

## Review

# Costs and benefits of induced resistance to herbivores and pathogens in plants

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## Abstract

While once considered noise in the background of constitutive resistance, the phenomenon of induced resistance to herbivores and pathogens is now firmly accepted as an integral component of plant defence. As for other forms of adaptive phenotypic plasticity, fitness costs and benefits of induced resistance are presumed to exist and may be realized in numerous ways; with their relative importance depending on when, where, and how induced resistance is deployed. Carefully controlled studies in which induced resistance has been manipulated in the absence of attack have provided some of the best evidence for direct costs of resistance in plants. Similar studies in the presence of attackers have provided evidence for fitness benefits, but fitness benefits of induced resistance have been rarely measured directly, especially in long-lived plants. The growing interest in placing induced resistance in a broader context has revealed many potential ecological costs and benefits that are dependent on the environment, but their fitness effects have been little examined. Induced indirect resistance (that is, resistance mediated by interactions with the third trophic level) has been an increasingly popular topic that comes with a unique set of potential costs and benefits. Further progress in our understanding of induced resistance will benefit from an increased synthesis of the literature from both agronomic and ecological perspectives, the former containing more pathogen-oriented studies in agricultural crops and the latter containing more examples of induced resistance to herbivores in wild plants. Such a melding of information will also better inform applications of induced resistance in agriculture.

**Keywords:** Costs of resistance, Benefits of resistance, Ecological costs, Indirect defences

**Review Methodology:** We searched for information using CAB Abstracts, Agricola, Biosis, ISI Web of Science<sup>®</sup> and Google Scholar. We used reference sections of articles obtained by these methods to find additional materials.

## Introduction

Variation in constitutive resistance of plants to herbivores and pathogens within and among species and populations has been undoubtedly recognized for many centuries. In turn, environmental conditions have long been known to alter plant resistance. The phenomenon of induced changes in resistance after attack by herbivores or pathogens (particularly systemic changes, i.e., in undamaged tissues of locally attacked plants) was not noted in the scientific literature until the early 1900s (reviewed in

[1]). One early study by Gilpatrick and Weintraub [2], demonstrated that asymptomatic leaves of previously infected *Dianthus barbatus* plants exhibited a dramatic reduction in virus symptoms upon a subsequent challenge with the carnation mosaic virus, even in the absence of any virus in the leaves at the time of challenge. Ross provided another example of this phenomenon in 1961, showing that inoculation of the lower leaves of tobacco (*Nicotiana tabacum*) with tobacco mosaic virus (TMV) could enhance resistance to a secondary infection in upper leaves [3]. He termed this phenomenon 'systemic

acquired resistance' (SAR), differentiating it from 'local acquired resistance'. About a decade later, Green and Ryan [4] published a seminal paper in their own right, showing that tomato (*Solanum lycopersicon*, formerly *Lycopersicon esculentum*) and potato (*Solanum tuberosum*) plants responded to wounding or feeding by the Colorado potato beetle by producing defensive proteinase inhibitors in both damaged and undamaged leaves. The work of these early pioneers and their colleagues largely proceeded downscale to the molecular mechanisms governing induced changes in plant resistance and the signals involved in mounting inducible resistance. The adaptive nature of such responses was largely assumed and it was not long until models appeared describing the theoretical costs and benefits of the expression of inducible resistance, largely contrasting its expression to that of the expression of constitutive resistance (e.g. [5]). The several decades of work on induced resistance that has occurred since these early demonstrations has provided a much more mature view of induced resistance, from an increasingly detailed understanding of the molecular mechanisms of induced resistance [6] to theoretical models of the evolution of these responses [7]. This work has been propelled by a general interest in understanding the physiology, ecology and evolution of plant defence traits, but also because of the numerous practical applications of induced resistance in agriculture.

Several reviews have been published on costs and benefits of induced resistance in the last 10 years (e.g. [8–13]). However, these reviews have typically focused on only a limited number of aspects of this phenomenon, and none have fully integrated information on both induced resistance to herbivores and to pathogens. Here, we provide a comprehensive review of costs and benefits of induced resistance to both herbivores and pathogens. We first define induced resistance and then provide examples of the range of induced resistance responses to herbivores and pathogens that can be found across the plant kingdom. We then describe the range of theoretical benefits of induced resistance that may exist for plants, followed by separate sections devoted to the empirical evidence for such benefits from studies of either induced resistance to herbivores or to pathogens. We follow the same structure for sections devoted to costs of induced resistance. Throughout each of these sections, we pay particular attention to studies on costs and benefits that are important over longer ecological or evolutionary time scales and we integrate the emerging body of knowledge on induced indirect resistance into our cost-benefit framework. We devote a section to examples of the actual or potential use of induced resistance in agriculture and explain how knowledge of costs and benefits of induced resistance will inform such applications. We conclude by providing a synthesis of our current understanding of costs and benefits of induced resistance and provide a prospectus for future research efforts on this topic.

## Examples of Induced Resistance Abound

### Definitions and Examples of Induced Resistance

Induced resistance can be defined as an increase in resistance to an herbivore or pathogen that results from a plant's response to a prior attack by the same or another attacker or to chemical or mechanical factors that mimic enemy attack [14, 15]. Although mostly studied after feeding by herbivores or infection by pathogens, induced resistance responses have also been observed after egg deposition by herbivorous insects [16, 17]. Induced resistance represents an important aspect of the phenotypic plasticity of a plant, and is typically contrasted with constitutive resistance, which can be defined as the basal level of resistance that does not change in response to attack. Changes in resistance resulting from prior damage can be assessed operationally, when artificially or naturally induced plants are later exposed to a challenge attack and their level of resistance compared with that of previously undamaged plants. Alternatively, induced resistance can be assessed through qualitative or quantitative changes in putative or known defence traits, which can either directly affect plant quality for the attacker or be involved in indirect defence. These can be chemical traits that disrupt herbivore or pathogen feeding, growth, and reproduction, physical deterrents of attack such as papillae formation, cell wall reinforcements, thorns or trichomes or traits involved in the attraction of predators or natural enemies such as extrafloral nectar (EFN) and parasitoid-attracting volatile compounds [15, 18]. Regardless of the type of inducible defence employed, the most complete studies of induced resistance have provided a quantitative relationship between changes in levels of putative defence traits and the corresponding changes in resistance phenotypes [19].

Mechanisms of induced resistance are typically multifaceted, even within an individual plant. Transcriptomic and metabolomic analyses of induced resistance have revealed wholesale changes in the transcriptome of attacked plants that are typically accompanied by changes in the levels of at least some of the secondary metabolites that a plant contains (although their defensive function is not always known) [20–22]. Representatives from many classes of secondary compounds and defensive proteins have been shown to be inducible, including terpenoids, phenylpropanoids, glycosides, alkaloids, phytoalexins and pathogenesis-related (PR) proteins, while some particular compounds, such as cyanide, have been consistently shown to be non-inducible [15, 23, 24]. Besides these 'defensive' traits, changes in levels of primary nutritional metabolites that can directly alter tissue quality, serve as signals, or promote plant tolerance to damage can also be part of the induced response [25]. In the case of indirect defences involving predators and parasitoids, the strength and speed of induction may be quantified by measuring the recruitment of bodyguards or monitoring changes in their behaviour [26].

Induced resistance can be mounted in response to a diversity of attackers. Induced resistance to the same or unrelated organisms has been noted in response to feeding by mammals, insects and other arthropods, nematodes, exposure to both beneficial and pathogenic fungi and bacteria, viruses and even parasitic plants [15, 27]. The strength and speed of induction can vary quantitatively and qualitatively with the identity of particular attackers, both among and within herbivore feeding guilds [28, 29] or among pathogen nutritional types (e.g. biotroph versus necrotroph) [30], and can even vary with the time of day [31]. Qualitative variation in induced resistance to many pathogens is dependent upon gene-for-gene recognition events [32], while this phenomenon has been less frequently noted for insect resistance [33]. At the molecular level, induction is triggered by the detection of defence elicitors in cells of wounded tissues that can be derived from the plant, the attacker, or both [34–40]. The degree of induction can vary quantitatively with the amount of elicitor detected (which usually correlates with the intensity of the attack). In some cases, subthreshold levels of herbivore attack or other stimuli alter resistance very little, but prime stronger responses to later attacks [41–43]. In turn, the ubiquitous defence hormones jasmonic acid (JA) and salicylic acid, along with some others, such as ethylene, are regarded as essential components of many signal transduction pathways leading to induced resistance [44]. Many of these individual signals or signal patterns are highly conserved and reveal that induced resistance and the mechanisms required to mount it are ancient and widespread in the plant kingdom, being present even in algae [45]. Moreover, it is increasingly understood how these signal pathways interact to help fine-tune plant responses in the face of multiple attackers [30, 46–48] and how herbivores and pathogens can sometimes deceive plants by manipulating signal production or release to minimize inducible responses [32, 37, 49–51], or to change assimilate allocation patterns to optimize plant metabolism for their own benefit [52, 53]. Importantly, use of these signalling compounds or elicitors has provided a high degree of experimental control in studies of fitness effects of induced resistance, which has helped to isolate costs and benefits of such responses from, for example, the costs of damage itself (e.g. [54]).

