PATHOGENS AND PLANT POPULATION DYNAMICS: THE EFFECTS OF RESISTANCE GENES ON NUMBERS AND DISTRIBUTION[1]

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INTRODUCTION

The scenario that has stimulated this workshop is a scary one: resistance genes developed for protecting our crops escape into natural populations of weeds and crop relatives. These populations then become resistant to the pests and pathogens that hold them in check. Resistant populations explode in abundance and invade back into our crop fields, or displace and disturb the ecological balance of our natural communities.

Circumstantial evidence that this scenario might be a cogent one comes from natural experiments that result from the inadvertent introductions of weeds from different continents. Success of such introductions is often attributed to the absence of native pathogens and pests that previously kept the plants in check in their original habitats. The success of biological control agents subsequently introduced to control these alien weeds is then cited as supporting evidence for the importance of pests and pathogens in regulating the natural populations. Conversely, introduced pests can devastate native populations, and this is further cited as evidence for their controlling influence.

However, there are many reasons why the natural experiments provided by introductions and biological control may not be good models for assessing the risks of the escape of resistance genes. First, we only focus on extreme cases and "horror stories"—the many introductions and biological control agents that fail are never at the forefront of our minds. Biological control itself is often preceded by intensive screening and deliberate selection for agents that will have a large effect. Should we then be surprised that they are sometimes effective? Second, there is the assumption that losing a whole suite and community of ecological interactants is equivalent to acquiring a resistance gene. Resistance genes are very diverse in their effects and may carry substantial fitness costs. Third, introductions and biological-control activities disrupt population genetic structure, and this itself may have a large impact on the outcomes of host-pathogen interactions. For example, it has been shown that biological control is more effective when the weed is inbred or largely clonal, than when it is outcrossing (Burdon and Marshall 1981). Understanding the relationship between disease and mating systems remains one of the most important issues in evolutionary biology.

How then do we get an alternative, perhaps more balanced view? The approach I want to take is to examine how resistance to pests might be expected to impact the abundance of their host populations, focusing on plant pathogens in particular. We can get considerable insight by examining how pathogens impact natural populations of plants, and then "imagining" what the consequences would be if those plants became resistant to the pathogens.

This paper describes some simple models of host-pathogen dynamics to establish some principles and generalities. Very similar and no more complex models are then used in a real-world context to better understand the impact that pathogens have on abundance and distribution of plants in nature. Understanding these impacts for species capable of acquiring resistance genes from crops will provide a more scientific basis for attempting to "reverse predict"

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the consequences of eliminating pathogens through the introduction of resistance.

EFFECTS OF PATHOGEN RESISTANCE GENES ON PLANT ABUNDANCE: EXISTING EVIDENCE

Learning from Theory

Although comprehensive reviews on the subject have appeared only recently, there is abundant evidence that plant diseases affect components of plant fitness in nature (Burdon 1987; Alexander 1988). However, the effect that a pathogen (or any pest) has on an individual is a poor guide to predicting the effects that the pathogen will have on a population. Far fewer studies have investigated the effect of pathogens on the abundance of species in natural populations or on the structure of whole communities.

Basic models

We will focus on models of so-called "micro-parasitic" infections (e.g., fungi, bacteria, and viruses). These models consider the host population to consist of healthy and diseased individuals and disregard the degree to which specific individuals are diseased or infected. This is in contrast to the so-called "macro-parasitic" models, where the number of pathogens or parasites per individual is considered to be an important variable.

In a diseased population, the rate at which healthy individuals become diseased is determined not just by their physiological resistance but also by the likelihood that they receive infectious stages of the pathogen from other diseased individuals. This is a function of the number and proximity of other diseased individuals in the population and on the transmission mode. In the most basic models, "resistance" is often represented by a disease transmission parameter (often denoted by the symbol β). A low value of β implies that the host is resistant, while a high value indicates it is susceptible. Healthy individuals produce new individuals (by birth or seed production) at a rate b and they die at a rate d. Disease either lowers reproductive output or increases mortality of the hosts. The magnitude of this effect is often represented by the symbol α. This parameter represents the "aggressiveness" of the pathogen (the term "virulence" is often used instead in animal and human contexts). The inverse of α represents the "tolerance" of the plant to the disease. Many such models also include the rate of recovery of diseased hosts, but to avoid parameter overload, I will ignore this for the moment. Full account of such models and their analysis is given in Anderson and May (1981).

