

Induced plant defence and the evolution of counter-defences in herbivores

Shea N. Gardner¹ and Anurag A. Agrawal^{2*}

¹*Biology and Biotechnology Research Program, Lawrence Livermore National Laboratory, PO Box 808, L-448, Livermore, CA 94551, USA and* ²*Department of Botany, University of Toronto, 25 Willcocks Street, Toronto, Ontario M5S 3B2, Canada*

ABSTRACT

We examine how induced plant defences affect the evolution of resistance in herbivores (i.e. the ability to overcome plant defences) compared with constitutive defence strategies. Since resistance of herbivores may evolve as a result of major monogenic and/or quantitative (polygenic or gene amplification) genetic sources, and the selective pressure imposed by plant defences affects the rate of evolution of each genetic source of resistance, we incorporate both into a model of herbivore evolution. We combine Mendelian single-locus and quantitative genetic models with a logistic population growth model based on an empirical plant–herbivore system. Induced defences may delay the evolution of both quantitative and major gene resistance and thus depress herbivore population size for more than 50 herbivore generations longer than constitutive defences. This increased longevity in the effectiveness of plant defence is associated with the production of substantially less plant defence over the long term, hence maximizing the benefit to cost ratio from the plant's perspective.

Keywords: evolution of resistance, induced versus constitutive defence, major gene resistance, phenotypic plasticity, plant–insect interactions, quantitative characters.

INTRODUCTION

Host defences can take many forms, including those that are expressed all of the time (constitutive defences) and those that are only expressed after an initial cue that predators or parasites are present (phenotypically plastic, or induced defences) (Karban and Baldwin, 1997; Tollrian and Harvell, 1999). Constitutive and induced defences are likely to have fundamentally different consequences for populations of predators or parasites in ecological and evolutionary time. For example, induced plant defences have the potential to regulate herbivore populations because they act in a density-dependent manner; constitutive defences do not have this potential (Haukioja and Hakala, 1975; Seldal *et al.*, 1994; Agrawal and Karban, 2000). In this study, we examine how induced plant defences affect the evolution of resistance in herbivores (i.e. the ability to overcome plant defences) compared with constitutive defence strategies using combined Mendelian single-locus and quantitative genetic models.

* Author to whom all correspondence should be addressed. e-mail: agrawal@botany.utoronto.ca
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The speed at which resistance evolves depends crucially on the interaction between the selection pressure applied and the genetic mechanisms responsible for resistance (Gould, 1998). Quantitative resistance evolves gradually as a result of selection with low or incrementally increasing doses of a mortality agent (Via, 1986); quantitative resistance may evolve by the accumulation of many resistant alleles at different loci, each of small effect, by gene amplification, or by sequential mutations within a gene. In contrast, major gene (or monogenic) resistance, conferred by a single gene of large effect, rises exponentially at a rate that depends on the selection pressure applied. Monogenically resistant populations usually appear to emerge suddenly after several successive exposures to strong selective agents (Georghiou and Taylor, 1977; Gardner *et al.*, 1998). Both quantitative and monogenic variation in herbivores have been observed for host plant use and for detoxification of defensive compounds (Via, 1990; Berenbaum and Zangerl, 1992; Futuyma *et al.*, 1995; Nielsen, 1997; Gould, 1998). In addition, quantitative or major gene resistance may evolve in response to the same selective agent in different populations of the same species (Lande, 1983; Gardner *et al.*, 1998). Thus, it is critical to allow for the possibility that herbivores may evolve resistance to plant defences through quantitative genetic or major monogenic mechanisms, or both.

If induced defences reduce the ability of herbivores to evolve resistance compared with constitutive strategies, and adapted herbivores are more damaging than unadapted herbivores, then natural selection may favour or at least maintain inducible defence. The key notion is that when herbivore densities are low, a plant may produce no or low levels of defence, saving limiting resources and reducing selection on the herbivores. However, when herbivore densities rise, the plant sharply increases defence. Various factors may affect the relative benefits of induced versus constitutive defence. These include the number of herbivores required to trigger the defence, the concentration or strength of selection provided by the defence when it is induced, and how long the defence persists after herbivore numbers have dropped as a result of control by that defence.

In this paper, we consider the effects of these factors on the ability of induced versus constitutive resistance to suppress herbivore populations and to delay the evolution of resistance to host defences using a combined population and genetic modelling approach. We integrated both quantitative genetic and Mendelian single-locus models with a logistic model of population growth. In particular, we parameterized our model based on a system of spider mite herbivores that colonize novel cucurbit host plants. Cucurbits are characterized, in part, by terpenoid chemicals called cucurbitacins, the most bitter compounds known (Metcalf and Lampman, 1989). In several experiments, including ones with cucurbits, spider mites have been shown to adapt locally to atypical host plants, evolutionarily overcoming the effectiveness of plant defences (Gould, 1979; Fry, 1989; Agrawal, 2000). Thus, our modelling efforts were motivated and parameterized by previous empirical studies.

METHODS

Overview

We consider how three responses of herbivore populations are affected by plant defence: logistic population growth, evolution of quantitative resistance and evolution of major monogenic resistance. For constitutive defence, a plant produces toxins in every herbivore

generation, regardless of the herbivore population size. For inducible defence, at low herbivore densities the plants produce no toxin. Once the herbivore population size exceeds a threshold size of N_{induce} , we assume that herbivores induce plants to produce toxins. These toxins reduce herbivore survival by an amount that depends on the toxin concentration z_d , as we have observed in the spider mite system. Survivors mate randomly and produce offspring in which both quantitative genetic and major monogenic resistances have increased from the parental generation, assuming diploid genetics. In our model and in nature, both types of resistance are selected for and potentially evolve simultaneously, although not independently. If the herbivore population size drops below N_{induce} , then after q herbivore generations, host plants cease to express the defence. Thus, q is a parameter characterizing the longevity of the defence. Herbivores are assumed to have many generations per plant generation (i.e. plants are perennial). We examine how four factors affect the length of time required until herbivores evolve resistance to host plant toxins: (1) the herbivore population growth rate; (2) the threshold herbivore population size, N_{induce} , for induction; (3) the toxin concentration z_d ; and (4) the persistence, q , of defence. For simplicity, our model assumes that plants either employ constitutive or induced defence. As much as possible, we have relied on empirical data from the mite–cucurbit system to parameterize our model.

We selected parameter values based on experimental data from a system of generalist spider mite (*Tetranychus urticae*) herbivores that were new colonists on *Cucumis sativus* plants (Agrawal *et al.*, 1999; Agrawal, 2000). Spider mites are broadly distributed generalist herbivores (>900 recorded hosts) with rapid generation times (7–10 days). Mites are cell-content feeders, their survival is affected by cucurbitacins and they are relatively poor dispersers (i.e. they do not fly). Calculations were performed using True BASIC software and the program is available upon request from S.N.G.