### ***Induced Responses Vary at Several Scales***

The nature of any costs or benefits of induced resistance depends upon when, where, and how it is deployed. While much of the work on induced resistance has focused on short-lived herbaceous plants [15], induced resistance has been demonstrated in algae [45, 55], herbaceous perennials [56], woody shrubs [57] and short- and long-lived trees [17, 58–63]. Induced resistance can be detected in both vegetative and reproductive tissues and can be confined to tissues that are actually attacked

(local induction) or it can spread systemically via mobile signals to as yet undamaged parts of the plant (systemic induction) [15]. Changes in resistance in particular tissues can result from local up-regulation of defences or by transport of defences made in other parts of the plant to damaged tissues [64, 65]. Although not often isolated in ecological studies, induced responses can be confined to only certain parts of single plant tissues [66] and often to very specific cell types within plant tissues [61]. In addition to effects confined to the attacked plant, long-distance signalling through the phloem can lead to systemic induction in clonal plants where individual ramets are connected to a ‘maternal’ plant [67], while airborne signalling through volatiles can induce resistance in plant parts that lack vascular connections to the damaged part, and even in neighbouring individuals of the same or different species [43, 68–71].

The duration of significant alterations in resistance partly determines the extent of any costs and benefits that resistance may confer. Increases in levels of defence traits and resistance following a single inducing event typically ranges from a few days through several months in most herbaceous plant studies [72–78]. In woody plants, induced resistance can be rapidly deployed in damaged tissues (rapid induced resistance), deployed much later in the same season as the original attack but in undamaged tissues (intermediate delayed induced resistance), or delayed entirely until the following season (delayed induced resistance) [59, 79, 80]. While most induced chemical defences relax to basal levels after some period of time in the absence of attack, partly because of down-regulation of defence genes and turnover of defences [81, 82], induction of increases in permanent physical defences, such as trichomes and thorns, cannot relax in tissues where they have been induced. However, in tissues produced later in the season or in following years in the absence of attack, densities of these sorts of inducible structures typically relax to basal levels [83–85]. While the duration of induction would seem inherently limited in annual plants to a single season, a few examples of trans-generational induced resistance have been demonstrated, where resistance of the progeny of a plant increases as a result of damage to the maternal parent (e.g. [86]). This tremendous variation in ways that induced resistance can be mounted, the defences involved, and the duration of induction can make it challenging to make generalizations about costs and benefits of induced resistance.

### **The Potential Fitness Benefits of Induced Resistance**

#### ***Induced Resistance as an Example of Adaptive Phenotypic Plasticity***

Induced resistance is presumably beneficial to plant fitness and has evolved as a result of natural selection. To that

end, several authors have explored induced resistance as an example of adaptive phenotypic plasticity [54, 87–91]. As such, induced resistance is thought to allow plants to respond dynamically to changing attacker identities and intensities and is more effective than possessing no resistance, and more flexible than possessing high constitutive resistance. The default condition is often thought to be one of induced resistance evolving as a derivative of constitutive resistance, given that possession of both strategies would seem to be redundant. However, the detection of contemporary trade-offs between constitutive and induced resistance remain equivocal [12, 78, 92–95], Bingham and Agrawal, unpublished data). One modelling study suggested that both high constitutive resistance and induced resistance could evolve jointly if the cost of inducibility and of the actual defences involved are relatively low, but that low constitutive resistance and high inducibility are favoured if defence is especially costly [7]. While several studies have attempted to detect trade-offs between constitutive and inducible resistance in single plant species, only two studies have placed empirical data on relationships between constitutive and inducible defences in a phylogenetic framework. One study that examined the phylogenetic distribution of resistance strategies in the genus *Gossypium* indicated that both strategies may be derived and can evolve independently [96]. In another EFN study, Heil *et al.* [97] showed that ant-attracting EFN production moved from an inducible strategy to a constitutive one in the genus *Acacia*. Further confusion about the relationships between constitutive and induced resistance is added for species that may express high levels of some defence constitutively, but have different defences that are inducible [93, 98].

To be subject to natural selection, genetic variation in inducibility (or plasticity) must exist in plant populations. Several studies have now documented either quantitative or population variation in inducibility of resistance (separately from variation in constitutive resistance) [99–103], Bingham and Agrawal, unpublished data). Several others have reported the detection of genotypes of plants that vary in inducibility without quantifying genetic variation [75, 104]. In particular, many examples of quantitative variation in induced resistance to insects and disease can be found in agronomic plants (e.g. [105]). Qualitative variation in inducibility is also inherent in gene-for-gene systems where inducibility in response to a particular attacker is determined by the possession of appropriate plant *R* genes. Since polymorphisms in *R* gene expression are known to exist, an inducibility of resistance that is dependent upon *R-Avr* gene matching will necessarily vary within and among populations [32, 33]. While still lacking a multitude of ecologically oriented studies, sufficient variation in inducibility in plant populations upon which natural selection can act has been found when it has been investigated.

### ***The Currency of Direct Benefits is Fitness***

In order for induced resistance to evolve, it must benefit the fitness of the plant. In most studies, fitness benefits of induced resistance have not been carefully measured, but are usually inferred by the well-documented reduction in subsequent pathogen or herbivore attack or performance that can follow induction [15]. Although reduced attack rates or attacker performance can correlate with increased plant fitness in the face of attack [106], this is not always the case [102], thus measures of plant fitness following induction are necessary to fully demonstrate direct fitness benefits to the plant. In studies of pathogens or herbivores that can kill their host, the benefit of induced resistance to host fitness is often very clearly shown in increased chances of survival (e.g. [107]). Moreover, studies using mutant plants compromised in their ability to appropriately express inducible responses to insects or pathogens have clearly indicated the fitness benefit of possessing induced resistance over no resistance [108, 109]. While few studies have actually quantified increases in growth or reproduction in induced plants in the face of subsequent herbivore or pathogen attack, the best examples of direct fitness benefits of induced resistance in the field were shown using annual plants, in which effects on plant reproduction can be readily observed [54, 110, 111], see below). Benefits of induced resistance involving some aspect of plant performance have also been noted in some herbaceous perennial plants [56], but direct fitness benefits have never been measured in any long-lived woody plant [59]. Clearly, challenges associated with estimating fitness in a long-lived plant make it difficult to estimate lifetime fitness benefits of induced resistance in such plants. In general, the few studies in which fitness effects of resistance induction have been adequately quantified reported evidence for positive net outcomes when herbivore pressure was high (see below, under section 'Benefits of induced direct resistance to herbivores: the empirical evidence'). However, many more studies including plant species with different life histories and growing in different ecosystems will be required to provide support for the assumption that induced resistance expression has generally positive effects on plant fitness.

