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Impacts of *Bt* Transgenic Cotton on Integrated Pest Management

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ABSTRACT: Transgenic cotton that produced one or more insecticidal proteins of *Bacillus thuringiensis* (*Bt*) was planted on over 15 million hectares in 11 countries in 2009 and has contributed to a reduction of over 140 million kilograms of insecticide active ingredient between 1996 and 2008. As a highly selective form of host plant resistance, *Bt* cotton effectively controls a number of key lepidopteran pests and has become a cornerstone in overall integrated pest management (IPM). *Bt* cotton has led to large reductions in the abundance of targeted pests and benefited non-*Bt* cotton adopters and even producers of other crops affected by polyphagous target pests. Reductions in insecticide use have enhanced biological control, which has contributed to significant suppression of other key and sporadic pests in cotton. Although reductions in insecticide use in some regions have elevated the importance of several pest groups, most of these emerging problems can be effectively solved through an IPM approach.

KEYWORDS: *Bacillus thuringiensis*, transgenic crop, regional pest suppression, nontarget effects, insecticide use patterns, pest damage, biological control, integrated pest management

INTRODUCTION

The cultivation of crops that have been genetically engineered (GE) to tolerate certain herbicides and resist specific insect pests has become dominant in several countries worldwide. Between 1996 and 2009 GE crops were grown on nearly 1 billion hectares of farmland globally.[1] Adoption continues to grow at a rapid pace with an average of about 10 million additional hectares of production added annually since 1996.[1] In 2009, GE crops were grown on 134 million hectares of farmland in 25 countries. Total GE crop production continues to be dominated (63% in 2009) by the cultivation of plants tolerant to the herbicides glyphosate or glufosinate. Insect-resistant crops producing the toxins of *Bacillus thuringiensis* (*Bt*) comprise most of the remaining market share (57% of these as stacked varieties with both insect resistance and herbicide tolerance) with <1% of crops engineered for resistance to several viral diseases.[1]

Cotton accounts for about 40% of the world's natural fiber production and is commercially cultivated in 78 countries from temperate, subtropical, and tropical regions of the world.[2] Surveys have cataloged >1300 species of herbivorous insects inhabiting cotton,[3] but even though only a tiny fraction of these are considered pests of economic significance, cotton has historically been one of the largest users of insecticides worldwide.[4] There have been many improvements in the management of insect pests in cotton that have contributed to a reduction of insecticide use in this crop in the past two decades[5,6] with perhaps the most notable being advances in biotechnology that have allowed engineering of plants to provide highly effective and selective control of caterpillar (Order Lepidoptera) pests, the most significant pest group of cotton globally.

Given the importance of this pest group, it is no surprise that *Bt* cotton technology has been rapidly adopted. Australia, Mexico, and the United States first allowed commercial production of *Bt* cotton in 1996 and Argentina, China, and South Africa joined these early adopters in the next two years (Table 1). Commercial production of *Bt* cotton in India, the largest producer of cotton by land area, was first legally allowed in 2002, and adoption rates there have risen dramatically, with 87% of production in *Bt* varieties by 2009. Burkina Faso was the latest large-scale cotton-producing nation, and the second nation on the African continent, to allow *Bt* cotton cultivation, joining the list of adopters in 2008. Costa Rica permitted production in 2009, but all of its small output is for seed export. A total of 11 countries now grow *Bt* cotton, including four of the top five cotton-producing nations in the world, three of which have adoption rates over 60% (Table 1). As a result, it is estimated that *Bt* cotton comprised about half of all the cotton grown worldwide in 2009.[1,2]

This paper compliments several recent treatises on the subject[7−9] by highlighting specific elements of the impact of *Bt* cotton on integrated pest management (IPM). I will focus on the role of *Bt* cotton in regional target pest suppression, its impact on pest damage and insecticide use, interactions with nontarget pests in the system, and the role and impact of *Bt* cotton on the ecological services provided by biological control. This paper will not cover resistance management, a key component in *Bt* crop sustainability. The reader is referred to Naranjo et al.[9] for a discussion of resistance management in *Bt* cotton and to Ferré et al.,[10] Tabashnik et al.,[11] and Carrière et al.[12] for a broader discussion of resistance and resistance management in *Bt* crops.

TARGETS OF *BT* COTTON

As noted, *Bt* cotton has specific activity against lepidopteran insects, a characteristic that is governed by the specific receptors and conditions in the caterpillar's gut allowing activation of the *Bt* crystal (Cry) proteins.[13] Roughly 30 species of lepidopteran pests

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Table 1. Summary Production Statistics for *Bt* Cotton Adopting Countries, 2009[a]

country	yield (M kg)	total ha (1000s)	% Bt	first *Bt* production
Argentina	181	430	70	1998
Australia	384	200	86	1996
Brazil	1252	836	14	2005
Burkina Faso	152	420	29	2008
China	7076	5300	68	1997
Colombia	30	38	64	2002
Costa Rica	0.2	1		2009
India	5117	10260	87	2002
Mexico	92	70	58	1996
South Africa	8	10	88	1997
United States	2654	3047	63	1996

[a] Compiled from James[1] and the National Cotton Council.[2]

are important in *Bt* adopting countries, and the vast majority are highly susceptible to *Bt* cotton[9] even though the primary targets of the technology are various bollworms and budworms such as *Helicoverpa* and *Heliothis* spp., *Pectinophora gossypiella*, and *Earias* spp. As recent as a few years ago, most *Bt* cotton produced only a single Cry protein (e.g., Cry1Ac in Bollgard), but many countries are now using *Bt* cotton in which two different Cry proteins are produced in the plant (e.g., Bollgard II and Widestrike). These provide for a broader spectrum of activity against the Lepidoptera, enhanced control of caterpillars that were already susceptible to single-toxin transgenic plants, and better opportunities for managing insect resistance to Cry proteins.[10] Growers in Australia have been exclusively using two-toxin *Bt* cotton since 2004.[9] In the United States, Monsanto's registration of *Bt* cotton that produces only one Cry toxin (Bollgard) expired in 2009. Bollgard has been replaced primarily by *Bt* cotton that produces two toxins (Bollgard II and Widestrike). Thus, *Bt* cotton varieties with two Cry proteins is becoming common, and most *Bt* cotton is also genetically engineered to be herbicide tolerant.

AN IPM PERSPECTIVE

For over five decades IPM has been the paradigm for pest control in agricultural systems globally. IPM has been defined by Kogan[14] as "a decision support system for the selection and use of pest control tactics, singly or harmoniously coordinated into a management strategy, based on cost/benefit analyses that take into account the interests of and impacts on producers, society, and the environment". Figure 1 depicts one way in which this broad concept can be visualized. Within this tactically based context, *Bt* crops in general can be characterized in one of two ways; they can be considered as vehicles for the novel delivery of a selective insecticide or as simply another example of host plant resistance that affects the insect's growth and development (antibiosis). The former characterization is perhaps a consequence of the way in which regulatory agencies view transgenic plants. For example, the U.S. Environmental Protection Agency (EPA) considers a *Bt* protein to be a "plant incorporated protectant" (PIP), and thus, they regulate transgenic plants with pesticidal properties much as they do any synthetic or organic pesticide. This characterization has raised debate on the question of whether or not *Bt* crops are compatible with one of the primary tenets of IPM, the delivery of control methods on an as-needed or prescriptive basis (Figure 1, two upper layers of the pyramid). *Bt* proteins are produced in *Bt*

