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Durability of resistance and cost of virulence

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Abstract

A seasonal model, where a growing season is defined as the time between sowing and harvest and alternates with an inter-crop period, was derived to study the effects of the 'cost of virulence' and cropping ratio on durability of resistance. We assumed a single strain of virulent pathogen, a single strain of avirulent pathogen and two cultivars (one resistant and one susceptible) and studied two measures of durability of resistance ('take-over time' and 'usefulness time'). Take-over time is defined as the time needed for the virulent strain of the pathogen to reach a preset threshold and predominate over the previous pathogen population. Usefulness time is the time needed before the estimated gain in green canopy area duration per plant through the use of the resistant cultivar becomes negligible. The model suggested that, although it could take several seasons before the virulent strain of the pathogen predominated over the previous pathogen population, the usefulness time of the resistant cultivar was always much shorter. Furthermore, increasing selection for the virulent strain of the pathogen (through increasing the cropping ratio of the resistant cultivar) caused the virulent strain of the pathogen to invade the system more rapidly. Cost of virulence, reflecting differences in pathogen infection rates between the four possible combinations of cultivar/pathogen strain, significantly affected durability of resistance, with the dynamics of the virulent and avirulent strains ranging from a case where the virulent strain of the pathogen died out to a case where the virulent strain of the pathogen invaded the resident pathogen population. An intermediate state, where the system reached equilibrium and the virulent strain of the pathogen neither became predominant nor died out, was defined as 'coexistence' of both strains of the pathogen. Occurrence of coexistence was directly related to the cost of virulence since it did not occur when virulence of the pathogen did not have a fitness cost. Two methods to include cost of virulence in the model gave similar results in relation to the two measures of durability of resistance studied.

Introduction

Growth in the productivity of agriculture during the last 50 years has relied, to a large extent, on the development of strategies for crop protection (pesticides, resistant cultivars or specific farming practices). It is generally recognized that both pesticides and cultivar resistance face major durability problems (Regev, 2002). Once such a crop protection technique is introduced, it is often only a matter of time before it loses its efficiency as a growing proportion of the targeted pest/pathogen becomes resistant (e.g., to fungicides). This problem can be managed as long as farmers have access to a wide range of alternative efficient crop protection techniques. However, the recent introduction of regulations for market approval has greatly decreased the number of commercialized active ingredients used in pesticides. In future, farmers may need to rely on a narrow range of chemical crop protection techniques and consequently will need to depend more on genetic resistance. Therefore, understanding and developing strategies for managing the durability of resistance in cultivars is a scientific issue with major economic stakes.

This problem of durability is particularly important in the case of the pathogen *Leptosphaeria maculans* that causes phoma stem canker in oilseed rape. Currently, the control of the disease through the use of fungicides is frequently only partially effective (Aubertot et al., 2006) and farmers often rely on cultivar resistance and specific cultural practices. Under some circumstances, major gene resistance used in cultivars has broken down shortly after its introduction into commercial cultivars. For example, the major resistance genes *Rlm1* and *Rlm6* were rendered ineffective within, respectively, 4–5 years and 3 years in France (Rouxel et al., 2003) and the major resistance gene in cultivar Surpass 400 was broken down in 3 years in Australia (Li et al., 2003).

Although mapping work has been done on *L. maculans* avirulence genes (Kuhn et al., 2006), the genetic basis of much of the resistance is not well understood in oilseed rape (Delourme et al., 2006) and strategies to maximize durability of resistance in commercial crops remain poorly developed and have mainly concentrated on crop rotation (Marcroft et al., 2002), burning or disposal of stubble (Marcroft et al., 2003) or ploughing (Turkington et al., 2000). Known major genes for resistance to *L. maculans* are scarce. In Europe, of the 10 such genes (*Rlm*) known in oilseed rape (Howlett, 2004), many have already been overcome. As a result, correct advice on optimum strategies for deployment of resistant cultivars is crucial to maximize durability of resistance.

