

Delivering on the Promise of Pheromones

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It has been 50 years since the first successful experiments were performed demonstrating the effectiveness of sex pheromone-based mating disruption and its potential for protecting agricultural crops from damage by insect pests. The results were reported in two papers from Harry Shorey's group in 1967 (Shorey et al. 1967), the second of which appeared in *Nature* (Gaston et al. 1967). These papers provided a new perspective on the possible practical applications of pheromones, and captured the imagination of the scientific community because these behavior-manipulating chemicals were so obviously powerful and species-specific. This class of compounds presented an exciting new opportunity to reduce or replace the use of toxic insecticides with benign control methods that targeted specific pests and suppressed their populations without affecting other organisms.

Indeed, the promise of pheromones was such that in the 1960s and early 1970s, entomology departments and government agencies specifically hired chemists, insect physiologists, and ecologists to explore the use of sex pheromones

for pest management. The goal of these efforts was to develop pheromones for mating disruption of targeted pests, and for monitoring pest populations to better time applications of insecticides in order to minimize the number of applications and consequently, the overall pesticide burden to the environment. Fifty years later, a wide range of pheromone-based products are commercially available and used for managing insects on millions of acres of agricultural crops and forests (Witzgall et al. 2010; Miller and Gut 2015). In addition, millions of pheromone lures are used annually in monitoring traps for detecting the movements of invasive pests and as crucial components of integrated pest management (IPM) plans for hundreds of pest species worldwide (Witzgall et al. 2010).

The intensity and commitment of the early researchers in their efforts to isolate, identify, and develop practical applications of pheromones and related semiochemicals led to the founding of a new journal, the *Journal of Chemical Ecology*, in 1975. The journal was formed in large part to provide a focused venue in which to publish and disseminate results from research on insect pheromones to entomologists, ecologists, chemists, and the greater scientific community.

In subsequent years, the rapidly developing research on insect sex pheromones stimulated interest in other types of insect pheromones, and spread more broadly to encompass the study of semiochemicals in general, comprising any molecules that convey signals or information between organisms of the same or different species. The focus of research also broadened into efforts to understand the sensory neurophysiological, biochemical, and neuroanatomical pathways involved in insect olfaction and gustation. These studies led to major breakthroughs with regard to animal olfaction in general, such as the first characterization of members of the large family of insect odorant receptor proteins (Clyne et al. 1999), a discovery that trailed by only a few years the Nobel Prize-

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winning research on the first characterization of the large family of putative mammalian odorant receptors (Buck and Axel 1991).

Our current wealth of knowledge about insect olfaction and intra- and interspecific insect and plant interactions is a direct offshoot of the enthusiasm generated by the promise implicit in the early days of pheromones, specifically, that pheromones would provide highly specific and safe methods of reducing and eventually replacing toxic insecticides, with all their negative aspects. But, how much of the decades of pheromone- or semiochemicals-related research has resulted in the development of effective technologies that are used routinely by growers and other end-user clientele? How much of the research has translated into commercial products, and have new companies arisen to manufacture and deliver effective and cost-effective products? In short, how much of the large societal investment in semiochemical research has paid off, making good on this initial promise to society?

We hope that some of these questions will be answered by the mixture of reviews and new research articles in this special issue of the Journal. In fact, the theme proved to be so popular that it was not possible to publish all the manuscripts in one issue, so this issue will be followed by a second one that continues the theme of practical applications of chemical ecology. Overall, we hope that the review articles will illustrate how and why some semiochemically-based methods of insect management have been successful, and the various biological, technological, and regulatory issues that have been overcome. Along the same lines, the research articles highlight systems that are still actively being optimized and developed for commercialization, with a broader scope than just insects and their pheromones.