### ***Benefits Can Come in a Variety of Ways***

The most obvious benefit of induced resistance is the direct increase in fitness that arises from a reduction in the amount of damage or disease incurred by a plant after attack. In this sense, induced resistance should always be more beneficial than possessing no resistance in the face of herbivore or pathogen attack [109, 112]. Once inducible resistance mechanisms are stably mounted, however, such benefits are not conceptually different from those conferred by constitutive resistance. However,

possessing induced resistance may have several other benefits over constitutive strategies [113–115]. Firstly, possession of inducible resistance with some level of specificity toward different attackers provides a plant with the ability to carefully fine tune defences to appropriate targets [28, 29, 47, 48, 115]. To be equally effective in a constitutive context would require the continuous production of a suite of broadly effective defences, which would probably come at a high cost. Secondly, by creating spatial and temporal variation in plant quality, induced resistance may function to disperse damage around an individual plant or plant population, which may reduce the often more negative fitness effects of highly localized damage ([59, 60, 66, 116], but see [117]). These sorts of benefits may be particularly important for long-lived trees, whose generation time far exceeds that of its attackers. On an ecological time scale, induced resistance may create chemical diversity in a plant population that may affect herbivore or pathogen population dynamics [59]. For example, modelling studies have indicated that induced resistance can regulate population dynamics of herbivores, sometimes causing fluctuations in population sizes, although constitutive resistance may have stronger effects on population growth rate [112, 118]. Thirdly, possessing induced resistance may provide long-term benefits by altering evolutionary responses of attackers to plant defence traits. One modelling study based on data from a real plant–herbivore system revealed that the existence of inducible resistance in a plant population can substantially delay the evolution of both quantitative and qualitative resistance to plant defences in herbivore populations relative to a population possessing only constitutive resistance. Prerequisites were, however, that induced resistance is mounted in a density dependent fashion, relaxes after some time period, and the herbivore population has limited dispersal ability [119]. Fourthly, the use of induced indirect defences may be a low-cost way to protect the plant by employing the third trophic level, and alarm signals involved in induced indirect defence only work if the signals are intermittent (inducible). Except for cases such as in obligate ant–plant interactions [97], constitutive attraction of parasitoids or predators in the absence of herbivore presence would probably be disfavoured quickly by selection, because sufficient positive feedback cannot be guaranteed to the third trophic level. Fifthly, some inducible responses may benefit plant tolerance. A recently identified phenomenon, termed ‘induced storage’, can occur whereby carbohydrate export to storage organs from source leaves can increase following damage [120]. While this may be temporarily costly to current growth, it may benefit plant tolerance by protecting valuable resources until later in the season, or until the following year in perennial plants, and requires a long-term examination in order to capture the fitness benefits of such an inducible response. This mechanism contrasts with studies showing inducible sink strength in damaged organs that fuels the production of certain

defences [25, 121] and could also enhance the growth of important parts of the plant. Finally, induced resistance may be accompanied by several types of ‘ecological benefits’ that are dependent upon the environment. For example, since some of the proteins and secondary compounds involved in induced resistance may have multiple roles in defence and protection from other forms of abiotic and biotic stress, induction of resistance by certain herbivores or pathogens may confer ‘cross resistance’ to a variety of other stresses. Such benefits may act to counterbalance some of the costs of induced responses in ecologically relevant environments [47, 89, 122, 123].

### Benefits of Induced Direct Resistance to Herbivores: the Empirical Evidence

The two most widely cited examples of direct fitness benefits of induced resistance to herbivores come from studies of the annual plants, wild radish and wild tobacco. These studies are notable in that they examined fitness of wild plants in natural field settings, either minimized or accounted for tissue loss, and quantified plant reproduction. In the first study, Agrawal [110] showed that leaves of wild radish plants induced by controlled feeding with *Pieris rapae* had higher glucosinolate contents and trichome densities than previously uninduced plants. Induced plants subsequently supported less damage by a suite of herbivores and had higher fitness than previously uninduced plants by the end of the season. With similar objectives, but using JA as an elicitor of induced resistance, Baldwin [54] showed that JA-induced wild tobacco (*Nicotiana attenuata*) plants had much higher leaf nicotine contents than uninduced plants. In turn, induced plants had higher fitness than paired uninduced plants in the face of sufficient herbivore pressure in natural post-fire field environments, but the inverse was true when plants were largely protected from herbivore damage. Using genetic transformation coupled with phenotypic manipulations, Zavala and Baldwin [106] subsequently showed that constitutive and inducible trypsin proteinase inhibitor production in wild tobacco was substantially beneficial in the face of herbivore attack, partly by directly reducing herbivore growth and partly by constraining herbivore feeding to less valuable parts of the plant. They also showed a strong negative relationship between herbivore performance (growth) and plant fitness. An agronomic example of clear fitness benefits of induced resistance to herbivores is the wheat–Hessian fly system, in which induced resistance is qualitatively controlled in a gene-for-gene manner [33]. In this case, when induced resistance is mounted in response to attack by avirulent biotypes, early instar larvae (which are closely associated with the plants in a gall-like structure) often die and plants incur minimal damage. When attacked by a virulent biotype of Hessian fly that is unrecognized by the wheat *R* genes, then plants can suffer severe damage to their stems, which can result

in major yield losses [124]. Finally, mutant *Arabidopsis* and tomato plants lacking the ability to either produce or perceive JA fail to mount induced resistance to herbivore attack and can receive much more severe damage by herbivores than fully competent plants [109, 125]. Expression of inducible resistance would most certainly have been shown to benefit fitness in these studies, had it been directly measured.

Most other studies of benefits of quantitative resistance traits have inferred fitness benefits through alterations in the intensity of subsequent attacks or effects on plant survival after induction. Where quantitative relationships between mass or area of specific tissues and their contribution to fitness are known [126], then fitness benefits can be reasonably estimated by the percent reduction in damage to those tissues caused by a certain level of induced resistance, coupled with knowledge of the fitness costs in the absence of attack that are incurred in order to acquire a particular level of resistance. For example, in the absence of attack, three treatments of wild-type *Arabidopsis* with JA across the growing season reduced total seed mass of plants by ~18% [127]. Since every 1% of the area of young leaves lost on bolting plants (the most valuable leaf class on rosette plants) results in the loss of about 0.8% of the total seed mass [126], costs of induced responses noted in Cipollini [127] are equivalent to losing about 23% of the young leaf area of bolting plants. A one-time treatment with the same concentration of JA reduced larval growth and feeding damage by a generalist caterpillar by 20% in a short-term bioassay [19]; effects that would probably increase with additional JA treatments to match that in Cipollini [127] and with a lengthening of the bioassay. Together, these studies indicate that the fitness benefit via the amount of leaf area preserved by induction of resistance in the face of generalist herbivore attack would probably not completely account for the costs of resistance induced by JA in this semi-natural system. This outcome could be the case in many systems, and argues for the need to actually measure fitness benefits along with costs, but these links have typically not been fully developed in most systems. In the case of delayed induced resistance [59], long-term benefits of induced resistance through alterations in herbivore population dynamics may be particularly important, for example, through moderations in the amount of damage done on a yearly basis. Benefits are also quite obvious in cases where the insect may kill its tree host in the absence or exhaustion of inducible host resistance mechanisms, such as in the case of bark beetle–fungus–conifer systems [107, 128]. Despite the dearth of studies actually measuring plant reproduction, there is good evidence that induced resistance can directly benefit fitness, especially in short-lived plants. However, fitness benefits of most of the other theoretical benefits of induced resistance described above have not yet been quantified [115] and clearly represent gaps in our understanding.

### Benefits of Induced Indirect Resistance to Herbivores: an Emerging Area of Study

While induced direct resistance traits most probably benefit the plant that is expressing them, it is less clear whether induced indirect defence mediated by facultative plant–carnivore mutualisms can decrease herbivory and lead to net fitness benefits for the plants. Since the first reports of herbivore-damaged plants becoming more attractive to predatory mites or parasitoid wasps [129–131], hundreds of studies have found changes in the quantity and quality of volatile organic compounds (VOCs) that are released from plants in response to herbivore damage [131–133]. Carnivorous mites and parasitic wasps use such VOCs to locate their herbivore prey [133–139] and many of these species rely on plant-derived traits to locate their prey or host animals [138, 140]. For example, caterpillars suffered higher parasitism rates when caged near tomato plants that were induced with JA to release VOCs [141] and more parasitic wasps were trapped near induced maize plants in a corn field [142]. Studies using artificial VOCs found confirming evidence: artificially applied VOCs increased predation rates of *Manduca sexta* eggs on *N. attenuata* plants [143], methyl salicylate increased populations of predators in grape vineyards and hop yards [144, 145], and (*E*)- $\beta$ -caryophyllene released from corn plant roots was attractive to entomopathogenic soil nematodes [146].

Responding to herbivore-induced VOCs clearly benefits predators and parasitoids, but does this phenomenon benefit the VOC-emitting plant? In the laboratory, feeding by parasitized caterpillars reduced the fitness of *Arabidopsis* plants less than did feeding by unparasitized ones [147]. Thus, if induction of VOCs leads to higher parasitism rates, then plant fitness should benefit. Lima bean (*Phaseolus lunatus*) plants treated with JA in the field released more VOCs, suffered less herbivory, and produced more leaves, flowers and fruits than untreated controls [56]. The same result was found for plants to which VOCs and EFN had been applied exogenously, in order to isolate the benefits of these traits from putative direct, JA-responsive defence traits [148]. Applying VOCs also reduced herbivore populations and/or herbivory rates in several other experiments [143, 145, 146]. Unfortunately, none of these studies was able to directly attribute the observed defence effects to the attraction of the third trophic level by VOCs [18], because VOCs have other defence-related roles. Studies conducted on more than 30 plant species have demonstrated that herbivore-induced VOCs can induce and prime resistance-related traits in neighbouring yet intact plants (e.g. [41, 68, 149–152]). VOCs even serve as systemic signals within plants and hence function as plant hormones [43, 69–71, 153], which may benefit plants in ways unrelated to plant defence. Overall, determining specific fitness benefits of VOCs has been a challenge because most studies in which VOCs were manipulated experimentally were not able to

isolate their beneficial effects that function via the third trophic level from those resulting from the effects of VOCs on other inducible defence traits.