We will use the convention that X represents the number of healthy hosts, Y the number of diseased hosts, and N the total population size (= X + Y). If disease transmission to a healthy host increases linearly with the number of diseased individuals in the population, then β N is the rate at which healthy individuals become diseased. Assuming further that the disease only affects the mortality rate of the hosts, we can generate a simple dynamical model that describes the rate of change over time in numbers of healthy and diseased individuals.

$$dX/dt = (b - d)\,X + b\,Y - \beta\,X\,Y$$

$$dY/dt = \beta\,X\,Y - (d + \alpha)\,Y$$

The sum of these gives an equation for the rate of change of total population size:

$$dN/dt = (b-d)\,N - \alpha\,Y$$

If the host is susceptible enough for the disease to spread (β large), a population represented by this model reaches an equilibrium population size (which we will call N*). In this model, N* is actually given by a somewhat involved expression ($N^* = \alpha\,(\alpha + d) / \beta\,(\alpha - b + d)$), which tells us immediately that the effect of a disease on population size is not a simple function of host resistance and disease aggressiveness.

With regard to resistance, the outcome meets our qualitative expectations. More resistance (smaller value of β) leads to a larger population size, but the effects are very non-linear. With regard to aggressiveness affecting mortality, translation of individual effect to population effect fails completely. Indeed, pathogens that are of intermediate aggressiveness have the largest effects on reducing population. By killing their

own hosts, very lethal pathogens have much less of an impact on the equilibrium population size. Resistance to very aggressive pathogens may therefore have negligible consequences for the population! This result is different for pathogens that reduce the reproductive output of their hosts without affecting their survival; in this case increasing sterility results in increasingly reduced population size, albeit in a non-linear manner.

What is the effect of the spread of a gene for complete resistance on population size? Obviously, when the disease is eliminated (β is set to zero), the population increases exponentially to infinity. Here then, in algebra, is our "scary scenario."

Effects of population regulation

We know that very few populations grow exponentially for any length of time. In most ecological settings, the birth and death rates of a host will be influenced by factors such as limited resources, predators, or alternative parasites. In other words, the population size of the host itself will be subject to "density-dependent" regulation in addition to the pathogen of interest.

When there is density-dependent regulation, the effects of a newly acquired resistance gene in increasing the population size are much less than if there is unconstrained growth of a healthy population. The population cannot "explode" because it is limited by other factors. A critical parameter now becomes the intensity of this regulation. All other things being equal, when the effects of density-dependent population regulation are more severe, the impact of a particular pathogen on equilibrium population size will be less. Therefore, an escaped resistance gene is likely to have much more effect on populations that have weak density-dependent regulation. The effect of a gene that causes broad-scale or multiple-pest resistance would be to eliminate a number of other pests, perhaps causing a concomitant loss of a suite of ecological interactions important in regulating the host population. Thus a broad scale resistance gene would have the effect of decreasing the severity of density dependence.

Effects of transmission mode

The disease transmission mode will change the model construction, as well as our predictions about the effects of introduced resistance genes. Such a transmission process may be applicable to a number of diseases important in agriculture such as fire-blight of pears and the pollen borne virus diseases.

Here, the rate at which healthy individuals become diseased is more likely to be a function of the fraction of individuals in the population that are diseased rather than a function of the absolute number that are diseased (Antonovics *et al.* 1995). In the case of such "frequency-dependent" disease transmission, the increase in population size due to resistance becomes independent of the level of density dependent regulation. Therefore, the proportional effect of introducing a resistance gene will be the same regardless of the intensity of density-dependent regulation, and knowledge of only four parameters (b, d, α, and β) is necessary to predict the magnitude of such an effect.

Genetic models

Genetic models also make the point that simplistic, seemingly "intuitive" approaches are likely to fail. Consider the matter of resistance costs. It may seem that if a resistance gene had a large cost, then it could still escape into the natural environment and spread if the benefits to the host were sufficient. It is likely that some broad scale resistance genes might be costly to the plant, e.g., constitutively induced systemic acquired resistance that activates a whole suite of pathogenesis related proteins. For example, resistance of *Silene alba* to an anther-smut disease can have costs approaching 30% (Alexander 1989; Biere and Antonovics 1996).

Analysis of a simple genetic model of resistance costs, in which resistance variation in the host was controlled by a single locus with two alleles and there was no genetic variation in the pathogen, showed that an allele that gave a very high resistance could spread even if it resulted in a large decrease in reproductive output (Antonovics and Thrall 1994). Despite an initial increase, however, the allele did not spread completely but remained in a polymorphic equilibrium with the alternative more susceptible

allele which did not lower reproductive output. Moreover, the disease could persist in such populations even if it could not persist in a population that was completely fixed for the resistance allele. The advantage of the resistance allele depended on its frequency in the population—once it reached a high frequency, disease frequency decreased and the advantage of the allele declined.

