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BASICS

Gene-Modified Ants Shed Light on How Societies Are Organized

Dr. Daniel Kronauer, shown in a double exposure, above, studies ants with altered DNA in order to understand complex biological systems. Credit Béatrice de Géa for The New York Times

By Natalie Angier

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Whether personally or professionally, Daniel Kronauer of Rockefeller University is the sort of biologist who leaves no stone unturned. Passionate about ants and other insects since kindergarten, Dr. Kronauer says he still loves flipping over rocks "just to see what's crawling around underneath."

In an amply windowed fourth-floor laboratory on the east side of Manhattan, he and his colleagues are assaying the biology, brain, genetics and behavior of a single species of ant in ambitious, uncompromising detail. The researchers have painstakingly hand-decorated thousands of clonal raider ants, Cerapachys biroi, with bright dots of pink, blue, red and lime-green paint, a color-coded system that allows computers to track the ants' movements 24 hours a day — and makes them look like walking jelly beans.

The scientists have manipulated the DNA of these ants, creating what Dr. Kronauer says are the world's first transgenic ants. Among the surprising results is a line of Greta Garbo types that defy the standard ant preference for hypersociality and instead just want to be left alone.

The researchers also have identified the molecular and neural cues that spur ants to act like nurses and feed the young, or to act like queens and breed more young, or to serve as brutal police officers, capturing upstart nestmates, spread-eagling them on the ground and reducing them to so many chitinous splinters.

Dr. Kronauer, who was born and raised in Germany and just turned 40, is tall, sandy-haired, blue-eyed and married to a dentist. He is amiable and direct, and his lab's ambitions are both lofty and pragmatic.

"Our ultimate goal is to have a fundamental understanding of how a complex biological system works," Dr. Kronauer said. "I use ants as a model to do this." As he sees it, ants in a colony are like cells in a multicellular organism, or like neurons in the brain: their fates joined, their labor synchronized, the whole an emergent force to be reckoned with.

"But you can manipulate an ant colony in ways you can't easily do with a brain," Dr. Kronauer said. "It's very modular, and you can take it apart and put it back together again."

Dr. Kronauer and his co-authors describe their work in a series of recent reports that appear in Proceedings of the National Academy of Sciences, The Journal of Experimental Biology and elsewhere.

A color-coded system allows computers to track the ants' movements 24 hours a day. Credit Béatrice de Géa for The New York Times

The researchers hope to turn the clonal raider ant into a so-called model organism, right up there with such laboratory stalwarts as E. coli and Drosophila. But while bacteria and fruit flies have proved invaluable for addressing fundamental questions of how genes operate or body plans arise during development, Dr. Kronauer's model ants offer scientists the chance to explore, under controlled conditions, the origin and evolution of animal societies.

"His system is unbelievably promising for anyone who wants to study social behavior," said Corina Tarnita, an associate professor of ecology and evolutionary biology at Princeton University who has worked with termites and microbial communities.

"You can ask, what are the basic ingredients, the elementary operations that nature has used repeatedly to produce societies — whether you're talking about ants, slime molds, baboons or even the very first human societies."

Gene Robinson, a honeybee expert and director of genomic biology at the University of Illinois at Urbana-Champaign, said, "Social insect colonies are the quintessential complex system, and Daniel has developed a very powerful set of tools addressing big questions of how they operate, and how, in the absence of central control, local interactions can give rise to global patterns."