Total survival

Individuals may survive as a result of either major gene resistance or quantitative resistance. A fraction $w_m(z_d)$ survive due to major gene resistance and, of the $1 - w_m(z_d)$ that would have died, a fraction $w_q(z_d)$ survive due to quantitative resistance (the converse argument yields the same equation). Thus, the total fraction of the population that survives is

$$w_{\text{tot}}(z_d) = w_m(z_d) + w_q(z_d) - w_m(z_d)w_q(z_d) \quad (1)$$

Major gene resistance

Selection increases the frequency of the major allele R conferring resistance at a rate determined by the relative fitnesses w_{RR} , w_{Rr} and w_{rr} of the resistant genotype RR, heterozygote Rr and susceptible genotype rr, respectively. The relative fitnesses, which in this case are the survival probabilities, are $w_{RR} = 1$, $w_{Rr} = 1 - ks(z_d)$ and $w_{rr} = 1 - s(z_d)$, respectively. The function $s(z_d)$ is the dose-dependent strength of selection against susceptible individuals exposed to toxin concentration z_d , and k is the dominance of R over r. The resistant allele R is dominant when $k = 0$, the effects are additive when $k = 0.5$ and R is recessive when $k = 1$. If p_t is the frequency of the R gene in generation t , and $1 - p_t$ is the frequency

of r , the change in p after one generation of selection is given by (modified from Crow, 1986):

$$p_{t+1} = \frac{(1 - w_q) [p_t^2 + p_t(1 - p_t)(1 - ks(z_d))] + w_q p}{w_{\text{tot}}(z_d)} \quad (2)$$

The first term in the numerator indicates that a fraction $1 - w_q$ of individuals that do not survive as a result of quantitative resistance experience selection for major gene resistance. Those that do survive as a result of quantitative resistance (the second term in the numerator) do not undergo selection for an increase in major gene resistance. The mean fitness $w_m(z_d)$ associated with the major locus for resistance is

$$w_m(z_d) = p_t^2 + 2p_t(1 - p_t)(1 - ks(z_d)) + (1 - p_t)^2(1 - s(z_d)) \quad (3)$$

This represents the fraction of the population that survives a dose z_d as a result of major gene resistance. Sometimes $w_m(z_d)$ may be written simply as w_m . For the dose-dependent strength of selection, we used

$$s(z_d) = 0.0082z_d \quad (4)$$

where z_d is in units of μg cucurbitacin per gram dry weight of plant tissue, estimated from experiments comparing spider mite fitness (measured in terms of survival) at different cucurbitacin concentrations (Agrawal *et al.*, 1999). The initial frequency of R in the herbivore population is p_0 , determined by mutation–selection balance of a population that uses undefended plants assuming a mutation rate to resistance of 10^{-6} per generation (Falconer, 1989), yielding $p_0 = 10^{-6}$. We discuss briefly the effects of variation in the initial frequency p_0 of the major resistance allele.

Quantitative resistance

A fraction $f_i(z)$ of individuals in generation t have resistance z . The probability that an individual with resistance z survives a dose z_d due to quantitative resistance is $p(z, z_d)$. The total fraction of the population surviving a dose z_d due to quantitative resistance is

$$w_q(z_d) = \int_{-\infty}^{\infty} p(z, z_d) f_i(z) dz \quad (5)$$

where the subscript q represents quantitative resistance. As with w_m , $w_q(z_d)$ may be written simply as w_q . We assume that the defence does not kill herbivores with a resistance of at least z_d , but that the survival probability of individuals with resistance below z_d is reduced, giving

$$p(z, z_d) = \begin{cases} \exp\left(-\frac{(z - z_d)^2}{2\sigma_s^2}\right) & z < z_d \\ 1 & z \geq z_d \end{cases} \quad (6)$$

Other sources of mortality that may act independently of plant defence and herbivore resistance, such as predation, do not differentially affect resistant and susceptible pests, so are included by their effects on population growth rate (see ‘Size of the herbivore population’ below). Although individuals with resistance below z_d are only partially resistant to the

toxin concentration in the plant, some may survive for a number of reasons. For example, they may survive because they augment their diet with less toxic material, because they are in a less susceptible stage of development or because they have more stored fat reserves. These survivors with resistance below z_d may mate with other fully or partially resistant individuals, and recombination may result in offspring that can survive even higher doses. The parameter σ_s determines the width of the selection curve. In the limit as σ_s goes to 0, truncation selection results. In the limit as σ_s goes to infinity, there is no selection, since $p(z, z_d) \rightarrow 1$ for all z .

We model the evolution of quantitative resistance using standard Gaussian models (Lande, 1976; Falconer, 1989), with some modifications to incorporate the effects of major gene resistance. In generation t , the distribution $f_t(z)$ of individuals with resistance z is normal with mean \bar{z}_t and phenotypic variance σ_t^2 :

$$f_t(z) = \frac{1}{\sigma_t \sqrt{2\pi}} e^{-\frac{1}{2}((z - \bar{z}_t)/\sigma_t)^2} \quad (7)$$

In induced cucumber plants, first true leaves produce up to 100 μg cucurbitacin per gram of dry weight plant tissue, approximately 50% more than in uninduced controls (Agrawal *et al.*, 1999). Based on these empirical results, we use a value for the concentration of plant defence in uninduced plants of 60 $\mu\text{g} \cdot \text{g}^{-1}$. We assumed that initially in a mite population that has not been exposed to cucurbitacins, $\bar{z}_0 = 60 \mu\text{g} \cdot \text{g}^{-1}$. Cotyledons may produce substantially more, up to 800 $\mu\text{g} \cdot \text{g}^{-1}$ (Agrawal *et al.*, 1999). Phenotypic variance σ_t^2 is the sum of the additive genetic variance $V_A(t)$ and environmental variance V_E . We assume that there is no non-additive genetic variance and that V_E is constant over time. $V_A(t)$ changes with selection as a result of linkage disequilibrium (see below). Thus, $\sigma_t^2 = V_A(t) + V_E$ and narrow sense heritability is $h_t^2 = V_A(t)/\sigma_t^2$, which we assume starts at 0.5 in an unexposed population of herbivores (e.g. Berenbaum and Zangerl, 1992).

Dynamics of the quantitative mean resistance

After selection and before reproduction, the mean quantitative resistance of the population is

$$\bar{z}_{tw} = \frac{(1 - w_m) \int_{-\infty}^{\infty} zp(z, z_d) f_t(z) dz + w_m \int_{-\infty}^{\infty} zf_t(z) dz}{w_{\text{tot}}(z_d)} \quad (8)$$

The first term in the numerator represents selection on the quantitative mean for the fraction $1 - w_m$ of individuals that do not survive as a result of major gene resistance. The second term in the numerator indicates that a fraction w_m that survive from major gene resistance do not experience selection for an increase in quantitative resistance, so their quantitative mean resistance remains the same as before selection:

$$\int_{-\infty}^{\infty} zf_t(z) dz = \bar{z}_t$$

Substituting in equations (1), (5) and (6) gives

$$\bar{z}_{tw} = \frac{(1 - w_m) \left(\int_{-\infty}^{z_d} z \exp(-(z - z_d)^2 / (2\sigma^2)) f_t(z) dz + \int_{z_d}^{\infty} z f_t(z) dz \right) + w_m \bar{z}_t}{(1 - w_m) \left(\int_{-\infty}^{z_d} \exp(-(z - z_d)^2 / (2\sigma^2)) f_t(z) dz + \int_{z_d}^{\infty} f_t(z) dz \right) + w_m} \quad (9)$$

Methods for computing the integrals in equation (9) are presented in the Appendix.