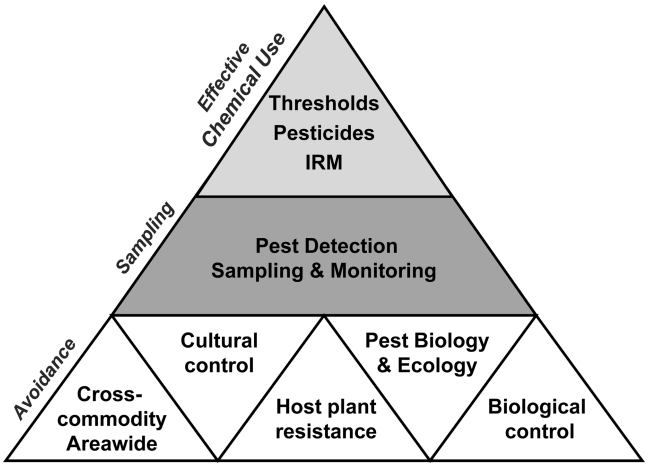

Figure 1. Conceptual model of IPM organized into three layers identifying the major pest control components and their inter-relationships. *Avoidance* tactics provide the foundation of a management system by delaying or preventing potential pests from ever achieving economic status. In instances when the foundation is unable to supply the necessary pest suppression, *Sampling* and *Effective Chemical Use* provide for prescriptive pest control strategies Reprinted with permission from ref 9 with permission from Elsevier and Springer.

cotton and other *Bt* crops continually and not just when economic infestations of pests might be feeding, leading to the perception of *Bt* crops as prophylactic control. The concept of IPM is of course much broader and includes both prescriptive and preventive components; these latter components are depicted as the base of the pyramid (Figure 1) and are composed of tactics that may lead to the avoidance of pest problems. Host plant resistance is one such preventive tactic and has long been recognized as a key component of IPM.[15] Thus, if *Bt* crops are correctly classified as a form of host plant resistance, then they are entirely compatible with IPM. In general, the development of conventional host plant resistance to key insect pests through breeding and selection efforts has been limited.[15] For example, cotton germplasm with variable levels of insect resistance (including that against pests that are the targets of *Bt* cotton) have been developed, but relatively few of these traits have been incorporated into commercially viable cultivars.[6,16] *Bt* crops have simply accelerated the process of developing high levels of host plant resistance through recombinations of specific genetic material followed by crossing into multiple elite lines.

Regardless of how one characterizes *Bt* crops, they represent only one tactic that must be comprehensively integrated to allow effective and sustainable management of all pests in the system.[9,17−20] This is particularly true of cotton, which, as noted above, suffers from the depredation of many pests. The key lepidopteran pests of cotton are typically perennial threats, and thus the deployment of *Bt* cotton in a preventative manner is warranted.[6] However, beyond an understanding of historical pest distribution patterns, a grower's deployment of *Bt* cotton should also be based on experience, personal levels of risk aversion, and a weighing of the costs and benefits of the technology. These factors cannot always be evaluated scientifically, and ultimately the decision to use *Bt* crops or any other form of host plant resistance is up to the producer.

REGIONAL TARGET PEST SUPPRESSION

It has long been recognized that control actions applied synchronously to subpopulations within a region may result in

large reductions in total pest populations.[21] The general concept of area-wide management has been developed and applied to insect pests in many systems.[22] The wide-scale adoption and use of *Bt* cotton represents a very successful implementation of such a synchronous control approach. Thus, it is no surprise that regional populations of target pests have been negatively affected in areas where rates of *Bt* cotton adoption have been high, benefitting both adopters and nonadopters of the technology.

Carrière et al.,[23] using historical data from 1992 to 2001 encompassing 15 cotton-producing regions in Arizona, showed declining populations of the pink bollworm, *P. gossypiella*, which feeds almost exclusively on cotton, as a function of an increasing proportion of *Bt* cotton starting three years after the initial introduction of the technology in 1996. These changes were corrected for natural variations in weather that can affect *P. gossypiella* overwinter survival. The authors further concluded that these regional declines in target pest populations were associated with a threshold value in *Bt* adoption of ≈65%. The nearly 100% efficacy of *Bt* cotton against this cotton specialist[24] along with the potential of this technology to cause regional declines in pest populations was largely responsible for the inception of a phased, cooperative eradication program among growers and state and federal agencies that was initiated in 2001. The program goal is the elimination of this exotic pest from the continental United States and northern Mexico by 2011.[25] In addition to *Bt* cotton, the eradication program uses several methods that were developed for management of *P. gossypiella*,[26] including pheromone-based mating disruption, mass release of sterile insects, various cultural control tactics, and insecticides. In 2006, the EPA granted Arizona an exemption from the mandatory refuge requirement, thus allowing producers to plant 100% *Bt* cotton. This unprecedented decision was based on the assumption that sterile insect releases would substitute for non-*Bt* refuges. To date, the program has nearly eliminated *P. gossypiella* from the Unites States and greatly reduced populations in the northern bordering states of Mexico.[27,28] This result would probably have been impossible without the use of *Bt* cotton. There is little doubt that the rapid success in Arizona was driven largely by the nearly 100% planting of *Bt* cotton since 2006.

Similar large-scale patterns of target pest suppression have been seen for several other major target pests of *Bt* cotton. On the basis of 20 years of pheromone trap captures for the polyphagous *H. zea* and *H. virescens*, Adamczyk and Hubbard[29] examined regional trends in pest densities from a county in the Mississippi delta. From 1986 to 1996 moth captures averaged about 15 moths per trap per day for *H. zea* and about 20 for *H. virescens*, with neither species showing a consistent decreasing trend over that period. However, between 1997 and 2005 populations of both moth species have been declining, but at different rates. *H. virescens* has declined approximately 23-fold, whereas *H. zea* has declined only about 6-fold during this same period. As cotton is the primary host of *H. virescens* during the summer months, *Bt* cotton cultivation is the likely cause of declining abundance in this species. This association is less clear for the more polyphagous *H. zea*. The authors note that several other factors including greater use of preplant herbicides eliminating weed hosts and changes in soybean phenology and thus their attractiveness to *H. zea* relative to cotton may have contributed to these changes in abundance. In addition, *H. zea* is less susceptible to the Cry proteins in single-toxin *Bt* cotton, and better monitoring of their populations in cotton has resulted in increased management of this species with foliar insecticides.

A final example comes from the *H. armigera*/cotton system in northern China. This polyphagous cousin of *H. zea* is a major pest of cotton, corn, peanuts, soybeans, and various vegetables in this region of China. Wu et al.[30] used extensive historical data to show a linear decline in populations of *H. armigera* on cotton in six provinces in northern China associated with increasing years since the adoption of *Bt* cotton in 1997. In addition, this pattern of decline in *Bt* and non-*Bt* cotton has been mirrored in many of the other crops affected by *H. armigera* in this region and is likely to lead to reduced insecticide use on a large scale in multiple crops. The authors suggest that *Bt* cotton is acting as a dead-end trap crop (*sensu*[31]) for this pest.

Overall, these examples from China and the United States clearly demonstrate the "halo" effect of an extremely effective pest control technology deployed on an area-wide basis.

NONTARGET PESTS

As emphasized above, the use of host plant resistance in the form of *Bt* cotton still represents only a single tactic in an overall IPM program. This has been reinforced in some part of the world where other pests not affected by *Bt* toxins have become more problematic.[9] Many of these nontarget pests in cotton are important in both *Bt* and non-*Bt* cotton and continue to be managed effectively in both types of crops by the judicious use of insecticides and other tactics. Others have risen in importance relative to other pests in the system but are no more problematic than in the past. For example, the plant bug, *Lygus hesperus*, which is a sucking insect pest and not susceptible to *Bt* proteins, is now considered to be the number one pest of cotton in Arizona on the basis of the proportion of total insecticide sprays targeting this pest.[32,33] However, insecticide use has plummeted to historic lows in Arizona cotton, and insecticide use for *L. hesperus* has declined as well [33] (see below). On the contrary, large reductions in insecticide use for target lepidopteran pests (see below) in *Bt* cotton have acted to release certain pests that are not susceptible to *Bt* proteins and were once controlled with insecticides applied for these lepidopteran pests. For example, in Australia, the green mirid, *Creontiades dilutus*, green vegetable bug (*Nezara viridula*), leafhoppers (*Austroasca viridigrisea* and *Amrasca terraereginae*), and thrips (*Thrips tabaci*, *Frankliniella schultzei*, and *Frankliniella occidentalis*) have increased in importance.[34,35] Sprays for the former species have in turn been linked with increased risk of spider mite, *Tetranychus urticae*, aphid, *Aphis gossypii*, and whitefly, *Bemisia tabaci*, outbreaks due to the disruption of natural enemies.[36,37] In India, reduction in insecticide sprays has precipitated the resurgence of some minor pests such as mealybugs (*Pseudococcus corymbatus*, *Pulvinaria maxima*, and *Saissetia nigra*), thrips (*T. tabaci*), and leafhoppers (*A. biguttula biguttula*).[38] Mirid plant bugs (*Lygus* spp., *Neurocolpus nubilus*) and stinkbugs (e.g., *N. viridula*) have risen in pest status since the adoption of *Bt* cotton in the midsouthern and southeastern cotton-producing regions of the United States.[39] Many of these emergent pests are easily controlled with insecticides and other pest management tactics. Despite their increased importance, growers have adapted, particularly in Australia and the United States, such that overall use of insecticides for cotton pest management has continued to decline over the past decade[9] (see below).