Large costs therefore do not necessarily prevent the spread of resistance alleles into diseased populations. However, if such genes do invade, they may have much less effect than would be predicted from a model where the population was monomorphic for those alleles. Monomorphism is an implicit assumption in models that only consider changes in numbers, such as those described at the beginning of this section.

Effects on a regional scale

The models developed above can be scaled up to a regional metapopulation (a collection of populations) level, with very little loss of generality. Individual populations within the larger metapopulation have a dynamic that is determined by their colonization and extinction dynamics. A region is thus conceptualized as consisting of habitat patches that may be occupied or empty. Empty patches are created by extinction of the local population and become colonized by dispersal from occupied patches.

When plant pathogens cannot exist independently of the host (as we have assumed throughout), three kinds of patches are possible: unoccupied (= "empty"), occupied by the host alone (= "healthy"), and occupied by the host and its disease (= "diseased"). Such a scenario results in a model that closely resembles the dynamics of a pathogen in a single population with density-dependent regulation. The empty patches can be seen as equivalent to a limiting resource, the occupied patches represent individual healthy hosts, and the diseased patches represent individual hosts that are diseased. A model of the form presented above is therefore usable (in a heuristic sense) to gain understanding of host-pathogen interactions at a metapopulation level.

By drawing certain parallels, it can be seen that the spread of a resistance gene may both decrease the population extinction rate and increase the reproductive (= seed) output of individual patches. However, the consequences for the regional abundance of a host now depend on the population level effects of the pathogen. The hierarchical structuring of this simple model shows that the effects of a pathogen on the individual are now subsumed two levels below its effect on abundance at a regional effect. Therefore, the magnitude of regional effects is only predictable by a study of metapopulation dynamics.

The extension of metapopulation models to include the details of host-pathogen interactions and their genetics has barely begun (Frank 1993; Thrall and Burdon 1997). This is an exciting area in which more research is needed if we are to gain anything more than an anecdotal understanding of how diseases impact plant populations of weeds, weeds harboring resistance genes from crops, or endangered species.

Disease and range extension

Limits to distribution along local ecological gradients occur when immigration and recruitment rates no longer exceed the local death rates (Watkinson 1985; Antonovics and Via 1988). At a metapopulation level, geographical limits occur as suitable patches become farther and farther apart, or as emigration from those patches or their persistence decreases (Carter and Prince 1988). The question of how disease presence (or absence due to invasive resistance genes!) affects distribution of a plant along a habitat or geographical gradient has not yet been explored.

The precise outcomes are hard to predict, especially as there will be feedback between host and pathogen dynamics. The explicit study of how pathogens limit range distribution is an area that needs serious inquiry and promises rich dividends in the future. It is critical for understanding both the risks associated with release of genetically engineered organisms and the overall impact of pests and pathogens on species distributions.

Learning from Nature: Getting Data That Says More Than the Models

The models presented here have enormous practical utility. Such models capture the essential features of the life cycles of both the host and the pathogen. They are iterative and therefore they can be used as a starting point for estimation and prediction purposes.

In most ecological settings, one simply cannot control all the factors that ecologists are prone to study (e.g., light, nutrients, soil, water, or temperature). Predicting the effects of resistance genes on population size is therefore best done by direct study of the population dynamics of the organisms at risk, rather than by extensive studies of factors that may affect these populations.

For over a decade, we have been studying the population biology of *Silene alba* (= *S. latifolia*, or white campion) and its pathogen *Ustilago violacea* (= *Microbotryum violaceum*, or anther-smut disease). The disease, somewhat unusual in being pollinator transmitted, sterilizes the host rather than increases its mortality. As a model system, it incorporates approaches that might be useful for examining both the local and regional dynamics of any naturally occurring host-pathogen system. It illustrates how population data on disease incidence, gathered over a number of years, can provide critical information for predicting the potential effects of resistance escape.

Local predictions

A minimal model of the kind described above has very few parameters and these can often be estimated from field and experimental studies (Alexander *et al.* 1996). The assumptions inherent in the model can also be confirmed by experimental and field studies (e.g., that the disease transmission term is non-linear rather than linear, and that transmission is a function of frequency of disease in the population rather than density of disease; Antonovics and Alexander 1992).