Dynamics of the mean quantitative resistance after reproduction

We computed the evolutionary dynamics of herbivore resistance to plant defence following reproduction using the fundamental equation of quantitative genetics. To account for the fact that the population is finite, however, we modify this equation slightly so that, if survival is very low, then no individuals with quantitative resistance survive, since it does not make sense for only a fraction of an individual to survive. The size of the population in generation t is $N(t)$. If at least one individual survives [$w_{tot}(z_d) \geq 1/N(t)$], then the usual equation for the mean holds:

$$\bar{z}_{t+1} = \bar{z}_t + h^2 (\bar{z}_{tw} - \bar{z}_t) \quad (10)$$

The mean after selection but before reproduction is \bar{z}_{tw} and the mean after selection and reproduction is \bar{z}_{t+1} . Since individuals are discrete rather than continuous entities, if the surviving fraction is smaller than $1/N(t)$, it is improbable that any individuals will live, since the population is finite. As a result, when a single individual is unlikely to survive toxin exposure [$w_{tot}(z_d) < 1/N(t)$], the mean is reset to a low starting value:

$$\bar{z}_{t+1} = \bar{z}_0 \quad (11)$$

and $N(t+1) = N_{min}$. If no mites survive, the herbivore population can only persist if a mite colonizes the plant. Because mites do not fly and dispersal is so dangerous, mites typically only disperse when conditions are very poor or when the population is seriously overcrowded. We assume new colonist mites come from a source population that does not have quantitative resistance. The immigration of a few susceptible mites is important for recolonization, but has virtually no effect on population mean resistance if these mites immigrate into a substantially larger population. In contrast, for the evolution of major monogenic resistance, the allele frequency p_t increases in every generation of toxin exposure according to equation (1), regardless of the herbivore population size, rather than being reset to the initial p_0 . Otherwise, if the major monogenic frequency is reset to p_0 , major monogenic resistance is never predicted to evolve even under strong selection. This does not reflect those empirical cases in which herbivores can and do evolve the major monogenic resistance that we are attempting to model.

Changes in heritability with recurrent selection

Because selection alters additive genetic variance due to departures from linkage equilibrium, the heritability of quantitative resistance changes with selection (Bulmer, 1980). Although linkage disequilibrium is not responsible for changes in the mean in the absence of epistatic interactions (such changes result instead from altered allele frequencies), linkage disequilibrium may influence the response to selection by changing heritability. After t generations of selection, the heritability is

$$h^2(t) = \frac{V_A(t)}{\sigma_t^2} \quad (12)$$

When $w_q(z_d) \geq 1/N(t)$, the additive genetic variance after $t + 1$ generations of selection is

$$V_A(t + 1) = \frac{1}{2}(1 - h^2(t)c(c - y))V_A(t) + \frac{1}{2}V_A(0) \quad (13)$$

where

$$y = \frac{z_d - \bar{z}_t}{\sigma_t} \quad \text{and} \quad c = \frac{1/(\sqrt{2\pi})e^{-(y^2/2)}}{w_q(z_d)} \quad (14)$$

(Bulmer, 1980). When $w_q(z_d) < 1/N(t)$, then $V_A(t + 1) = V_A(0)$.

Alternatively, heritability could depend on the mean resistance \bar{z}_t . When resistance alleles are at low frequencies, additive genetic variance and, therefore, heritability, are also low. Initially, heritability rises with the frequencies of resistant alleles, but then declines again as alleles near fixation. The results were qualitatively and quantitatively similar to those assuming that heritability changes only as a result of linkage disequilibrium, so are not presented here.

Size of the herbivore population

The herbivore population grows in a density-dependent fashion, following a discrete analog of logistic growth:

$$N(t + 1) = (N(t) + N(t)\lambda(1 - N(t)/N_{\max}))w_{\text{tot}}(z_d) \quad (15)$$

where N_{\max} is the maximum size (carrying capacity) of the mite population on a plant. If $N(t) = N_{\max}$, then population size the following generation depends only on survival $w_{\text{tot}}(z_d)$. If $N(t) < N_{\max}$, then the population in $N(t + 1)$ depends on both the rate of increase $\lambda(1 - N(t)/N_{\max})$ and $w_{\text{tot}}(z_d)$. We used $\lambda = 0.3$ based on experimental data from Agrawal (2000) and Agrawal *et al.* (1999), and assumed that N_{\min} individuals colonize a plant. The population growth parameter λ takes into account predation, assuming that predators do not discriminate on the basis of herbivore resistance. If $N(t)$ drops below N_{\min} , then we assume that recolonization occurs, so that $N(t + 1) = N_{\min}$.

RESULTS

Evolutionary implications of constitutive plant defence

A herbivorous spider mite population on an undefended plant is predicted to reach carrying capacity after approximately 35 herbivore generations, while the same population (naive to defensive cucurbitacins) on a constitutively defended plant producing a cucurbitacin concentration of $100 \mu\text{g} \cdot \text{g}^{-1}$ dry leaf [initially reducing herbivore fitness by $1 - w_{\text{tot}}(z_d) = 82\%$] does so after 70 generations (Fig. 1a). On the constitutively defended plant, major gene resistance evolves after about 30 herbivore generations, and herbivore numbers subsequently explode (Fig. 1b). Because selection for resistance is strong from the outset, gradual evolution of quantitative resistance is not predicted and, once major gene resistance

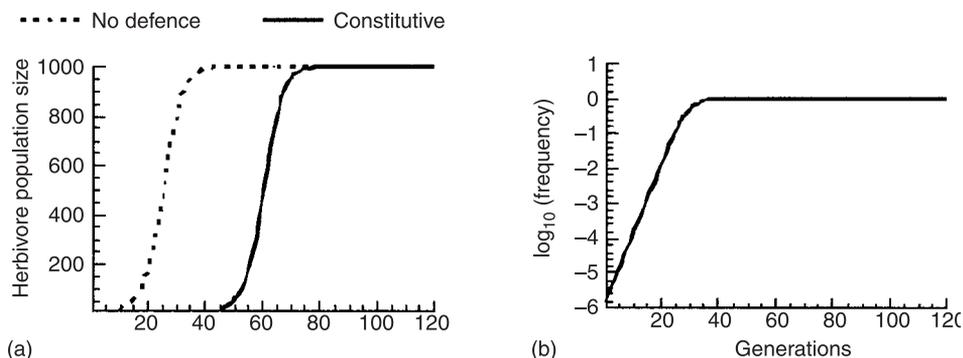


Fig. 1. (a) Herbivore population size over time on undefended and constitutively defended plants at a concentration of $100 \mu\text{g}$ cucurbitacin per gram of dry weight plant tissue. (b) The frequency of the major allele for resistance on plants with constitutive defence. The frequency of the major allele for resistance in the herbivore population increases rapidly in response to constitutive defence at this concentration. The number of colonists N_{\min} is one individual. Parameters used in this and subsequent figures, unless otherwise specified, are $k = 0.5$, $p_0 = 10^{-6}$, $\lambda = 0.3$, $N_{\max} = 1000$ and $N_{\min} = 1$.

confers survival to the herbivores, there is no selection for quantitative resistance. In the case of undefended or constitutively defended plants, the rapid growth of herbivore populations is likely to result in severe reductions in plant fitness (e.g. Agrawal and Karban, 1997).