However, because of the cost and time needed, few field experiments to study resistance durability have been done (Brun et al., 2000) and, in some situations, they may not be feasible. For instance, pyramiding and non-pyramiding of major genes of resistance have never been compared in field experiments, although pyramiding has been recently suggested as a way to improve durability of oilseed rape resistance to *L. maculans* (Li et al., 2004a). Models can be used to provide plant pathologists with a better insight into the relative effects of different agricultural practices and characteristics of the pathosystem on durability of resistance. Agricultural practices and strategies which can be investigated include crop rotation and spatial deployment of resistance genes (McDonald and Linde, 2002). However, before examining such strategies in detail, it is necessary to define a *base-line model*, discuss the assumptions it relies on and establish its validity as a starting point for further analysis. This is the aim of this paper. Hence, the emphasis of this work is on qualitative (rather than quantitative) analysis.

Van den Bosch and Gilligan (2003) developed a continuous model for a polycyclic disease epidemic and compared several ways to define durability of resistance. However, as they acknowledge in that paper, "the model used [...] is the simplest possible model that shows the effects of population dynamics and population genetics on durability" and does not include spatial nor temporal patterns. To incorporate spatial and temporal heterogeneity, it is necessary to introduce seasonality into the model. Here, we discuss differences caused by the introduction into the model of seasonality, with a sowing and a harvest date, when studying a polycyclic disease. When comparing models for monocyclic epidemics and polycyclic epidemics, we had found no significant difference in the effects studied (Pietravalle et al., 2004), possibly because a polycyclic epidemic can be considered as a series of successive monocyclic epidemics. Consequently, we decided to restrict this study to polycyclic epidemics as this led to a simpler model. Furthermore, and most importantly, we also introduced a cost of virulence. The aims of this paper are therefore (1) to explain the relationship between cropping ratio and durability of resistance, (2) to explain the relationship between cost of virulence and durability of resistance, (3) to compare two measures of durability of resistance and (4) to compare two models for introducing cost of virulence.

Materials and methods

The model

We consider a pathosystem with two host cultivars (resistant or susceptible) and two strains of the pathogen (virulent or avirulent). As well as introducing seasonality into the model, we also include two definitions of cost of virulence to represent the differences in 'total' infection rate between the four possible combinations of pathogen strain and cultivar. Further, in the context of this model, we include both qualitative resistance (complete resistance, mediated by a single gene) and quantitative resistance (incomplete resistance, mediated by one or more genes). Thus, where resistance is incomplete, it is possible for the avirulent pathogen to infect the resistant cultivar. These assumptions lead to a system of six linked ordinary differential equations (ODE) to describe the system within each growing season and a set of rules for the transfer of the pathogen and crop densities between seasons. Two equations describe the dynamics of the uninfected host, according to its susceptibility (resistant or susceptible), whereas four equations describe the dynamics of the pathogen, according to its virulence (virulent or avirulent) and the cultivar it infects (resistant or susceptible). We now derive the two models studied and define the two measures of durability used in this paper.

Within season dynamics

The densities of healthy tissue on susceptible and resistant cultivars are called S and R, respectively. In the absence of disease, both these densities increase logistically as the crop grows, between sowing and harvest. However, the increase in both healthy crop densities is slowed down or even reversed because of pathogen infection. Similarly, when present, each strain of the pathogen increases as a result of new infections and decreases as a result of death or cessation of sporulation. This is expressed as a set of six differential equations:

$$\frac{\mathrm{d}S}{\mathrm{d}t} = [\text{crop growth}]_{\mathrm{S}} - \left[\begin{array}{c}\text{disease due to the}\\ \text{virulent strain}\end{array}\right] - \left[\begin{array}{c}\text{disease due to the}\\ \text{avirulent strain}\end{array}\right]$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = [\text{crop growth}]_{\mathrm{R}} - \left[\begin{array}{c}\text{disease due to the}\\ \text{virulent strain}\end{array}\right] - \left[\begin{array}{c}\text{disease due to the}\\ \text{avirulent strain}\end{array}\right]$$

