

# Editorial overview: Pests and resistance: Shedding the albatross of resistance starts by embracing the ecological complexities of its evolution

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Current Opinion in Insect Science 2017, 21:v–viii

For a complete overview see the [Issue](#)

doi:10.1016/j.cois.2017.07.003

2214-5745/Published by Elsevier Inc.

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Thomas W Sappington is a Research Entomologist with USDA-ARS. He received his PhD in Systematics & Ecology at the University of Kansas. He is an insect ecologist with primary expertise in movement ecology, especially of agricultural pests in corn and cotton production systems. He combines a variety of experimental approaches to help characterize insect dispersal at different spatial scales, including mark-recapture, laboratory flight mills, and population genetics. His current research is focused on characterizing long-distance dispersal of western corn rootworm, and the drivers underlying this behavior, in the context of insect resistance evolution and management.

Ah! well a-day! what evil looks  
 Had I from old and young!  
 Instead of the cross, the Albatross  
 About my neck was hung.

Samuel Taylor Coleridge, 1798

In *The Rime of the Ancient Mariner*, Samuel Taylor Coleridge's great poem, a mariner tells the tale of his ship trapped in Antarctic ice. An albatross appears, the ice splits, and a south wind helps the ship escape. The sailors befriend the good-luck albatross, which follows the ship as it sails northward. One day, for no apparent reason, the mariner shoots the albatross with his crossbow. The ship's luck changes, becalmed for days in windless seas. The crew, dying of thirst, hangs the dead albatross around the mariner's neck, an inescapable reminder of the curse now laid upon them all for killing the harmless bird that had rescued them.

In some ways, evolution of resistance by insect pests to human control tactics is a curse as burdensome as an albatross hung round our necks: a reminder of our all-too-human hubris, an oppressive hindrance to our attempts to protect ourselves and our domesticated crops from the ravages wrought by pests. Of course the analogy is not fully transferable, in that pests are not exactly our innocent friends (though we may become fond of the organism we spend so many intimate hours with each day . . . ). But like the curse of the albatross, resistance is difficult to avoid when we are generating strong selection pressure via the bolts of our latest crossbow, and its wrath is inescapable once it has evolved to the point of repeated field failure [1].

To escape the curse of resistance, we scientists seek to understand the molecular, biochemical, and physiological mechanisms that shield the insect from our crossbow, as well as the genes ultimately responsible for these proximate mechanisms. Such knowledge of resistance mechanisms is usually essential to designing effective countermeasures in the form of different management tactics or improved strategies of applying existing tactics. But to truly shed the albatross of pest resistance from around our necks for a given system, we must also come to grips with the evolutionary ecology behind its rise, spread, and maintenance in and among populations.

Adaptation of a species to a pest control measure, such as an insecticide, involves essentially the same evolutionary processes as adaptation to any environmental stressor [2,3]. The living insects targeted by a control tactic are the latest product of countless generations of natural selection by a

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complex history of stressors on their ancestors. New chemical insecticides, or transgenic crops using engineered DNA from *Bacillus thuringiensis* (Bt) to produce an insecticidal protein, are often deployed widely and quickly by humans, putting pest populations under intense selection pressure. Some pest species may adapt rapidly, like Colorado potato beetle (*Leptinotarsa decemlineata*) has to many insecticides [4] and like western corn rootworm (*Diabrotica virgifera virgifera*) has to Bt corn [5]. Others, such as the European corn borer (*Ostrinia nubilalis*) in corn [6] and pink bollworm (*Pectinophora gossypiella*) in U.S. cotton [7], have remained susceptible to transgenic Bt toxins for many generations.

Adaptations to environmental stressors can pre-adapt insects to either tolerate or evolve resistance to human-imposed stressors, that is, control tactics. Several of the reviews in this issue touch on the phenomenon of pre-existing resistance mechanisms, how they arise and how they are maintained. Hoffmann examines what we can learn about rapid adaptation of insect pests to climatic stresses, something of interest and increasingly researchable given the accelerating pace of climate change [3]. Research on the ability of pest populations to adapt to ongoing climate change is not only of direct importance to predicting life history responses or range expansions. In addition, they can help us understand the underlying patterns and potential of adaptive response to control measures like insecticides. Hoffmann finds that the few examples available so far suggest pests can adapt rapidly to changes in climate, but, importantly, they also reveal constraints to rapid adaptation. Understanding the nature of such adaptability and constraints will be facilitated as more pest genomes are used in comparative studies to identify markers associated with adaptive shifts.

Plants do not sit idly by, evolutionarily (and metaphorically) speaking, allowing themselves to be grazed on by every herbivorous insect that happens along. They are usually protected by a toxic cocktail of chemical compounds, which the herbivore must be adapted to detoxify or otherwise circumvent [8]. Alyokhin and Chen explore the connection between the evolution of detoxification mechanisms in insects that allow them to feed on certain host plants, and the ability to adapt to synthetic chemical insecticides by adjusting expression of pre-existing detoxification genes. Insects associated with host plants protected by abundant or novel secondary metabolic compounds tend to be primed to detoxify pesticides. In their review, French-Constant and Bass point out the common assumption that resistance to an insecticide carries a fitness cost, and that resistance allele frequencies will decline in the absence of selection by the insecticide because of those costs. However, they find that evidence for fitness costs of resistance rarely comes from experiments using genetically related strains, which is important for avoiding confounding effects of strain-specific variation. Instead, molecular studies show that pre-existing resistance alleles can be maintained in a population by sexual antagonism and by mechanisms promoting permanent heterozygosity.