A slightly different pattern has emerged in northern China,[40] where populations of a complex of mirid plant bugs (*Adelphocoris suturalis*, *Adelphocoris lineolatus*, *Adelphocoris fasciaticollis*, *Lygus*

lucorum, and *Lygus pratensis*) have risen dramatically in association with reduced insecticide use in *Bt* cotton. Lu et al.[40] show a strong positive correlation between both plant bug densities and the number of insecticide sprays targeting plant bugs in cotton with an increasing proportion of *Bt* cotton adoption on the basis of surveys at multiple sites in six provinces in northern China. In contrast to the findings of this same group that showed significant regional reductions of *H. armigera*, plant bug populations have apparently grown regionally and are now affecting a number of different crops outside cotton, including apples, grapes, peaches, pears, and dates.[40] Although other agronomic and environmental factors may be involved in influencing these patterns, the lack of developed management systems for plant bugs in China has exacerbated the problem. It is likely that once such management systems are put in place, the problem in China will diminish as it has in Australia and the United States. In the end, total insecticide use in cotton has declined in this region of China despite increasing usage for plant bugs since the early 2000s.[40]

In general, it would appear that many of these more problematic pests were not under good biological control prior to the introduction of *Bt* cotton and thus were unaffected by reductions in insecticide use that may have benefited natural enemy populations. With overall reductions in insecticides, more emphasis should be placed on improving biological control of these pests through augmentation, introduction, or conservation. There has been no evidence that *Bt* cotton itself is having any direct effect on population changes in these emergent pests.[40−44] Instead, the phenomenon ironically seems to be closely tied to reduced insecticide use, an indirect effect of the technology.

PEST DAMAGE AND INSECTICIDE USE

Historically, cotton has been one of the largest users of insecticides in the world,[4,45] a trend largely driven by the presence of numerous arthropod pest species, including lepidopteran pests, which are the most important worldwide.[9] In the past 15 years or so this insecticide use pattern has undergone significant change. This can be attributed to several factors such as the availability of newer and more effective insecticides, eradication efforts targeting insects such as the boll weevil, historically one of the most significant pest of cotton in the United States and elsewhere, better overall IPM practices, and the adoption and deployment of *Bt* cotton.[6,45] Using comparative farm-level data in adopting countries, Brookes and Barfoot[46] continue to compile the most comprehensive estimates available on the impact of GE crops on pesticide use, crop production, economics, and various environmental variables. They estimate that GE crops of all types have reduced the volume of pesticide active ingredient use by 352 million kilograms globally between 1996 and 2008. Reductions in insecticide use in *Bt* cotton alone account for nearly 40% of this change, a 141 million kilogram total decrease and a 22% change for this crop over the 13 year period. Reductions in the overall environmental toxicity of the insecticides used can be measured by changes in the environmental impact quotient (EIQ).[47] Brookes and Barfoot[46] estimate that the EIQ for *Bt* cotton has been reduced by 24.8% over this 13 year period. These benefits continue to accrue to developing nations disproportionately, with a 13.8:1 ratio of reductions in insecticide EIQ in developing nations relative to developed nations.[46] This is in large part driven by heavy rates of *Bt* cotton adoption by millions of farmers in India and China. A side benefit of reduced insecticide application in *Bt* cotton has been an estimated cumulative savings of 125 million liters of tractor fuel and an associated reduction of 344 million kilograms of CO_2 emissions.[46]

The remainder of this section will focus on pest damage and insecticide usage patterns in U.S. cotton as a case study relative to *Bt* target and nontarget pests. Total damage by all pests in U.S. cotton averaged 7.4% from 1986 to 1995 and declined to an average of about 5.4% from 1996 to 2009, a 27% reduction[48] (Figure 2). Damage inflicted by the three main targets of *Bt* cotton in the United States, *H. zea*, *H. virescens*, and *P. gossypiella*, averaged 2.2% prior to *Bt* cotton and dropped 33% to an average of ≈1.5% from 1996 onward. During these same pre- and post-*Bt* cotton periods, damage due to plant bugs collectively declined about 22% from an average of ≈1.2 to 1%, whereas low levels of stink bug damage increased about 4-fold to ≈0.5%. Damage statistics are of course influenced by the amounts of insecticides that are applied to control pest populations, and the inclusion of insecticide use statistics provides a more complete picture of pest impacts. The average number of total sprays per hectare averaged ≈5.5 in the pre-*Bt* cotton era but dropped 44% to an average of just over 3 per hectare following the introduction of *Bt* cotton (Figure 2). A large portion of this reduction was realized in the control of the three major lepidopteran pests, with a 61% reduction in sprays for these pests between the pre- and post-*Bt* cotton period. Eradication of the boll weevil from many cotton-producing states also contributed to reductions in overall usage. On the contrary, sprays for plant bugs nearly doubled, albeit the average application rate was only 0.6 spray per hectare from 1996 to 2009. Likewise, sprays for stinkbugs increased from 0 prior to *Bt* cotton to an average of a little over 0.2 from 1996 onward.

These patterns of yield loss and insecticide use in the United States demonstrate how *Bt* cotton has contributed to greatly reducing the impact of the key lepidopteran pests while also slightly exacerbating problems with plant bugs and stink bugs due to reductions in overall insecticide use in the system. Regardless of these nontarget pest issues, total insecticide use in cotton has been nearly cut in half as a result of *Bt* cotton and other advances in pest management since 1996. Overall, the use of *Bt* cotton and associated advances in IPM over the past two decades has led to dramatic global reductions in insecticide use in a crop once characterized as one of the largest users of insecticides in the world.

ENABLING BIOLOGICAL CONTROL

In addition to the large number of herbivores known to inhabit cotton worldwide,[3] the crop supports a large and diverse array of arthropod predators and parasitoids.[49−54] This community keeps many potential pests from being economic problems and contributes to control of perennial key pests.[36,55−61] Thus, a key component of any strategy for effectively managing cotton pests is maximizing biological control through conservation of the natural enemy community (see Figure 1).