$$\frac{\mathrm{d}A_{\mathrm{S}}}{\mathrm{d}t} = \left[\begin{array}{c}\text{disease due to avirulent}\\ \text{spores transferred from}\\ \text{susceptible to susceptible cultivar}\end{array}\right] + \left[\begin{array}{c}\text{disease due to avirulent}\\ \text{spores transferred from}\\ \text{resistant to susceptible cultivar}\end{array}\right] - \left[\begin{array}{c}\text{pathogen death}\\ \text{or sporulation}\\ \text{cessation}\end{array}\right]$$

$$\frac{\mathrm{d}A_{\mathrm{R}}}{\mathrm{d}t} = \left[\begin{array}{c}\text{disease due to avirulent}\\ \text{spores transferred from}\\ \text{susceptible to resistant cultivar}\end{array}\right] + \left[\begin{array}{c}\text{disease due to avirulent}\\ \text{spores transferred from}\\ \text{resistant to resistant cultivar}\end{array}\right] - \left[\begin{array}{c}\text{pathogen death}\\ \text{or sporulation}\\ \text{cessation}\end{array}\right]$$

$$\frac{\mathrm{d}V_{\mathrm{S}}}{\mathrm{d}t} = \left[\begin{array}{c}\text{disease due to virulent}\\ \text{spores transferred from}\\ \text{susceptible to susceptible cultivar}\end{array}\right] + \left[\begin{array}{c}\text{disease due to virulent}\\ \text{spores transferred from}\\ \text{resistant to susceptible cultivar}\end{array}\right] - \left[\begin{array}{c}\text{pathogen death}\\ \text{or sporulation}\\ \text{cessation}\end{array}\right]$$

$$\frac{\mathrm{d}V_{\mathrm{R}}}{\mathrm{d}t} = \left[\begin{array}{c}\text{disease due to virulent}\\ \text{spores transferred from}\\ \text{susceptible to resistant cultivar}\end{array}\right] + \left[\begin{array}{c}\text{disease due to virulent}\\ \text{spores transferred from}\\ \text{resistant to resistant cultivar}\end{array}\right] - \left[\begin{array}{c}\text{pathogen death}\\ \text{or sporulation}\\ \text{cessation}\end{array}\right]$$

In the absence of disease, healthy crop densities of both resistant and susceptible cultivars increase logistically, with equal growth rate r ($r = r_R = r_S$) and with carrying capacities K_R and K_S. The pathogen has a polycyclic development with a base-line infection rate β (defined as the new area infected per lesion per unit time for the avirulent strain of the pathogen on the susceptible crop) and a rate of pathogen death and sporulation cessation μ. We also introduce a cost of virulence that affects the pathogen infection rate. To do so, we define parameters ε_1, ε_2 and ε_3 that represent the relative decreases in infection rates of the virulent pathogen on the susceptible crop, the avirulent pathogen on the resistant crop (possibly to zero) and virulent pathogen on the resistant crop, respectively. The parameters ε vary between 0 (no infection possible) and 1 (no decrease in infection rate). We also need to introduce the number (g) of lesions produced per infected area. In this study, to investigate the four objectives presented in the 'Results' section, we chose to keep the eight parameters ($r, K, \beta, \mu, g, \varepsilon_1, \varepsilon_2$ and ε_3) constant across growing seasons.

In a first approach, we assume that the cost of virulence ε affects infection and does not affect spore production (model 1) (Pietravalle et al., 2004). Within growing season, this leads, after setting $A = A_S + A_R$ and $V = V_S + V_R$, to a set of four differential equations, with parameters described in Table 1.

$$
\begin{aligned}
\frac{dS}{dt} &= r_S S\left(1 - \frac{S}{K_S}\right) - \beta SA - \varepsilon_1 \beta SV \\
\frac{dR}{dt} &= r_R R\left(1 - \frac{R}{K_R}\right) - \varepsilon_2 \beta RA - \varepsilon_3 \beta RV \\
\frac{dA}{dt} &= g\beta A(S + \varepsilon_2 R) - \mu A \\
\frac{dV}{dt} &= g\beta V(\varepsilon_1 S + \varepsilon_3 R) - \mu V
\end{aligned} \tag{1}
$$