Today, numerous semiochemical products are commercially available, covering the spectrum from routine monitoring for detecting the presence and/or population densities of particular organisms, sentinel traps for the sensitive detection of incursions of invasive species, to mass trapping, mating disruption, attract-and-kill, and other biologically based methods for large-scale control of pest populations. These products are developed, produced, and distributed by a network of companies worldwide, usually with input from academic researchers and growers, and the semiochemical industry perspective is covered in several articles. Our intent is to provide a glimpse of how the fundamental science of chemical ecology has developed from its initial relatively narrow focus on insect pheromones, to the situation today in which chemical ecology is studied across essentially all taxa. The breadth of science also has widened substantially, with studies ranging from the molecular and cellular levels, to whole organisms, and all the way up to whole ecosystems. Thus, today's chemical ecology encompasses molecular biology, biochemistry, organic chemistry, animal behavior, and landscape and microbial ecology, among numerous other disciplines. Many of these disciplines

are showcased in this special issue, with a particular emphasis on the synergy among disciplines that is required for the development of effective methods of exploiting semiochemicals to manage pest populations. This issue presents a few of the many examples of these signaling molecules being used at a commercial or transition-to-commercial level. It must be emphasized that each successful development of a widely adopted semiochemical product invariably results in reduced insecticide applications, with corresponding benefits to human and environmental health and our overall quality of life.

This special issue begins with an article by Cui and Zhu that describes the historical development of semiochemical research and applications in China, with an overview of the current widespread pheromone research, development, and commercialization taking place that is positively impacting Chinese integrated pest management efforts. This is a story that has never before been shared in English language publications. This article is followed by several papers describing the development of sex pheromones for management of pests of fruit crops. First, the evolution of sex pheromone-based mating disruption against moth pests on apples and grapes in the mountainous Trentino-South Tyrol region of northern Italy is reported by Ioriatti and Lucchi. The authors describe how focused, iterative research and development by a consortium of growers, researchers, and industry produced optimized pheromone dispensers and protocols for their use, resulting in widespread acceptance and adoption by growers and effective management of the major pests. Suckling et al. then describe the development and use of a novel pheromone-based mating disruption dispenser system in New Zealand, in which a blend of the sex pheromones of four different moth pests of apples effectively controls all four pests. This unusual system, which through careful design overcomes the potential cross-species interference when such pheromone blends are co-emitted, is likely to be widely adopted because of its ease of use for control of four pests simultaneously.

The next paper by Lance et al. details the complexities involved with the US Department of Agriculture's Animal and Plant Health Inspection Service's (USDA-APHIS) use of pheromone-based mating disruption as a key factor in trying to fulfill the USDA-APHIS mandate of eradicating invasive insect pests. In addition to the purely scientific issues, USDA-APHIS has to deal with numerous societal and logistical issues in both suburban and agricultural landscapes that may affect the chances for success of their efforts, regardless of the effectiveness of the mating disruption technique itself. The paper by Hoshi et al. then illustrates the types of experiments involved in optimizing mating disruption for a particular species, en route to commercializing the technique. A not inconsiderable problem in this case stems from working with a pest species in a poorly known lepidopteran family, which has an

unusual pheromone. The series of papers regarding mating disruption ends with a paper by McGhee et al. regarding experiments using aerosol “mega-dispensers”. These were conducted against the codling moth, and illustrate the importance for any mating disruption technology of optimizing dispenser design and performance in order to achieve effective levels of disruption while lowering cost. The authors show, by reducing by 50 % the amount of codling moth pheromone contained in each aerosol canister, while also reducing by over 90 % the number of nightly sprays emitted by the machines, that levels of codling moth mating disruption can remain high. This substantially reduces cost to growers.

The next two papers deal with the use of sex pheromones and aggregation-sex pheromones in species from two large families of beetles: the Curculionidae (weevils) and Cerambycidae (longhorned beetles). Oehlschlager’s paper describes the successful control of two devastating weevil pests that attack oil palm and date palm, respectively, using semiochemically-based mass trapping. The success of these projects single-handedly elevated the mass trapping technique from a theoretical concept to a widely accepted practice and commercial success, which is now used worldwide on hundreds of thousands of hectares. Hanks and Millar then review the explosion of knowledge during the last decade on the volatile pheromones used by cerambycid beetles, which has provided the key information required to develop practical applications of these pheromones. These applications include monitoring/detection of invasive species, of which there are many in the Cerambycidae, monitoring and conservation of rare and threatened species, and the possible implementation of mating disruption or mass trapping for some species. The enumeration and illustration of the variety of chemical structures in this group, and their parsimony across many of the species groups as well as their within-group differences, will make this paper a valuable resource for years to come for researchers and practitioners alike.

