A Simple Model of Selection for Fungicide Resistance in Plant Pathogen Populations

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ABSTRACT


A simple model is proposed for studying changes in pathogen populations in response to selection by fungicide and for estimating pathogen fitness. Its implications are discussed in relation to other current models of fungicide resistance. Simulations indicate that the outcome of selection is largely dependent on a fine balance between the relative fitnesses of sensitive and resistant populations and the proportion of host plants treated with the fungicide. Analysis of data on selection by benomyl genotypes on treated (T) and untreated (U) areas of a susceptible host may be described as follows:

\[ S(\beta) = \begin{cases} 1 & \text{T} \\ 0 & \text{U} \end{cases} \]

\[ R(\alpha) = \begin{cases} 1-s & \text{T} \\ 1 & \text{U} \end{cases} \]

in which \( s \) represents the selection coefficient against the resistant genotype in the absence of the fungicide. For simplicity, an equal selection coefficient is assumed on the treated host and the sensitive genotype fails completely against the fungicide.

If the initial frequencies of \( S \) and \( R \) are \( \beta_0 \) and \( \alpha_0 \), respectively, and the proportion of \( U = \theta \), then after one cycle of selection:

\[ \text{frequency of } S(\beta) = \beta_0 \theta / (\alpha_0 W + \beta_0 \theta) \]

\[ \text{frequency of } R(\alpha) = \alpha_0 W / (\alpha_0 W + \beta_0 \theta) \]

in which \( W = 1 - s \) is the relative fitness of \( R \), and

\[ \alpha_3 = \alpha_1 W / (\alpha_1 W + \beta_1 \theta) \]

\[ = \alpha_0 W^2 / (\alpha_0 W + \beta_0 \theta) \]

\[ + \beta_0 \theta / (\alpha_0 W + \beta_0 \theta) \]

\[ + \beta_0 \theta / (\alpha_0 W + \beta_0 \theta) \]

By induction

\[ \alpha_i = \alpha_0 W^{i-1} / (\alpha_0 W^i + \beta_0 \theta^i) \] (1)

\[ \beta_i = \beta_0 \theta / (\alpha_0 W^i + \beta_0 \theta^i) \] (2)

From equations 1 and 2,

\[ \alpha_i / \beta_i = \alpha_0 W^i / \beta_0 \theta^i \] (3)

\[ W^\theta = \alpha_0 \beta_0 \theta / \alpha_0 \beta_0 \theta \]

\[ \ln W^\theta = (1/\theta) \ln (\alpha_0 \beta_0 / \alpha_0 \beta_0) + \ln \theta \] (4)

On the treated host alone (i.e., \( \theta = 1 \)), equation 4 becomes:

\[ \ln W^\theta = (1/\theta) \ln (\alpha_0 \beta_0 / \alpha_0 \beta_0) \]

\[ = (1/\theta) \ln (\alpha_0 (1 - \alpha_0) / \alpha_0 (1 - \alpha_0) \]

\[ = (1/\theta) [\ln (\alpha_0 / (1 - \alpha_0) - \ln (1 - \alpha_0)] \] (5)
which is identical to the model by MacKenzie (16)

\[ \frac{q/p}{q_0/p_0} \exp (r_1 - r_2) t \]

in which \( p_0 \) and \( p \) are initial and final proportions, respectively, of a pathogen race \( x \); \( q_0 \) and \( q \) the initial and final proportions, respectively, of a second, more fit race \( y \) after time \( t \); and \( r_1 \) and \( r_2 \) are the apparent infection rates of \( x \) and \( y \). Since

\[ \ln W = r_1 - r_2 \]

(where \( W \) is the relative fitness of the less fit race),

\[ \frac{q/p}{q_0/p_0} (W). \]

This may be rearranged to give

\[ \ln W = 1/t [\ln (1-q/(1-q)) - \ln q_0/(1-q_0)] \]

which is identical to equation 5.