Surprisingly, much more evidence exists for the beneficial effects of ENF secretion than for VOC emission. Hundreds of studies in a wide range of ecosystems demonstrated that the presence of ants, which are attracted to ENF, benefits the ENF-secreting plant (see [18, 154, 155] for reviews). Because the JA-dependent inducibility of ENF in response to herbivory was discovered less than ten years ago [26], less circumstantial evidence exists for the beneficial effects of ENF induction than for other forms of induced resistance. However, inducing ENF secretion in *Macaranga tanarius* with exogenous JA reduced the presence of herbivores and leaf damage; an effect that disappeared when ENFs were removed before the induction treatment [26]. Likewise, applying artificial ENF exogenously to wild lima bean plants at amounts that mimicked induced ENF secretion reduced herbivory and increased growth rates and flower numbers [156]. In summary, we have evidence that ENF secretion alone can benefit plants under natural conditions while the respective data for the emission of VOCs are still missing.

### **Benefits of Induced Direct Resistance to Pathogens: the Empirical Evidence**

The broad spectrum resistance that is conferred when SAR is mounted has long been investigated for its beneficial effects on agronomic crops [157–159]. Many studies have consequently searched for (and found) inhibitory effects of SAR induction on disease development under greenhouse and agronomic field conditions. Many of the early studies employed an initial local infection to induce resistance, then a subsequent challenge infection to determine the resistance level (the design used originally by Ross [3] to detect SAR) and found enhanced disease resistance against the original or other pathogens [160–163]. Later studies made use of chemical SAR elicitors such as benzothiadiazole (BTH; see [164, 165]), then challenged plants with biotrophic pathogens and generally found successful disease suppression in the treated plants (e.g. [166–170]). Studies of mutant plants that either under- or overexpress certain inducible responses have also revealed the effectiveness of SAR in protection of plants from disease [171]. A successful reduction of disease symptoms is, however, no guarantee for a higher yield (or plant fitness). For example, Kover and Schaal [102] showed that variation in effects of the bacterial pathogen *Pseudomonas syringae* on plant fitness were not always correlated with its ability to grow or the symptoms it produced in several accessions of *Arabidopsis*. Indeed, several examples exist of where BTH treatment failed to improve yields despite the successful reduction of disease [167, 172–174].

Few studies have determined net fitness consequences of resistance expression (but see [175]) and even fewer studies have been conducted under natural field conditions. Because SAR expression causes substantial allocation costs (see below), studies employing artificial pathogen challenges under greenhouse or agronomic field conditions (conditions being characterized by high pathogen pressure and high resource availability) are not likely to represent natural conditions (which are generally characterized by low pathogen pressure and low resource availability). A screening of the activity of several PR-proteins in wild plant species indicated that several species had impaired capacities to express components of SAR [176]. While this would appear to be detrimental, these species may be able to phenologically escape from pathogens and lack the need for fully competent inducible resistance mechanisms. In fact, abiotic conditions partly determine whether SAR expression benefits plants. For example, wild-type *A. thaliana* plants had a higher fitness than mutants that could not activate SAR when plants were challenged with a pathogenic oomycete under low-nutrient conditions, whereas these effects disappeared under high-nutrient conditions [177]. The only study showing the fitness benefits of SAR expression under natural pathogen pressure in a wild plant was by Traw *et al.* [111]. Here, the authors showed that field-grown *Arabidopsis* plants induced with SA had lower natural bacterial titres and higher fitness than untreated controls. The net effect of disease resistance expression on plant fitness depends on many factors, such as plant genotype, developmental stage at induction, pathogen pressure and resource availability [8]. Many more studies will be needed before we can predict the outcome of the non-linear interactions among all these factors under certain conditions.

### **The Potential Costs of Induced Resistance**

#### **Costs Remain the Major Explanation for Inducibility**

While some potential benefits of induced resistance are not dependent upon the existence of fitness costs (see section 'The Potential Fitness Benefits of Induced Resistance'), fitness costs of resistance remain the major explanation for the evolution of inducibility. A quantification of costs can only be undertaken in environments in which the beneficial effects of resistance cannot obscure its costs, that is, when plants express resistance without being exposed to their enemies [9, 178, 179]. Based on this principle, three general approaches have been used to assess costs of resistance; the comparison of plant species, races, or inbred lines with different levels of resistance expression, the controlled induction of resistance by natural or artificial elicitors and the investigation of mutants that over- or underexpress certain resistance-related genes.

Despite some notable examples that have failed to detect costs of resistance, the detection of costs has increased with increasing experimental control [9, 11, 57, 180]. In fact, the results of studies of inducible resistance (as opposed to variation in constitutive resistance) are probably the major reason why a consensus now exists for the existence of costs of resistance. Studies using single genotypes of plants in which induction has been manipulated have greatly advanced the detection of costs of resistance by minimizing genetic variation between experimental replicates. However, studies that have examined costs and benefits of induced resistance have often failed to control or account for tissue loss during the induction event. Use of minimal, but inducing, damage levels, herbivore oral elicitors, or signals and their mimics have all been used to circumvent this problem [54, 101, 127, 181]. Finally, genetic transformation techniques have allowed careful examinations of the costs and benefits of particular inducible defence pathways or specific defence genes and have contributed greatly to the progress made in this area [106, 122, 127, 182, 183].

### **Allocation Costs Have Been Well Studied**

Allocation costs are the fitness costs of the actual production of defence-related compounds and proteins, and are widely assumed to exist. The assumption is that, under limiting resource conditions, allocation of resources to defence production necessarily prevents use of the same resources in other fitness-enhancing functions [184, 185]. The costliness of a particular defence varies with the biochemical makeup of the defence, its half-life and turnover rates, and metabolic requirements [81, 186]. Studies attempting to estimate costs of particular kinds of chemical defences have indicated that compounds such as alkaloids and furanocoumarins seem to be particularly costly [187–189], while VOCs [190] are not. Costs are likely to vary greatly between physical and chemical defences, given that resources used in physical defences cannot be recovered by the plant, and between large-molecular-weight-direct and low-molecular-weight-indirect defences [22, 191]. Costs of plants transformed with single defence genes that are inducible have revealed large costs of certain defences, such as trypsin proteinase inhibitors [192]. This is somewhat surprising given the numerous defence genes that a single species can possess. Likewise, the sensitivity of the expression and the costs of resistance to environmental conditions may depend on the degree of matching between the biochemical makeup of the major defences, and the nature of any particular resource limitation in the environment [22]. In addition to direct production costs, induction of defence-related transcripts and metabolites is typically accompanied by a temporary down-regulation of photosynthetic machinery as resources are shifted to defence production, which may contribute to the initial costs of induced resistance

[21, 22]. In particular, SAR expression often has negative effects on the amount or activity of proteins functioning in plant carbon or nitrogen assimilation [193–195], which can reduce net photosynthetic rates [196, 197]. Recently, a gene associated with the growth suppressing effects of JA was identified in *Arabidopsis* [198]. This discovery lends additional support to the idea that induction of resistance is accompanied by an active down-regulation of growth processes as the plant elevates its defence. Sometimes the defence itself directly impacts plant development, such as is the case for some defence-related oxidative enzymes that directly inhibit elongation rates through their effect on cell wall toughening [199]. When such mechanisms are induced, then growth rates of certain plant tissues will slow down as a consequence.

