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Trends in theoretical plant epidemiology

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Abstract

We review trends and advances in three specific areas of theoretical plant epidemiology: models of temporal and spatial dynamics of disease, the synergism of epidemiology and population genetics, and progress in statistical epidemiology. Recent analytical modelling of disease dynamics has focused on SIR (susceptible–infected–removed) models modified to include spatial structure, stochasticity, and multiple management-related parameters. Such models are now applied routinely to derive threshold criteria for pathogen invasion or persistence based on pathogen demographics (e.g., Allee effect or fitness of fungicide-resistant strains) and/or host spatial structure (e.g., host density or patch size and arrangement). Traditionally focused on the field level, the scale of analytical models has broadened to range from individual plants to landscapes and continents; however, epidemiological models for interactions at the cellular level, e.g., during the process of virus infection, are still rare. There is considerable interest in the concept of scaling, i.e., to what degree and how data and models from one scale can be transferred to another (smaller or larger) scale. Despite assertions to the contrary, the linkages between epidemiology and population genetics are alive and well as exemplified by recent efforts to integrate epidemiological parameters into population genetics models (and *vice versa*) and by numerous integrated studies with an applied focus (e.g., to quantify sources and types of primary and secondary inoculum). Statistical plant epidemiology continues to rely heavily on the medical and ecological fields for inspiration and conceptual advances, as illustrated by the recent surge in papers utilizing ROC (receiver operating characteristic), Bayesian, or survival analysis. Among these, Bayesian analysis should prove especially fruitful given the reliance on uncertain and subjective information for practical disease management. However, apart from merely adopting statistical tools from other disciplines, plant epidemiologists should be more proactive in exploring potential applications of their concepts and procedures in rapidly expanding disciplines such as statistical genetics or bioinformatics. Although providing the scientific basis for disease management will always be the *raison d'être* for plant epidemiology, a broader perspective will help the discipline to remain relevant as more resources are being devoted to genomic and ecosystem-level science.

Introduction

It is perhaps somewhat atypical that this commentary on theoretical plant epidemiology is authored by a group of investigators who consider themselves experimentalists rather than theoreticians. However, our role as dispassionate observers allows us to take a bird's-eye view of recent developments in the area and assess their impact on the science and practice of plant pathology without being influenced by predetermined notions.

The Encyclopaedia Britannica defines a scientific theory as a 'systematic ideational structure of

broad scope, conceived by the human imagination, that encompasses a family of empirical (experiential) laws regarding regularities existing in objects and events, both observed and posited' (Anon., 2005). In practice, this 'systematic ideational structure' is usually formalized as a model, either conceptual or mathematical. Both forms of models have been influential in plant epidemiology (Jeger, 2000; Zadoks, 2001). Although theory can be developed without mathematical models, the two concepts are often used synonymously in the epidemiological literature.

One of the most commonly voiced criticisms surrounding the use of theory and mathematical models in the broader ecological literature has been the lack of interaction between modellers and experimentalists during model development, testing, and validation (Caswell, 1988; Hall, 1988b). Theoretical epidemiology has largely escaped this controversy, presumably because some of the most influential epidemiological modellers in plant pathology (or at least some members of their laboratories) are superb experimentalists in their own right. The resulting synergism between models and experimental data in advancing theory is typified in the work of JM Jeger and CA Gilligan, among others (e.g., Jeger, 2000; Gilligan, 2002). It is important to note that testing and validation of models need not occur at the same time for a model to be useful. For instance, the theory of dispersive epidemic waves (focal epidemics that spread with increasing frontal velocity) was formalized by Ferrandino (1993) based on physical principles of spore transport, with limited empirical support. Although additional observational (Scherm, 1996) and experimental (Frantzen and van den Bosch, 2000) backing for this theory was presented in the interim, it took more than a decade after publication of Ferrandino's paper until large-scale disease gradient experiments by Cowger et al. (2005) demonstrated convincingly that epidemics of wheat stripe rust spread consistently with increasing frontal velocity.