In a second approach, we assume the cost of virulence ε affects spore production and does not affect infection (model 2). This leads to six differential equations:

$$
\begin{aligned}
\frac{dS}{dt} &= r_S S\left(1 - \frac{S}{K_S}\right) - \beta S(\varepsilon_1 V_S + \varepsilon_3 V_R) \\
&- \beta S(A_S + \varepsilon_2 A_R) \\
\frac{dR}{dt} &= r_R R\left(1 - \frac{R}{K_R}\right) - \beta R(\varepsilon_1 V_S + \varepsilon_3 V_R) \\
&- \beta R(A_S + \varepsilon_2 A_R) \\
\frac{dA_S}{dt} &= g\beta(A_S + \varepsilon_2 A_R)S - \mu A_S \\
\frac{dA_R}{dt} &= g\beta(A_S + \varepsilon_2 A_R)R - \mu A_R
\end{aligned}
$$

Table 1. Variables and parameters used in the models

	Description	Dimension
Variables		
R	Density of uninfected resistant crop	L^2L^{-2}
S	Density of uninfected susceptible crop	L^2L^{-2}
A_R	Density of avirulent lesions on resistant crop	L^{-2}
A_S	Density of avirulent lesions on susceptible crop	L^{-2}
V_R	Density of virulent lesions on resistant crop	L^{-2}
V_S	Density of virulent lesions on susceptible crop	L^{-2}
Parameters		
r_R, r_S	Logistic growth rate of resistant or susceptible crop	t^{-1}
K_R, K_S	Carrying capacity of resistant or susceptible crop	L^2L^{-2}
g	Number of lesions produced per infected area	L^{-2}
μ	Rate of pathogen death and sporulation cessation	t^{-1}
β[a]	New area infected per lesion per unit time (base-line)	L^2t^{-1}
$\varepsilon_{1,2,3}$[a]	Cost of virulence	1
λ	Rate of transfer of pathogen between seasons	1
θ	Proportion of crop sown which is resistant	1

[a] New area infected per lesion per unit time for the avirulent pathogen on the susceptible and resistant crops are β and $\varepsilon_2\ \beta$ respectively and new area infected per lesion per unit time for the virulent pathogen on the susceptible and resistant crops are $\varepsilon_1\ \beta$ and $\varepsilon_3\ \beta$ respectively.

$$\frac{dV_S}{dt} = g\beta(\varepsilon_1 V_S + \varepsilon_3 V_R)S - \mu V_S$$
$$\frac{dV_R}{dt} = g\beta(\varepsilon_1 V_S + \varepsilon_3 V_R)R - \mu V_R \qquad (2)$$

Transition between seasons

Having described the derivation of the *within season* model, we describe the dynamics between two growing seasons. The parameter (λ) for transfer of pathogen between seasons represents the proportion of infected material left in the field from one cropping season to the next as a result of environmental factors and farming practices (e.g. burning of stubble, ploughing, etc.). Because one aim of this study was to investigate the similarities and differences between a continuous and a seasonal model, rather than to investigate agricultural practices, we decided to keep constant across seasons the initial total crop density H_0 and the proportion θ of crop sown in the region which was resistant. Consequently, the initial total crop density and carrying capacity for each cultivar are given by

$$K_R = \theta K, \quad K_S = (1-\theta)K,$$
$$R(0) = \theta H_0, \quad S(0) = (1-\theta)H_0$$

where K is the total (i.e. over both cultivars) carrying capacity and $t=0$ is the start of each growing season.

Furthermore, the initial density of pathogen present at the start of a season is a fraction λ of the total density remaining at the end of the previous season. $V(0)$ and $A(0)$ are initial conditions to be chosen the first season they are in the system. Then, for each subsequent growing season:

$$V(0) = \lambda V(\text{end of previous season})$$
$$A(0) = \lambda A(\text{end of previous season})$$

Numerical simulations and measures of durability of resistance

All simulations are started with only the susceptible cultivar and the avirulent strain of the pathogen. This system was solved numerically until a steady state was reached. Stabilization of the system was assessed by comparing both final densities (A and S) at the end of two consecutive seasons. The system was considered to be stabilized if both densities (A and S) differed by less than 1% when measured at the end of two consecutive seasons, that is $\frac{A(t_{i+1})-A(t_i)}{A(t_i)} < 0.01$ and $\frac{S(t_{i+1})-S(t_i)}{S(t_i)} < 0.01$ where $A(t_i)$ and $S(t_i)$ are densities of the avirulent pathogen and susceptible crop at the end of season i and the pathogen was considered as extinct for a density smaller than 10^{-14} at the end of any season.