Toxin concentration of inducible defence

In a plant with inducible defence at a modest dose of $80 \mu\text{g} \cdot \text{g}^{-1}$ cucurbitacin (initially reducing herbivore fitness by 53%), the herbivore population is predicted to begin to expand after about 90 generations and to reach carrying capacity after about 120 generations (Fig. 2a). Although the number of herbivores in this case is 10–100 individuals higher for the early generations than in the case of constitutive defence at $100 \mu\text{g} \cdot \text{g}^{-1}$ cucurbitacin, inducible plants produce only 83% of the cucurbitacin that constitutive plants produce over 100 herbivore generations ($8320 \mu\text{g} \cdot \text{g}^{-1}$ for the inducible and $10,000 \mu\text{g} \cdot \text{g}^{-1}$ for the constitutively defended plant). This calculation assumes that the plant continues to produce toxin even after the herbivores have evolved resistance. At the relatively low dose of $80 \mu\text{g} \cdot \text{g}^{-1}$, some individuals survive as a result of quantitative resistance, enabling the population to evolve greater quantitative resistance after multiple bouts of induction (Fig. 2b). If the plant produces inducible defence at a higher concentration of $100 \mu\text{g} \cdot \text{g}^{-1}$ (the amount in our empirical measurements from Agrawal *et al.*, 1999), herbivore numbers remain at or below the threshold for induction for over 100 herbivore generations (Fig. 2c). The major resistance allele reaches a high frequency at 90–100 generations, but quantitative resistance does not yet evolve (Fig. 2d). The fraction of the herbivore population that survives as a result of quantitative resistance spikes down and up because survival is high in generations in which plant defences are relaxed and low in generations in which defences are induced. Surprisingly, the total amount of toxin produced after 100 herbivore generations is only $6600 \mu\text{g} \cdot \text{g}^{-1}$, since induction is turned on for relatively few herbivore generations compared to the case of constitutive defence or induced defence at a lower concentration of $80 \mu\text{g} \cdot \text{g}^{-1}$. With inducible defence at a higher concentration of $120 \mu\text{g} \cdot \text{g}^{-1}$ (98% fitness reduction in an

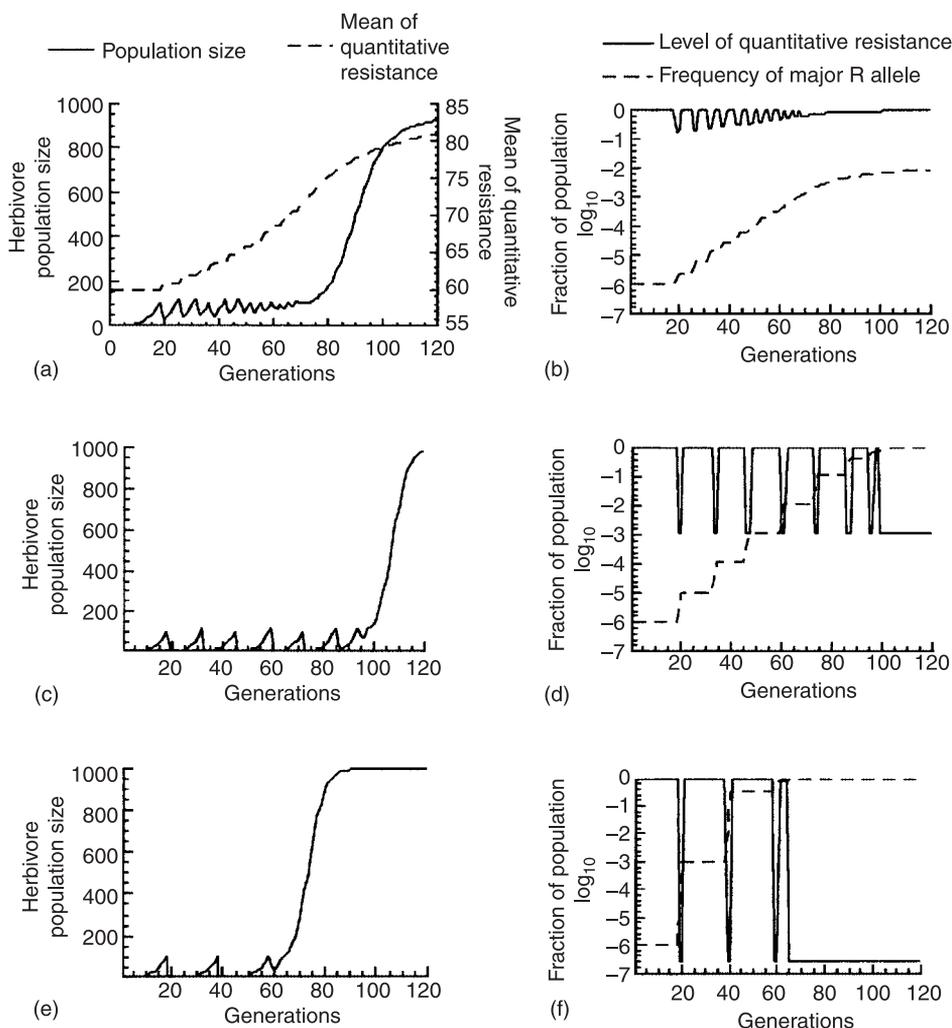


Fig. 2. (a, c, e) Herbivore population size over time on plants with induced defences; (b, d, f) survival due to quantitative resistance and the frequency of the major allele for resistance on plants with induced defence. In (a) and (b) the cucurbitacin concentration is $80 \mu\text{g} \cdot \text{g}^{-1}$, in (c) and (d) $100 \mu\text{g} \cdot \text{g}^{-1}$, and in (e) and (f) $120 \mu\text{g} \cdot \text{g}^{-1}$. In (b), (d) and (f), survival due to quantitative resistance fluctuates sharply up and down because in the herbivore generations in which defences are not induced, all herbivores survive. In herbivore generations exposed to induced plant defences, survival as a result of quantitative resistance may be reduced by orders of magnitude. Other parameters in this and subsequent figures, unless otherwise specified, are $N_{\text{induce}} = 100$, $N_{\text{min}} = 1$, $q = 1$, $\sigma_s = 10 \mu\text{g} \cdot \text{g}^{-1}$ cucurbitacin, $\bar{z}_0 = 60 \mu\text{g} \cdot \text{g}^{-1}$, $V_E = 10 \mu\text{g} \cdot \text{g}^{-2}$, $V_A(0) = 10 \mu\text{g} \cdot \text{g}^{-2}$ and $h_0^2 = 0.5$.

unexposed herbivore population), the herbivore population is predicted to suffer more dramatic declines and take longer to rebound to N_{induce} than with inducible defence at $100 \mu\text{g} \cdot \text{g}^{-1}$. However, major monogenic resistance evolves sooner (Fig. 2e) and herbivores reach carrying capacity after 90 generations (Fig. 2f). At this high concentration of induced

defence, the amount of toxin produced over 100 herbivore generations is nearly doubled ($11,040 \mu\text{g}\cdot\text{g}^{-1}$).

When the concentration of induced defence is $80 \mu\text{g}\cdot\text{g}^{-1}$ (Fig. 3), the mean quantitative resistance of the herbivore population rises quickly to tolerate greater than $80 \mu\text{g}\cdot\text{g}^{-1}$ of plant toxin. At the induced defence concentration of $100 \mu\text{g}\cdot\text{g}^{-1}$, quantitative mean resistance only increases slightly above $60 \mu\text{g}\cdot\text{g}^{-1}$, the concentration of toxin in uninduced plants. Although this concentration is not high enough to reset the mean quantitative resistance back to \bar{z}_0 when defences are induced, it is high enough that most survivors do so as a result of major gene resistance and not by an increase in mean quantitative resistance (see equation 8). At $120 \mu\text{g}\cdot\text{g}^{-1}$, the quantitative mean is reset every time defences are induced, and major gene resistance evolves instead.

