Chemical ecology in retrospect and prospect

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Chemical ecology deals with molecularly mediated biological interactions. Its scope includes the production and chemical characterization of signal molecules, their emission and transmission mechanisms, their detection in recipient organisms, the transduction of these signals, and the neuroendocrine-mediated behavioral or developmental responses they evoke. Inevitably, given the breadth of its mandate, the discipline is the direct beneficiary of advances in analytical and synthetic chemistry, protein chemistry, genetics, neurobiology, ecology, and evolution and, in fact, in virtually every field of the chemical and biological sciences. Because all living organisms emit, detect, and respond to chemical cues, the number and kinds of interactions are essentially limitless. Nonetheless, it is these interactions that underlie and generate the biotic environment in which we live. Certainly, chemical ecology is one of the most fertile research fields of contemporary science.

Because of the extremely broad scope of this field, we found it particularly challenging to decide which topics to include in our Chemical Ecology Special Feature. We obviously had to pick and choose, and our choices may have been somewhat arbitrary. The final result should be seen as a collage of "snapshots from the frontier," and we acknowledge that many other topics might have been chosen. The Special Feature contains 11 articles on a wide variety of subjects, each of which we believe tells an interesting story and illuminates an important area of chemical ecology. We hope that most PNAS readers will find at least a few of these articles to be as fascinating as we did.

We introduce our collection of articles with Thomas Hartmann's essay, "The Lost Origin of Chemical Ecology in the Late 19th Century" (1). Although the discipline of chemical ecology is often considered to be only half a century old, Hartmann reminds us that it has a much longer history. The idea that many natural products found in plants serve as chemical defenses—specifically for protection against herbivores—was put forward many years ago but was subsequently ignored and almost forgotten. The following five articles deepen our understanding of the chemistry of plant/insect interactions by using techniques unimaginable in the 19th century. The articles also illuminate some of the subtle aspects of the evolution and genetic underpinnings of these interactions.

Arthur Zangerl *et al*. (2) quantify, under natural conditions, the selective impact of an herbivore on the defensive chemistry of its host plant. An inquiry into the behavioral responses of aphids and their parasitoids to uninduced and *cis*-jasmone-induced host plants is provided by Toby Bruce *et al.* (3). Shree Pandey *et al.* (4) elucidate the role of small RNAs, elicited by herbivore attack, in activating a plant's chemical defenses.

Joaquín Goyret *et al.* (5) report on the remarkable role of a primary metabolite—carbon dioxide produced by a night-blooming flower—in attracting pollinating hawkmoths. Coby Schal and colleagues (6), adding another dimension to the domain of plant/insect interactions, explore the subject of plant seed dispersal by insects and describe the chemistry underlying ant–seed mutualism in the Amazonian rainforest.

The development of ever-more-sensitive chemical instrumentation for the detection and characterization of signaling compounds continues to play a key role in advancing chemical ecology. Biologists also benefit directly from the exploitation of new technology. Thus, it was the use of high-precision GPS loggers and stomach temperature recorders that allowed Gabrielle Nevitt *et al.* (7) to show that olfactory cues are important in guiding wandering albatross in their foraging for food over thousands of square miles of open ocean.

To understand the factors that promote marine invasions, Ernesto Mollo *et al.* (8) studied the possible relevance of chemical defense mechanisms in permitting sea slugs to take advantage of new niches. The article by William Gerwick and coworkers (9), which also deals with marine chemical ecology, illustrates the promise of a new analytical technique—in this case, newly developed mass spectrometric imaging technology—in determining the distribution of secondary metabolites in marine microbial communities. These investigations take on particular importance because they should allow us to establish which organisms are actually responsible for the biosynthesis of rare secondary metabolites of potential medicinal value.

The final two articles offer further insight into the extremely important subject of secondary metabolite biosynthesis. Chaitan Khosla and coworkers (10) discuss how bacterial polyketide antibiotics have evolved and diversified in nature and point out the value of elucidating these processes for the biosynthetic engineer interested in the production of urgently needed antimicrobial agents. Finally, Michael Fischbach *et al.* (11) present an analysis of the grand theme of how natural selection may drive chemical innovation, resulting in the creation of new natural products. It should be clear to anyone, from the questions addressed in these articles, that chemical ecology has entered a new age.