In what follows we consider current trends in three specific areas of theoretical plant epidemiology: models of temporal and spatial dynamics of disease, the synergism of epidemiology and population genetics, and advances in statistical epidemiology. The purpose here is not to provide a comprehensive review, but rather to give selected examples illustrating these trends. Inevitably, these examples reflect our personal views of what is interesting and important in theoretical epidemiology. We limit our discussion largely to work published since the last International Workshop on Plant Disease Epidemiology in Ouro Preto, Brazil, in 2001. Selected aspects of theoretical work carried out during the 1990s have been synthesized recently (Jeger, 2000; Gilligan, 2002).

Models of temporal and spatial disease dynamics

The development of mathematical models to describe disease dynamics has been and continues to be the mainstay of theoretical epidemiology. Recent research in the area has focused on incorporating spatial structure, elucidating the consequences of stochasticity and spatial scale, identifying threshold criteria for pathogen or strain establishment, and predicting the effects of selected management strategies on disease dynamics. A detailed account of the use of analytical models to address these objectives has been given by Gilligan (2002). Based on his review and the subsequently published literature, a number of trends may be inferred.

SIR models have entered the mainstream and become more versatile

In its most basic form, an SIR model consists of a set of linked differential equations describing the dynamics of susceptible (healthy), infected, and removed (post-infectious) host tissue; commonly, the infected tissue is divided into exposed (latently infected) and infectious compartments, leading to an SEIR model (Madden, 2005). This type of analytical model, first formalized by Kermack and McKendrick (1927) for human diseases, was popularized by Jeger (1982) for use in plant epidemiology. Almost 20 years later, Segarra et al. (2001) formally derived the SEIR model for plant epidemics from the more general Kermack–McKendrick model based on first principles. In addition, Segarra et al. (2001) provided a detailed comparison of the behaviour of the latter two models with that of Van der Plank's widely used differential-delay equation (Van der Plank, 1963).

Recent work has added considerable complexity to SIR-type models (Gilligan, 2002), including demographic and environmental stochasticity (Park et al., 2003; Gibson et al., 2004; Otten et al., 2004a), seasonal disturbance and multi-year

disease dynamics (Madden and van den Bosch, 2002), dynamics of host growth and susceptibility (Gibson et al., 2004), virus vectoring mode and vector performance (Madden et al., 2000; Holt and Colvin, 2001), interactions with biocontrol agents (Gibson et al., 2004), spatial structure and metapopulation dynamics (Park et al., 2001, 2003), and the presence of pesticide-resistant subpopulations (Hall et al., 2004), among others. The inclusion of stochasticity and spatial structure is especially significant as models featuring these attributes can produce qualitatively very different predictions regarding pathogen establishment and persistence than their deterministic mean-field counterparts. Most importantly, invasion thresholds in stochastic models are higher and the pathogen or strain may be unable to persist following successful invasion due to chance events, especially at low population densities (Gilligan, 2002).

The increased complexity of contemporary SIR models adds realism and allows their application to a wider range of problems. Indeed, models are now routinely formulated to accommodate parameters useful in exploring specific management strategies (Jeger, 2000; Gilligan, 2002; Stacey et al., 2004). For instance, a linked *African cassava mosaic virus*–whitefly vector model (Jeger et al., 2004) includes four management-related parameters, namely the roguing rate of infected host plants, the insecticide-induced death rate of the vector, and the virus acquisition and transmission rates of the vector, both of which are determined by the level of host resistance. Analysis of this model indicated that roguing applied once per month in combination with a modest level of host resistance (specifically one that reduces the product of acquisition rate and transmission rate below 80% of the value of the susceptible host) is sufficient to eradicate the disease, while a combination of roguing and insecticide application is less effective. This example illustrates that analytical models have come a long way in their capacity to provide specific management recommendations that have traditionally been considered in the realm of more complex simulation models.

Nonetheless, a few words of caution are appropriate as there are some well publicized examples from the broader ecological literature where the extension of theoretical models to management has met with disastrous results (Hall, 1988a). Perhaps we need to remind ourselves occasionally that the purpose of theory is to explain rather than to predict, and that theoretical problems without practical applications are just as legitimate as empirical studies that do not contribute to the development of new theories.