Zalucki and Furlong examine the evidence for behavioral resistance to insecticides. Though often posited as a resistance mechanism, they point out the widespread problem of confusing pre-existing behavioral mechanisms promoting avoidance of a toxic compound or toxic environment, with true behavioral resistance. The latter requires demonstration of a heritable increase in a protective behavior in a population over generations. Unambiguous evidence for true behavioral resistance is not at all common. Although Zalucki and Furlong focus on behavior as a resistance mechanism, it occurs to us that the same principle applies to all pre-existing mechanisms

that can protect an individual insect from the negative effects of an insecticide. For example, pre-existing detoxification mechanisms that allow an insect to feed on a host plant, may also render it naturally tolerant to certain insecticides. As a research community, we usually recognize the difference between pre-existing tolerance and evolved resistance in the context of chemical insecticides or transgenic Bt toxins (e.g. [9]), but for some reason we tend to overlook the difference when addressing behavioral mechanisms. Awareness of the difference is important when characterizing efficacy of a control tactic, and when predicting and managing evolution of resistance to it.

When we consider the dynamics of resistance evolution of a pest to a control tactic, we usually envision the effects of a single, well-defined selective agent on a population of individuals that vary in susceptibility, and the heritable change in susceptibility over generations. As complex as this process can be, the array of potential relevant interactions is dwarfed by that when the selective agent also is a living organism, and even moreso when the agent is a group of living organisms with their own population dynamics, ecologies, and capacity to evolve. Cory reviews the literature on evolution of resistance in pests to pathogens, which are often deployed or being developed for use as biocontrol agents. As we saw in the case of behavioral resistance, true resistance of a pest to a pathogen is not easy to demonstrate or characterize, although there are some examples. When attributing causes of change in susceptibility to a pathogen, it can be very difficult to distinguish heritable changes in the pest from changes due to other factors such as virulence of the attacking pathogen strain, virulence of various mixtures of pathogen isolates, endosymbiont-mediated resistance, or immune priming of offspring to fight off attack by the same pathogen in the next generation. Multiple toxins may be produced by the attacking pathogen (e.g. Bt formulations), and it has long been assumed that this kind of diversity will make it difficult for the pest to evolve resistance. After all, pyramiding Bt toxins of different modes of action in transgenic crops is a key insect resistance management (IRM) recommendation [10]. While this predicted pattern appears to hold for at least some baculoviruses, the situation is by no means clear for other entomopathogens, and much more study is needed.

Because we entomologists have seen enough over the decades to know the albatross of pest resistance is a serious threat to our latest crossbow darts, including really expensive ones like transgenic crops, we have undertaken to intervene in clever ways to slow its evolution. And once resistance does evolve, we sometimes can intervene to contain and mitigate its effects on crop production. Intervention with IRM strategies to preserve efficacy of Bt crops has been a fascinating evolutionary experiment implemented on a grand spatial scale over the last 20+

years [11]. Brown and Staňková develop a game theory approach to understanding pest management under conditions where resistance evolution is a threat to a farmer's ability to protect a crop. The essential tension in the models developed by the authors is that of the time horizon over which a farmer makes pest control decisions. Under the 'ecologically enlightened' time-frame of concern, the farmer is focused on short-term consequences and response of the pest population. This corresponds to the typical IPM approach that relies on economic thresholds to guide treatment decisions. Under the 'evolutionarily enlightened' approach, the temporal scale of concern is much longer, where the goal is to retain efficacy of a management tool by slowing resistance evolution. The modeling framework developed by the authors promises to bring fresh insights to bear on development of pest management strategies that maximize the joint benefits of both ecological and evolutionarily enlightened time horizons.

Most current IRM programs involve a structured refuge (from selection) strategy, where a non-Bt variety of the same crop is purposely planted as a nursery of susceptible insects, which will emerge in overwhelming numbers to mate with rare resistant insects emerging from nearby Bt fields [12]. An underlying assumption is that resistant and susceptible individuals disperse from their natal habitat to find one another and mate [13]. This assumption exposes the critical role of pest dispersal in resistance evolution, a topic explored by Miller and Sappington. Accounting for the fundamental phenomenon of dispersal is necessary to designing effective IRM strategies and predicting evolutionary outcomes such as rate of resistance development, likelihood of independent evolution in resistance hotspots, the spatial spread of resistance from a hotspot, and the spatial scale at which mitigation may be effective. The dynamics of resistance spread are affected by the interplay of many factors, including whether resistance alleles are invading an established population or whether the resistant population itself is spreading into new habitat.

Not all countries have agricultural and socio-economic systems amenable to systematically deploying structured non-Bt refuges. But for polyphagous pests, natural refuges of wild host plants or different non-Bt crops may serve the same purpose [14]. Li *et al.* assess the value of natural refuges in different crop/pest agricultural systems. Because there is little or no direct control over the spatial arrangement or even the species composition of potential natural refuges, reliance on them for IRM can be problematic. The factors that have resulted in their successful use in certain scenarios, and those that have led to their failure in others are reviewed. Understanding when a natural refuge will and will not work well is important in predicting the useful lifespan of a new transgenic product or release of an old product in a new region where structured refuges essentially are not an option.

Most studies address evolution of insecticide resistance in a population, focusing on binary interactions between a single pest species and the selective agent. While it is understandable, logical, and useful to simplify the questions being asked and hypotheses to be tested, especially when resistance management and regulatory decisions must be made quickly to keep up with adoption of new pest management products, *Guedes et al.* invite us to pause and consider a larger community-level view. They point out that application of selection pressure, for example, by an insecticide, against a particular target insect in a particular crop will almost inevitably apply collateral pressure to other exposed, off-target organisms [15]. The effects may not include acute mortality, but sublethal effects are potentially important with consequences not only to the affected species themselves, but to the functioning of the larger community, as they extend or even amplify through webs of ecological interactions. Though such studies are daunting, they are not impossible as recent examples illustrate, and represent an important, wide-open field for future research.

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