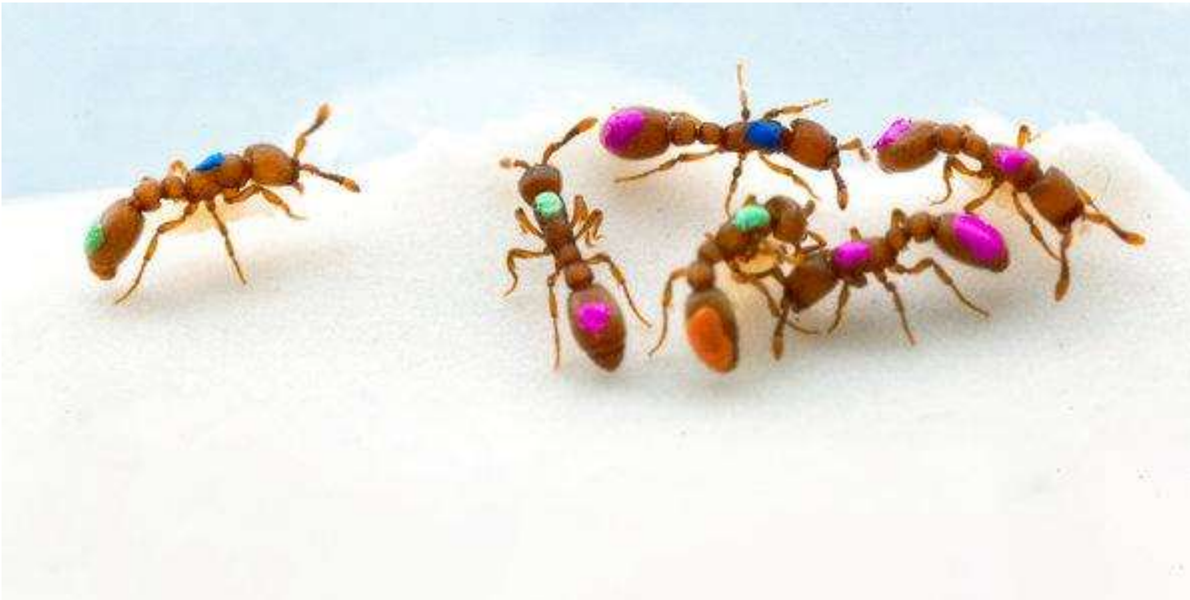
Ant Research, Human Insights

One key to the raider ant's potential as a laboratory workhorse is its adaptability. Many ants are finicky. Not so Cerapachys.

"It's a weedy species," Dr. Kronauer said. "That's true of a lot of model organisms — they have a global distribution, they're good at invading disturbed habitats, and they're good at being raised in a lab."

To trace the knotted skeins of antly social life, the researchers take a battery of approaches. They knock out ant genes or edit the lettering of ant genes and see how the ants respond. They ply ants with radioactively labeled neurochemicals and check where in the ants' brains the signaling molecules gain purchase.

They measure ant movements by fractions of a millimeter as the insects perambulate along finely calibrated grids traced in ceramic. They overfeed the ants and starve the ants; they mix and match ants of varying age, life experience and transgenicity.



By using gene knockout techniques, the researchers made some raider ants display asocial behavior. Credit Béatrice de Géa for The New York Times

The project represents basic research at its most seductively cerebral, yet it may well reveal insights into human disease, like why cancer cells ignore all stop signals from their surroundings, or why the brain turns in on itself during depression.

“By studying the neuromodulators that make ants so sensitive to their social environment,” Dr. Kronauer said, “we could learn something fundamental about autism and depression along the way.”

The five-year enterprise has not been glitch free. Early on, the ants were stricken by a mite infestation. “It came out of nowhere and killed off 80 percent of the colonies,” Dr. Kronauer said. “I went home and told my wife, we’re done.”

Now the protocols are established, the ants are thriving and members of Dr. Kronauer’s lab handle their subjects with deft efficiency. In one experiment, Vikram Chandra, a graduate student, plucked individual ants from a dish with a small pair of pliers and passed the tool over to Amelia Ritger, a research assistant.

She peered through a microscope to inject a dose of hormone into each ant’s abdomen and then returned the pliers to Mr. Chandra for a refill. “We’ll go through a few hundred of these over the next couple of hours,” Ms. Ritger said.

“In structuring our work routine,” Mr. Chandra said dryly, “we decided to take a tip from the ants.”

Dr. Kronauer said his students and postdoctoral fellows designed everything from scratch: computer algorithms, tracking devices, the incised mazes. “They’re engineers, code writers, neuroscientists,” Dr. Kronauer said. “Me, I’m just the guy who knows about ants.”

In fact, Dr. Kronauer spent years studying ants in the field, working with slave-making ants in Arizona and army ants in Costa Rica. But as much as he loved fieldwork, he began to feel that chasing army ants through the forest was like chasing chimpanzees.