There are numerous examples of the direct and indirect interactions between arthropod natural enemies and plants that are resistant to certain herbivore species; these interactions may result in negative, positive, or neutral effects on biological control (see, e.g., refs 62−67). It is not surprising, then, that despite the long history of safety associated with *Bt* sprays,[13,68] the season-long expression of these proteins in crop plants through genetic transformation has prompted extensive research to address

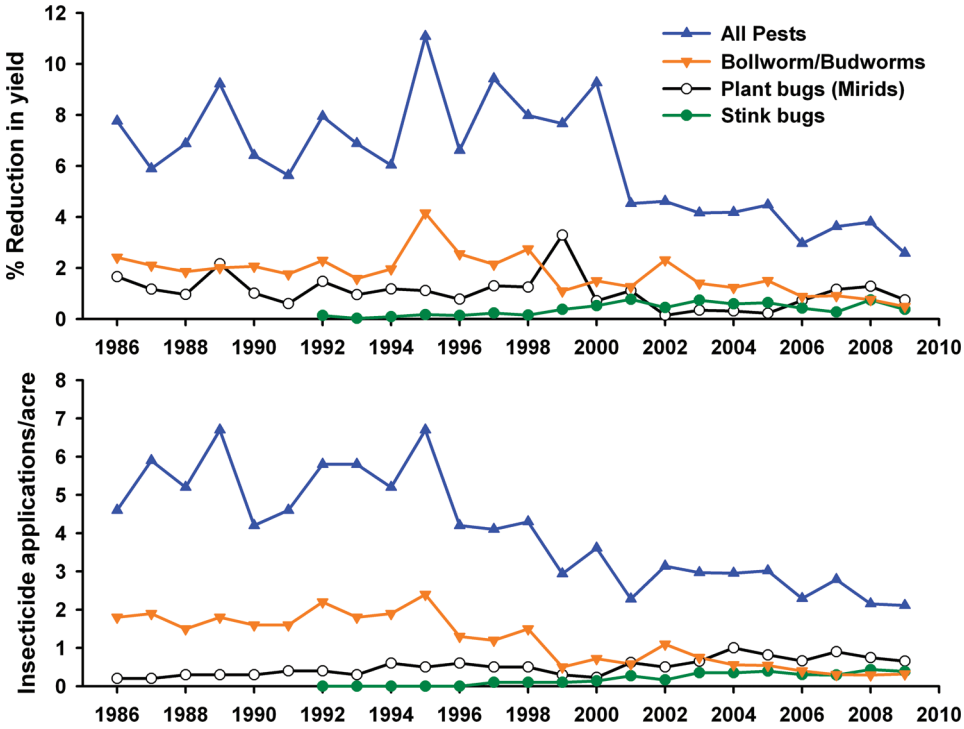

Figure 2. Pest damage and insecticide use patterns in U.S. cotton, 1986−2009, for major caterpillar pests (*H. zea*, *H. virescens*, *P. gossypiella*), two pest groups that have become more problematic with the introduction of *Bt* cotton, and all pests combined. Compiled from data of the National Cotton Council[48] (modified from ref 9).

effects on nontarget organisms, particularly the arthropod predator and parasitoid communities that provide essential ecological services[69] in pest control.

As of late 2008, more than 360 published research studies have examined the potential effects of *Bt* crops on nontarget invertebrates (including nontarget pests),[70] and numerous reviews (see, e.g., refs 8, 13, and 71−79) and several meta-analyses[44,70,80,81] have explored and generalized the results of this extensive research. Overall, unlike conventionally bred insect-resistant plants that may sometimes be detrimental to both the pest and its associated natural enemies, *Bt* crops have been documented to be essentially benign to a wide range of nontarget invertebrates. Laboratory studies that have reported negative effects on species of arthropod natural enemies have largely resulted from the indirect effects of the *Bt* proteins wherein parasitoids or predators were exposed to compromised, low-quality target prey or hosts feeding on *Bt* containing plants or diets.[77] This pattern was further confirmed through meta-analyses that took into account prey or host quality.[70] The presentation of sublethally compromised target hosts led to a general decline in developmental, reproductive, and survival rates in insect parasitoids. In contrast, removal of this effect through the use of *Bt*-resistant caterpillars or hosts not susceptible to *Bt* proteins led to neutral or even positive effects on these life history traits in insect parasitoids exposed indirectly to *Bt* proteins. Insect predators were generally less affected by prey quality, but meta-analysis showed a significant reduction in survival when predators were fed sublethally affected target prey. Again, the effect was eliminated when predators were presented with healthy prey not directly affected by *Bt* proteins. Thus, many of the claims of negative effects of *Bt* proteins on natural enemies (see, e.g., ref 82) have not been based on measuring direct toxic effects, but instead on indirect effects mediated through prey or host quality. In fact, based on laboratory studies published through late 2008, approximately 63% of those examining tritrophic interactions among prey, natural enemies, and *Bt* proteins were measuring effects of prey or host quality and not the direct effects of *Bt* toxicity.[70,83] In the 37% of tritrophic studies that controlled for prey or host quality, the results are unequivocal in demonstrating no effects of *Bt* proteins on natural enemies.

The general lack of a direct hazard of *Bt* proteins to natural enemies and other nontarget groups, including nontarget pests, in the laboratory has been confirmed through meta-analyses of numerous field studies.[44,70,80] A recent meta-analysis to examine the tier-testing system used by many regulatory agencies in fact demonstrated that laboratory studies of toxicity accurately or conservatively predict effects in the field.[84] A summary of the most recent meta-analyses for field studies in *Bt* cotton is presented in Figure 3. In studies in which no insecticides were used on either the *Bt* or the non-*Bt* crop, a meta-analysis can test the hypothesis that the *Bt* protein or other characteristics of the *Bt* plant affected arthropod abundance directly and/or indirectly. Effects were neutral for parasitoids, omnivores, herbivores, and detritivores but slightly negative for predators, indicating that, as a whole, this group was found at slightly lower densities in *Bt* cotton compared with non-*Bt* cotton (Figure 3A). Further analyses indicated that this result was largely driven by one family of insect predators (Nabidae) that are known to prey on caterpillars, a prey that would be expected to occur at very low densities in *Bt* fields.[44] Thus, this likely represents an indirect ecological effect of prey scarcity and not one caused by *Bt* toxicity per se. Not surprisingly, *Bt* crops generally tend to adversely affect natural enemies that specialize on the target pest by reducing prey or host abundance (a goal of all pest management tactics). Perhaps the most striking example of this comes from the *Bt* corn system, for which meta-analyses have shown large

negative impacts on a specialist parasitoid of the European corn borer, the major target of *Bt* corn in the United States.[44]

Insecticide use has clearly declined as a result of *Bt* cotton adoption (see above), and this would be expected to alter arthropod dynamics relative to cotton that is being managed in a more conventional manner. Thus, another way to measure the effects of *Bt* cotton on nontarget organisms is to test the hypothesis that abundance is influenced by the method used to control the target pests in the system. Although fewer field studies have examined this contrast, meta-analyses demonstrate a greater reduction in nontarget abundance in non-*Bt* cotton treated with insecticides compared with untreated *Bt* cotton[44,70, 80] (Figure 3B). A final comparison is relevant to the cotton system in which other pests not targeted by the *Bt* crop may need to be controlled with insecticides. When both *Bt* and non-*Bt* cotton are treated with insecticides, the general results are neutral (Figure 3C). Although fewer insecticide sprays are generally needed in *Bt* cotton, the impact of even a few broad-spectrum sprays are detrimental and result in nontarget densities being equivalent in the two systems. However, Torres and Ruberson[85] showed that a common coccinellid predator was more abundant in non-*Bt* fields. They suggest this phenomenon is related to the fact that this predator has known resistance to one of pyrethroid insecticides applied to the non-*Bt*, but not the *Bt*, fields in their study system. Such results point to the need to carefully consider underlying mechanisms when the impact of *Bt* crops is assessed.

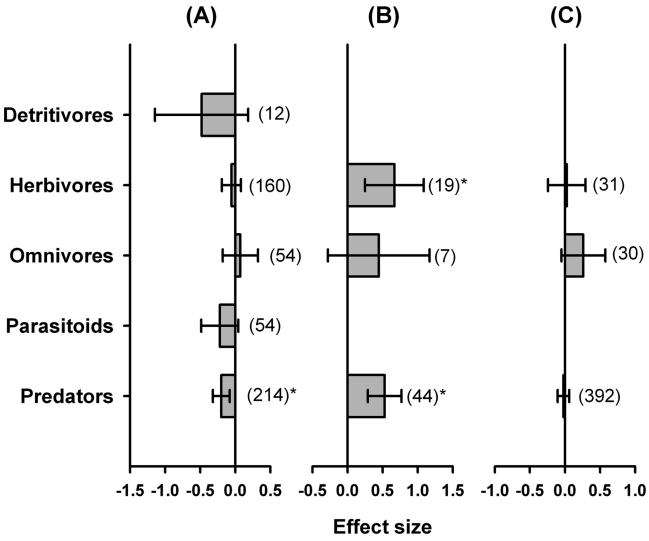

Figure 3. Meta-analyses of field studies examining the abundance of nontarget invertebrates in transgenic *Bt* cotton organized by ecological functional guilds: (A) *Bt* cotton compared with non-*Bt* cotton, neither treated with insecticides; (B) *Bt* cotton compared with insecticide-treated non-*Bt* cotton; (C) *Bt* cotton compared with non-*Bt* cotton, both treated with insecticides. Effect sizes were estimated such that negative values depict lower abundance on *Bt* cotton compared with non-*Bt* controls. Numbers next to bars indicate the total number of observations, and error bars denote 95% confidence intervals; error bars that do not include zero indicate significant effect sizes (∗, $P < 0.05$). Modified from ref 70, with permission from the Centre for Agricultural Biosciences International.