Broadened scale of investigation

With few exceptions, epidemiological models have traditionally focused on the field scale, a logical choice considering the importance of individual fields as the spatial unit for tactical disease management by growers. In recent years, however, the scale of analysis has broadened to include both finer and larger scales. At one end of the spectrum is the individual plant scale, where theoretical models have been developed, for instance, to describe transmission of *Rhizoctonia solani* from an infected to a healthy plant based on models of hyphal and colony growth of the fungus through soil (Stacey et al., 2001; Otten et al., 2004b). At the cellular level, effects of phenomena such as viral cross-protection (Zhang and Holt, 2001) and synergism among different viruses (Zhang et al., 2000; Naylor et al., 2003) have been modelled with respect to their effects on field-level disease dynamics. However, epidemiological models that explicitly describe molecular processes and interactions within individual plant cells, e.g., during virus replication or virus- or transgene-induced gene silencing, are still lacking in plant pathology, even though they are common in medical epidemiology (e.g., Phillips et al., 2001).

At the other end of the spectrum are models for disease development at landscape (Park et al., 2001, 2003; Otten et al., 2004a; Stacey et al., 2004) and continental (van den Bosch et al., 1999) scales. With the rising interest in area-wide pest management and the increasing exotic species problem (Scherm and Coakley, 2003), this scale of investigation will become more important in the future. In landscape models, spread among fields has been implemented via percolation theory (Otten et al., 2004a), cellular automata (Gilligan, 2002), or in a metapopulation framework (Park et al., 2001, 2003) in which habitable patches are made up of aggregates of susceptible fields. The models allow for the analysis of disease spread in relation to within-patch pathogen dynamics, the strength of coupling among patches, and patch size, density, and arrangement.

Closely related to the issue of scale is the concept of scaling, i.e., to what degree and how data and models from one scale can be transferred to another (smaller or larger) scale. This has been an active area of research in both theoretical and statistical epidemiology (Turechek, 2005). For instance, statistical procedures to extrapolate disease incidence data from a lower hierarchical level (e.g., leaves) to a higher level (e.g., shoots) and *vice versa* have been developed (Hughes et al., 1997; Hughes and Gottwald, 1998; Madden and Hughes, 1999; McRoberts et al., 2003; Turechek and Madden, 2003) and are now increasingly being applied to develop more efficient sampling and disease assessment protocols through approaches such as cluster sampling and group testing. In a recent example, Xu et al. (2004) used a distribution-based approach to derive relationships between the incidence of spikelet infection and the more easily determined incidence of ear infection for the Fusarium head blight pathosystem on wheat. These particular relationships may be useful for making decisions in cases where management thresholds are based on the incidence of infected spikelets.

On a more process-based level, Stacey et al. (2001) developed a mathematical model to scale up from the behaviour of individual hyphae (of *R. solani* in this example) to fungal colony growth through soil and to infection of individual plants. The approach was based on a spatially explicit model of hyphal expansion incorporating the relationships between hyphal growth and fungal biomass as well as between fungal biomass, proximity of the mycelium to a susceptible root, and the probability of disease transmission. A stochastic, cellular automaton-based model for scaling up from individual plants to plant populations infected with *R. solani* had been developed previously (Kleczkowski et al., 1997), and it may be possible to combine this probabilistic model with the more detailed fungal growth-based model of Stacey et al. (2001) to arrive at estimates of both the mean and variance of the spatio-temporal dynamics of *R. solani*.

In the broader ecological literature, fractal geometry has been applied for scaling among different spatial or temporal hierarchies if the pattern or process of interest is scale-invariant, i.e., repeats itself at progressively larger scales (Brown et al., 2002; Li, 2000). In practice, scale-invariance is suggested by a straight line in a log–log plot of the measure of interest against the scale of observation. The slope of the line is interpreted as the fractal dimension, which summarizes the properties of the pattern across scales. In general, scale-invariance might be expected for organisms occurring at a population density near their lower critical threshold, e.g., due to human intervention (Cousens et al., 2004). In a recent pest management-related example, Cousens et al. (2004) counted numbers of five agricultural weeds in up to 202,500 contiguous 0.2×0.2-m quadrats in a single arable field. Counts from adjacent quadrats were pooled into progressively larger quadrats with up to 90 m-long sides. This allowed for the calculation of incidence values for different quadrat sizes and an understanding of how these incidence values vary with scale. Calculation of the fractal dimension showed that spatial patterns of those weed species that were most aggregated and/or occurred at the lowest densities were scale-invariant, indicating that patterns observed at small scales repeated themselves at progressively larger scales. Although there are theoretical reasons why such scale-invariance would be unlikely for plant pathogens (e.g., different mechanisms for long- vs. short-distance dispersal along with changes in the physical environment at different spatial scales), it would be interesting to test the null hypothesis of scale-variance for different types of pathogens, e.g., those causing aerial vs. soilborne or monocyclic vs. polycyclic diseases. Scale-invariance, if it occurs in plant pathogens, would allow for extrapolation and prediction over a wide range of spatial scales with potentially useful applications in areas such as precision agriculture.