Effects of population growth rate and number of colonists

Contour plots (Fig. 4) illustrate the sensitivity of the predictions to variation in parameter combinations. The number of generations until the herbivore population size surpasses 500 individuals can be delayed the longest using constitutive defence if that defence is produced at a low dose of $70 \mu\text{g}\cdot\text{g}^{-1}$ (Fig. 4a). This contour plot shows that there is an interaction of dose and the herbivore population growth rate: the herbivore population expansion can only be delayed for 75 or more generations if the population grows at a rate not more than $\lambda = 0.3$. Induced defences, in contrast, are predicted to delay herbivore population explosion for at least 75 generations for herbivore population growth rates up to $\lambda = 0.5$ (Fig. 4b). A $90\text{--}100 \mu\text{g}\cdot\text{g}^{-1}$ dose of induced defence delays population expansion the longest.

For induced defence, the number of generations q that the defence persists after herbivore numbers have dropped below the threshold (Fig. 4c) and the value of the threshold N_{induce}

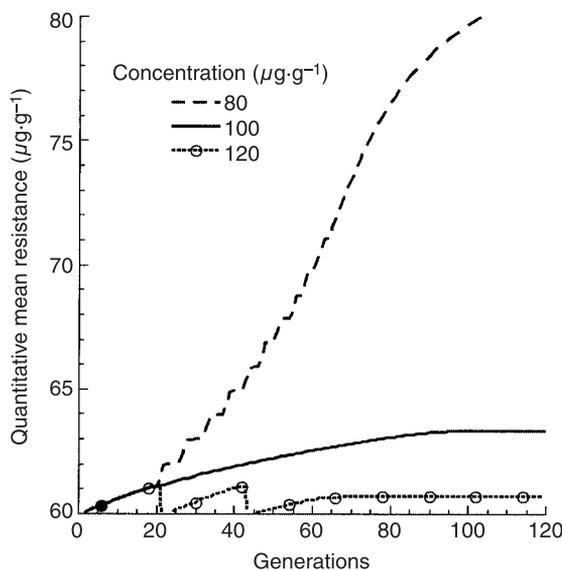


Fig. 3. Mean quantitative resistance over time on plants with a concentration of induced defence of 80, 100 or $120 \mu\text{g}\cdot\text{g}^{-1}$. Other parameters are as specified in Figs 1 and 2.

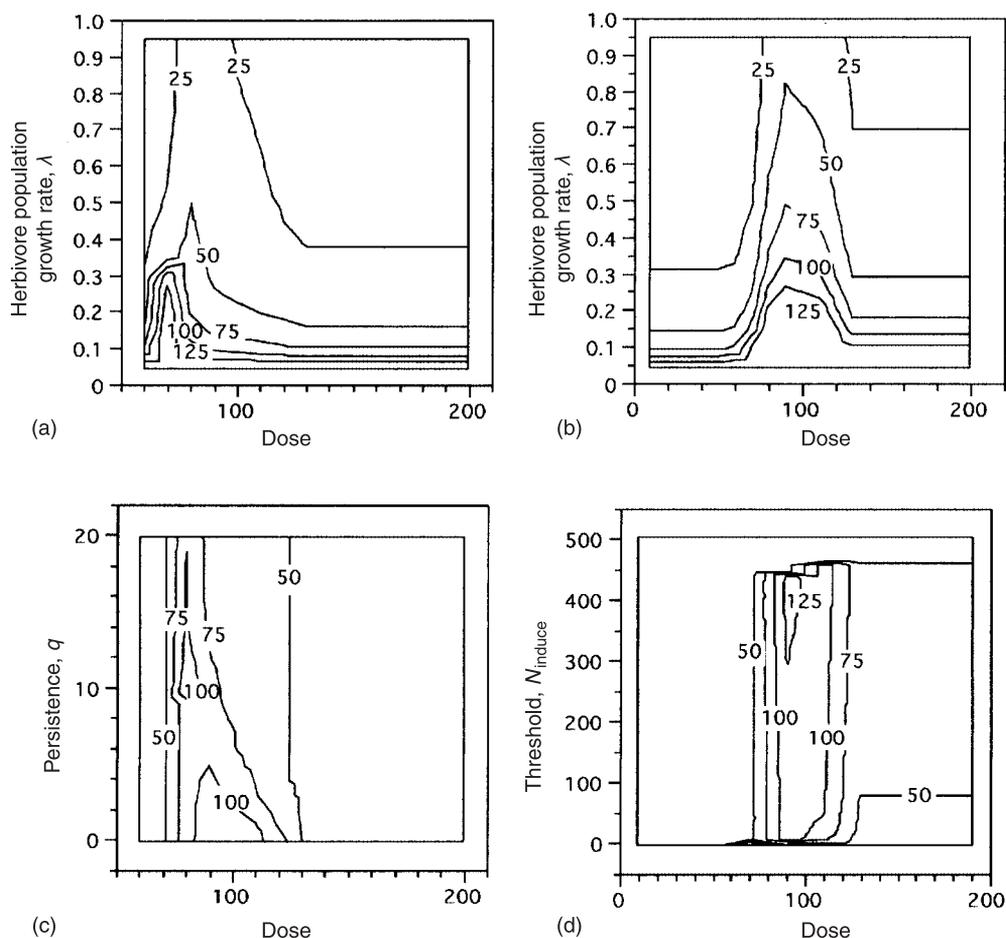


Fig. 4. Contours of the number of herbivore generations until the herbivore population grows to half its carrying capacity for combinations of the herbivore population growth rate λ and the concentration of defence for (a) constitutive and (b) induced plant defence. (c) Contours of the number of herbivore generations until the herbivore population grows to half its carrying capacity for combinations of the persistence q (in units of herbivore generations) of the defence and the concentration of defence (in units of $\mu\text{g}\cdot\text{g}^{-1}$). (d) Contours of the number of herbivore generations until the herbivore population grows to half its carrying capacity for combinations of the threshold N_{induce} herbivore population size (in units of numbers of individuals) and the concentration of defence (in units of $\mu\text{g}\cdot\text{g}^{-1}$). In (b) $q = 1$ and $N_{\text{induce}} = 100$; in (c) $\lambda = 0.3$ and $N_{\text{induce}} = 100$; in (d) $\lambda = 0.3$ and $q = 1$. In all plots, $N_{\text{min}} = 1$.

(Fig. 4d) are predicted to have only a minor effect on the time that herbivore populations can be controlled. There is a slight advantage for a short persistence of $q \leq 4$ generations, which only occurs if the concentration lies in the range $85\text{--}110 \mu\text{g}\cdot\text{g}^{-1}$. There is another peak in length of time for which herbivore populations are predicted to be controlled that occurs at much longer persistence times of $10\text{--}18$ generations, but the range of concentrations at which this is predicted is very narrow: $80\text{--}90 \mu\text{g}\cdot\text{g}^{-1}$.

The threshold N_{induce} has virtually no effect on the duration of herbivore control, illustrated by the fact that all contours are vertical, except at the most extreme values of 1 or greater than 450. At the extreme value of $N_{\text{induce}} = 1$, induced defence is effectively the same as constitutive defence in our model. Even with a threshold of $N_{\text{induce}} = 2$, induced defence is predicted to delay herbivore population explosion by 20 generations compared with constitutive defence. Only the concentration of the defence is predicted to play a major role in delaying herbivore population explosion past half its carrying capacity.

