demics and focusing control efforts. Some countries already use a relatively unsophisticated trap developed by the U.S. Centers for Disease Control and Prevention (CDC) to keep track of pathogens. But this trap, which relies on just CO_2, light, or a combination, catches a motley array of insects—often not those most relevant to human health. To catch *An. gambiae*, says Takken, a human needs to be nearby, and because the attractiveness of people varies, so does the nightly catch. Spiking such a trap with a specific odor blend could lead to a much better and more reproducible haul, he says.

Other mosquito-thwarting strategies on the drawing board are clever new repellents. If, for instance, researchers could find compounds that overstimulate crucial odor receptors, they might be able to disorient the insects, dooming them to a life of aimless buzzing, Zwiebel says. It might even be possible, he says, to tinker with the receptors that help mosquitoes find nectar or places to lay their eggs.

In the meantime, attraction studies with human volunteers suggest another, more down-to-earth approach to keeping mosquitoes at bay. Among his human subjects, chemist Ulrich Bernier of the U.S. Department of Agriculture in Gainesville, Florida, has found some people who are almost never bitten. His team has isolated compounds from their skin—he declines to discuss which ones—that he believes might be a clue to the protection. Someday, he speculates, they could serve as a natural, less toxic alternative to DEET.

Splashing yourself or your house with somebody else's body odor might not sound all that enticing. But at the levels needed to keep bugs away, Bernier assures, humans won't smell a thing. **–MARTIN ENSERINK**

NEWS

Lab v. Field: The Case for Studying Real-Life Bugs

Molecular entomology is all well and good, some researchers say—but what about studying insects where they live and breed: in the field?

These querulous observers don't want to sound like curmudgeons. Nor do they want to take away anyone's scientific glory. But some tropical disease researchers say they just can't get very excited about the sequence of the *Anopheles gambiae* genome, published in this issue of *Science*. To be sure, the sequence promises to reveal the inner workings of the mosquito in unprecedented detail, shedding light on everything from its metabolism to insect evolution. But skeptics aren't convinced it will actually help control malaria—or, as Chris Curtis of the London School of Hygiene and Tropical Medicine puts it, "pass the so-what test."

For more than a decade now, Curtis and other vector ecologists have argued that the field of insect-borne diseases—whether malaria, dengue, West Nile virus, or Lyme disease—is betting too many of its scarce research dollars on high-tech work like DNA sequencing and too few on studies of insect behavior and ecology, the type of fieldwork that gets your back sweaty and your hands dirty. To figure out how these diseases behave, they say, you have to don your boots rather than start your sequencer (see p. 87).

The riposte from molecular researchers is that ecological studies are important, but given the lack of progress in the fight against insect-borne diseases, new strategies are needed. "If ecology had all the answers, there wouldn't be molecular biology," says Anthony James, a molecular entomologist at the University of California, Irvine. In the past few years, the sparring has gotten especially intense over molecular biologists' boldest plan: to control malaria by releasing transgenic mosquitoes (see Morel Viewpoint on p. 79). Some ecologists have dismissed the scheme as a grandiose folly—a Star Wars of infectious disease—that is diverting money from more "down to earth" research. James chalks up part of the bickering to the "impoverished mentality" that afflicts all of tropical disease research. When funding is tight, he explains, "people start fighting over whose work is more important."

Handsome devil
Sabethes cyaneus

credit: W. A. Foster

Males of this mosquito species, one of the most beautiful on Earth, display an elaborate courtship dance in which they wave one of their legs and swing their bodies back and forth. They sometimes court other males, too.

Distribution: New World tropics, from Belize to northern Argentina.
Breeding habitat: Deep rot holes in trees, where the low evaporation rate allows breeding throughout the dry season.
Feeding: Most likely a daytime biter; hosts unknown (monkeys?).
Diseases: Not incriminated as a vector, although a close relative transmits yellow fever to monkeys.

