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Biological Bulletin Virtual Symposium: The Neuroecology of Chemical Defense

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In 2006, *The Biological Bulletin* initiated the idea of publishing "virtual symposia," a series of papers, in a single issue, on a compelling theme that is central to the scope of this journal. The inaugural virtual symposium, on marine invertebrate models of learning and memory, was introduced in an article by McPhie and Miller (2006). Here, we present the second chapter, focusing on "The Neuroecology of Chemical Defense."

The present symposium was inspired by recent discoveries in chemical ecology, which itself is derived from multiple infusions of new ideas over the last half century. Studies in chemical ecology share the common trait of using chemistry to explain biological interactions at the level of individual organisms, populations, or communities. Chemical ecology currently has at least two major, independent branches. The first, chemical communication, developed through pioneering investigations by notable ethologists. For example, Karl von Frisch (1941) described the behavioral reactions of European minnows to alarm substances from skin from damaged conspecifics. These compounds are emitted only after successful predatory attack and thus serve as an early warning to other, yet-unharmed, minnows. Such studies ultimately inspired physiologists to seek to understand the cellular basis of behavior, giving rise to the field of neuroethology. Today, investigations linking chemistry, physiology, and behavior flourish, with a common goal of understanding the molecular basis and evolutionary ecology of chemical communication systems. The second branch of chemical ecology, allelopathics and defense, arose as a consequence of insights by organic chemists. Working mainly on plants, they discovered a variety of unique natural products that lack primary metabolic function. Some of these "secondary" metabolites occur at extraordinarily high concentrations and are synthesized only at considerable energy investment. This interesting paradox was solved using a combination of elegant laboratory and field investigations. Secondary metabolites were found to act as critical determinants of allelopathy, by inhibiting growth or survivorship of competitive plant species, and of chemical defense, by reducing herbivory. In addition to incorporating the idea of defense and allelopathics into general theories on plant ecology at population and community levels, contemporary research in chemical ecology involves topics such as mechanisms of genetic regulation of biosynthesis, models of the acquisition and sequestration of toxins, and contributions of constitutive *versus* inducible defenses.

Over time, the two branches of chemical ecology have merged into a single, unified trunk. No longer is there a clear distinction between bioactive molecules acting either in communication or in defense. Many herbivorous animal species, for example, exhibit resistance, borrowing plant toxins for their own defense and using these same compounds or their metabolites in courtship and mate attraction. Moreover, toxins act as feeding attractants for consumer species that are resistant to its adverse effects. Similarly, plants use volatile chemical constituents for communicating with each other at a distance. Airborne substances released in response to herbivore attack are carried downwind, reaching plants not yet in contact with the predator and activating inducible chemical defenses in their tissues. Thus, lines are blurred between experimental studies on animal and plant taxa, and between chemical communication and defense.

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This virtual symposium synthesizes ideas and approaches in neuroecology, with the goal of promoting a continued fusion of disciplines.

In fact, this symposium renovates and refocuses the term "neuroecology," which has had limited usage and in disparate contexts. It was first applied to describe the interactions of neurons during development as they compete for survival in their extracellular environment (Purves and Lichtman, 1985). Next, it was used to describe the specializations of nervous systems, especially the evolution of cognitive functions of vertebrates. This second definition was criticized by Bolhuis and Macphail (2001), and then defended by Sherry (2005) among others. Currently, we co-opt the term neuroecology for a different use. Nervous systems are sculptured by evolution through natural selection. Many ecological interactions among individual organisms are mediated by behavioral processes. The outcomes of these organismal-level encounters have profound consequences for populations and communities. Thus, neuroecology synthesizes neuroethological and ecological principles, embodying both the neural basis for behavior and the role of behavior in establishing patterns of organism abundances and species distributions within natural habitats. It scales from molecules to communities or ecosystems.

This symposium presents six papers from leading scientists in the emerging field of neuroecology. Collectively, they develop concepts from research performed within diverse native environments (freshwater, marine, terrestrial), using a wide range of taxa (mammals, salamanders, fish, insects, snails, crustaceans, seaweeds, bacteria), across many disciplines (behavioral and community ecology, neuroscience, molecular biology, evolution, and systematics).

The first paper is "Neuroecology, Chemical Defense, and the Keystone Species Concept," by Richard Zimmer and Ryan Ferrer of The University of California, Los Angeles. The authors present the idea that neurotoxins function in keystone roles, by affecting species interactions at multiple trophic levels. Two potent neurotoxins, tetrodotoxin in riparian stream environments and saxitoxin in coastal ocean environments, are introduced into communities by limited sources as a means of chemical defense. Once in the environment, these compounds are borrowed by consumer species that are resistant to their effects, and used either as chemical defenses against their own natural predators or as signals in chemical communication. The consequences of the broad distribution of these molecules in natural communities include changes in species compositions and rates of material exchange.