The minimum arithmetic mean herbivore population size over 100 herbivore generations is minimized over the same range of concentrations that maximize the time for the herbivore population to reach half its carrying capacity (Fig. 5a). For concentrations below this range, the population has high levels of quantitative resistance (Fig. 5b). Above this range, most individuals are predicted to have major gene resistance after 100 herbivore generations.

If more herbivores colonize a plant than in the cases pictured above with $N_{\text{min}} = 1$, then the advantage of induced over constitutive defences is magnified further. For example, if $N_{\text{min}} = 10$, then constitutive defences are predicted to delay herbivore population expansion only for 50–100 generations and only if population growth rates λ are not more than 0.3 (Fig. 6a). Induced defences, in contrast, may delay pest population expansion for 50–125+ herbivore generations for λ up to 0.7 (Fig. 6b). Similar patterns emerge for even higher values of N_{min} but are not illustrated here. Prolonged control by constitutive defences fails with more numerous colonists because those colonists have sufficient variation to enable quantitative resistance to evolve early. If higher concentrations are produced to preclude the evolution of quantitative resistance, then major gene resistance soon impedes herbivore control. In contrast, when very few herbivores colonize a plant, genetic variation is so low that quantitative resistance is not predicted to evolve when defences are constitutively expressed, even at fairly low levels of $70\text{--}80 \mu\text{g}\cdot\text{g}^{-1}$, so constitutive defence may control pests

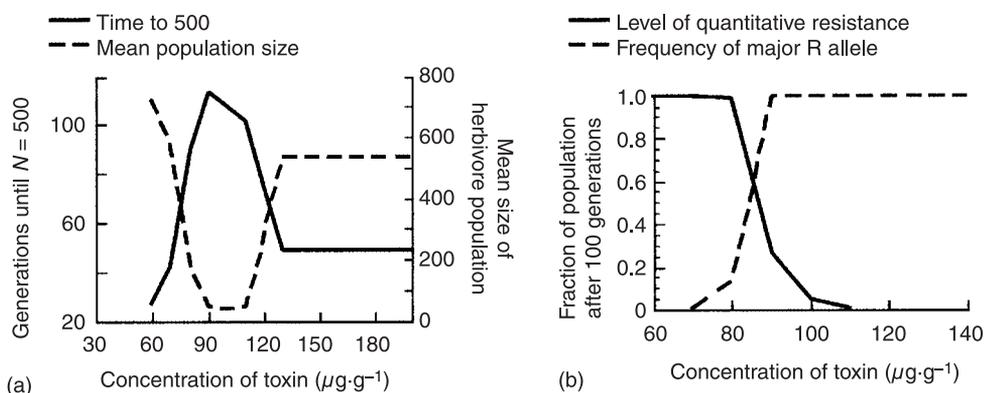


Fig. 5. (a) The number of herbivore generations until the herbivore population reaches 500 individuals (one half the carrying capacity) (left y-axis) and the mean size of the herbivore population over 100 generations (right y-axis) versus the concentration of cucurbitacin produced by a plant with inducible defences. (b) The fraction of the herbivore population that survives due to quantitative resistance and the frequency of the major resistance allele after 100 herbivore generations versus the concentration of defence produced by a plant.

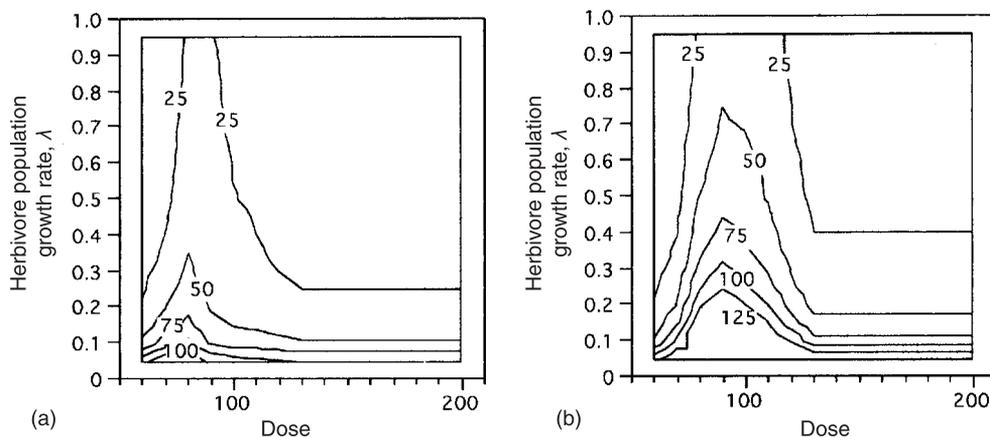


Fig. 6. Contours of the number of herbivore generations until the herbivore population grows to half its carrying capacity for combinations of the herbivore population growth rate λ and the concentration of defence for (a) constitutive and (b) induced plant defence. N_{\min} in both plots is 10 individuals. Comparing Figs 4a and 6a shows that constitutive defences perform worse if there are more colonists. The similarity of Figs 4b and 6b, however, illustrates that the success of induced defences in delaying herbivore population explosion is relatively insensitive to the number of colonists.

almost as long as induced defences if the herbivore population grows slowly (see Fig. 4a). With induced defences, however, the success of prolonged herbivore control remains relatively unaffected by the number of colonists. Since pest numbers must reach $N_{\text{induce}} > N_{\min}$ before the plant deploys the defence, a larger number of colonists means that intervals between induction will shorten so that major gene resistance might evolve slightly sooner (this effect is small, as shown by the similarity of Figs 4b and 6b), but that there will be little impact on the evolution of quantitative resistance.

Sensitivity to variation in other parameters

If the allele conferring major monogenic resistance is dominant or has additive effects (variation in the value of k), then the evolution of herbivore resistance is more rapid than if the allele is recessive. If the resistance allele is completely recessive, major gene resistance may never evolve over relevant time frames (thousands of generations, so quantitative resistance will probably evolve first).

We also examined other quantitative and qualitative forms of the function characterizing the dose-dependent strength of selection $s(z_d)$, both concave and convex, as well as other initial frequencies p_0 (ranging from 10^{-1} to 10^{-10}), and the models lead to the same qualitative predictions. Using higher initial allele frequencies of the major resistance allele (e.g. $p_0 = 0.1$) results in more rapid evolution of major gene resistance and makes it less likely that quantitative resistance will evolve before major gene resistance. The relative advantage of induced over constitutive defence in delaying pest population explosion is smaller at higher initial frequencies p_0 : when $p_0 = 0.1$, the model predicts that induced defences suppress pest numbers for 10–15 herbivore generations longer than constitutive

defences, compared with the much larger advantages of induced defence when $p_0 = 10^{-6}$ that are illustrated in Figs 1 and 2.

In addition, a range of values of σ_s between 1 and $40 \mu\text{g}\cdot\text{g}^{-1}$ were examined, and the model leads to the same qualitative predictions about constitutive versus induced defence, so detailed results are omitted here. However, higher toxin concentrations are required with large values of σ_s , since more individuals with resistance below z_d survive. Readers are referred to Gardner *et al.* (1998) for additional discussion. Also, the results were qualitatively similar across a wide range of values of heritability in the range of those commonly observed ($h^2 = 0.05\text{--}0.9$; Mousseau and Roff, 1987; Head *et al.*, 1995, and references therein) and, for the sake of brevity, are not presented here. Changes in heritability as a result of the linkage disequilibrium were minor: with a starting value of $h^2(0) = 0.5$, for subsequent times $h^2(t > 0)$ ranged between 0.46 and 0.5.