Most field studies examining nontarget effects have focused on comparative abundance, but from the standpoint of assessing impacts on biological control, this is only a surrogate measure. Nonetheless, from the relatively few studies in the cotton system that have examined biological control function, the results are consistent with findings relative to field abundance. For example, in a three year field study, Naranjo[86] found that rates of predation on sentinel eggs and pupae of the target pest (*P. gossypiella*) were the same in both unsprayed *Bt* and non-*Bt* cotton (Figure 4). A similar result was reported by Sisterson et al.[87] for sentinel *P. gossypiella* egg masses placed in commercial cotton fields. Furthermore, field life table studies on *B. tabaci*, another key cotton pest in the southwestern United States, showed that marginal rates of parasitism, predation by sucking predators, and dislodgement (partially the action of chewing predators) were equivalent in unsprayed *Bt* and non-*Bt* cotton[86] (Figure 4).

Reductions in insecticide use associated with *Bt* cotton, the increased availability and deployment of selective materials when insecticides are needed, and the general enhancement in other

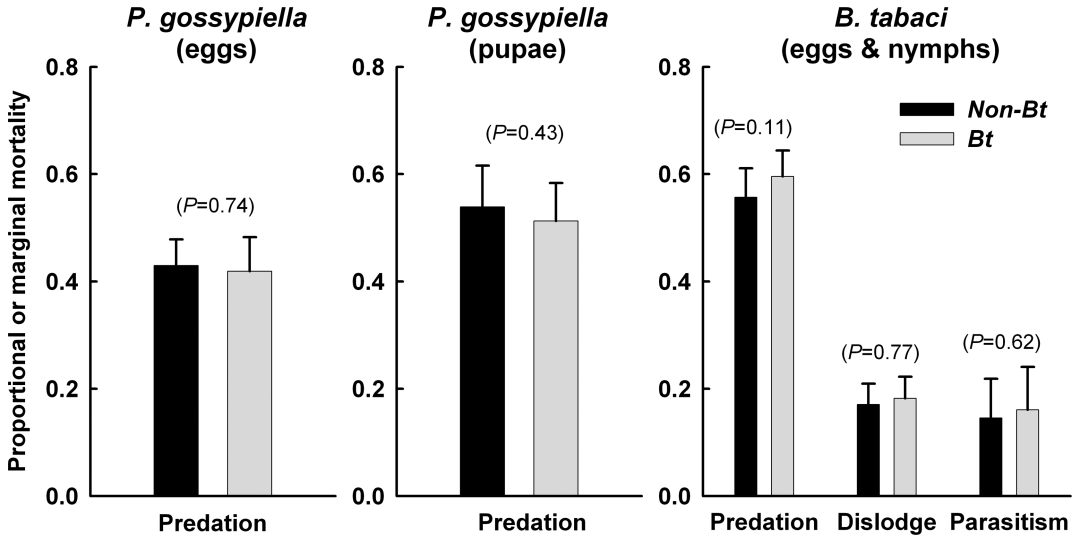

Figure 4. Comparison of predation on sentinel *P. gossypiella* eggs and pupae, and sucking predation, parasitism, and dislodgement (partially chewing predation) on natural cohorts of *B. tabaci* between unsprayed *Bt* and non-*Bt* cotton over a three year period. Numbers above paired bars denote *P* values for analysis of all years combined. Error bars represent 95% confidence intervals. Results are based on two to four separate experiments in each year. Modified from ref 86 with permission from the Entomological Society of America.

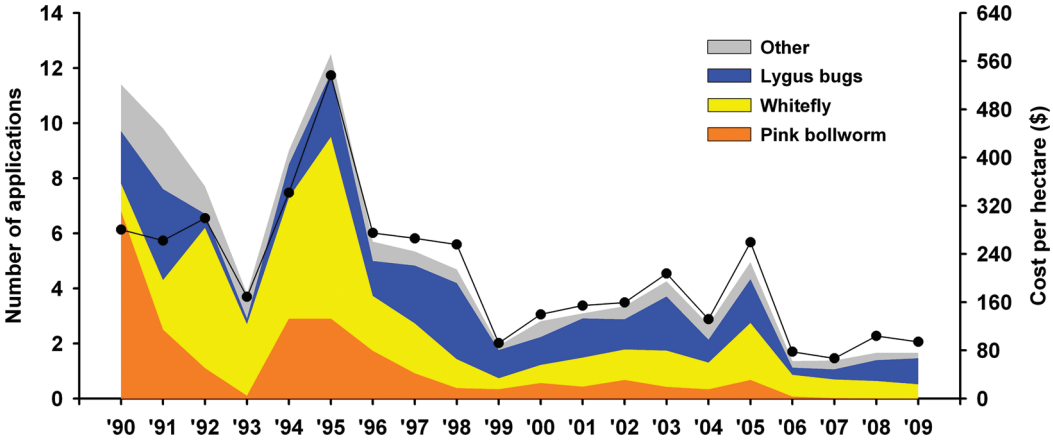

Figure 5. Statewide average foliar insecticide intensity (number of applications per hectare; area graph) and cost (line graph) for multiple pest groups in cotton, 1990−2009, Arizona. Compiled from Ellsworth et al.[33]

pest management tactics have greatly facilitated biological control by creating an environment in which natural enemies can flourish. Greater abundance of natural enemies has been noted in several cotton-producing nations that have adopted *Bt* cotton and other pest management practices,[5,88−90] and the tangible benefits have been repeatedly demonstrated. For instance, in northern China, cotton aphids that are resistant to various insecticides used to control bollworms in cotton are being effectively suppressed by natural enemies in *Bt* cotton fields where such sprays are unnecessary, whereas insecticides used to control bollworms in non-*Bt* cotton fields are leading to secondary aphid outbreaks because of natural enemy destruction.[91] In the western United States, whiteflies (*B. tabaci*) are suppressed long-term in cotton fields, often with only a single application of selective insecticides, whereas fields sprayed with broad-spectrum insecticides require repeated applications.[92] In this system the key contribution of *Bt* cotton has been the almost complete elimination of such broad-spectrum sprays for *P. gossypiella*,[93,94] particularly the common early-season sprays intended to protect flower buds and early fruit formation.[95] The success of the whitefly management program was followed by the development and widespread adoption of selective insecticides to control western tarnished plant bug, *L. hesperus*.[96] As a result of *Bt* cotton, selective control options for other key pests in the system along with a complete IPM program infrastructure allowing for the efficient utilization of all component tactics (see Figure 1), insecticide use in Arizona cotton has been driven to historically low levels[94,97] (Figure 5). Thus, although *Bt* cotton is only a technology for controlling one key pest in this system, it has played a key role in facilitating and enabling biological control. This in turn has allowed biologically based IPM programs to flourish and insecticide use to be nearly eliminated in a system once dominated by chemical control.

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ABBREVIATIONS USED

Bt, *Bacillus thuringiensis* (to denote a type of transgenic crop); IPM, integrated pest management; GE, genetically engineered; EPA, United States Environmental Protection Agency; EIQ, environmental impact quotient.

REFERENCES

(1) James, C. Global Status of Commercialized Biotech/GM Crops: 2009. *ISAAA Briefs* **2009**, *No. 41* (http://www.isaaa.org/resources/publications/briefs/41/executivesummary/default.html).