Opportunity costs are the loss of a fitness benefit associated with activation of defence rather than continuing with active growth or some other fitness-gaining mechanism, and may be conceptualized as 'lost opportunities' because of allocation of resources to defence. These costs are not usually separately isolated in studies addressing allocation costs. When inducible responses are fully expressed, their allocation costs should not differ from those of the expression of constitutive defence, but opportunity costs may increase in importance. For example, while the optimal timing of the allocation decisions made by the plant may be more fine-tuned by selection for constitutive defences, activating inducible defences at inopportune times in plant development may compete strongly with other functions and represent large opportunity costs. Despite their presumed defensive value, different inducible defences can show tissue-specific and ontogenetic variation in expression, suggesting that plants may regulate when and where induced resistance is expressed to avoid opportunity costs [22, 73, 200]. Thus, to protect against undue opportunity costs, one key for the plant is not activating induced resistance until it is really needed, and only when abiotic conditions allow its expression at affordable costs. In fact, resistance expression in *Arabidopsis* can be quantitatively reduced when nutrients are limiting [201].

Further adjustments may be obtained at the level of systemic responses because local attack is not always indicative of future systemic attack. Defence priming may be a way to save opportunity costs whereby sub-threshold levels of attack do not induce significant increases in levels of resistance traits, but they prime plants to respond more strongly to a subsequent, more threatening attack. Studies with *Arabidopsis* have indicated that there is a substantial fitness benefit to priming at a minimal cost [42].

### **Costs of Maintaining Sensory Systems and Plasticity Genes Can Exist**

Costs of the molecular mechanisms governing inducibility, including the sensory proteins that recognize specific

elicitors or signal patterns from herbivores or pathogens, are presumed to exist, and have been incorporated in some modelling efforts [7]. Agrawal *et al.* [101] provided some evidence that more inducible genotypes of wild radish had lower fitness in the absence of attack than less inducible genotypes, but the mechanistic basis of the variation in inducibility is unknown. Likewise, *Solidago altissima* plants that fail to actively respond to attack by gall-making flies grew faster than resistant plants in the absence of attack [202]. In a seminal study, Tian *et al.* [203] showed that *Arabidopsis* plants transformed with the *Rpm1* gene, a resistance gene that detects and binds bacterial effectors in gene-for-gene interactions, produced 9% less seed than empty-vector controls in a field experiment (a subtle result that benefited from the use of up to 500 experimental replicate plants in each treatment group). This study revealed that *Rpm1*, one representative of a large family of *R* genes, is a surprisingly costly gene to carry. Brown [8] discussed the need to understand how induced responses and their sensory systems are fine-tuned in order to mitigate these costs, given that plants may possess many *R* genes that would be exceedingly costly for the plant to carry if each incurred this level of fitness cost. In turn, producing and maintaining other components of the metabolic machinery necessary to mount induced resistance (as opposed to that needed for constitutive resistance) presumably carries costs, but these remain theoretical for the most part.

#### **Lag Time and Threshold Effects Have Been Understudied**

These are associated with the damage that a plant must bear until induced resistance is mounted, and these have not been studied empirically. These 'induction' costs may be minimal if the induced resistance is mounted quickly, given that plants can often tolerate substantial amounts of damage before significant fitness effects are seen [126]. The fitness effects of such costs, however, may have particular relevance for examples of delayed induced resistance, whereby significant changes in resistance do not appear until later in the current season or in the next season [59]. Here, the delayed fitness benefit of resistance (which would be difficult for the plant to predict) may not account well for the tissue loss incurred during the initial induction event. The existence of lag times and threshold effects may also lead to indirect costs because of their effects on herbivore behaviour at the population level. One modelling study, confirmed empirically, indicated that induced resistance that is dependent upon acquiring threshold levels of damage and that is mounted after a significant lag time can lead to spatially aggregated herbivore populations [117]. Concentrated damage by aggregated herbivores may have larger fitness effects at the individual plant or plant population level than damage by randomly or evenly distributed herbivores.

#### **Ecological Costs Have Received Increased Attention**

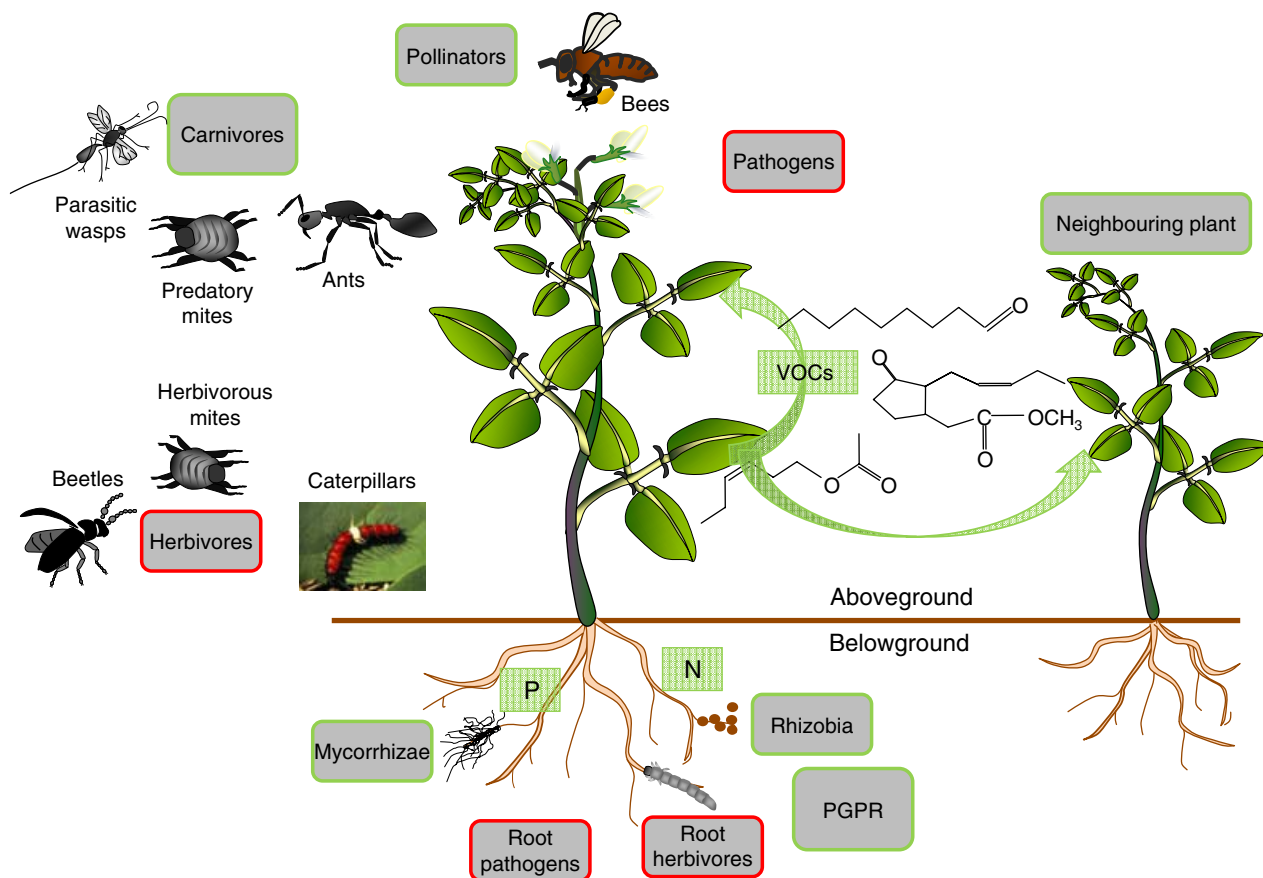
Negative effects of induced responses on a plant's interaction with its biotic or abiotic environment are referred to as 'ecological' costs [10, 77, 204–207] (Figures 1 and 2). Such costs are generally not detected in laboratory or field studies when plants are grown under optimal conditions or are excluded from interacting with parts of their environment. Ecological costs have received increased attention as interest in placing induced resistance in a broader ecological context has increased, but the fitness effects of such costs still largely remain unexamined. There are numerous ways in which expression of inducible resistance may alter the plants ability to simultaneously respond to other aspects of its biotic and abiotic environment. For example, expression of induced resistance may impact a plant's ability to compete for resources with other plants [208] or to tolerate damage by herbivores [122]. Expression of induced resistance to one attacker may have direct positive effects for a non-target attacker, as is the case for specialist herbivores that use certain inducible defences as oviposition cues [29]. Trade-offs may occur between defence pathways involved in mounting inducible resistance to alternate attackers through inhibitory pathway cross-talk [19, 48, 77, 204, 205]. Expression of induced resistance may negatively affect plant mutualists, including beneficial microbes and pollinators [209, 210]. Finally, expression of induced resistance may at least temporarily impact a plant's ability to express other forms of phenotypic plasticity in response to the abiotic environment [89, 90, 182].