We then assumed that the virulent strain of the pathogen was already present in very small quantities in the background of the system and could start to spread when the resistant crop was introduced. As a result, we introduced the resistant cultivar and virulent strain of the pathogen at the start of the season following stabilization of the initial system. The virulent strain of the pathogen was introduced at a very low density $V(0)=A(0)/1000$, where $A(0)$ and $V(0)$ are the densities of the avirulent and virulent strains of the pathogen, respectively, at the time of introduction of the virulent strain of the pathogen.

Two measures of durability of resistance were studied. Firstly, the widely recognized time until take-over of the virulent pathogen is defined as the time for the virulent pathogen to reach a given threshold (95% in this work) in the pathogen population, that is the time until $V/(A+V) \geq 0.95$ (van den Bosch and Gilligan, 2003). Secondly, because it is often thought that yield is related to green canopy area duration (Gaunt, 1995), we also introduced a measure of durability of resistance based on the crop estimated green canopy area duration. We calculated this as the sum, over the entire growing season, of the healthy tissue for each crop separately. Soon after the resistant cultivar was introduced, it had an advantage over the susceptible cultivar but this advantage decreased with time as the virulent strain of the pathogen developed, so that differences in green canopy area duration between the resistant and susceptible cultivars became small. As a result, we define the usefulness time of the resistant crop as the number of seasons before the estimated gain in green canopy area duration per plant due to the use of the resistant cultivar becomes negligible (<5%), that is the time until there is no advantage for the farmer to use a resistant cultivar rather than a susceptible cultivar.

Results

In this section, we successively demonstrate whether (1) durability of resistance responds to cropping ratio and compare this to results from the previously published continuous model (van den Bosch and Gilligan, 2003), (2) cost of virulence (through ε_1, ε_2 and ε_3) affects durability of resistance, (3) the two measures of durability of resistance differ and (4) the two models introduced differ.

(1) Increasing the proportion of resistant cultivar θ significantly reduces the time until take-over (Figures 1 and 2). This result was comparable to that obtained when using a continuous model. On the other hand, usefulness time is not affected by increasing cropping ratio θ.

(2) Figures 1 and 2 also show that, when the cost of virulence affects infection (model 1), take-over time decreases with increasing ε_1 and ε_3 (results not shown for ε_3) and increases with increasing ε_2. Small values of ε_1 and ε_3 and large values of ε_2 produce extreme cases where both strains of the pathogen coexist (infinite take-over time) or the virulent strain of the pathogen dies out. Coexistence, defined as an equilibrium state where the virulent strain of the pathogen neither dies out nor takes over, is therefore directly related to the cost of virulence. When usefulness time is the measure of durability of resistance, similar trends are observed, with the yield per plant for the resistant cultivar only remaining significantly greater than that for the susceptible

