unrealized, and therefore need to be evaluated more critically. The rapid increase in the popularity of this area has been made possible, in part, by the easy accessibility of genetic markers, as a result in advances in technology of molecular biology, and the perception that it is fashionable to use these techniques. Unfortunately, these developments have led to a method-oriented approach to research. Significant advancement in this field requires taking a problem-oriented approach, where the most appropriate methods are used to address the questions. Furthermore, we need a synthesis of population genetics and epidemiology (two disciplines that have developed separately), resulting in a population biology perspective of plant pathology. No simple formula can be applied to studying the population biology of plant pathogens that can effectively contribute to disease management. Instead, every pathosystem must be considered on a case-by-case basis, in both genetic and ecological contexts, with the questions unique to each system determining what research should be done. In this paper, I discuss a few selected examples in which population genetics and epidemiology have been integrated to provide greater insights into pathogen population biology and disease management.

Key words: population biology, population genetics, epidemiology, molecular markers, genetic variation.

INTRODUCTION

The increasing trend in the interest in genetic variation is evident by the fact that the theme for 5th Congress of the European Foundation for Plant Pathology is biodiversity. In choosing this theme, the conference organizers explicitly recognized that variation in virulence, fitness and fungicide resistance are among the major constraints to plant disease management. The increasing trend to study genetic variation in plant pathogens is also reflected by the numbers of papers published on genetic variation in recent years. For example, more than twice as many papers dealing with genetic variation of pathogens were published in Phytopathology in 1999 than in 1989. Interestingly, the number of papers dealing with epidemiology has decreased concomitantly. There were approximately three times as many epidemiology papers as genetic variation papers in Phytopathology in 1989, but roughly equal numbers in 1999. This crude assessment is based on very broad interpretations of genetic variation and epidemiology, nonetheless, I believe that the shift in emphasis of published papers over the last decade in Phytopathology is indicative of the general trend in plant pathology.

At this time, it would be worthwhile to reflect on why genetic variation of plant pathogens has become so popular to study, and what value we can derive from these studies, especially with respect to plant disease management. In a previous paper (Milgroom, 1997), I summarized the applications of genetic variation, especially with regard to improving our understanding of diagnosis, taxonomy, systematics and population genetics of plant pathogens. Diagnosis, taxonomy and systematics are distinct from population genetics, however, in that they are not asking questions about evolutionary processes in populations [although some studies successfully cross the interface between systematics and population genetics (e.g., Carbone and Kohn, 2001)].

The challenge that I address in this paper is how
population genetics can be integrated with epidemiology to contribute to disease management. One often reads claims, especially in funding applications, that knowledge of population genetics will contribute to better disease management. While it is clear that improved diagnosis or more accurate and rapid identification of pathogens can benefit disease management, the connections between population genetics and management are often indirect and much less clear. My colleague and I argued previously that there are no generalizations that can be made to apply population genetics to disease management; instead, each situation needs to be evaluated on a case-by-case basis (Milgroom and Fry, 1997). Compounding the problem are a number of misconceptions that have led to myths or half-truths about population genetics in plant pathology (Milgroom and Fry, 1997).

My goal in this paper is not to dissect the misconceptions about population genetics further, but to express one perspective for integrating population genetics with epidemiology. Population biology can be viewed as the synthesis of epidemiology and population genetics. Studies combining these two fields have great potential for addressing both basic and applied questions in plant pathology, and yet this potential is not being realized in many cases. The aim of this paper is to outline some of the obstacles to reaching this goal, and to illustrate a few examples in which this synthesis has been successful. There are three parts to this paper. First, I discuss why there are so many studies of genetic variation, and how we need to take a problem-oriented approach to research. Second, I compare and contrast concepts of population genetics and epidemiology, and suggest how they might be integrated. Finally, I highlight a few recent studies in which population genetics concepts have been integrated with epidemiological studies to address questions in population biology of plant pathogens. The take-home message from this paper is that a synthesis of population genetics and epidemiology would increase the benefits of studying genetic variation in populations of plant pathogens. This can be done by broadening our views beyond the currently narrow – and all too separate – perspectives of population genetics and epidemiology, and taking a general biological perspective.

PROBLEM-ORIENTED RESEARCH

I believe that many studies of genetic variation of plant pathogens are done for the wrong reasons. There are two contributing factors: first, genetic variation is studied because the tools are now readily accessible; and second, it has become fashionable to use the tools of molecular biology, even if only to describe genetic variation in a sample of pathogens. These are the wrong reasons to study genetic variation because they are motivated more by methods than by a desire to solve problems.