Ferrandino (2004) recently proposed a sampling approach for disease incidence based on a nested fractal design, i.e., one in which sampling points at distances of, say, 1, 2, 4, 8, and 16 m are represented equally. Using simulated spatial epidemics, he showed that this design was more efficient in detecting aggregation than either regular, random, or spatially clustered sampling designs, in addition to providing spatial information over a wider range of scales.

Fascination with thresholds

Van der Plank (1963) expressed his threshold theorem as $iR_c > 1$, which states that an epidemic will not occur unless the product of infectious

period i and basic corrected infection rate R_c exceeds 1. For consistency with the medical and ecological literature, the theorem has been rewritten as $R_0 > 1$, where R_0 is the basic reproductive number, i.e., the number of new infected individuals resulting from one introduced infected individual (Madden, 2005). Although the interest in thresholds for plant epidemics has been longstanding (e.g., Jeger and van den Bosch, 1994a, b), we note a recent surge of activity in this area, mostly derived from analyses with SIR-type models. This has included derivation of threshold criteria based not only on pathogen demographics (e.g., fitness of fungicide-resistant strains; Hall et al., 2004), but also on host spatial structure (e.g., host density, patch size, and coupling among patches; Bailey et al., 2000; Gubbins et al., 2000; Park et al., 2001; Otten et al., 2004a). One of the reasons for the current preoccupation with thresholds in plant epidemiology is the wider availability of stochastic models, which allows for the calculation of not only the risk of pathogen invasion, but also the probability of subsequent persistence in the face of chance events that can lead to extinction at low population densities.

Apart from stochastic forces, the establishment of a pathogen following its successful introduction may be limited by certain demographic features, such as the difficulty to find a compatible mating partner at very low population densities for species with an obligate sexual cycle (Taylor and Hastings, 2005). This feature leads to an intermediate optimum in the relationship between population growth rate and population density (Allee effect; Figure 1). In a deterministic population model of the heterothallic Karnal bunt fungus *Tilletia indica*, inclusion of an Allee effect resulted in a teliospore threshold for establishment about two orders of magnitude higher than in a version of the model without this constraint (Garrett and Bowden, 2002). This finding has potentially important implications for risk assessments of *T. indica* and other quarantine pathogens with an obligate sexual cycle.

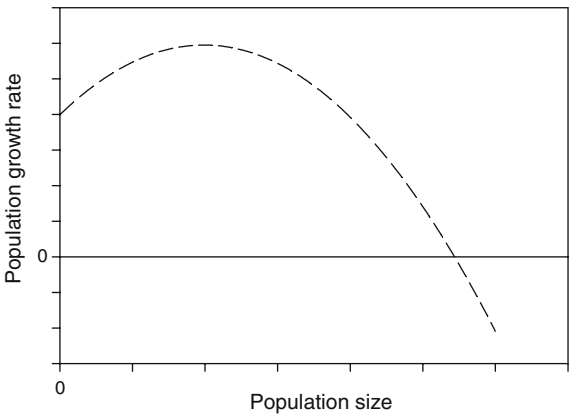

Figure 1. Graphical representation of the Allee effect showing an intermediate optimum in the relationship between population growth rate and population density, e.g., due to the difficulty to find a compatible mating partner at very low population densities for species with an obligate sexual cycle.