Defining symbols as described earlier, we use the following model:

$$dX/dt = (b - d)\,X - \beta\,X\,Y/N$$

$$dY/dt = \beta\,X\,Y/N - d\,Y$$

The sum of these gives an equation for the rate of change of total population size:

$$dN/dt = bX - d\,N$$

The above model contains only three parameters, and if we can estimate these, we can estimate the increase in population size due to acquisition of resistance by the host. Data obtained by averaging the results from several field experiments gave values of $b = 2.0$, $d = 0.5$, and $\beta = 5.86$ (Antonovics *et al.* 1998). Using these data in the above model and adjusting the density dependence so that the size of a healthy population would be 100, results in 18.2 healthy and 17.1 diseased individuals in the equilibrium population of 35.3. The disease reduces the population to 35% of its normal equilibrium size. Introducing a resistance gene into a diseased population of *Silene alba* would increase the population size by around 200%.

The ability of "minimal" models to predict the dynamics of single populations was elegantly shown by Thrall and Jarosz (1994a,b) also using the *Silene-Ustilago* system. They used model parameterization from field experiments in one year to predict outcomes in the following year. Their experimental populations were started either with hosts that were susceptible or hosts that were relatively resistant and were replicated over a range of initial disease frequencies. They showed that the theoretically predicted dynamics closely matched the observed dynamics and that the long-term predictions for resistant and susceptible populations were quite different. They predicted population sizes of generally around 20-40 individuals (depending on model details) in disease susceptible populations, and population sizes of 80-100 individuals in resistant (and usually disease free) populations. This is direct evidence that resistance genes have a substantial effect on the size of *Silene alba* populations.

Regional predictions

Just as it is dangerous to extrapolate the effects of a disease on an individual into population level effects, so it is potentially very misleading to extrapolate from single populations to a

regional level. This is best illustrated by first doing an overly simplistic calculation of how a 200% increase in population size due to introduction of a disease resistance gene might translate into a regional effect. For example, in our study area only about 20% of the populations are diseased. Assuming this value, four-fifths of the populations (i.e., the healthy ones) would have a size of 100, while a fifth (i.e., the diseased ones) would have a size of 35.3. Eliminating the disease would increase only this latter fifth to a size of 100. The overall impact of the resistance gene at a regional scale (about 15%) is therefore almost negligible from a practical standpoint.

However, such a simple summation fails to take into account the overall metapopulation dynamics. We have used the *Silene-Ustilago* system to model disease effects at a regional level (Thrall and Antonovics 1995; Antonovics *et al.* 1998). The main effect of the disease at a metapopulation level is that the number of sites occupied by the plant in the presence of disease is much less than in the absence of disease (17.4% vs. 51.7%; average of 10 simulation runs). The spread of a gene for complete resistance to the fungus would therefore result in a 300% increase in numbers of host populations, and this is an order of magnitude greater than predicted by summing individual population effects. There are two main reasons for this effect. First, the increased seed output of resistant populations increases the rate at which new sites are colonized. Second, the extinction rates in the model are dependent on the size of the populations (based on empirical data), and therefore the increase in the population size as a result of disease resistance also decreases extinction risk.

Our results therefore confirm a general expectation that hosts and their pests and pathogens would regulate each other to low levels in natural populations. This has the important corollary that simply assessing disease incidence at one period of time or estimating the magnitude of disease effect on individuals is a poor predictor of the impact of these agents on populations. There is a real danger in recourse to casual natural history or feelings that "well, we don't see a lot of disease." More importantly, these studies show how it is possible to understand the consequences of disease for the abundance and distribution of any species. These methodologies and principles can be applied to understanding the impact of pests and pathogens of crop relatives that may acquire resistance genes. A challenge for the future is to do precisely this and to move the regulation and management process away from being based on general impressions derived from hearsay, anecdote, and familiarity.

FUTURE RESEARCH STRATEGIES: OBTAINING EVIDENCE

Studying the effects of pathogens on plant population dynamics is a very recent enterprise. A paper on the dynamics of the anther-smut disease (Alexander and Antonovics 1988), published only a decade ago, was perhaps the first study to deal exclusively with joint numerical dynamics of a plant host and its pathogen! Only within the last few years has there been a surge of interest in applying these approaches explicitly to plant populations in natural and agricultural contexts (Thrall *et al.* 1997; Gilligan and Kleczkowski 1997; Gilligan *et al.* 1997).

The example cited here is perhaps unique in being the only case in which we have any substantial understanding of how a pathogen influences plant abundance at either a local or regional level. It is therefore not surprising that our current ability to predict pathogen effects is so often limited to discussions focused around scary scenarios and circumstantial evidence.

Experimental studies of disease effects at a population level are urgently needed to assess the role of pathogens in population regulation at both local and regional scales. We simply don't know if plant species are strongly limited in their abundance by resources or if pests play a substantial role. If pests and pathogens have a minimal effect on these species, then we have little to fear. If, however, pathogens are an important regulatory force on those populations, then the escape of resistance genes could cascade into population and community effects that might parallel the drastic effects of introduced species.

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