(2) National Cotton Council, Memphis TN. *Cotton Crop Database*, 2010; http://www.cotton.org/econ/cropinfo/cropdata/index.cfm.

(3) Hargreaves, H. *List of the Recorded Cotton Insects of the World*; Commonwealth Institute of Entomology: London, U.K., 1948.

(4) Allan Woodburn Associates Ltd. Cotton − the crop and its pesticide market. *Pestic. News* **1995**, *30*, 11.

(5) Wilson, L. J.; Mensah, R. K.; Fitt, G. P. Implementing integrated pest management in Australian cotton. In *Novel Approaches to Insect Pest Management in Field and Protected Crops*; Horowitz, A. R., Ishaaya, I., Eds.; Springer-Verlag: Berlin, Germany, 2004; pp 97−118.

(6) Naranjo, S. E.; Luttrell, R. G. Cotton arthropod IPM. In *Integrated Pest Management*; Radcliff, E. B., Hutchison, W. D., Cancelado, R. E., Eds.; Cambridge University Press: Cambridge, U.K., 2009; pp 324−340.

(7) Fitt, G. P.; Wilson, L. J. Genetic engineering in IPM: Bt cotton. In *Emerging Technologies for Integrated Pest Management: Concepts, Research and Implementation*; Kennedy, G. G., Sutton, T. B., Eds.; APS Press: St. Paul, MN, 2000; pp 108−125.

(8) Benedict, J. H.; Ring, D. R. Transgenic crops expressing Bt proteins: current status, challenges and outlook. In *Transgenic Crop Protection: Concepts and Strategies*; Koul, O., Dhaliwal, G. S., Eds.; Science Publishers: Enfield, NH, 2004; pp 15−84.

(9) Naranjo, S. E.; Ruberson, J. R.; Sharma, H. C.; Wilson, L.; Wu, K. M. The present and future role of insect-resistant genetically modified cotton in IPM. In *Integration of Insect-Resistant Genetically Modified Crops with IPM Systems*; Romeis, J., Shelton, A. M., Kennedy, G. G., Eds.; Springer: Berlin, Germany, 2008; pp 159−194.

(10) Ferré, J.; Van Rie, J.; MacIntosh, S. C. Insecticidal genetically modified crops and insect resistance management (IRM). In *Integration of Insect-Resistant Genetically Modified Crops with IPM Systems*; Romeis, J., Shelton, A. M., Kennedy, G. G., Eds.; Springer: Berlin, Germany, 2008; pp 41−86.

(11) Tabashnik, B. E.; Van Rensburg, J. B. J.; Carriere, Y. Field-evolved insect resistance to Bt crops: definition, theory, and data. *J. Econ. Entomol.* **2009**, *102*, 2011–2025.

(12) Carrière, Y.; Crowder, D. W.; Tabashnik, B. E. Evolutionary ecology of insect adaptation to Bt crops. *Evol. Appl.* **2010**, *3*, 561–573.

(13) Glare, T. R.; O'Callaghan, M. *Bacillus thuringiensis: Biology, Ecology and Safety*; Wiley: New York, 2000.

(14) Kogan, M. Integrated pest management: historical perspectives and contemporary developments. *Annu. Rev. Entomol.* **1998**, *43*, 243–270.

(15) Kennedy, G. G. Integration of insect-resistant genetically modified crops within IPM programs. In *Integration of Insect-Resistant Genetically Modified Crops with IPM Systems*; Romeis, J., Shelton, A. M., Kennedy, G. G., Eds.; Springer: Berlin, Germany, 2008; pp 1−26.

(16) Jenkins, J. N.; Wilson, F. D. Host plant resistance. In *Cotton Insects and Mites: Characterization and Management*; King, E. G., Phillips, J. R., Coleman, R. J., Eds.; Cotton Foundation: Memphis, TN, 1996; pp 563−600.

(17) Cohen, M. B.; Chen, M.; Bentur, J. S.; Heong, K. L.; Ye, G. Y. Bt rice in Asia: Potential benefits, impacts and sustainability. In *Integration of Insect-Resistant Genetically Modified Crops with IPM Systems*; Romeis, J., Shelton, A. M., Kennedy, G. G., Eds.; Springer: Berlin, Germany, 2008; pp 223−248.

(18) Grafius, E. J.; Douches, D. S. The present and future role of insect-resistant genetically modified potato cultivars in IPM. In *Integration of Insect-Resistant Genetically Modified Crops with IPM Systems*; Romeis, J., Shelton, A. M., Kennedy, G. G., Eds.; Springer: Berlin, Germany, 2008; pp 195−221.

(19) Hellmich, R. L.; Albajes, R.; Bergvinson, D.; Prasifka, J. R.; Wang, Z. Y.; Weiss, M. J. The present and future role of insect-resistant genetically modified maize in IPM. In *Integration of Insect-Resistant Genetically Modified Crops with IPM Systems*; Romeis, J., Shelton, A. M., Kennedy, G. G., Eds.; Springer: Berlin, Germany, 2008; pp 119−158.

(20) Shelton, A. M.; Fuchs, M.; Shotkoski, F. A. Transgenic vegetables and fruits for control of insects and insect-vectored pathogens. In *Integration of Insect-Resistant Genetically Modified Crops with IPM Systems*; Romeis, J., Shelton, A. M., Kennedy, G. G., Eds.; Springer: Berlin, Germany, 2008; pp 249−272.

(21) Levins, R. Some demographic and genetic consequences of environmental heterogeneity for biological control. *Bull. Entomol. Soc. Am.* **1969**, *15*, 237–240.

(22) Vreysen, M. J. B.; Robinson, A. S.; Hendrichs, J. *Area-wide Control of Insect Pests: From Research to Field Implementation*; Springer: Dordrecht, The Netherlands, 2007.

(23) Carrière, Y.; Ellers-Kirk, C.; Sisterson, M.; Antilla, L.; Whitlow, M.; Dennehy, T. J.; Tabashnik, B. E. Long-term regional suppression of pink bollworm by *Bacillus thuringiensis* cotton. *Proc. Natl. Acad. Sci. U.S. A.* **2003**, *100*, 1519–1523.

(24) Ellsworth, P. C.; Moser, H.; Henneberry, T. J.; Majeau, G.; Subramani, J. Transgenic comparisons of pink bollworm efficacy and response to heat stress. In *Cotton, A College of Agriculture and Life Sciences Report*, Series P-130; College of Agriculture and Life Sciences, University of Arizona: Tucson, AZ, 2002; pp 147−157.

(25) National Cotton Council. *Pink Bollworm Eradication*; National Cotton Council: Memphis, TN, 2001.

(26) Henneberry, T. J.; Naranjo, S. E. Integrated management approaches for pink bollworm in the southwestern United States. *Integrated Pest Manage. Rev.* **1998**, *3*, 31–52.

(27) Antilla, L.; Liesner, L. Program advances in the eradication of pink bollworm, *Pectinophora gossypiella*, in Arizona cotton. In *Proceedings of the Beltwide Cotton Conference*; National Cotton Council: Memphis, TN, 2008; pp 1162−1168.

(28) Allen, C. T.; Herrera, E.; Smith, L. E.; Patton, L. W. Status report of pink bollworm eradication in Texas. In *Proceedings of the Beltwide Cotton Conference*; National Cotton Council: Memphis, TN, 2009; pp 1015−1022.

(29) Adamczyk, J. J.; Hubbard, D. Changes in populations of *Heliothis virescens* (F.) (Lepidoptera: Noctuidae) *and Helicoverpa zea* (Boddie) (Lepidoptera: Noctuidae) in the Mississippi Delta from 1986 to 2005 as indicated by adult male pheromone traps. *J. Cotton Sci.* **2006**, *10*, 155–160.

(30) Wu, K. M.; Lu, Y. H.; Feng, H. Q.; Jiang, Y. Y.; Zhao, J. Z. Suppression of cotton bollworm in multiple crops in china in areas with Bt toxin-containing cotton. *Science* **2008**, *321*, 1676–1678.