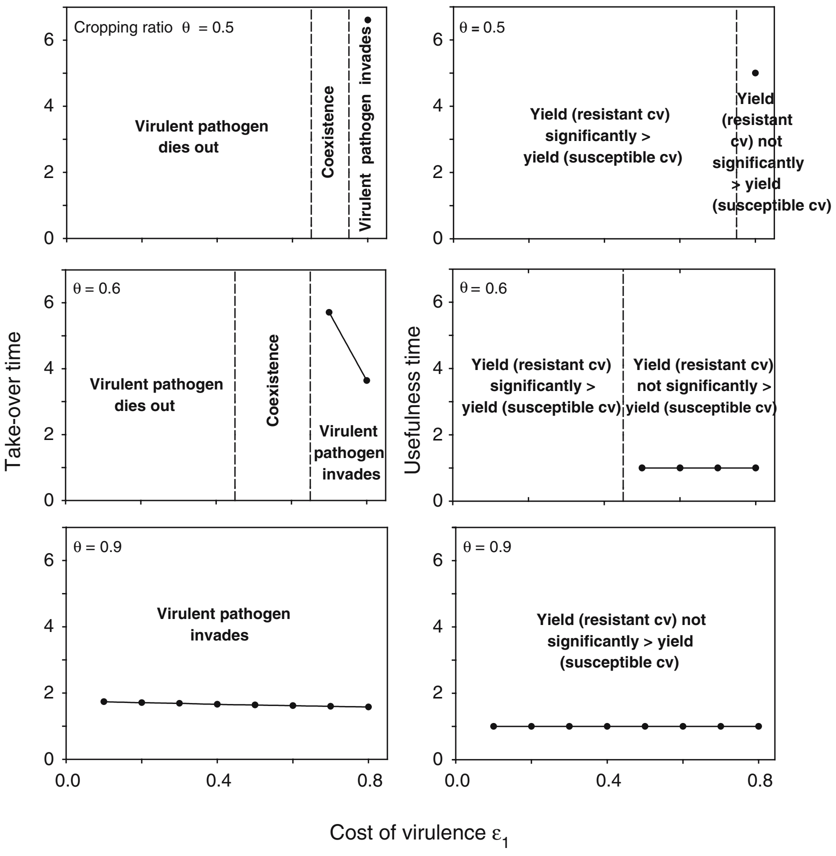

Figure 1. Effects of cost of pathogen virulence (ε_1) and cropping ratio (θ) on the two measures of durability of host resistance (take-over time and usefulness time) to when the cost of virulence is assumed to affect infection (model 1). Model parameter (Table 1) values used in these simulations are $\beta = 0.015$, $\lambda = 0.05$, $\varepsilon_2 = 0.6$, $\varepsilon_3 = 0.9$, $\mu = 30$, $g = 2000$, $r_S = 18.4$, $r_R = 18.4$, $K = 3.5$, $H_0 = 0.01$, $A(0) = 0.2$ and $V(0) = 0.001\ A(0)$. A smoothed spline was fitted to the calculated take-over and usefulness times.