Pathogen population biology

Epidemiology is a holistic discipline (Zadoks, 1990), and the development of epidemiological theory thus requires an interdisciplinary approach. This includes not only mathematics and statistics, but also concepts and tools from population genetics. The main focus of population genetics is to understand the evolutionary processes driving and maintaining genetic variation within and among populations (McDonald, 2004). Because host and pathogen populations consist of distinct genetic entities, the fundamental theory of their population dynamics in space and time must coincide with that of their genetic composition. Conceptually, there is thus a considerable overlap between epidemiology and population genetics. Here, we take an heuristic look at the interplay between the two disciplines in the development and application of epidemiological theory and highlight areas that may best be served by an interdisciplinary approach. An in-depth review of the nature of the synergy between epidemiology and population genetics is outside the scope of this paper but is available elsewhere (Milgroom, 2001; Milgroom and Peever, 2003).

It has been suggested that, over the past 20 years, a schism appears to have developed between epidemiology and population genetics (Milgroom, 2001; Milgroom and Peever, 2003). Indeed, it is tempting to conclude that such a split was a consequence of both disciplines becoming more specialized as they responded to new technologies; epidemiology to the availability of advanced modelling techniques and increased computing power, population genetics to advances in molecular biology. In practice, however, the two

disciplines often have been utilized jointly to address applied epidemiological questions such as source and type of primary inoculum (Gobbin et al., 2003; Peever et al., 2004), dispersal of secondary inoculum (Cortesi et al., 2000; Cortesi and Milgroom, 2001; Loskill et al., 2004), or host specificity (Peever et al., 2000; Akimitsu et al., 2003; Flier et al., 2003). A notable example in a theoretical sense is the recent work by plant pathologists on the appropriateness of the application of measures of genotypic diversity to microbial populations (Grünwald et al., 2003; Kosman and Leonard, 2005). From these examples it should be obvious that plant epidemiology can benefit greatly from concepts and tools developed in population genetics (and *vice versa*), including in studies designed to test theoretical ideas.

Eriksen et al. (2001) used numerical simulations to address a question that had been the subject of vigorous theoretical discussions. The problem, broadly put, was to determine the role of ascospores in development and microevolution of septoria tritici blotch of wheat caused by *Mycosphaerella graminicola*. Population genetics studies in the United States in the 1990s had provided indirect evidence for sexual reproduction by *M. graminicola* during the growing season (McDonald et al., 1995; Chen and McDonald, 1996). An important question was how to determine the relative contribution of immigration (gene flow) and sexual reproduction to the genetic structure of the pathogen during the course of an epidemic, and which of these two evolutionary forces is of greater epidemiological importance within a season. This was resolved, not without some debate, through mark-release-recapture experiments (Zhan et al., 1998) and a theoretical analysis (a subject of two letters to the editor in *Phytopathology*) of the data to estimate the rates of recombination and migration (Brown, 2000; Zhan et al., 2000). Nonetheless, these studies did not answer the question of the relative contribution of ascospores vs. pycnidiospores to disease development, nor of the extent of genetic recombination. Through simulation modelling Eriksen et al. (2001) showed that the extended latent period of pseudothecia compared with that of pycnidia leads to the release of ascospores too late in the season to have a major effect on final severity of septoria tritici blotch epidemics in northern Europe. However, ascospores contributed appreciably to the genetic composition of the pathogen population (as indicated by the proportion of sexual descendants among lesions at the end of the season), especially in dry conditions unfavourable for the dispersal of pycnidiospores.

With regard to analytical modelling approaches, one of the key challenges has been to integrate epidemiological parameters into population genetics models (and *vice versa*) while at the same time keeping model complexity at a manageable level. Jeger (1997) illustrated this by incorporating host-pathogen gene-for-gene interactions into an analytical SIR model. This resulted in a set of six linked differential equations, one each for homozygous and heterozygous genotypes of both host and pathogen. Although the model was not very tractable analytically, it allowed for the derivation of threshold criteria for persistence of specific pathogen and host genotypes. Subsequent simplification of the model allowed the effects of host density dependence, fitness cost for virulence in the pathogen, and fitness cost for host resistance to be incorporated and analyzed.