**IMPLICATIONS OF THE MODEL**

Equation 3 suggests that the outcome of selection depends on (i) the initial frequencies of \( S \) and \( R \); (ii) the fitness of resistant genotypes relative to sensitive genotypes; (iii) the proportion of treated plants; and (iv) the number of pathogen generations. The equation for the change in frequency of \( R \) after one pathogen generation \( G \) is given by:

\[ \Delta \alpha = \alpha_1 - \alpha = \frac{\alpha W - \alpha (W + \beta \theta)}{(a W + \alpha \theta)} \]

\[ = \alpha \beta (W - \theta) / (a W + \beta \theta). \]

At equilibrium, \( \Delta \alpha = 0 \), and \( W = \alpha \). \( \alpha \) and 1 are trivial solutions. The stability of the equilibrium is given by the solution of:

\[ \partial \Delta \alpha / \partial \alpha = (W - \theta) (\beta^2 \theta - \alpha^2 W) / (\alpha (W - \theta) + \theta). \]

At equilibrium, \( W - \theta = 0 \), and \( \partial \Delta \alpha / \partial \alpha = 0 \). The equilibrium is therefore neutral and the genotypic frequencies remain unchanged irrespective of their actual values when \( W = \theta \). If \( W > \theta \), then \( \Delta \alpha > 0 \), and the frequency of \( R \) increases until it is fixed in the pathogen population; there is no internal equilibrium. If \( W > \theta \), then \( \Delta \alpha < 0 \), and the frequency of \( R \) declines until it is lost from the population.

**Changes in frequency of \( R \) with time.** In this series of simulations (Fig. 1), the value of \( W \) is set at 0.8 and changes in the frequency of \( R (\alpha) \) are plotted against time for different values of \( \theta \). When \( \theta = W = 0.8 \), the value of \( \alpha \) is constant with time. When \( \theta < W \) (i.e., the untreated area is less than the relative fitness of the \( R \) genotype), then \( \alpha \) increases with time and \( R \) is ultimately fixed in the pathogen population.

With \( \theta = 0.5 \) (i.e., 50% of area treated), the frequency of \( R \) increases from 0.1 to 0.54 in five generations. Corresponding values are 0.1 to 0.99 if \( \theta = 0.2 \) (i.e., 80% of area treated). The model demonstrates the rapidity with which the pathogen population can respond to extensive fungicide applications if the resistant genotypes have a high level of relative fitness.

**Changes in frequency of \( R \) with increase in \( 1 - \theta \).** Figure 2 illustrates the final frequencies of \( R (\alpha) \) attained after 10 cycles of simulated selection on different proportions of treated host and with three levels of selection coefficient, 0.2, 0.5, and 0.8. In each case, \( \alpha \) increases above the initial level \( \alpha = 0.1 \) as soon as the treated area \((1 - \theta) \) exceeds the selection coefficient.

When the area treated is small, resistant genotypes need to be very fit (high \( W \)) to survive. After 10 generations, \( R \) is virtually undetectable when the treated area is \( < 0.3 \) if \( W < 0.5 \) (Fig. 2). Even if pathogen genotypes are very fit \((W = 0.8)\), they increase relatively slowly with increases in the proportion of treated area. For example, an increase of \( 1 - \theta \) from 0.2 to 0.3 increases \( \alpha \) from 0.10 to 0.30 in 10 cycles of selection when \( s = 0.2 \).
infection in disease nurseries for 3 days. Following incubation in a clean greenhouse for a further 3 days, spores from 50 lesions in each box were isolated, multiplied on agar culture, and reinoculated on fresh trays of seedlings identical to the original treatments. Spores produced from the second inoculation had therefore undergone two cycles of selection and were tested for resistance by germination tests on agar plates containing benomyl at 3.2 ppm.

The frequency of resistant genotypes increased from 0.115 to 0.295 after two selection cycles. As half of the plants were not treated with benomyl, $\theta = 0.5$. Substituting into equation 4,

$$\ln W = \frac{1}{2} \ln (0.295) (0.885)/(0.115) (0.705) + \ln 0.5$$

$$W = 0.897$$

$s = 0.103.$

(Alternatively, when $s$ is small, $\ln W \sim -s$ and $s = 0.108$.)

Since the selection coefficient against the resistant genotype is small, benomyl resistance is likely to increase rapidly in response to moderate use of the fungicide. For example, if 30% of the plants in an area are treated with benomyl, then the frequency of the resistant genotype may increase from 0.1 to 0.57 in 10 cycles of selection.