Finally, for the results presented here, we assumed $N_{\text{max}} = 1000$, although we also examined model predictions using $N_{\text{max}} = 10^6$, and found the results to be virtually identical, so we omit them from this presentation.

DISCUSSION

Induced defences create many types of spatial and temporal variability within individual plants. We show that induced defences can suppress herbivore populations and delay the evolution of resistance to those defences longer, using less defensive compounds than constitutive strategies. Many herbivores, including mites, thrips and aphids, have short generation times and these herbivores are classically known for their rapid adaptation (as low as 5–10 generations) to novel host plants and toxins (Edmunds and Alstad, 1978; Gould, 1979; Fry, 1989; Karban, 1989; MacKenzie, 1996; Agrawal, 2000). Van Zandt and Mopper's (1998) recent meta-analysis of local adaptation of insect herbivores to host plants indicated that local adaptation was strong, even among herbivores with high dispersal ability. In the system we modelled, induced cucurbitacin production at concentrations between 90 and $105 \mu\text{g}\cdot\text{g}^{-1}$ minimizes the evolution of quantitative and major monogenic resistance in herbivorous mites. This prediction matches our observation of induced cucurbitacin production at $100 \mu\text{g}\cdot\text{g}^{-1}$ in *Cucumis sativus* (Agrawal *et al.*, 1999). Our model predicts that relaxation of the induced defence within 0–4 herbivore generations would be most beneficial in terms of reducing evolution of resistance in herbivores; although limited data exist, this is well within the realm of empirical observations (Haukioja, 1991; Underwood, 1998).

Our model can be generalized to either: (1) a long-lived tree with short-lived insect herbivores, in which case hundreds of herbivore generations occur on a single plant, or (2) a field of plants whose herbivores are well dispersed, so that insect numbers rise and fall in tandem through the field, with the hosts' induced defences synchronized across plants. Again, the herbivore population would live tens to hundreds of generations for every plant generation. Finally, the model could be envisioned as the herbivore population on a single plant, provided that herbivores rarely disperse between hosts. In this case, defence induction in different hosts would not have to be synchronized, although for our model to apply it is necessary to assume that herbivores do not travel between hosts except in rare instances of colonization. Our model does not apply to cases in which host induction is asynchronous among plants and herbivores disperse frequently among plants.

Consequences of density-dependent induced defence

The dependency of induced defences on the density of attacking herbivores may have a strong influence on the ecology and evolution of the interaction between host plants and their herbivores (Karban and Baldwin, 1997). Recent work in the soybean–Mexican bean beetle association has shown that plants have thresholds for induction and delayed relaxation times, and that these parameters can be variable among plant genotypes (Underwood, 1998, 2000). Our model predicts that the induction of high levels of defence at high herbivore densities hinders the gradual evolution of quantitative resistance that might occur when defences are expressed at lower levels. Monogenic resistance will emerge more slowly than if high levels of defence were expressed constitutively. Although considering both quantitative and major monogenic evolution in tandem is more complicated than modelling each separately, organisms can and do evolve resistance via both genetic mechanisms simultaneously (Lande, 1983; Via, 1990; Berenbaum and Zangerl, 1992; Futuyma *et al.*, 1995; Nielsen, 1997; Gould, 1998). Thus, it is critical to allow for the possibility that herbivores may evolve resistance via both quantitative genetic and major monogenic mechanisms, as is the case in nature. As the concentration and schedule of the selective agent affects the rate at which organisms evolve, we have attempted to incorporate both mechanisms of genetic change into a model to predict patterns of herbivore evolution in response to plant defence.

The number of herbivore colonists affects the relative benefits of induced over constitutive defences; the more colonists there are, the more favourably induced defence is predicted to perform relative to constitutive defence. Although constitutive defence is effective when there are only a few colonists, it is predicted to fail when even a modest number of herbivores (e.g. 10) colonize a plant. When only one or two individuals from a susceptible population colonize a plant, it is unlikely that these individuals will survive a defence if that defence is expressed constitutively before the colonists increase in number. With a larger group of colonists, however, the chance that there is at least one individual that can survive the constitutive defence is increased. In this case, only higher concentrations of defence would be effective at delaying the evolution of quantitative resistance. Higher constitutive concentrations, however, also select more strongly for major gene resistance.

In contrast, the success of induced defence is more robust to variation in the number of colonists. Irrespective of the number of colonists, hosts express the defence when herbivore numbers expand past the threshold for induction. Although the concentration must be sufficiently high to preclude quantitative resistance for the level of genetic variation present in the threshold number of individuals, major gene resistance takes many generations to evolve because the host does not express defence in those generations when few herbivores remain on the plant. Many plants that employ induced defences dynamically express defences to match levels of damage above some threshold (Agrawal and Karban, 2000; Underwood, 2000; Agrawal, 2001). Thus, an added long-term benefit of an inducible strategy may be higher durability of defence to variation in colonist numbers than that of constitutive defences.

We also note, however, that our model is deterministic, and thus predicts mean times for the suppression of herbivore numbers averaged across populations. Stochastic models such as genetic simulations would be appropriate tools to explore this subject.

Additional factors that may influence the evolution of resistance in herbivores

Our model does not consider costs of adaptation to plant defences in the parasites (Berenbaum and Zangerl, 1992; McKenzie, 1996; Nielsen, 1997). Although herbivores can eventually evolve to reduce costs of adaptation to toxins (McKenzie, 1996), initial costs may further delay or reduce the ability of herbivores to overcome inducible defences. Costs of counter-adaptations to plant defence functionally weaken the selection pressure to evolve resistance in the herbivore. For example, in herbivore generations when an inducible plant relaxes its defence, the resistant herbivores may realize the cost of counter-adaptation and thus decrease in frequency compared to unselected herbivores that do not pay such a cost. However, for constitutively defended plants, unselected herbivores would never have this competitive advantage, and selective pressure in every herbivore generation would favour resistant individuals. Thus, costs of adaptation to plant defences in herbivores may further delay resistance evolution and potentially prevent genes for resistance to fix in the population of herbivores. By preventing fixation of resistance genes, including such a cost to resistance might also result in more sustainable dynamics of herbivore populations and their hosts.

Our theoretical results simply suggest a delay in the onset of resistance evolution when plants employ inducible versus constitutive defences. However, many other sources of variation, including natural enemies, may influence the evolution of resistance in herbivores (e.g. Johnson *et al.*, 1997; Hochberg and Van Baalen, 1998). These other factors may widen the gap between the strength of selection for adaptation to constitutive and induced plant defences. For example, if individual herbivores grow more slowly on constitutively defended plants, predators and parasitoids are more likely to kill them than if the herbivores were growing faster (i.e. the slow-growth-high-mortality hypothesis; Benrey and Denno, 1997). Natural enemies that preferentially prey on susceptible herbivores may thus amplify selection for adaptation to constitutive plant defences.