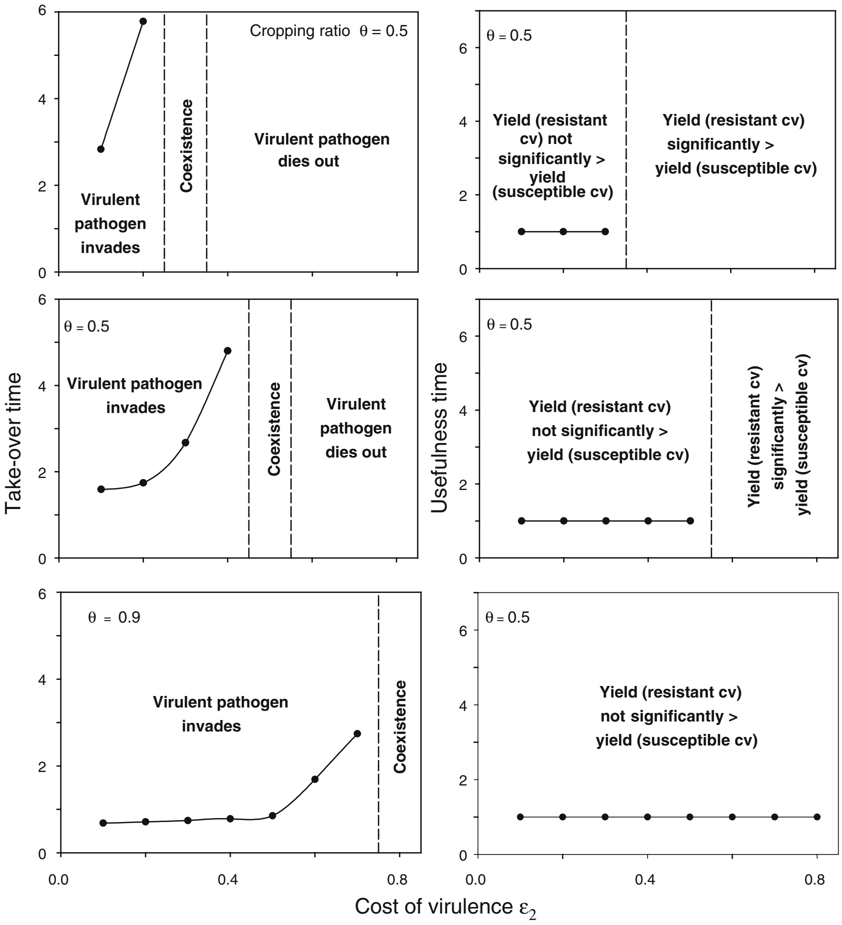

Figure 2. Effects of cost of pathogen virulence (ε_1) and cropping ratio (θ) on the two measures of durability of host resistance (take-over time and usefulness time) to when the cost of virulence is assumed to affect infection (model 1). Model parameter (Table 1) values used in these simulations are $\beta = 0.015$, $\lambda = 0.05$, $\varepsilon_1 = 0.4$, $\varepsilon_3 = 0.9$, $\mu = 30$, $g = 2000$, $r_S = 18.4$, $r_R = 18.4$, $K = 3.5$, $H_0 = 0.01$, $A(0) = 0.2$ and $V(0) = 0.001\ A(0)$. A smoothed spline was fitted to the calculated take-over and usefulness times.

cultivar for small values of ε_1 and ε_3 (results not shown for ε_3) and large values of ε_2.

(3) The two measures of durability of resistance used in this paper are measured in the same units (number of seasons) and are therefore directly comparable. Although it might be expected that the advantage of the resistant cultivar over the susceptible cultivar would decrease as the population of the virulent strain of the pathogen increases, and that the two measures of durability of resistance are similar, Figures 1 and 2 show that this is not the case. For instance, even with the virulent and avirulent strains of the pathogen coexisting, the resistant cultivar may produce a yield (as measured by green canopy area duration) not significantly greater than that of the susceptible cultivar. Furthermore, when the virulent strain of the pathogen does take over, making the resistant cultivar 'useless', the time until take-over is always larger than the usefulness time.

(4) Although results for simulations when cost of virulence was assumed to affect the pathogen spore production (model 2) are not illustrated, there was no difference between the two models in terms of usefulness time and take-over time.

Discussion

Introduction of seasonality into the continuous model of van den Bosch and Gilligan (2003) did not qualitatively change the effect of cropping ratio on the durability of resistance. However, introduction of a cost of virulence (ε) greatly affected the dynamics of the virulent and avirulent pathogen strains and the measures of durability of resistance. The most important effect on the dynamics of the pathogen is the possibility of coexistence of the two strains for certain values of ε. Since results were qualitatively similar for the two measures of durability of resistance and similar patterns were observed for increasing ε_1 or increasing ε_3, we will concentrate on the cases where take-over time is used as the measure of durability of resistance and where cost of virulence is expressed through ε_1 and ε_2. To understand the possibility of coexistence in relation to cost of virulence, let us assume a very simple case where ε_2 is very small and ε_1 and ε_3 are equal ($\varepsilon_1 = \varepsilon_3 = \varepsilon$). If we consider an initial system in equilibrium with only the avirulent strain of the pathogen and the resistant and susceptible cultivars present, it follows that, if ε is 'large enough' and the fraction of S at equilibrium is 'not too large', the virulent strain of the pathogen will invade. Similarly, if we consider an initial system at equilibrium with only the virulent strain of the pathogen and the resistant and susceptible cultivars present, it follows that the avirulent strain of the pathogen will invade provided the fraction of S at equilibrium is 'large enough'. Thus, in a system where both strains of the pathogen are present, this shows that, for some costs of virulence (i.e. combinations of ε^s), coexistence can occur since both strains can re-invade the system if they reach small proportions of the population. This result seems in accordance with observed field data; even when a major gene for resistance has broken down, coexistence has occurred (Brun et al., 2004).