**DISCUSSION**

The model presented is simple because it does not include competition between pathogen genotypes for available infection sites at the late phase of an epidemic. Also, aspects of fitness other than parasitic fitness affect survival of the pathogen in nature. The model may, however, be particularly useful in wet tropical areas where environmental variations are less severe and where parasitic fitness may be the most important component of biological fitness of plant pathogens.

The model assumes random distribution of spores over an area and the absence of age structure on the population. For example, Barrett (1) has considered that the proportion of spores ($1-\phi$) that lands on the same plant and causes self-infection may affect the outcome of selection of pathogen races in multilines and cultivar mixtures. High proportions of spores that are randomly distributed ($\phi = 0.9$ to $0.95$), as detected by Leonard (14) for oat stem rust and by Kiyosawa and Shiyomi (13) for blast, suggest that simple models may be a good approximation for these pathogens. Further, the model suggests that whereas selection in the pathogen population for resistance to fungicides may generally be related directly to the proportion $(1-\theta)$ of treated crop and the fitness $(W)$ of resistant phenotypes, interactions between the two factors may be complex.

Chemicals that select for resistant genotypes of low fitness $(W)$ values are likely to be more durable than those that do not. Persistency and systemicity of a compound also affect the rate of selection for resistance through their effects on $(1-\theta)$. For example, if the compound is non-systemic, $(1-\theta)$ is in practice likely to be smaller than the proportion of crop treated because of incomplete protection of susceptible tissue. If the compound has poor persistency, $(1-\theta)$ may be expected to decrease rapidly with time. Fungicides that lack persistency and are not systemic are therefore likely to be more durable in effectiveness than compounds that have these qualities, since selection for resistance is reduced. A similar opinion has been expressed by Wolfe (23).

Strategies for fungicide use that are intended to increase durability operate in a similar manner by reducing the extent or duration of exposure of the fungal population to the toxicant. Examples include limiting fungicide usage until disease exceeds economic threshold levels, alternating use of fungicides with different modes of action, or use on alternate crops when there are two or more crop seasons a year (6,25).

Fungicide mixtures have been advocated as presenting a more complex problem for pathogens to overcome than single fungicides. They may also have a synergistic effect (18). Wolfe (22) suggested the use of heterogeneous mixtures (different plants receiving different fungicides) because homogeneous mixtures (all plants receiving the same mixture) present a uniform environment for selecting resistant genotypes. Heterogeneous mixtures, particularly those where components vary in persistency, may allow sensitive genotypes to compete more successfully with resistant genotypes. Urech and Staab (19), however, considered prepacked mixtures to be the only practical strategy for delaying or preventing the development of resistance.

The model may be extended to follow selection for increased virulence by substituting susceptible and resistant hosts for $U$ and $T$. Both nonvirulent and virulent pathogen phenotypes for $S$ and $R$. The proportion of resistant hosts, and the number of pathogen generations in a manner similar to that discussed for the fungicide resistance model. A similar model for host resistance has been presented earlier by Groth and Person (9).

Some host resistances may be considered to have like systemic fungicides with maximum persistency, and selection for virulence may be expected to be intense. Other hosts that exhibit different degrees of resistance at different growth stages (e.g., adult resistance or susceptibility) may be more durable because selection for increased virulence occurs only in limited periods of time. Examples include adult resistance of some varieties of wheat and barley to rusts and powdery mildew. Rice cultivars that are susceptible to foliar blast but resistant to neck blast may be more durable in resistance than cultivars that are resistant to both phases of the disease.

Although it seems probable that cultivars possessing discontinuously expressed resistance are more durable than those that do not, other as yet unidentified factors may also be important in conferring durability. For example, attention has been drawn to the greater durability of resistance of the wheat cultivar Capelle-Depréz to *Puccinia striiformis* (West.) compared with that of other cultivars that possess a similar pattern of seedling susceptibility and adult plant resistance (11).

The mean fitness of pathogen populations may be further reduced by integrating fungicide use with host resistance. Wolfe (22) considered that a combination of intermediate resistance with low levels of fungicide application would provide adequate protection while extending the durability of both control measures. In controlled experiments, adaptation of *Pyricularia oryzae* to either resistance of the rice host or benomyl application was delayed by a combination of both measures (3).

**LITERATURE CITED**