The issue then switches topics to focus on practical applications of kairomones (interspecific chemical attractants) for pest control. Kairomonal baits have been studied for a number of years, but generally with less success than pheromone lures. However, the next three papers in this special issue describe the research and development behind two such baits that have resulted in effective and successful commercial products. Starting with Landolt and Zhang, they describe how an iterative series of carefully conceived and designed trapping experiments resulted in effective kairomonal lures that target stinging wasps in the genera *Vespula* and *Dolichovespula*. The research describes how trap design, as well as the kairomonal lure, was crucial to the development of effective, selective, and consumer-friendly trapping systems. The two subsequent papers by

Gregg and his colleagues describe the different stages in the development of an effective and commercially successful attract-and-kill system that combines a toxicant with a food bait, targeting adults of an important moth pest, *Helicoverpa armigera*. In the second of the two papers, the authors describe the possible, but so far negligible, effects of these aerially applied attract-and-kill baits on non-target insects such as beneficial predatory species.

The next article by Kahn et al. presents the results and the impacts of what has become a “classic” in the annals of chemical ecology: a semiochemically-based, “push-pull” agricultural strategy that has been implemented by and benefited over 100,000 small-acreage maize growers in Africa. The system involves planting an attractive trap crop for lepidopteran stem borers along with a leguminous intercrop that simultaneously repels the stem borers, inhibits growth of a pernicious weed that parasitizes maize, and provides nutrition to the maize through nitrogen fixation. This strategy represents the culmination of decades of research, and it has benefited thousands of subsistence farmers through its low cost, low inputs, sustainability, and its harmony with their agricultural practices in a difficult environment.

The explosion of publications on insect pheromones in the 1960s and ‘70s also stimulated research on chemical communication in vertebrates, and the article by Sorensen describes several promising strategies for use of semiochemicals from fish for control of pests such as sea lampreys and the common carp. Several pheromones have been identified from fish, and Sorensen reports encouraging research results that suggest how these pheromones might be used for population control, or for monitoring population levels of commercially desirable or even endangered species.

Progress in understanding the many elements in insects’ olfactory pathways has been facilitated by a detailed knowledge of the odorant receptor proteins (ORs) that have selective affinities with volatile molecules that convey information to the receiving organism. Because insect olfactory systems are so sensitive and selective, biosecurity and related agencies have explored whether these systems can be exploited as chemosensors for detection and classification of potential agents of harm. In this vein, the final paper by Termtanasombat et al. reports the expression of several insect ORs in Sf21 cells, each of which is differentially tuned to different odors, and the adhesion of these cells to different regions of a sensor plate array without diminishing their responses to their preferred ligands. This technology presents new opportunities for creating durable arrays of odorant-specific cells whose patterns of differential responses to complex odor mixtures can be strategically engineered for different target odors. Their outputs (differential increases in levels of fluorescence) can be read by pattern recognition algorithms to detect and classify both natural and xenobiotic volatiles. Thus, this last paper represents the true integration of tuneable living tissues with machines,

showing how far we have come since the first identification of a pheromone almost 60 years ago.

We are pleased with the wide-ranging scope of the papers comprising this special issue of the Journal, and the follow-on issue containing a second group of papers focused on the topic of practical applications of semiochemicals. Overall, these papers represent just a tiny subset of examples in which semiochemical research has already delivered and continues to deliver practical solutions to pest problems in safe and cost-effective ways. They also give a glimpse of the massive expansion of chemical ecology from its relatively narrow beginnings in the sex pheromones of Lepidoptera, to its current status, in which chemical ecology is recognized as an integral part of the biology and life history of all living organisms.

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