(31) Shelton, A. M.; Nault, B. A. Dead-end trap cropping: a technique to improve management of the diamondback moth. *Crop Prot.* **2004**, *23*, 497–503.

(32) Ellsworth, P. C.; Jones, J. S. Cotton IPM in Arizona: a decade of research, implementation and education. In *Proceedings of the Beltwide Cotton Conference*; National Cotton Council: Memphis, TN, 2001; pp 1088−1096.

(33) Ellsworth, P. C.; Fournier, A.; Smith, T. D. *Arizona Cotton Insect Losses*, Publication AZ1183; College of Agriculture and Life Sciences, Cooperative Extension, University of Arizona: Tucson, AZ, 2007 (http://cals.arizona.edu/crops/cotton/insects/cil/cil.html).

(34) Lei, T.; Khan, M.; Wilson, L. Boll damage by sucking pests: an emerging threat, but what do we know about it? In *World Cotton Research Conference III: Cotton for the New Millennium*; Swanepoel, A., Ed.; Agricultural Research Council, Institute for Industrial Crops: Cape Town, South Africa, 2003; pp 1337−1344.

(35) Wilson, L.; Hickman, M.; Deutscher, S. Research update on IPM and secondary pests. In *Proceedings of the 13th Australian Cotton Conference*; ACGRA: Gold Coast, Australia, 2006; pp 249−258.

(36) Wilson, L. J.; Bauer, L. R.; Lally, D. A. Effect of early season insecticide use on predators and outbreaks of spider mites (Acari: Tetranychidae) in cotton. *Bull. Entomol. Res.* **1998**, *88*, 477–488.

(37) Farrell, T.; Mensah, R.; Sequeira, R.; Wilson, L.; Dillon, M. Key insect and mite pests of Australian cotton. In *Cotton Pest Management Guide 2006−07*; Farrell, T., Ed.; New South Wales Department of Primary Industries: Australia, 2006; pp 1−17.

(38) Sharma, O. P.; Bambawale, O. M.; Dhandapani, A.; Tanwar, R. K.; Bhosle, B. B.; Lavekar, R. C.; Rathod, K. S. Assessment of severity of important diseases of rainfed *Bt* transgenic cotton in southern Maharashtra. *Indian Phytopathol.* **2005**, *58*, 483–485.

(39) Williams, M. R. Cotton insect losses 2005. In *Proceedings of the Beltwide Cotton Conference*; National Cotton Council: Memphis, TN, 2006; pp 1151−1204.

(40) Lu, Y.; Wu, K.; Jiang, Y.; Xia, B.; Li, P.; Feng, H.; Wyckhuys, K. A. G.; Guo, Y. Mirid bug outbreaks in multiple crops correlated with wide-scale adoption of Bt cotton in China. *Science* **2010**, *328*, 1151–1154.

(41) Head, G.; Moar, M.; Eubanks, M.; Freeman, B.; Ruberson, J.; Hagerty, A.; Turnipseed, S. A multiyear, large-scale comparison of arthropod populations on commercially managed Bt and non-Bt cotton fields. *Environ. Entomol.* **2005**, *34*, 1257–1266.

(42) Naranjo, S. E. Long-term assessment of the effects of transgenic Bt cotton on the abundance of nontarget arthropod natural enemies. *Environ. Entomol.* **2005**, *34*, 1193–1210.

(43) Whitehouse, M. E. A.; Wilson, L. J.; Fitt, G. P. A comparison of arthropod communities in transgenic Bt and conventional cotton in Australia. *Environ. Entomol.* **2005**, *34*, 1224–1241.

(44) Wolfenbarger, L. L.; Naranjo, S. E.; Lundgren, J. G.; Bitzer, R. J.; Watrud, L. S. Bt crops effects on functional guilds of non-target arthropods: a meta-analysis. *PLoS One* **2008**, *3*, e2118 (DOI: 10.1371/journal.pone.0002118).

(45) Fitt, G. P. Have Bt crops led to changes in insecticide use patterns and impacted IPM? In *Integration of Insect-Resistant Genetically*

Modified Crops with IPM Systems; Romeis, J., Shelton, A. M., Kennedy, G. G., Eds.; Springer: Berlin, Germany, 2008; pp 303−328.

(46) Brookes, G.; Barfoot, P. Global impact of biotech crops: environmental effects 1996−2008. *AgBioForum* **2010**, *13*, 76–94.

(47) Kovach, J.; Petzoldt, C.; Degni, J.; Tette, J. A method to measure the environmental impact of pesticides. *New York Food and Life Sciences Bulletin*; New York State Agricultural Experiment Station, Cornell University: Geneva, NY, 1992 (http://www.nysipm.cornell.edu/publications/eiq/default.asp).

(48) National Cotton Council. *Cotton Crop Loss Data*; National Cotton Council: Memphis, TN, 2010 (http://www.entomology.msstate.edu/resources/tips/cotton-losses/data/).

(49) Whitcomb, W. H.; Bell, K. Predaceous insects, spiders and mites of Arkansas cotton fields. *Arkansas Agric. Exp. Stn. Bull.* **1964**, *690*, 1–84.

(50) Van den Bosch, R.; Hagen, K. S. Predaceous and parasitic arthropods in California cotton fields. *Calif. Agric. Exp. Stn.* **1966**, *820*, 1–32.

(51) Bishop, A. L.; Blood, P. R. B. A record of beneficial arthropods in South East Queensland cotton. *PANS* **1977**, *23*, 384–386.

(52) Zhao, J. Z. Species distribution and population fluctuation of predacious spiders in cotton fields in China. *Nat. Enemies Insects* **1984**, *6*, 1–12.

(53) Romeis, J.; Shanower, T. G. Arthropod natural enemies of *Helicoverpa armigera* (Hübner) (Lepidoptera: Noctuidae) in India. *Biocontrol Sci. Technol.* **1996**, *6*, 481–508.

(54) Dippennaar-Schoeman, A. S.; van den Berg, A. M.; van den Berg, A. Spiders in South African cotton fields: species diversity and abundance (Arachnida: Araneae). *Afr. Plant Prot.* **1999**, *5*, 93–103.

(55) Eveleens, K. G.; van den Bosch, R.; Ehler, L. E. Secondary outbreak induction of beet armyworm by experimental insecticide application in cotton in California. *Environ. Entomol.* **1973**, *2*, 497–503.

(56) Bottrell, D. G.; Adkisson, P. L. Cotton insect pest management. *Annu. Rev. Entomol.* **1977**, *22*, 451–481.

(57) Abdelrahman, A. A.; Munir, B. Sudanese experience in integrated pest management of cotton. *Insect Sci. Appl.* **1989**, *10*, 787–794.

(58) Trichilo, P. J.; Wilson, L. T. An ecosystem analysis of spider mite outbreaks: physiological stimulation or natural enemy suppression. *Exp. Appl. Acarol.* **1993**, *17*, 291–314.

(59) Devine, G. J.; Ishaaya, I.; Horowitz, A. R.; Denholm, I. Effects of piperonyl butoxide on *Bemisia tabaci* Genn. (Homoptera: Aleyrodidae): mortality, development, parasitism and predation in Israeli cotton fields. *Crop Prot.* **1998**, *17*, 717–726.

(60) Naranjo, S. E.; Ellsworth, P. C. Mortality dynamics and population regulation in *Bemisia tabaci*. *Entomol. Exp. Appl.* **2005**, *116*, 93–108.

(61) Sharma, H. C.; Arora, R.; Pampapathy, G. Influence of transgenic cottons with *Bacillus thuringiensis cry1Ac* gene on the natural enemies of *Helicoverpa armigera*. *BioControl* **2007**, *52*, 469–489.

(62) Price, P. W.; Bouton, C. E.; Gross, P.; McPheron, B. A.; Thompson, J. N.; Weis, A. E. Interactions among three trophic levels: Influence of plants on interactions between insect herbivores and natural enemies. *Annu. Rev. Ecol. Syst.* **1980**, *11*, 41–65.