Clonal raider ants are adaptable, which could make them a good laboratory workhorse. Credit Béatrice de Géa for The New York Times

“They move, you follow. You can’t really do experiments,” he said. He wanted to delve deeper, take ants back to the lab, do sequencing, transgenics, knockouts, molecular work, the whole fruit fly buffet. But what sort of ants would comply?

As a rule, biologists who study ants in the lab must constantly replenish their stocks from the wild, which would preclude the precise genetic research Dr. Kronauer had in mind. Then he happened on three papers about the obscure C. biroi, and he knew he’d found his ant.

Mixed Signals

Beyond its amenable weediness, the clonal raider ant seems almost custom-tailored for experimentation. The world’s 12,000 known species of ants display a variety of reproductive and survival strategies. The most familiar examples are the fully eusocial ants, in which many sterile female workers do all the chores, a single large queen lays all the eggs, and a sprinkling of male ants, or drones, supply the sperm.

Among clonal raider ants, there are no permanently designated workers and queens. Instead, all the ants in a colony switch back and forth from one role to the other. About half the time, they behave like workers, gathering food for their young — generally, by raiding the nests of other ants and stealing their larvae.

The rest of the time, they go into queen mode and all colony members lay eggs together. Moreover, there are no male raider ants: The eggs develop parthenogenetically, without sperm, creating phalanxes of genetically identical female clones.

The ants' unusual mix of genetic uniformity and wildly protean conduct offers a powerful tool for cracking the old nature-versus-nurture conundrum, and the Kronauer researchers have been mapping out the interplay between genes and environmental cues in shaping essential behaviors like reproduction and sociality.

Sequencing the genome of the ant, the scientists found that one class of odorant receptor genes had been "massively expanded," Dr. Kronauer said, suggesting that C. birois may be even more dependent than the average ant on chemical communication. The researchers then used gene knockout techniques to eliminate that category of odorant receptors from some ants, and the results were startling.

The knockout ants had no trouble detecting food. In fact, Dr. Kronauer said, "they would eat much more than other ants do." Their appetite for socializing was another matter.

"Our ultimate goal is to have a fundamental understanding of how a complex biological system works," Dr. Kronauer said of his work with ants. Credit Béatrice de Géa for The New York Times

Whereas normal raider ants will happily pile on top of one another whenever possible, the knockout ants avoided the crowd, instead wandering around on their own for days at a time, as though they were nothing more than the average asocial beetle.

The results suggest that the diversification and specialization of olfactory receptors were keys to the evolution of ant sociality.

The researchers are also exploring the biochemistry of caretaking, asking which signals prod ants to leave the nest and find food for their young.

Preliminary results suggest that volatile pheromones exuded by newborn larvae stimulate the brains of adult ants to begin generating the hormone inotocin, the ant's equivalent of oxytocin, which is famed for its role in promoting nurturing behavior among mammals.

For raider ants, an inotocin surge galvanizes the urge to venture forth and start plundering, and ants with the greatest number of inotocin-making neurons, Dr. Kronauer said, "are the first ones out the door."

Some ants, by contrast, ignore the community cues altogether, and they pay dearly for their scoffery.

Reporting in the journal Current Biology, Dr. Kronauer and his colleagues described the strictness with which a colony of clonal ants synchronized its schedule: Now everyone lays eggs, now the eggs hatch into larvae, now the adults shut down their ovaries and instead attend to the hungry young.

On occasion, though, an ant's ovaries remain animated when they should be suspended, and other ants can detect the illicit activity through telltale hydrocarbon signatures on the offender's cuticle. Policing ants soon move in on the hyperovarian individual, drag it out of the nest, hold it down and pull it apart, an execution that can take hours or days.

"These ants are like little tanks," Dr. Kronauer said.

Why is it important to kill off an ant that might breed off-season when that ant is your genetic twin? Dr. Kronauer compared the police ants to the body's immune system, and the rebel ant to cancer.

"An ant colony faces similar problems as a multicellular organism," he said. "You can't have components that don't respond to regulatory cues and start to replicate out of control."

When the ant police come knocking, there's no rock big enough to hide you.