Technology is an essential component of any scientific endeavor. New technologies let scientists think about addressing questions that before were either technically intractable or logistically unattainable because of the expense and effort required. New technologies, therefore, raise the hopes that doors can be opened to research on exciting new questions. These hopes give rise to higher expectations that scientists can advance knowledge rapidly, which, in turn, leads to research funding and research activities applying the new technology. What are the results? Sometimes there is a pay-off, sometimes not. For example, look at plant disease epidemiology in the 1970s and early 1980s. The rapid advances in computer technology gave rise to the hopes that computer modeling could be applied to systems analysis and improved disease management. For a while, there was great activity in developing complex disease and crop models. Although there were some successes in applying complex models to disease management, the majority of them languished unused. The same pattern is being repeated for studies of genetic variation of plant pathogen populations (not to mention other areas of science). Technological advances in the late 1980s and 1990s led to the development of easily accessible genetic markers (e.g., RFLPs, RAPDs, AFLPs, microsatellites, etc.). These methods became popular and generated a lot of hope that by studying genetic variation we could improve disease management. Numerous studies have been conducted, but few contribute directly to disease management (Milgroom and Fry, 1997).

A method-oriented phase, such as that experienced with genetic markers and describing variation, may be a natural consequence of technological advances, and it is possible to occur in many fields. However, when technology – along with the perception that it is fashionable – sets the research agenda, it is a case of the tail wagging the dog. In an eloquent and inspiring essay on scientific method, Platt (1964) distinguished between problem-oriented and method-oriented research, arguing that science should be directed towards answering questions not just applying techniques. I would argue that the majority of studies today of genetic variation of plant pathogens have been undertaken with methods taking primacy over questions. It is time now to reorient our efforts towards solving problems.

Gowin (1981) proposed a heuristic tool for illustrating the interplay of questions and methods (or technology) in problem solving or for production of
knowledge (Fig. 1). The question (or hypothesis) is symbolically placed at the top-center because research is ideally organized to answer a question. The sides of the \( V \) represent conceptual and methodological aspects of research. The experiment (or ‘objects/events’ in Gowin’s terminology) is placed at the union of both sides of the \( V \), representing the synthesis of the conceptual and methodological aspects. Imagine this diagram (Fig. 1) if we were conducting method-oriented research; without a question tying the components together the methods and experiments would be weakly supported by concepts, if at all. This latter case is not intellectually satisfying or efficient for conducting research. In contrast, all of these components interact in an integrated way in problem-oriented research, with the question being central to everything. This is the ideal for which we must strive in our studies of genetic variation of plant pathogens: problem-oriented research, with questions, not methods, driving research programs.

**POPULATION BIOLOGY: THE SYNTHESIS OF POPULATION GENETICS AND EPIDEMIOLOGY**

Over the past decade or so, epidemiology and population genetics have diverged and are now mostly independent subdisciplines within plant pathology. However, it has not always been this way. Genetic variation has long been recognized as a major constraint in disease management, which suggests that epidemiology and population genetics should be naturally allied. Some of the best examples of the integration of epidemiology and population genetics date back a long time. For example, race (or pathotype) variation has been discussed at length for almost a century and was featured in Vanderplank’s (1963) landmark book on epidemiology. Two books from the late 1980s (just before neutral genetic markers became easily available and popular) also attempted a synthesis of epidemiology and population genetics (Wolfe and Caten, 1987; Leonard and Fry, 1989). More recently, some of the best examples of this synthesis are in studies of resistance gene deployment; (e.g., studies of barley powdery mildew in Europe e.g. Brown and Wolfe, 1990; Wolfe and McDermott, 1994).

However, over the last decade, many studies reflect a distinct separation of these two fields. For example, the study of pathotype variation (let alone genetic variation for fungicide resistance or neutral genetic markers) seems to have diverged completely from epidemiology (sensu stricto). In their epidemiology textbook, Campbell and Madden (1990) do not discuss host plant resistance, pathotype variation or anything else about genetic variation. A more recent book on epidemiology (Jones, 1998) is more inclusive, devoting two of the 21 chapters entirely to topics related to genetic variation (Brown, 1998; Finckh and Wolfe, 1998). The schism that has developed has been detrimental to the study of plant pathogen populations and has worsened since neutral genetic markers have become so easily available. Researchers studying genetic variation or population genetics are just as guilty as the epidemiologists. Little effort has been made to apply their genetic findings to epidemiological questions, except in superficial ways. The narrow interpretation of genetic data, often devoid of biology or pathology, shows the myopia of some population geneticists also.