#### **Costs of Induced Resistance to Herbivores: the Empirical Evidence**

##### **Evidence for Allocation Costs of Direct Resistance Traits to Herbivores is Substantial**

Some of the earliest studies on costs of resistance focused on variation in constitutive resistance and found, for example, a negative correlation of tannin concentrations with plant growth rate for species such as *Cecropia peltata* [186] and *Bauhinia brevipes* [211]. On the other hand, similar attempts did not reveal significant costs of chemical defence in *Ipomoea purpurea* [212] and in several species of Asteraceae [213]. Increased precision through the use of inbred lines of *A. thaliana* that varied quantitatively in trichome density and total glucosinolate concentration [214] and with *Datura wrightii* lines that varied qualitatively in glandular trichome production [215], fostered the detection of high costs of resistance to herbivores in these studies.

The ability to manipulate inducible responses in single plant genotypes has greatly advanced the detection of costs of resistance. Several studies used JA application to induce plant resistance to herbivores and found allocation



**Figure 1** A plant in its biotic environment. Plants interact with multiple partners both aboveground and belowground and these partners can exert positive effects (frames with green margin) or negative effects (red margins) on the plant. Aboveground, plants are usually engaged in positive interactions with pollinators and with carnivores, which are attracted via EFN or volatiles (VOCs), the latter of which can also function in communication among different partners of the same plant and among different plants. Belowground, the most common positive interaction partners are mycorrhizal fungi, rhizobia and plant-growth promoting rhizobacteria (PGPR). Most important enemies are characterized as herbivores (animals) or pathogens (microorganisms) and both classes can attack both the shoot and the root system.

costs of resistance expression in, for example, native tobacco, *N. attenuata* [54], wild radish, *Raphanus raphanistrum* [178], tomato, *S. lycopersicon* [216], *Arabidopsis* [127] and the solanaceous species *Brugmansia suaveolens* [217]. Although exogenous application of JA probably does not cause completely natural patterns in resistance expression, the results of these elicitor-based studies apparently represent the natural situation. In an elegant effort to quantify reproductive costs of induced resistance to herbivory in wild radish plants, Agrawal *et al.* [178] induced resistance either naturally with *P. rapae* caterpillar feeding or chemically with JA application. To control for effects of tissue removal in the caterpillar treatment, the authors applied manual clipping to one control group. Clipping removes leaf tissue without exposing the plant to herbivore-associated molecular patterns (HAMPs) from the insect's saliva [38] and damages few cells, minimizing the release of elicitors that activate a plant's 'damaged-self recognition' system [39]. As a consequence, rapid whole-leaf removal by manual clipping causes a negligible resistance induction, as is also the case for some types of

mammalian browsing [218]. Induced plants exhibited increased concentrations of glucosinolates and reduced plant fitness, independent of leaf tissue removal [29]. The same approach was followed in a more recent study aiming at quantifying costs of trichome production by willows (*Salix cinerea*) and also found that natural herbivory caused stronger reductions in plant growth than removing the same amount of tissue by artificial clipping [85]. Costs of resistance induction were also observed after controlled herbivore attack of the clonal plant, *Trifolium repens* [67].

Significant control over defence expression can be achieved using genetic transformation, which has greatly informed studies of costs and benefits of resistance. Several studies have used such approaches and found that potato plants silenced in lipoxygenase (a gene that is involved in JA synthesis after wounding) produced larger tubers than wild-type plants under enemy-free conditions [219]. Likewise, growth rates of wild tobacco plants transformed to under- or overexpress proteinase inhibitors were consistent with large fitness costs of this inducible



indirect resistance traits have probably been lumped with costs of direct resistance traits in other studies. Physiological costs of VOCs synthesis are assumed to be low because of the low molecular weight and quantity of VOCs that are typically induced [191, 222]. However, significant costs of VOCs release have been found in a study on different cultivars of maize, *Zea mays* [190]. Allocation costs of EFN synthesis have apparently never been investigated, but EFN secretion by young leaves requires the net transport of assimilates from mature to the younger leaves [223] and thus probably causes costs, at least when carbon assimilation limits future plant growth. Some indirect evidence for costs of indirect defence in ant-plants comes from the observation that ant-attracting traits relax when these plants are released from their herbivores [224–228]. Since indirect defences often consist of a certain degree of ‘advertisement’ of various plant traits, then they are, however, subject to a number of relevant ecological costs (see below).

### **Empirical Evidence for Ecological Costs of Induced Resistance to Herbivores is Growing**

Many environmental factors can potentially influence the magnitude of costs of resistance, including the presence of plant competitors and limited soil resource availability. For example, the expression of JA-dependent resistance traits impairs the capacity of wild tobacco to compete for nitrogen [208, 229]. As a result, fitness costs of induction by JA in wild tobacco, while weakly detectable in induced plants that are grown alone, become particularly apparent when induced plants compete with an uninduced neighbour [208, 230]. In this case, induced plants experience opportunity costs due to a temporary reduction in competitive ability, while the uninduced neighbour experiences opportunity benefits because of the freeing of soil resources. A similar result has been found for *Arabidopsis* in paired plant studies competing either induced wild-type plants or MeJA-overproducing mutants with controls [122]. These effects are not surprising given that the expression of JA-inducible genes transiently inhibits root growth in both of these species [231, 232]. Likewise, induced responses of *Lepidium virginicum* to herbivory were associated with greater reductions in root biomass when plant density was high [28, 29] and JA-induced *Alliaria petiolata* plants exhibit increased costs of JA-induction as soil fertility declines (D. Cipollini, unpublished data). In contrast, Cipollini [127] found that costs of JA-induction in *Arabidopsis*, which is more detectable in single plants than in wild tobacco, did not continually increase as neighbour density increased. Costs of JA-treatment of *Solanum carolinense* were actually higher under high fertility conditions [233], as was the difference in fitness between MeJA-overproducing genotypes of *Arabidopsis* and empty vector controls [182]. Even the fitness differences between paired induced and control wild tobacco

plants noted above were greater under high nitrogen conditions than under low nitrogen conditions [208]. These apparently idiosyncratic results may be due to constraints on the expression of phenotypic plasticity to resource availability in induced plants that prevents them from responding to resource opportunities as readily as uninduced plants [122, 182]. It is clear that the presence of competitors or otherwise modified resource environments can influence the magnitude of costs of induced resistance, if not always in the direction one would predict.

As a consequence of these non-linear interactions between soil fertility, competition and the occurrence of resistance costs, plants can potentially increase their fitness by reducing defence when competition with other plants is likely [89]. For example, Cipollini and Bergelson [234] showed that *Brassica napus* plants maintained growth in the presence of competition or reduced nutrient availability at the expense of constitutive or wound-inducible expression of defences. Future competition can be sensed by the quality of light reaching the plant's shoot. Light enriched in far-red wavelengths that passes through a canopy is detected by specific phytochrome receptors that allow plants to induce shade avoidance responses before competition affects their future growth [235, 236]. Indeed, a trade-off between far-red sensing and defence induction was reported for a native tobacco species, *Nicotiana longiflora*: when far-red light signalled the presence of putative competitors, the plants suppressed defence expression even when under attack [237]. Recent evidence suggests that this response could be explained by negative effects of far-red sensing on the sensitivity to jasmonates [238]. The inverse trade-off can also occur. Cipollini [90] showed that JA-induction could inhibit part of the shade avoidance response in *Arabidopsis*, which may have partly explained the tendency for fitness costs of JA-induction to be higher in lower light environments in this study.

Other ecological costs stem from the ability of induced defence responses to both attract and repel different members of the community. One such cost is a direct consequence of the continuous co-evolutionary arms-race between plants and their herbivores: many defensive traits are used by specialist herbivores to locate their host plants. Examples include direct defences such as cyanide [239], iridoid glycosides [240], cucurbitacins [241] and glucosinolates [242]. Induction of any of these compounds may increase resistance to generalist herbivores, but simultaneously increase attractiveness to specialists [178]. Attracting herbivores instead of defending against them is also a common problem of plants that use indirect defence strategies. Herbivore-induced VOCs can be used by specialist herbivores to locate their host plants [243–250] and several adult insects with herbivorous larvae feed on ant-attracting EFN [251, 252]. Ant-plants can sometimes exhibit reduced contents of certain direct resistance traits that are directed against herbivores and

pathogens, suggesting a trade-off between direct and indirect defences [181, 253], but this pattern cannot be regarded as a general one [254]. These trade-offs function in both directions, because direct defence by glandular trichomes can reduce the time spent by natural enemies of herbivores on plants and thereby reduce a plant's indirect defence [255]. Finally, some induced defences can directly inhibit fitness through impacts on pollinator exposure or behaviour. Delays in flowering noted in plants expressing induced resistance may cause plants to miss important windows of pollinator availability, and delayed development may inhibit fitness when it exposes plants to unfavourable abiotic conditions [182, 216]. In the case of indirect defence, Ness [210] showed that cactus plants defended by the most effective ant defenders actually suffered decreased fitness due to pollinator repulsion by the ants. Now that a number of ecological scenarios have been described that may contribute to the costliness of induced resistance, progress will be made through increased efforts to quantify the actual fitness costs of these environmentally dependent effects.