Chemical ecology, as a hybrid discipline within the natural sciences, is bound to flourish in decades to come, driven by both its exploratory and explanatory potentials. Advances in analytical instrumentation are making it possible to detect and characterize messenger molecules on the basis of ever-smaller quantities of material. By the same token, increased appreciation of the importance of chemical interactions in nature has created an enhanced awareness on the part of both the chemically and biologically minded that much of what remains to be known about the ecological panorama of life has a chemical basis. The truth is, we have only begun to access the molecular treasury of nature and have yet to comprehend the full range of functions associated with these molecules.

Chemoecological relationships of the most unsuspected kinds remain to be discovered: between animal and plant, parasite and host, predator and prey; between the unicellular and multicellular, the social and nonsocial, the kin and non-kin. Pheromones will continue to be characterized, including, one would hope, those elusive ones that are almost certainly produced by humans. Structures and meanings will be found for specific molecules, or blends of mole-

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cules, by which organisms convey information about their mating readiness, state of development, defensive capability, or any number of other parameters. Wide open is the exploration of the microbial frontier, where the spectacular diversity of kind is bound to be matched by the diversity of chemical expression.

It will be highly important to establish cooperative partnerships, such as are only now beginning to be formed, between the chemical ecologist and the genomicist. The capabilities of organisms to generate and receive chemical messages are subject to genetic control, as is the cascade of molecular events by which the messages are relayed systemically and translated into overt action or developmental response. Manipulation of the genes that determine chemoecological capacities has vast biotechnological potential, particularly in agriculture and the pharmaceutical industry. There is also every reason to expect that "chemical prospecting"—the search for, and characterization of, natural products of signal value that is at the very heart of chemical ecology—will continue to yield compounds of unanticipated molecular architecture, from unexpected sources, and of unforeseen (including medicinal) use. Discovery in the realm of chemical ecology, especially insofar as it could reveal imitable mechanisms, could also find application in the emergent field of nanotechnology. In short, chemical ecologists, in the immediate future and beyond, are in for some real fun.

1. Hartmann T (2008) The lost origin of chemical ecology in the late 19th century. *Proc Natl Acad Sci USA* 105:4541–4546.
2. Zangerl AR, Stanley MC, Berenbaum MR (2008) Selection for chemical trait remixing in an invasive weed after reassociation with a coevolved specialist. *Proc Natl Acad Sci USA* 105:4547–4552.
3. Bruce T, *et al.* (2008) *cis*-Jasmone induces Arabidopsis genes that affect the chemical ecology of multitrophic interactions with aphids and their parasitoids. *Proc Natl Acad Sci USA* 105:4553–4558.
4. Pandey SP, Shahi P, Gase K, Baldwin IT (2008) Herbivory-induced changes in the small-RNA transcriptome and phytohormone signaling in *Nicotiana attenuata*. *Proc Natl Acad Sci USA* 105:4559–4564.
5. Goyret J, Markwell PM, Raguso RA (2008) Context- and scale-dependent effects of floral CO_2 on nectar foraging by *Manduca sexta*. *Proc Natl Acad Sci USA* 105:4565–4570.
6. Youngsteadt E, Nojima S, Häberlein C, Schulz S, Schal C (2008) Seed odor mediates an obligate ant–plant mutualism in Amazonian rainforest. *Proc Natl Acad Sci USA* 105:4571–4575.
7. Nevitt GA, Losekoot M, Weimerskirch H (2008) Evidence for olfactory search in wandering albatross, *Diomedea exulans*. *Proc Natl Acad Sci USA* 105:4576–4581.
8. Mollo E, *et al.* (2008) Factors promoting marine invasions: A chemoecological approach. *Proc Natl Acad Sci USA* 105:4582–4586.
9. Simmons TL, *et al.* (2008) Biosynthetic origin of natural products isolated from marine microorganism–invertebrate assemblages. *Proc Natl Acad Sci USA* 105:4587–4594.
10. Ridley CP, Lee HY, Khosla C (2008) Evolution of polyketide synthases in bacteria. *Proc Natl Acad Sci USA* 105:4595–4600.
11. Fischbach MA, Walsh CT, Clardy J (2008) The evolution of gene collectives: How natural selection drives chemical innovation. *Proc Natl Acad Sci USA* 105:4601–4608.