(63) Price, P. W. Ecological aspects of host plant resistance and biological control: interactions among three trophic levels. In *Interactions of Plant Resistance and Parasitoids and Predators of Insects*; Boethel, D. J., Eikenbary, R. D., Eds.; Wiley: New York, 1986; pp 11−30.

(64) Bottrell, D. G.; Barbosa, P.; Gould, F. Manipulating natural enemies by plant variety selection and modification: a realistic strategy? *Annu. Rev. Entomol.* **1998**, *43*, 347–367.

(65) Olff, H.; Brown, V. K.; Drent, R. H. *Herbivores: Between Plants and Predators*; Blackwell Scientific: Oxford, U.K., 1999.

(66) Cortesero, A. M.; Stapel, J. O.; Lewis, W. J. Understanding and manipulating plant attributes to enhance biological control. *Biol. Control* **2000**, *17*, 35–49.

(67) Hare, J. D. Plant genetic variations in tritrophic interactions. In *Multitrophic Level Interactions*; Tscharntke, T., Hawkins, B. A., Eds.; Cambridge University Press: Cambridge, U.K., 2002; pp 8−43.

(68) Federici, B. A. Effects of Bt on non-target organisms. *J. New Seeds* **2003**, *5*, 11–30.

(69) Daily, G. E. *Nature's Services − Societal Dependence on Natural Ecosystems*; Island Press: Washington, DC, 1997.

(70) Naranjo, S. E. Impacts of *Bt* crops on non-target organisms and insecticide use patterns. *CAB Reviews: Perspect. Agric. Vet. Sci., Nutr. Nat. Resour.* **2009**, *4*, No. 011 (DOI: 10.1079/PAVSNNR20094011).

(71) Cannon, R. J. C. Bt transgenic crops: risks and benefits. *Integrated Pest Manage. Rev.* **2000**, *5*, 151–173.

(72) Edge, J. M.; Benedict, J. H.; Carroll, J. P.; Reding, H. K. Bollgard cotton: an assessment of global economic, environmental and social benefits. *J. Cotton Sci.* **2001**, *5*, 121–136.

(73) Groot, A. T.; Dicke, M. Insect-resistant transgenic plants in a multi-trophic context. *Plant J.* **2002**, *31*, 387–406.

(74) Shelton, A. M.; Zhao, J. Z.; Roush, R. T. Economic, ecological, food safety, and social consequences of the deployment of Bt transgenic plants. *Annu. Rev. Entomol.* **2002**, *47*, 845–881.

(75) Conner, A. J.; Glare, T. R.; Nap, J. P. The release of genetically modified crops into the environment. Part II. Overview of ecological risk assessment. *Plant J.* **2003**, *33*, 19–46.

(76) O'Callaghan, M.; Glare, T. R.; Burgess, E. P. J.; Malone, L. A. Effects of plants genetically modified for insect resistance on nontarget organisms. *Annu. Rev. Entomol.* **2005**, *50*, 271–292.

(77) Romeis, J.; Meissle, M.; Bigler, F. Transgenic crops expressing *Bacillus thuringiensis* toxins and biological control. *Nat. Biotechnol.* **2006**, *24*, 63–71.

(78) Sanvido, O.; Romeis, J.; Bigler, F. Ecological impacts of genetically modified crops: ten years of field research and commercial cultivation. *Adv. Biochem. Eng./Biotechnol.* **2007**, *107*, 235–278.

(79) Romeis, J.; Van Driesche, R. G.; Barratt, B. I. P.; Bigler, F. Insect-resistant transgenic crops and biological control. In *Integration of Insect-Resistant Genetically Modified Crops with IPM Systems*; Romeis, J., Shelton, A. M., Kennedy, G. G., Eds.; Springer: Berlin, Germany, 2008; pp 87−118.

(80) Marvier, M.; McCreedy, C.; Regetz, J.; Kareiva, P. A meta-analysis of effects of Bt cotton and maize on nontarget invertebrates. *Science* **2007**, *316*, 1475–1477.

(81) Duan, J. J.; Marvier, M.; Huesing, J.; Dively, G.; Huang, Z. Y. A meta-analysis of effects of Bt crops on honey bees (Hymenoptera: Apidae). *PLoS One* **2008**, *1*, e1415 (DOI: 10.1371/journal.pone.0001415).

(82) Lovei, G. L.; Andow, D. A.; Arpaia, S. Transgenic insecticidal crops and natural enemies: a detailed review of laboratory studies. *Environ. Entomol.* **2009**, *38*, 293–306.

(83) Shelton, A. M.; Naranjo, S. E.; Romeis, J.; Hellmich, R. L.; Wolt, J. D.; Federici, B. A.; Albajes, R.; Bigler, F.; Burgess, E. P. J.; Dively, G. P.; Gatehouse, A. M. R.; Malone, L. A.; Rousch, R.; Sears, M.; Sehnal, F. Appropriate analytical methods are necessary to assess non-target effects of insecticidal proteins in GM crops through meta-analysis (response to Andow et al.). *Environ. Entomol.* **2009**, *38*, 1533–1538.

(84) Duan, J. J.; Lundgren, J. G.; Naranjo, S. E.; Marvier, M. Extrapolating non-target risk of *Bt* crops from laboratory to field. *Biol. Lett.* **2010**, *6*, 74–77.

(85) Torres, J. B.; Ruberson, J. R. Canopy- and ground-dwelling predatory arthropods in commercial Bt and non-Bt cotton fields: patterns and mechanisms. *Environ. Entomol.* **2005**, *34*, 1242–1256.

(86) Naranjo, S. E. Long-term assessment of the effects of transgenic Bt cotton on the function of the natural enemy community. *Environ. Entomol.* **2005**, *34*, 1211–1223.

(87) Sisterson, M. S.; Biggs, R. W.; Olson, C.; Carriere, Y.; Dennehy, T. J.; Tabashnik, B. E. Arthropod abundance and diversity in Bt and non-Bt cotton fields. *Environ. Entomol.* **2004**, *33*, 921–929.

(88) Sharma, H. C.; Ortiz, R. Transgenics, pest management and the environment. *Curr. Sci.* **2000**, *79*, 421–437.

(89) Naranjo, S. E.; Ellsworth, P. C.; Hagler, J. R. Conservation of natural enemies in cotton: role of insect growth regulators in management of *Bemisia tabaci*. *Biol. Control* **2004**, *30*, 52–72.

(90) Wu, K. M.; Guo, Y. Y. The evolution of cotton pest management practices in China. *Annu. Rev. Entomol.* **2005**, *50*, 31–52.

(91) Wu, K. M.; Guo, Y. Y. Influences of *Bacillus thuringiensis* Berliner cotton planting on population dynamics of the cotton aphid, *Aphis gossypii* Glover, in northern China. *Environ. Entomol.* **2003**, *32*, 312–318.

(92) Naranjo, S. E.; Ellsworth, P. C. The contribution of conservation biological control to integrated control of *Bemisia tabaci* in cotton. *Biol. Control* **2009**, *51*, 458–470.

(93) Ellsworth, P. C.; Martinez-Carrillo, J. L. IPM for *Bemisia tabaci*: a case study from North America. *Crop Prot.* **2001**, *20*, 853–869.

(94) Naranjo, S. E.; Ellsworth, P. C. Fifty years of the integrated control concept: moving the model and implementation forward in Arizona. *Pest Manage. Sci.* **2009**, *65*, 1267–1286.

(95) Ellsworth, P. C.; Meade, D. L. Validity of the pinhead square treatment program for pink bollworm suppression and impact of several insecticides on arthropod fauna in cotton. In *Cotton, A College of Agriculture Report*, Series P-96; Arizona Agricultural Experiment Station: Tucson, AZ, 1994; pp 267−277.

(96) Ellsworth, P. C.; Barkley, V. Transitioning Lygus chemical controls to more selective options for Arizona cotton. In *Cotton, A College of Agriculture Report*, Series P-142; University of Arizona: Tucson, AZ, 2005; pp 165−178.

(97) Naranjo, S. E.; Ellsworth, P. C. Fourteen years of Bt cotton advances IPM in Arizona. *Southwest. Entomol.* **2010**, *35*, 437–444.