Results of this work demonstrate that the two measures of durability of resistance studied are not equivalent (e.g. both strains of the pathogen can coexist (hence no take-over) while the yield per plant of the resistant cultivar becomes significantly less than that of the susceptible cultivar). This emphasizes the importance of clearly differentiating study of pathogen populations from study of plant productivity. Although different combinations of parameters produced different values for take-over time, the usefulness time was always shorter than the take-over time. This suggests that, although the virulent strain of the pathogen may sometimes take longer to invade the pathogen population, differences in take-over time will have little effect on the changes in green canopy area duration of the plant and can be explained, similarly to the appearance of coexistence of both strains of the pathogen, as another direct consequence of the introduction of costs of virulence in the model. For instance, if we consider the very simple case where both susceptible and resistant crops are present in similar proportion, the usefulness time would be expected to be much shorter than the take-over time because the loss of usefulness of the resistant crop can be due to the infection by the avirulent strain of the pathogen. Therefore, before such results can be used in practice, further model studies are needed to confirm our findings. For instance, one factor which should be tested is the period used to calculate the green canopy area duration and usefulness time. One alternative to the solution presented in this work would be to restrict the period for calculating the green canopy area duration to later stages of growth rather than to the entire growing season. If these results are shown to be robust, one consequence is that total annual increases in yield obtained through the introduction of resistant cultivars would be directly related to the proportion of the area sown with the resistant cultivar (θ). This suggests that it might be most profitable to introduce a resistant cultivar over a large area, to produce a larger gain in *total yield*, even though this strategy would decrease the time for take-over by the virulent strain of the pathogen.

To date, many field experiments investigating durability of resistance have concentrated on pathogen population frequencies (Brun et al., 2000; Rouxel et al., 2003). This work shows that such observations may not give the best insight into the effects of a breakdown in resistance and that the host green canopy area duration should also be investigated. The results also show that cost of virulence greatly affects durability of resistance, suggesting that experiments must focus on accurately estimating such fitness cost at each stage (Li et al., 2004b; Huang et al., 2006) of the pathogen life cycle to obtain an overall cost of virulence as defined for this model.

This model can be used to investigate the effects of spatial and temporal strategies for deployment of resistance genes on durability of resistance. For instance, spatial effects can be investigated further at the local scale. Temporal effects to be analysed could include agricultural practices such as crop rotation through varying cropping ratio, possibly combined with fungicide treatments (hence varying the rate of pathogen death and cessation of sporulation μ as a function of time) to investigate the issue of inoculum thresholds (Wherrett et al., 2004). Furthermore, some of the simplifying assumptions used in this model may be relaxed. For instance, it was assumed that the cost of virulence ε was constant with time. It can be argued that such a cost may diminish as a function of time. Other areas of research to be pursued include pyramiding of major resistance genes or introducing a probability of mutation (or gene deletion) for the pathogen.

Furthermore, the model developed can be used to analyse alternative measurements of durability, in particular through economic indicators. In the economic literature (Regev et al., 1983; Hurley et al., 2001), durability is generally measured by the accumulated profit for farmers over a long period of time (say 20 years). To implement such an indicator, a damage function that describes the fact that yield loss increases with increasing density of pathogen that can survive on each crop would need to be added. The damage is small if the frequency of the virulent pathogen is very small and if the resistant cultivar is efficient in reducing the density of the avirulent pathogen strains. However, the damage becomes significant as the frequency of the virulent pathogen and the density of pathogens increase. In an economic framework, a strategy is durable if it preserves the long-term economic gain without producing excessive short-term economic losses. Here, the long-term gain is generally obtained if the frequency of the virulent pathogen is kept small; the cultivar is then still efficient in controlling the damage caused by the pathogen. However, such an objective may be achieved only by preserving some avirulent pathogen strains in the short term, which would increase damage and give some short-term economic losses. Such an analysis would be worthwhile for two reasons. Firstly, most of the applied economic literature on the durability of resistance considers insect pests and, to our knowledge, no application has been made to fungal pathogens. Secondly, we expect the usefulness time indicator to be correlated with the accumulated economic profit indicator. If confirmed, this would increase the interest in using the 'usefulness time indicator'.

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