

Profile of Anurag A. Agrawal

Matthew Hardcastle, *Science Writer*

Anurag A. Agrawal once considered himself a “muddy boots ecologist,” but his career studying the interactions between plants and insects has led him to embrace a multidisciplinary approach, incorporating the latest tools from genetics and exploring the intricacies of chemical interactions. Much of his research has focused on the relationship between milkweeds (*Asclepias* spp.) and monarch butterflies (*Danaus plexippus*). Milkweed plants produce abundant toxins to repel insects and other herbivores, but the caterpillars of monarch butterflies have evolved to exclusively feed on toxic milkweed leaves. This relationship formed the subject matter of Agrawal’s popular science book, *Monarchs and Milkweeds* (1), published in 2017. Agrawal, who was elected to the National Academy of Sciences in 2021, is currently the James Perkins Professor of Environmental Studies at Cornell University in Ithaca, New York. In his Inaugural Article (2), Agrawal explores the dynamics of an evolutionary arms race between common milkweeds (*Asclepias syriaca*) and large milkweed bugs (*Oncopeltus fasciatus*).

Early Inspiration

Agrawal grew up in Allentown, Pennsylvania. Family camping trips and his mother’s love of gardening instilled in him an early appreciation of the outdoors, but he did not initially consider biology as a career. He enrolled at the University of Pennsylvania, in part because it was “close enough to home, but not too close,” with the intention of studying social sciences. However, as part of a bargain with his parents, he agreed to take some math and science courses. For introductory biology, Agrawal chose a course taught by evolutionary ecologist Daniel Janzen. “I thought, if I’m going to take a biology class, this is the one for me,” he says.

Janzen was known for his extensive field work in Costa Rica (3). “He was a super inspiring lecturer,” Agrawal says. “I took that class and was like, ‘Whoa, that’s mind blowing. Could I study this stuff?’” Janzen’s work on the ecological, evolutionary, and chemical interactions between plants and animals was particularly inspiring to Agrawal. The same topics would form the basis of his own academic career. Agrawal graduated from the University of Pennsylvania in 1994 with a Bachelor’s degree in biology and a Master’s degree in conservation biology.

For his Master’s research project, Agrawal followed in the footsteps of the American ecologist E. Lucy Braun. American chestnuts (*Castanea dentata*) were once a dominant tree species on the eastern coast of North America. As Agrawal explains, the trees once comprised 20 to 50% of many forest stands. In 1904, a fungal blight was accidentally introduced and wiped out nearly every American chestnut east of the Mississippi River in the span of two decades. Braun surveyed stands of American chestnuts as



Anurag A. Agrawal. Image courtesy of Anurag Agrawal (Cornell University, Ithaca, NY).

they were disappearing (4), and Agrawal returned to some of the same locations to explore how other tree species adapted to the rapid removal of a dominant species. By coring trees that predated the chestnut blight, Agrawal documented evidence of rapid growth in response to the light and nutrients made available by the American chestnuts’ disappearance.

Branching Out

When considering graduate schools, Agrawal was determined to move farther from home. He ultimately chose the University of California at Davis based on advice that going to a land-grant university would be beneficial for his career, given the scope for biological research at such institutes. Agrawal earned a doctorate in population biology from the University of California at Davis in 1999. His thesis project explored the costs and benefits of immune-like defensive strategies in plants (5).

“‘Immune-like’ is important for two reasons,” Agrawal says. “It’s not an actual immune system in plants like that in animals, but it functions in a similar way. Plants may hold back their defensive arsenal until after an herbivore starts munching. And once plants get the signals that they’re under attack, they upregulate toxins. My dissertation was about the economy of that adaptation.” Agrawal found that plants’ immune-like defensive strategy increased their fitness in terms of seed production. However, releasing an

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A monarch butterfly (*D. plexippus*). Image courtesy of Anurag Agrawal (Cornell University, Ithaca, NY).

unnecessary defensive response imposed a cost in the form of diminished pollen production.

As a postdoctoral researcher, Agrawal moved even farther from home to the University of Amsterdam. “I got more interested in the insect side of the plant–insect interaction,” he says. In the Netherlands he studied arthropods in the Tetranychidae family, called spider mites (6). The tiny mites are well-suited to population and evolutionary studies, given their short and prodigious reproductive cycles. “I also gained an appreciation for the mite as an individual organism with really interesting behaviors.”

Agrawal’s first faculty position was at the University of Toronto, in the botany department. While he enjoyed living and working in Toronto, a growing family at home prompted Agrawal to seek a change in favor of small-town life. In a return to the northeastern United States, Agrawal accepted a position at Cornell University, also a land-grant university, in Ithaca, New York, in 2004.