We need a genuine synthesis of population genetics and epidemiology. These two fields have common historical roots, and still overlap considerably in concepts. Table 1 lists some of the major concepts of plant

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**Table 1. Major concepts in epidemiology and population genetics in plant pathology.**

<table>
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<tr>
<th>Epidemiology</th>
<th>Population genetics</th>
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<tr>
<td>Source of inoculum</td>
<td>population structure</td>
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<tr>
<td>Dispersal</td>
<td>gene flow</td>
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<tr>
<td>Types of inoculum</td>
<td>recombination</td>
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<td>Host specialization</td>
<td>mating systems</td>
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<td>Gene deployment</td>
<td>selection</td>
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<td>Fungicide resistance</td>
<td>fitness</td>
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<td>Competition</td>
<td>genetic drift</td>
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<td>Disease progress</td>
<td>mutation</td>
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<td>Forecasting</td>
<td>coevolution</td>
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<td>Crop losses</td>
<td>phylogenetics</td>
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disease epidemiology and population genetics studied in plant pathogens; this list is not exhaustive but illustrates a fairly broad picture of the two fields. There are numerous commonalities between the two lists. For example (to name just a few), dispersal and gene flow are closely related; types of inoculum (e.g., sexual or asexual) strongly affects population structure; resistance gene deployment and fungicide resistance management are based as much in the concept of natural selection as in disease management. Granted, some of the concepts are unique to each list, but the overwhelming impression is that the two lists are highly interconnected. With such strong relationships between these two fields, isn’t it logical that they should be integrated and viewed as one synthetic discipline?

Fig. 2 shows one conception of the synthesis of epidemiology and population genetics in plant pathology. These two fields can be brought together within a framework that integrates concepts of evolution, epidemiology (ecology), and genetics. The intersection of these three fields defines population biology. A population biology perspective, synthesizing concepts and methodologies from the three individual fields is likely to result in a fruitful synergy, and a greater understanding of population processes that can potentially be exploited for better disease management.

**POPULATION BIOLOGY: EXAMPLES AT THE INTERFACE OF EPIDEMIOLOGY AND POPULATION GENETICS**

To illustrate how concepts from epidemiology and population genetics can be synthesized in a population biology perspective, I present several recent examples from the literature. I classify these examples by the epidemiological questions being addressed: (i) sources of primary inoculum, (ii) dispersal of secondary inoculum, and (iii) host specialization. The first study exemplifies the use of genetic variation to track specific genotypes; the other two are based more on concepts in population genetics and population biology. In all of them the goal is to understand the basic biology of a system in order to develop sound management programs.

**SOURCES OF PRIMARY INOCULUM.** Determining sources of primary inoculum is a question that can be addressed successfully in many systems by combining epidemiology and the use of genetic markers. Zwankhuizen et al. (1998) searched for the sources of primary inoculum of *Phytophthora infestans* that caused late blight foci and epidemics in potato fields in a region in The Netherlands. They combined a traditional epidemiological approach of studying the locations of disease foci and disease gradients in relation to potential sources (cull piles, organic farms or volunteers), with a population genetic approach of studying the spatial distribution of pathogen genotypes. By asking which pathogen genotypes (DNA fingerprints) were found in commercial fields and comparing them to genotypes found in potential inoculum sources these researchers were able to infer possible inoculum sources with a high degree of confidence. Equally important, they could rule out other sources of inoculum because the genotypes did not match. The combination of traditional epidemiological methods with identification of pathogen genotypes allowed them to make more definitive inferences about the sources of inoculum than could be made by each method alone.

This example highlights a relatively simple application of genetic markers to track specific genotypes in time and/or space. This type of study does not depend on an understanding of any evolutionary or genetic concepts beyond those needed to develop markers for distinguishing among different genotypes. Nonetheless, this simple use of genetic markers can greatly enhance epidemiological studies.

**DISPERAL OF SECONDARY INOCULUM.** Two grapevine diseases, Esca and Eutypa dieback, have been the subjects of recent studies of the dispersal of secondary in-
oculum within vineyards using a combination of epidemiological and genetic methods (Cortesi et al., 2000; Cortesi and Milgroom, 2001). First, spatial patterns of disease (symptomatic vines) were analyzed using a traditional epidemiological approach. No significant aggregation of disease was observed, although aggregations would be expected if dispersal of the pathogen occurred by mycelium during pruning or root-to-root contact. Second, studying the reproductive biology of the two pathogens, these researchers examined vines for fruiting bodies; basidiocarps of Fomitiporia punctata (Cortesi et al., 2000) and perithecia of Eutypa lata (Cortesi and Milgroom, 2001) were found associated with diseased grapevines. Third, genotypic diversity of the pathogens isolated from vines was studied. For both pathogens, genotypic diversity was very high, and each vine was colonized by different genotypes. This latter result also rejects the hypothesis that inoculum is spread clonally via pruning or roots, otherwise the same genotypes would occur on multiple vines. Furthermore, ascospore progeny from every individual perithecium of E. lata segregated for different genotypes, indicating that this fungus outcrosses under field conditions (Cortesi and Milgroom, 2001) (analogous studies could not be done with F. punctata because it is not possible to germinate basidiospores of this species in the lab). Looking at results from spatial patterns and genotypic diversity, together with finding sexual fruiting bodies, these authors rejected the hypothesis that asexual (clonal) secondary inoculum contributed significantly to these epidemics for either disease.