### Costs of Induced Resistance to Pathogens: the Empirical Evidence

#### *Studies of Costs of Induced Resistance to Pathogens and Herbivores Share Many Parallels*

Relative to costs of resistance to herbivores, which has long been a topic in ecology and evolution, costs of induced resistance to pathogens have been considered in detail only recently [206]. An early observation by Smedegaard-Petersen and Stolen [256] that resistance to powdery mildew (*Erysiphe graminis* sp. *hordei*) infection of barley had negative effects on grain yield was some of the first evidence of the existence of costs of induced resistance to pathogens. Other early studies compared growth rates of lines expressing different levels of pathogen resistance. For example, *Avena* genotypes that were susceptible to the fungal pathogen *Puccinia coronata* grew faster than resistant genotypes [257] and the potential growth rate of radish (*Raphanus sativus* L.) cultivars was negatively correlated with their resistance to fungal wilt disease caused by *Fusarium oxysporum* [258]. In general, studies comparing different cultivars found that resistant lines grew less well and exhibited lower fitness than less resistant lines when compared under pathogen-free conditions (for reviews, see [8, 13, 102, 159, 179, 259]). Comparing cultivars that vary in their levels of disease resistance, however, does not allow the separation of fitness effects of induced from constitutive resistance and does not allow control over other differences among the cultivars. As in the case of herbivore resistance, the breakthrough came with the use of artificial resistance elicitors, allowing the comparison of genetically identical plants that vary in resistance expression without having

a living pathogen in the system, and with the use of transgenic plants, which allows an investigation of the consequences of over- or under-expressing selected resistance genes.

### *Studies of Allocation Costs of Chemical Induction are Now Common*

Because of the ease of manipulating induction and its potential use in crop protection, many studies on costs of chemical elicitor treatment have now been conducted, particularly on agronomic plants. Treating wheat (*Triticum aestivum*) plants with the chemical resistance inducer, BTH (a chemical analogue of SA) impaired seed yield, particularly when plants were grown under low nitrogen supply [181], which paralleled findings of fitness costs of SA treatment in *Arabidopsis* [127]. Fitness costs of BTH might explain why combinations of BTH with fungicides did not result in any additional improvements in yield compared with fungicides alone, although a greater reduction in foliar diseases was observed in the combined treatment [174]. Similar results were observed in other systems: treatment with BTH reduced shoot fresh weight of sunflower [260], suppressed growth of tobacco plants [261] or seedlings of cauliflower [262] and strawberry plants [169], BTH treatment of melon seeds delayed germination [166], and cowpea seedlings pre-treated as seeds with BTH suffered from significant reduction in shoot growth and leaf enlargement [263]. Similarly, treating soybean seedlings with BTH affected their growth in a dose-dependent manner and reached a more than 50% growth suppression at a concentration of 0.5 g/l BTH [264]. Using BTH reduced disease severity of tomato, tobacco or bell pepper without increasing yield [167, 172, 173]: results which agree with the earlier observations by Stadnik and Buchenauer [174]. By contrast, no evidence of relevant costs of BTH treatment was observed in a study on bean, *Phaseolus vulgaris* [265].

The use of artificial resistance inducers has often been criticized because it does not yield truly natural levels of resistance expression. Other authors employed inhibitors of resistance expression and found, for example, that suppressing endogenous SA synthesis in *Salix pentandra* by applying an inhibitor of phenylalanine ammonia-lyase significantly increased plant growth rates [266]. Alternatively, one may use isogenic lines that do or do not contain a defined resistance gene. Using this approach revealed high fitness costs of R-gene-mediated resistance in *Arabidopsis thaliana* [203]. This result is in line with the general pattern that *Arabidopsis* mutants overexpressing resistance genes were characterized by 'stunted' phenotypes and lowered seed production, whereas mutants impaired in resistance grew faster and yielded more seeds than wild-type plants, as long as both were cultivated in a pathogen-free environment (e.g. [127, 177, 183]; see [9] for a review of earlier studies).

### **Ecological Costs of Pathogen Resistance Can Stem From Inhibitory Pathway Cross-talk or From Negative Effects on Beneficial Micro-organisms**

Ecological costs of induced resistance to pathogens have been little examined, with the major exception being studies that demonstrate trade-offs between resistance to herbivores and biotrophic pathogens. With the likely exception of *Arabidopsis* (see [267]), SA controls SAR to biotrophic pathogens whereas JA induces resistance to herbivores. SA inhibits the synthesis of JA at several steps [268, 269] and has direct negative effects on the expression of several JA-dependent genes [30, 46, 48, 269, 270]. As a consequence, plants induced to express SA-dependent resistance to biotrophic pathogens usually show an impaired capacity to develop a functioning resistance to insect herbivores at the same time: a trade-off that can cause significant ecological costs when both, pathogens and herbivores, are present in the environment [13, 19, 77, 123, 204, 271–273]. The fitness effects of such a trade-off have never been examined, however.

Besides herbivore resistance, JA in most plant species also controls induced resistance to necrotrophic pathogens, making a similar trade-off between resistance to necrotrophs and biotrophs highly likely. Indeed, infection with biotrophic *P. syringae*, which induces SA-mediated defence, suppressed the JA signalling pathway and consequently rendered *Arabidopsis* plants more susceptible to the necrotrophic pathogen *Alternaria brassicicola* [274]. This observation probably represents a general pattern: the gene *WRKY70* forms a central node integrating SA- and JA-mediated signalling events and modulates the balance between distinct defence responses. As a consequence, gain or loss of *WRKY70* function caused opposite effects on JA-mediated resistance to the fungal pathogen *A. brassicicola* and the SA-mediated resistance to *Erysiphe cichoracearum* [275]. In a recent review, Kliebenstein and Rowe [276] reported that plant interactions with biotrophic and necrotrophic pathogens in general use similar pathways with opposing effects and that the hypersensitive response, which is associated with increased biotroph resistance, usually leads to decreased resistance to necrotrophs. Thus, ecological costs resulting from impaired resistance to one type of enemy when plants express resistance to a different class of enemy probably play an important role in induced pathogen defence, as they do in the context of herbivore resistance.

Another form of ecological costs can result from the broad spectrum of micro-organisms against which SAR is targeted. Central causal agents of phenotypic resistance comprise PR-proteins such as chitinases and glucanases, which exert a damaging action on microbial structures [277, 278]. Fitness costs could arise from their induction if beneficial microbes, such as symbiotic foliar- and rhizobacteria and mycorrhizal fungi, are negatively affected by induced resistance. Probably as a consequence of their unspecific mode of action, several studies found reduced

colonization with rhizobia after resistance induction by chemicals [279, 280]. As of yet, no studies have attempted to isolate fitness costs of the potentially negative effects of induced resistance on mutualistic microbes. On the other hand, some studies have shown that plant associations with mutualistic microbes, including beneficial soil fungi, can decrease certain aspects of direct and indirect resistance mechanisms [281, 282]. These findings provide support that growth promotion can come at the expense of resistance, so the overall fitness effects of such mutualistic microbes could be altered substantially by the presence of pathogenic microbes or herbivores.

### **Environmental Conditions Affect Costs of Induced Resistance to Pathogens**

Separating the different types of costs is difficult even when using artificial resistance elicitors, because resistance expression interacts with so many other vital processes in the plant. For example, costs of resistance expression to the fungal pathogen *P. coronata* for *Avena fatua* cultivars varied with temperature: when growing at high temperatures in the glasshouse, the susceptible genotypes performed better than resistant genotypes, while the reverse pattern was observed at low temperatures in the field [257]. Allocation costs of pathogen resistance can depend on environmental conditions as described above for induced defence against herbivores: limited resource supply can increase the net costs of a given level of resistance expression [181, 283] and resistance expression *per se* can be constrained by environmental factors such as competition and nutrient supply [127, 201, 234]. Resource availability can also affect the capacity of plants to recover from transient effects of resistance expression on future growth. Growth reductions of induced soybean seedlings were transient and plants recovered in optimal growth conditions, but not when soil nutrients were limiting [264]. Likewise, induced *Arabidopsis* plants were able to compensate for induction given enough time and the availability of sufficient soil resources [283].