Implications of evolution of resistance in herbivores for the evolution of plant defence

Conventional wisdom has been that induced defences evolved as a strategy to save costs, with constitutive defences being the ancestral state of hosts (although the evidence is limited; see Thaler and Karban, 1997). An alternative view is that induced defences have other benefits (to energetic cost savings) that have led to their prevalence (Karbon *et al.*, 1997). Why else might organisms have inducible defences? Agrawal and Karban (1999) proposed that, since most organisms interact with multiple specialist and generalist parasites, various microbes and mutualists, there would be constraints on maintaining constantly high levels of defence. The temporal and spatial variability in food quality for parasites created by induction may be especially important to overcome these constraints (see table 1 in Agrawal and Karban, 1999). Variability may hinder parasite performance in ecological as well as evolutionary time, decreasing the ability of parasites to adapt to hosts (Denno and McClure, 1983; Whitham, 1983). In this study, we focused on the consequences of induced and constitutive defences for herbivores in terms of evolutionarily overcoming these defences. Our results may be general to other inducible defence systems where there are many parasite generations for each host generation (i.e. microbial parasites of vertebrates) (Tollrian and Harvell, 1999).

Induced defences may be favoured by natural selection over constitutive defences only if individual hosts benefit from induced defences (e.g. Agrawal, 1998). Here we start with the

assumption that herbivores, especially those that have overcome plant defences, reduce individual plant fitness. Ecological scenarios where herbivores have many generations for each plant generation are consistent with this idea because herbivores can adapt locally and overcome an individual's defences (Mopper, 1996; Van Zandt and Mopper, 1998). For example, individual oak and birch trees, well known to have induced defences (Haukioja, 1991), may live hundreds of years, supporting hundreds of generations of locally adapting herbivores (Mopper *et al.*, 1995). Herbaceous perennial plants with multivoltine herbivores such as aphids, mites and thrips may benefit from induced defences when individual plants lacking locally adapted herbivores have higher relative fitness than individual plants with constitutive defences that have devastating, adapted herbivores. For individual plants that do not benefit from induced defences as a resistance management strategy, other factors may favour the evolution of induced defences (Agrawal and Karban, 1999). Thus, even under these circumstances, a beneficial consequence of hosts having induced defences may be the long-term effectiveness of this strategy.

Empirically determined parameter values in the cucurbit–spider mite system we modelled fall within the range predicted by the model for inducibility to be favoured over constitutive defence as a strategy to minimize counter-adaptation by herbivores. Only in circumstances in which some constraint precluded plants from producing a sufficiently high concentration of inducible toxin and the number of herbivore colonists was very small were constitutive defences predicted to delay parasite population explosion longer than inducible defences. However, constitutive defence production at a low concentration requires that plants produce more total toxin over their lifetime than does the more effective inducible defence strategy. Thus, constitutive defence may only be favoured over induced defence if the production of high concentrations of toxin is constrained over a short time-frame of induction or if there is autotoxicity of higher concentrations of the defence. Across a broad range of other parameter values, however, we predict that induced defences will reduce counter-adaptation by herbivores, and thus potentially benefit plants more than constitutive defence strategies.

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APPENDIX: DERIVATION OF THE MEAN QUANTITATIVE RESISTANCE AFTER SELECTION AND BEFORE REPRODUCTION

The expression

$$\int_{z_d}^{\infty} f_i(z) dz = \int_{z_d}^{\infty} \frac{1}{\sigma_i \sqrt{2\pi}} \exp(-(z - \bar{z}_i)^2 / (2\sigma_i^2)) dz$$

in the denominator of equation (9) can be calculated rapidly by substituting $u = (z - \bar{z}_i)/(\sigma_i)$ and using the algebraic approximation for the cumulative Gaussian distribution (Abramowitz and Stegun,

1965: 932). The term $\int_{\bar{z}_d}^{\infty} z f_i(z) dz$ in the numerator is evaluated by substituting equation (7) and $u = (z - \bar{z}_i)/\sigma$ so that $z = \sigma u + \bar{z}_i$ and $dz = \sigma du$. Then

$$\int_{\bar{z}_d}^{\infty} z f_i(z) dz = \int_{\bar{z}_d}^{\infty} z \frac{1}{\sigma\sqrt{2\pi}} \exp(-(z - \bar{z}_i)^2/(2\sigma^2)) dz$$

$$= \sigma \int_{\frac{\bar{z}_d - \bar{z}_i}{\sigma}}^{\infty} u \frac{1}{\sqrt{2\pi}} \exp(-\frac{1}{2} u^2) du + \bar{z}_i \int_{\frac{\bar{z}_d - \bar{z}_i}{\sigma}}^{\infty} \frac{1}{\sqrt{2\pi}} \exp(-\frac{1}{2} u^2) du \tag{A1}$$

The second term on the right in (A1) is $\bar{z}_i \int_{\bar{z}_d}^{\infty} f_i(z) dz$. The first integral can be evaluated by integration by parts. In summary,

$$\int_{\bar{z}_d}^{\infty} z f_i(z) dz = \sigma \frac{1}{\sqrt{2\pi}} \exp\left(-\frac{1}{2} \left(\frac{\bar{z}_d - \bar{z}_i}{\sigma}\right)^2\right) + \bar{z}_i \int_{\bar{z}_d}^{\infty} f_i(z) dz \tag{A2}$$

The survival of individuals with $z < z_d$ as a result of quantitative resistance, in the denominator of equation (9), substituting in equation (7), is

$$w_{q,z < z_d} = \int_{-\infty}^{\bar{z}_d} \exp(-(z - z_d)^2/(2\sigma_s^2)) \frac{1}{\sigma\sqrt{2\pi}} \exp(-(z - \bar{z}_i)^2/(2\sigma^2)) dz \tag{A3}$$

Completing the square in the exponential term and simplifying yields

$$w_{q,z < z_d} = m \int_{-\infty}^{\bar{z}_d} \frac{1}{\sigma^* \sqrt{2\pi}} \exp(-(z - z_i^*)^2/(2\sigma^{*2})) dz \tag{A4}$$

where

$$\sigma^* = \frac{1}{\left(\frac{1}{\sigma^2} + \frac{1}{\sigma_s^2}\right)} \quad \text{and} \quad z_i^* = \frac{(\bar{z}_i \sigma_s^2 + z_d \sigma^2)}{\sigma_s^2 + \sigma^2} \tag{A5}$$

and

$$m = \frac{\sigma^*}{\sigma} \exp\left[\frac{(z_i^*)^2(\sigma_s^2 + \sigma^2) - (\bar{z}_i^2 \sigma_s^2 + z_d^2 \sigma^2)}{2\sigma_s^2 \sigma^2}\right] \tag{A6}$$

The first term in the numerator of equation (9) that is multiplied by $1 - w_m$ can be calculated in a similar fashion, giving

$$\int_{-\infty}^{\bar{z}_d} z \exp(-(z - z_d)^2/(2\sigma^2)) f_i(z) dz = m \int_{-\infty}^{\bar{z}_d} z \frac{1}{\sigma^* \sqrt{2\pi}} \exp(-(z - z_i^*)^2/(2\sigma^{*2})) dz \tag{A7}$$

This may be simplified by substituting and integrating as in equations (A1–A2), resulting in

$$\int_{-\infty}^{z_d} z \exp(-(z - z_d)^2/(2\sigma^2)) f_i(z) dz = m \left(-\sigma^* \frac{1}{\sqrt{2\pi}} \exp(-(z_d - z_i^*)^2/(2\sigma^{*2})) + z_i^* w_{q, z < z_d} \right) \quad (\text{A8})$$