Durability of host resistance, a key concept in population genetics, also has been examined from an epidemiological perspective (van den Bosch and Gilligan, 2003). This analysis considered three epidemiologically based measures of durability of resistance: (1) time to invasion by a virulent pathogen genotype; (2) time taken for the virulent genotype to dominate the pathogen population; and (3) time until a threshold proportion of the host population becomes diseased ('additional uninfected crop growth days'). These metrics differ conceptually from conventional population genetics-based measures of resistance durability in that they emphasize quantitative rather than qualitative aspects, i.e., they focus on the duration of resistance utility rather than the conditions under which durability is maintained. The model showed that if the virulent pathogen genotype is not already present, and the time between introduction (by mutation or immigration) and establishment is considered as a metric of resistance durability, both low and high proportions of resistant genotypes in the crop can prolong durability. This observation might explain the oft-encountered difficulty in trying to predict the durability of resistance genes (Hovmøller et al., 1997; Brown, 2002; Burnett, 2003). The results

also showed that the metric representing additional crop growth days without disease is unaffected by the proportion of the resistant host genotype in a cultivar mixture, thus concurring with data from experimental field studies in which varying the proportion of mixture constituents (of sorghum in this case) had no effect on time of disease onset (Ngugi et al., 2001).

Gudelj et al. (2004) investigated evolution of sibling fungal plant pathogens from an epidemiological perspective using adaptive dynamics methodology. They focused on the role of multiple host species involving a trade-off between the evolutionary benefit of being specialized and its cost (reduced virulence on other hosts). The results showed that this infectivity trade-off accounted for the evolution of only those pathogen siblings with non-overlapping host ranges (i.e., a high degree of host specialization such as observed with obligate parasites), and that other mechanisms (ecological and/or epidemiological) must account for the evolution of generalists with overlapping host ranges and that of groups containing both generalist and specialist siblings.

Several important generalizations about the role of spatial structure in host-pathogen coevolution can be drawn from the work by PH Thrall and JJ Burdon, who integrated population genetics and spatio-temporal analysis of epidemics in natural pathosystems (Burdon and Thrall, 1999, 2004). Key among these is that disease patterns in host–pathogen metapopulations are spatially and temporally asynchronous, whereby the magnitude of pathogen fluctuations varies between host populations but there is clustering of disease levels among populations. This prediction is supported by results of experimental studies (Burdon and Thrall, 2000; Thrall and Burdon, 2000, 2003; Bock et al., 2002; Thrall et al., 2002). Further, disease persistence, and hence its impact on coevolution, is higher at the local level. As a consequence, there is a tight evolutionary link between resistance and virulence of associated host–pathogen pairs whereby pathogen virulence (ability to infect many host genotypes) increases with increasing mean resistance of the host sub-population (Thrall and Burdon, 2003). These studies also provided evidence for a trade-off between virulence and aggressiveness (defined here as spore production per pustule), whereby selection for the former is favoured in resistant host genotypes while that for aggressiveness is favoured in susceptible host genotypes. Although the use of spore production as a measure of aggressiveness may be subject to debate, the study marks an important step toward documenting a virulence-aggressiveness trade-off for which previous evidence has been weak (Mundt, 2002), especially in natural systems.

Statistical epidemiology

Apart from forming a crucial link between theory and data, statistical concepts – in their own right – may result in new theoretical knowledge about plant pathosystems and plant epidemiology. For instance, distribution-based methods to characterize disease aggregation in a spatial hierarchy (Hughes et al., 1997; Madden and Hughes, 1999) have led to novel, testable hypotheses regarding disease dynamics in time and space, e.g., for incidence–severity relationships. With ever increasing computing power and a better understanding of how to utilize contemporary statistical tools, new opportunities for the application of statistics in plant epidemiology, both theoretical and applied, continue to emerge.

Generalized linear mixed models

Garrett et al. (2004) highlighted several statistical methods that are used relatively little but have the potential to improve inference from a range of epidemiological studies. Foremost among these are mixed-effects models, i.e., models to analyze data with fixed and random effects. At a theoretical level, the nature and properties of generalized linear mixed models (GLMMs) have been understood for decades (McCulloch and Searle, 2001), but until recently, without significant input from a specialist statistician, mixed-effects modelling has been very difficult in practice. Now, an increasing number of articles in application-oriented journals provide guidance for setting up mixed models and for implementing them in off-the-shelf statistical packages (Piepho, 1999; Madden et al., 2002; Piepho et al., 2003; Spilke et al., 2005). One of the most important advantages of these models is their applicability to unbalanced designs, for which exact statistical tests are usually not available. Therefore, one needs to resort to approximate methods such as the restricted maximum likelihood approach. Even for experimental designs for which traditional general linear models (GLMs)

are appropriate, analysis using the GLMM can produce more robust results when variances are unequal and/or sample sizes are small (Piepho, 1999). Madden et al. (2002) evaluated various GLMMs and recommended the fixed residual variance model (which is also the simplest GLMM) for analyzing disease incidence data from designed experiments.