Monarchs and Milkweeds

At Cornell, Agrawal began charting an interdisciplinary research program, with a focus on the biodiversity of the northeastern United States. “I can go hiking and also make observations—take my kids to these places,” he says. “Our local biodiversity is remarkable. You don’t have to go to the tropics to see the really beautiful organisms. They definitely bite you in the nose a bit more in the tropics, but there’s equally beautiful and amazingly adapted organisms in the Northeast.”

A significant focus of Agrawal’s research has been the interactions between monarch butterflies and milkweeds. “[Monarch butterflies] have spectacular biology,” he says. “By that, I mean everything, from their coloration, to their toxicity, to the long-distance migration.” Both Monarch butterflies and their caterpillars are brightly colored as a warning to potential predators of their toxicity, which is derived from toxins in the milkweed leaves that form the entirety of the caterpillars’ diet. In North America, monarch butterflies undergo long-distance seasonal migrations that can span 4,500 km.

As an added benefit, both monarch butterflies and milkweeds can be abundantly found in Agrawal’s backyard. “In ecology,” he says, “it’s important for some people to study the rare organisms. They’re rare for a reason. And they might be a conservation concern. But it can be a challenge to study rare organisms. The fact that milkweeds and monarchs are abundant and widely distributed makes them a great group to study.”

Agrawal’s research has also taken him to distant locales, including a sabbatical in Mexico. “At 10,000 feet of elevation,” he says, “on the tops of these mountains is where the monarchs go for the winter. Literally hundreds of millions of butterflies congregate in an area the size of New York City. Nearly all of them east of the Rockies fly south to Mexico and overwinter there.” He has also traveled across North America in search of milkweeds (7). “There are 130 milkweed species, believe it or not, in North America. One of the things that I do is travel to the different places where there are other milkweed species and try to understand their relationships with monarchs.”

Adaptive Defense in Milkweeds

In Agrawal’s Inaugural Article (2), he explores the evolutionary interaction between common milkweeds and large milkweed bugs, using monarch butterflies as a point of comparison. He also explores geographical patterns in milkweed defense by sampling common milkweed populations across almost 13° of latitude, from Quebec City, Canada, to Bishop, North Carolina.

“We found some evidence that defense expression is not linear as you move north to south, but it actually peaks in the range-center, where milkweed is most abundant.” Next, Agrawal and his colleagues took a closer look at the toxins produced by milkweeds. “The milkweeds make a group of toxins called cardenolides. They’ve been known for decades as being poisonous. And any one milkweed species might produce 20 to 30 different types of cardenolides.”

In particular, Agrawal was interested in the toxin labriformin, one of the few cardenolides that contains a nitrogen atom. Nitrogen tends to be a limited resource for plants, so it follows that milkweeds must have a solid reason for using valuable nitrogen in a toxin. Agrawal and colleagues tested the effectiveness of labriformin in disrupting enzymes extracted from the neural tissues of large milkweed bugs, monarchs, and other insects.

“Labriformin isn’t really much more toxic than any other cardenolide when applied to a nonmilkweed herbivore. And that tells us that the plant isn’t producing labriformin as a defense against the general insect population. As it turns out, labriformin has much higher toxicity when tested against organisms like the large milkweed bug.” Agrawal also found that monarch butterflies were more susceptible to the toxin than large milkweed bugs. “The monarch is totally suppressed by labriformin, even at low doses, but the large milkweed bug is able to tolerate 18 times more than monarchs.”

As Agrawal explains, the results suggest that, among the many toxins produced by milkweeds, labriformin is adapted as a defense against specialist herbivores. Indeed, the toxin is most concentrated in the seeds of milkweeds, which are eaten by large milkweed bugs. Large milkweed bugs have, in turn, developed a high tolerance for the toxin, reflecting the ongoing evolutionary interaction between the two organisms.

Monarch Conservation and Beyond

Over the past 30 years, monarch butterfly populations have been decreasing, drawing concern from researchers

and butterfly enthusiasts. As much as Agrawal has narrowly focused on monarchs and milkweeds in his research, he notes that in many ways they are representative of broad biological principles. "People want to conserve monarchs and milkweeds, and I tell them, that's great, but the goal isn't to conserve these two species. The goal is to conserve functioning ecosystems of all the species that can thrive there."

When it comes to the fate of monarch butterflies, Agrawal says, "I think I'm at once hopeful and pessimistic." On the pessimistic side, Agrawal notes that monarch butterfly populations are declining on the scale of the entire North American continent and mirror ongoing declines in many other migratory species. This suggests that the

problem may be on a continental scale and unlikely to be solved by well-intentioned but small-scale efforts, such as planting more milkweeds.

"The good news for monarchs in particular," Agrawal says, "is that they are an abundant species that is crafty and flexible. Monarchs have been introduced to other continents, and their [biology has] shifted in those places. They have a totally different seasonal migration in Australia. There are nonmigratory populations in Hawaii and Spain. So, the species isn't going extinct, but I think that we can learn something about its decline, to understand some general principles about what's happening on the continent, so that we can conserve ecosystems and the services they provide."

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