Although costs are usually investigated under pathogen-free conditions, Korves and Bergelson [284] used isogenic lines of *Arabidopsis* and found a net cost of R-gene-mediated resistance that was detectable only in the presence of disease: susceptible plants showed a higher capacity of overcompensation for disease, which occurred because of a developmental response to infection. Probably a consequence of non-linear interactions among nutrient levels and costs of resistance expression, a number of studies found no negative effects of induced resistance on plant growth and yield (reviewed in [13]). Intriguingly, wild-type *Arabidopsis* plants had a higher fitness than the mutant that could not activate SAR under low-nutrient conditions and after treatment with the pathogenic oomycete, *Hyaloperonospora parasitica*, while

mutants with constitutive SAR failed to show a fitness benefit in comparison with wild-type even under pathogen treatment [177].

Systemic induced plant resistance to insects or pathogens is the (probably evolved) consequence of highly concerted transcriptomic changes that comprise up- and down-regulation in the expression of hundreds of genes [20, 25, 195, 285, 286]: apparently, a normal inducible resistance is beneficial under most conditions whereas artificially changed expression patterns can result in negative effects on plant fitness. Comparisons among different studies are difficult, however, as long as detailed information on growing conditions and (particularly) comparisons of different levels of resource supply under otherwise unchanged environmental conditions are lacking.

In summary, the currently available information allows several general conclusions: First, overexpression of resistance genes in most cases reduced plant growth and fitness when it occurred under enemy-free conditions, and the same pattern showed up when artificial resistance elicitors were applied. Moreover, a general pattern appears to be that JA-dependent resistance traits and SA-dependent traits are subject to trade-offs, which restrict the capacity of plants to express resistance to different enemies at the same time. Finally, forcing plants to express resistance when important resources are limiting impairs plant growth and fitness more strongly as compared with resource-rich conditions.

### Induced Resistance in Sustainable Agriculture

Crop protection relies mainly on artificial and often highly toxic compounds, disregarding the high potential of the plant's own defensive arsenal [287]. Contemporary agricultural techniques with their heavy use of pesticides can damage ecosystems and affect human health [288, 289]. Therefore, there is an increasing demand for pesticide-free crop protection strategies and for residue-free high-quality products in the world market [290]. Moreover, many pesticides have recently been banned from usage in North America and Europe, causing an urgent need for the discovery of new and environmentally friendly alternatives for pest control. Still, most strategies aimed at a reduction of insecticide use are based mainly on plant defences that directly affect the attacking pest species. For example, *Bacillus thuringiensis* (Bt)-transformed plants are characterized by an enhanced resistance against various pest species due to the presence of a proteinaceous toxin. This attempt has repeatedly been criticized, since Bt-transformed plants may have negative effects on the environment that result from (1) outcrossing of the transgene into natural varieties of the same species, (2) negative influences on beneficial insects and, ultimately, (3) the likely evolution of counter-resistances by the target herbivores.

Inducing the plant's own resistance traits and breeding or transforming crops to increase their resistance potential provides a promising tool to reduce our reliance on chemical pesticides [291]. This idea has been around since at least 1933, when Chester speculated on the potential of inducing a plant's own natural immunity to pathogens as a pest management strategy. To that end, several elicitors of induced resistance, most of which activate SA-dependent resistance mechanisms, are now commercially available and are used in certain agronomic situations. Some commercial formulations and their active ingredients include BION and Actigard [acibenzolar-S-methyl (BTH)], Oryzmate (probenazole), Messenger (harpin proteins) and KeyPlex (yeast extract). These formulations each induce SAR-like resistance and are listed for prevention of a number of biotrophic pathogens. For example, inducing pathogen resistance by application of BTH was successfully employed for various crop plants [166–170]. By contrast, there are few elicitors used to activate JA-dependent direct resistance to herbivores, outside of JA itself [291], which is only now being marketed commercially. However, some important steps towards the application of induced indirect resistance to herbivores include the findings that induced release of VOCs from aboveground parts or certain intercropping strategies can enhance predation and parasitism pressure on leaf herbivores [141, 143, 292, 293]. Likewise,  $\beta$ -caryophellene release from maize roots could guide entomopathogenic nematodes towards root-feeding beetle larvae [146]. The application of these findings is still largely in its infancy and many contingencies will have to be examined before it is effectively used in practice.

Despite its apparent benefits, inducible resistance to pathogens and herbivores is still likely under-utilized because of the limited knowledge concerning how these traits affect crop performance and yield under realistic field conditions. Crop protection under agronomically feasible conditions requires a deep understanding of the underlying mechanisms, allowing concrete predictions on the effects of a certain resistance-improving treatment on the future development of disease symptoms and plant growth and, ultimately, on yield. In order to reach this understanding, we must disentangle the complex interplay of abiotic factors such as soil nutrients, light and water supply and of biotic factors such as pathogens, herbivores and beneficial micro-organisms, which all affect the net outcome of a given resistance induction treatment [287, 291]. Many questions remain to be answered before resistance induced biologically or by means of specific chemical elicitors can serve as a reliable, environmentally friendly strategy for crop protection. Most importantly, an intense, direct activation of defences can be costly, particularly if enemy pressure is low or non-existent. From a crop protection perspective, incurring costs and the possibly associated reductions in yield is likely to make direct induced resistance unpopular. By contrast, priming, with its triggering of defences only following pest or

pathogen challenge, allows a more efficient use of resources and indeed has been shown to provide benefits to plants under the pressure of pathogens [42] or herbivores [70]. Some elicitors, such as BTH, have the potential to both prime some responses and to directly induce other resistance responses [294]. If priming is to find a place in practical crop protection, it will be necessary to increase our understanding of the molecular, physiological and ecological aspects of the phenomenon. The ecology of priming is particularly important, since failure to understand priming in crops under field conditions is likely to result in inappropriate and ineffective use of the technology in practice.

## Conclusions and Outlook

Studies of induced resistance have been '*de rigueur*' in the field of plant–herbivore and plant–pathogen interactions for several decades. After debate over whether induced resistance is an active process (rather than a passive one) subsided, a great deal has been learned about the physiology, ecology and evolution of this phenomenon. With some exceptions, there is now substantial support for fitness costs of induced resistance to herbivores and pathogens. Mechanisms for how these costs arise continue to be debated, with allocation of resources forming a central aspect of most hypotheses. Many potential ecological costs exist, which may be particularly important as induced resistance is placed in broader ecological and agronomic contexts, but their fitness effects have yet to be described for the most part. There are still relatively few good studies of fitness benefits of induced resistance (particularly in the field), but a large amount of circumstantial evidence exists in support of them. Studies have revealed that, although induced resistance is costly, its benefits usually outweigh the costs. Still, gaps in our understanding of several aspects of the ecology and evolution of induced resistance remain. Firstly, specific predictions regarding induced resistance have not yet been fully incorporated in existing models of plant defence theory. Many of these theories were raised to describe patterns of constitutive defence allocation and have not been fully 'updated' with increased knowledge of induced resistance. Secondly, much of our understanding of induced resistance still stems from just a few annual herbaceous plant species. There is a dearth of studies on fitness costs and benefits done under realistic ecological conditions and almost no studies on long-lived woody plants. More studies of wild plants growing in the field under natural herbivore and pathogen pressure are needed to balance the wealth of studies on model plants amenable to genetic and phenotypic manipulation. There is a real need for some researchers to step forward with a long-term programme to study fitness costs and benefits of induced resistance in these plants. Induced indirect resistance is just now receiving the attention it requires,

and, because of its dependence upon specific animal behaviours, it comes with its own set of potential costs and benefits. Finally, agronomically oriented studies of induced resistance have often been ignored by those interested in ecology and evolution, but a wealth of information exists in this literature, with particular relevance to pathogen resistance. As early as 1933, Chester laid out a research agenda on ways to examine 'acquired immunity' (induced resistance) to pathogens in plants and on ways to apply this knowledge in agriculture. Since much of this work was oriented toward crop plants, this sort of information was largely overlooked in the realm of ecology. On the other hand, the application of induced resistance in agriculture will benefit from a broad ecological view of costs and benefits, which are particularly important given that widespread acceptance of this technology will require reasonably predictable results.

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