Survival analysis

Data on the occurrence and timing of events such as sclerotium germination, disease onset, or leaf abscission are routinely encountered in epidemiological studies. With such time-to-event data, several problems can arise that limit the usefulness of traditional statistical methods: (1) the times are unlikely to be distributed normally; (2) the data set will likely contain censored observations, i.e., observations for which the event has not occurred when the study was completed; and (3) the response may be influenced by time-dependent covariates, i.e., independent variables whose values change during the study period. Because of these properties, time-to-event data are now increasingly being modelled using survival analysis (Scherm and Ojiambo, 2004). This set of statistical methods not only allows the comparison of time-to-event distributions among treatment groups, but also the development of models for the effects of discrete and/or continuous covariates on event times. Recently published examples include analyses of the effects of landscape attributes on the time to invasion by an exotic plant pathogen (Jules et al., 2002); of orchard characteristics, environment, and disease status of neighbouring trees on the time of virus infection of individual orchard trees (Dallot et al., 2004); and of disease severity and other leaf attributes on the time of premature defoliation of diseased plants (Ojiambo and Scherm, 2005).

Decision analysis

Important advances have been made in the area of decision analysis for disease management, especially in relation to the quantitative evaluation of risk algorithms such as disease forecasters (Yuen et al., 1996; Hughes et al., 1999; Yuen and Hughes, 2002; Madden, 2005). Increasingly, ROC (receiver-operating characteristic) analysis is being employed to optimize risk algorithms and thresholds for making decisions. An ROC curve is a plot of the true positive rate (sensitivity) as a function of the false positive rate (1 – specificity) at all possible decision thresholds of the risk algorithm. This curve allows one to identify trade-offs between liberal and conservative thresholds in an attempt to identify the most suitable decision threshold for a given application. ROC analysis is best suited for responses that are inherently dichotomous, for instance the decision whether or not to apply a fungicide. In a recent example, Dewdney et al. (2002) used ROC analysis and historical data to evaluate parameters of MARYBLYT (a forecaster for fire blight of apple and pear) and to identify where key improvements were needed. MARYBLYT and Cougarblight (another fire blight forecaster) have been compared using ROC analysis and found to have equivalent action thresholds and thus perform similarly in their ability to predict blossom blight (Dewdney et al., 2003).

ROC analysis also can be applied in situations where the response is not dichotomous (Patil, 1991), for instance the decision on how much fertilizer to apply or how many fungicide applications to make. However, in plant epidemiology, ROC analysis of responses on a non-dichotomous scale has yet to be demonstrated.

Bayesian analysis

The evaluation of plant disease forecasters based on ROC analysis may be improved further when conducted in a Bayesian framework (Yuen and Hughes, 2002). This is accomplished by considering the prior probability of disease occurrence in addition to the likelihood ratios for positive and negative predictions by the risk algorithm. The latter two are calculated directly from sensitivity and specificity of the forecaster, while the former may be based either on the historical prevalence of the disease in the region of interest, or on growers' subjective estimates of disease risk. In either case, the result is a posterior probability of disease occurrence given the prediction by the forecaster. Yuen and Hughes (2002) illustrate this approach by means of risk algorithms for eyespot of wheat and Sclerotinia stem rot of canola (oilseed rape).

Apart from its application in the specific example of ROC analysis discussed above, Bayes's theorem presents a general framework for incorporating uncertainty and prior information into

epidemiological analyses and for updating current knowledge as new information becomes available (Mila and Carriquiry, 2004). The key feature is the calculation of posterior probabilities for the parameter of interest based on empirically derived prior probabilities in conjunction with the conditional probability of each possible outcome. This use of prior probabilities represents a powerful mechanism for incorporating subjective information such as growers' perceptions. This is illustrated in the work of Mila et al. (2003), who examined the effect of soybean growers' production decisions on Sclerotinia stem rot incidence using decision theory under uncertainty. Predictions of stem rot incidence and soybean yield based on regression-type models were updated with growers' subjective estimates of disease incidence via Bayes's theorem. The resulting posterior probabilities were then used to derive management criteria for profit maximization.