It is interesting to note that in both of these studies (Cortesi et al., 2000; Cortesi and Milgroom, 2001), genotypic variation in vegetative (or somatic) incompatibility was great enough that these relatively simple genetic markers were sufficient for answering the questions being addressed. Although these markers may be perceived by some as being old-fashioned (or low-tech), data could be obtained easily and cheaply. This is an example where the methods were determined by the questions, and not vice versa.

HOST SPECIALIZATION. Although there are several examples of studies of host ranges and specialization, I highlight one in which both epidemiological and genetic approaches were taken. Peever et al. (2000) sampled isolates of Alternaria alternata from various citrus cultivars. By using population genetic analyses of RAPD markers, they showed that Alternaria was significantly genetically differentiated among different host cultivars. This result suggests that there is restricted gene flow of pathogens among cultivars despite their close geographic proximity. Another way to interpret these results is that some degree of host specialization exists. In contrast, these researchers could not detect any evidence of host specialization with pathogenicity tests. If they had relied exclusively on traditional methods such as pathogenicity testing, their conclusions would have been completely different. Experimental assays may not be sensitive enough to detect host specialization, or they may not be indicative of fitness differences on the different hosts under field conditions (Peever et al., 2000). In these cases, population genetic approaches can augment epidemiological studies on host specialization, sometimes providing new insights and different interpretations.

ADDITIONAL EXAMPLES. The examples cited above are a small sample of epidemiological studies that combine concepts and methods from population genetics to give a broader population biology perspective on plant pathological problems. This is not meant to review the state of the field; a number of other examples could have illustrated these same points as well. Nonetheless, I want to conclude this section by briefly mentioning a few other recent efforts to combine epidemiology and population genetics. For example, the recent migrations of P. infestans has necessitated a reevaluation of the current management practices (Fry and Goodwin, 1997), including forecasting systems. New decision rules may be needed to account for the fact that current genotypes of P. infestans are generally more aggressive than those previously found (W.E. Fry, personal communication). Another example is the modeling of biological control of chestnut blight with transmissible hypovirulence (Liu et al., 2000). Successful biological (with both conventional and genetically-modified hypovirulent strains) is inextricably controlled by genetic variation for vegetative incompatibility in the target population. Therefore, knowledge of the population biology of the host is essential for implementing biological control in this system. Finally, Escriu et al. (2000) studied changes in the virulence of tomato necrosis caused by Cucumber mosaic virus in Spain. They showed that satellite RNAs responsible for high virulence behaved as predicted by evolutionary theory on the trade-off between virulence and transmission rates. The implications of this study for epidemiology are profound if virulence could be managed by manipulating transmission rates. This is a potentially exciting new way to look at the links between evolution and epidemiology. Each of these examples integrates epidemiology, population genetics and evolution in some way, instead of taking a restricted approach within a single discipline.
CONCLUSIONS

There are two conclusions to be drawn from this paper. First, the greatest advances in studying genetic variation within populations of plant pathogens will come from problem-oriented research, not method-oriented research. We have gone through a method-oriented phase, but greater advances can be achieved by focusing now on specific questions, in a problem-solving frame of mind. The second conclusion is that problems can be solved best if we take a broad population biology perspective that integrates classical epidemiology and population genetics. The examples discussed above will hopefully serve to illustrate the potential of combining the two fields.

In preparing this paper, I had the impression that history is repeating itself. Population genetics in plant pathology has undergone a method-oriented phase, just as epidemiology did a decade or more earlier (Madden and Teng, 1989). The parallels in the history of epidemiology and population genetics go even further. Zadoks (1990) called for viewing epidemiology as a holistic science, with a goal towards problem solving. We would benefit from the same advice in taking a more holistic approach to population genetics. The synthesis of population genetics and epidemiology would be a good step towards a more holistic view in population biology, and it would be one that might provide greater potential for problem solving.

REFERENCES