The second paper is "Chemical Defenses: From Compounds to Communities," by Valerie Paul, Karen Arthur, Raphael Ritson-Williams, Cliff Ross, and Koty Sharp, of the Smithsonian Marine Station at Fort Pierce, Florida. It considers some of the better-studied marine natural products with respect to their effects on marine organisms and communities. The chemicals of focus are okadaic acid, brevetoxins, lyngbyatoxin A, caulerpenyne, bryostatins, and isocyano terpenes. These examples take the reader to both benthic and pelagic communities, and include harmful algal blooms, invasive algae in coral reefs, microbial symbionts, and invertebrate chemical defenses. For each compound, the authors describe its biochemical synthesis; mechanisms of action at the cellular, systems, and organismal levels; and ecological effects, including trophic interactions and community composition.

John Glendinning, of Barnard College, Columbia University, contributes "How Do Predators Cope With Chemically Defended Foods?" He describes the abundance of chemically defended cuisine available to carnivorous, insectivorous, and herbivorous predators, and the resultant challenges the predators face. Findings are presented on how predators adapt to detect, and then avoid, tolerate, or otherwise overcome toxic and noxious defensive chemicals. To illustrate how generalist predators handle natural, chemically defended prey, two case studies are outlined: mice living in dense over-wintering populations of monarch butterflies in Mexico, and free-ranging livestock that face a diversity of chemically defended plants in the western United States.

"Has Vertebrate Chemesthesis Been a Selective Agent in the Evolution of Arthropod Chemical Defenses?" is the next contribution, by William Conner, Kerensa Alley, Jonathan Barry, and Amanda Harper, of Wake Forest University. This paper considers, from an evolutionary perspective, what factors determine the set of defenses used by terrestrial arthropods, especially insects. The authors apply multivariate statistics to compare the composition of defensive compounds in a range of arthropods and to examine the degree to which phylogeny and shared vertebrate predators shape the arsenal of defensive chemicals. The nature of the trigeminal system of vertebrates, which detects chemical irritants, has driven the evolution of chemical defenses of arthropods. Furthermore, the authors propose the use of their methodology to identify new irritant receptors of vertebrates.

"Escape by Inking and Secreting: Marine Molluscs Avoid Predators Through a Rich Array of Chemicals and Mechanisms," by Charles Derby, Georgia State University, is the next paper. This review focuses on ink as a chemical defense, especially for marine molluscs such as sea hares, cuttlefish, squid, and octopuses. These inks are often considered to operate in the visual modality, although experimental demonstrations of their protective effects against predators are virtually nonexistent. The author describes experimental studies demonstrating that sea hares use ink to enhance their chances of escaping predatory attacks; the studies include identification of bioactive molecules and demonstration that they act through the chemosensory systems of predators. Among the defensive mechanism are some surprises—phagomimicry and sensory disruption—in addition to the more typical mechanisms employing distasteful or toxic compounds. The review also describes initial attempts to extend these themes from sea hares to other inking molluscs among the cephalopods.

Florian Weinberger, of Leibniz-Institut für Meereswissenschaften, contributes the final paper, "Pathogen-Induced Defense and Innate Immunity in Macroalgae." Most investigations of plant chemical defenses focus on their interactions with herbivores, as detailed especially in the contribution by Paul *et al*. (2007). Weinberger's article broadens this discussion by exploring the use of chemical defenses in plant-microbe interactions. Whereas neither plants nor microbes have nervous systems, they have sensory and response elements that make plant-microbe interactions relevant to neuroecology and instructive about the evolution of chemical defenses from mechanistic and ecological perspectives. Weinberger describes receptor-mediated immunities in seaweeds as defensive mechanisms that are induced by attack from and infection with microbes.

We hope that taken as a whole, this virtual symposium inspires interest in neuroecology and imparts an appreciation for combining diverse approaches, methodology, and experimental systems to answer fundamental research questions. The organizers thank each participant for providing excellent contributions in a timely manner, James Olds for graciously encouraging and supporting the ideas, Carol Schachinger for outstanding administrative assistance, Cheryl Ann Zimmer for applying her incredible editorial prowess to this introduction, and Victoria Gibson for effective editing of the symposium as a whole.

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