Economic criteria (which often exhibit considerable uncertainty) and growers' perceptions are among the most important drivers affecting disease management decisions, yet they are routinely ignored by plant pathologists developing decision algorithms. The continued penetration of Bayesian analysis into the epidemiological mainstream should lead to a greater appreciation of the importance of these drivers and – it is hoped – their more widespread incorporation into disease management models.

Statistical genetics and bioinformatics

As shown in the above examples, statistical plant epidemiology has relied heavily on the medical and ecological fields for inspiration and conceptual advances. This trend will likely continue in the future as plant epidemiologists become more familiar with the theories and tools of statistical genetics and bioinformatics. In a recent example, Parsons and Te Beest (2004) used genetic algorithms to optimize fungicide applications on winter wheat relative to spray date as well as choice, number, and dose of active ingredients. Genetic algorithms use biologically derived concepts such as inheritance, mutation, natural selection, and recombination to 'evolve' a large population of possible solutions ('individuals') to the best ('fittest') solution ('survivor'). The evolution starts from a population of completely random individuals, and in each subsequent generation multiple individuals are selected stochastically and modified (mutated or recombined) to form a new population. Although the concept of evolutionary computing may be intuitively appealing to biologists, the approach is computationally intensive and effectively treats the optimization problem as a black box. Its theoretical and practical impact on plant epidemiology remains to be seen.

Apart from merely adopting statistical tools from other disciplines, plant epidemiologists should be more proactive in exploring potential applications of their concepts and procedures in rapidly expanding disciplines such as statistical genetics or bioinformatics. Conceptually, for instance, there are many parallels between the dynamics of plant pathogens in populations of plants and those of genetic loci or markers within a genome (Delwiche, 2004). The key here is to remain imaginative and keep an open mind toward broader applications, without being confined to the organismal level that has historically dominated statistical applications in plant epidemiology.

Conclusions

Based on the selected examples given above there can be little doubt that significant progress has been made in theoretical plant epidemiology since the turn of the century. New theories and models continue to be developed, and sincere efforts are being made to relate them to the broader field of theoretical biology on one hand and practical disease management on the other. As analytical models of plant disease dynamics have become more realistic, they also have become considerably more complex, and solutions often can be obtained only numerically. As such, the division between analytical and simulation models, an important distinction some 20 years ago (Jeger, 1986), is narrowing. It seems that we have come back full circle to the medium-sized models advocated by Botkin's (1977).

Although theoretical problems need not be tied to practical applications to be valid, the image of theoretical epidemiology within the larger field of plant pathology could benefit from a clearer documentation of its impact on practical disease management. In medical epidemiology, such evaluations are commonly achieved by comparing

model outputs with long-term morbidity data sets, e.g., in the case of models for the impact of vaccination on childhood diseases (Rohani et al., 2000). We would like to call attention to the need for similar analyses in plant epidemiology, especially with pathosystems for which long-term data are available (e.g., the cereal rusts). Establishment of additional long-term data collection standards, even if only for a limited number of pathosystems, would provide a more solid data base from which to evaluate the impact of interventions suggested by current theoretical knowledge.

While plant epidemiology, by definition, is concerned with the study of populations of pathogens in populations of plants, there exists ample opportunity to broaden the scale of investigation and apply the concepts of theoretical epidemiology to both sub-organismal and ecosystem scales. Examples of such non-traditional applications could include models of virus cross-protection in individual plant cells, temporal and spatial dynamics of molecular markers or of molecules such as mycotoxins, biotechnology risk assessment, microbial forensics, or the quantitative analysis of ecosystem health. We would argue that plant epidemiologists, including theoreticians, are not yet taking advantage of these new opportunities sufficiently. Although providing the scientific basis for disease management will always be the *raison d'être* for plant epidemiology, a broader perspective will help the discipline to remain relevant as more efforts and resources continue to be devoted to genomic and ecosystem-level science. Plant epidemiology, both theoretical and applied, will remain as integrating a discipline as it has ever been, but the individual components that require integration are changing.

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