Sabethes cyaneus

Sexier science

Field studies of mosquitoes, which peaked during the vector biology heyday of the 1940s and 1950s, were dealt their first heavy blow when DDT and other insecticides promised to end insect-borne disease. By the time insecticide resistance and growing opposition to chemical use shattered that dream, the molecular biology revolution was well under way, and chasing mosquitoes in the field seemed old-fashioned and obsolete. "People just find molecular biology sexier," concedes Duane Gubler, chief of the division of insect-borne infectious diseases at the U.S. Centers for Disease Control and Prevention (CDC) in Fort Collins, Colorado. "It's seen as the future."

Indeed, for the last 15 years or so, molecular scientists have dominated mosquito research grants and high-profile publications. Of more than 130 mosquito studies currently funded by the U.S. National Institute of Allergy and Infectious Diseases (NIAID), only about one in five includes fieldwork, while DNA work booms. The World Health Organization (WHO) has also made the transgenic mosquito one of its top priorities in fighting malaria.

The funding shift, some say, created a self-perpetuating cycle: Universities hired molecular researchers because they could pull in grants, and vector biology departments took on a decidedly molecular bent. "The molecular people are multiplying like flies," laments Yale medical entomologist Durland Fish. Even if they would like to do field studies, he says, young scientists are forced to follow the money and end up in molecular research.

As a result, studies that could make a dent in disease transmission are lacking, ecologists say. Dengue fever, a debilitating and sometimes fatal disease transmitted by a mosquito species called *Aedes aegypti*, is a case in point, says CDC entomologist Paul

Reiter. Until a vaccine is available, the best way to block its continued spread is to reinvigorate mosquito-control programs, which aren't working well now, says Reiter.

The problem, he says, is that researchers still don't know certain cornerstones of dengue vector ecology, such as the mosquitoes' longevity—a crucial factor in their ability to transmit diseases—and the relation between mosquito density and human infection risk. With better information, he adds, scant resources for vector control—insecticides, reduction of breeding sites, and biological control—could be employed more effectively.

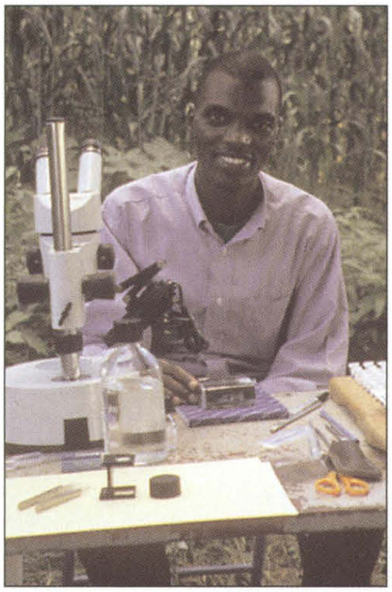
A similar lack of knowledge is hampering the control of West Nile virus, which landed in New York City in 1999 and has now spread across most of the continental United States, says Fish. Scientists aren't sure which mosquito species are the primary "bridge vectors" that shuttle the virus from birds to humans. It's also unclear how best to control them or the mosquitoes that infect birds, West Nile's primary hosts. But presumably, Fish says, research could identify a better alternative than sending out the spray trucks whenever citizens turn in large numbers of dead birds.

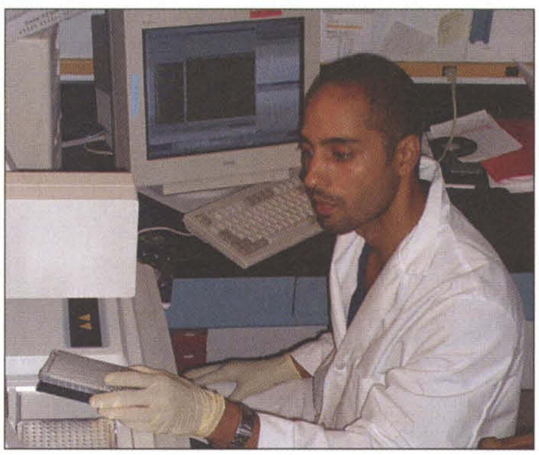
Designer mosquitoes

Of all the molecular projects, it's the diversion of malaria funds to the genetic engineering of mosquitoes that makes entomologists the most apoplectic. "It's pie in the sky," says Fish. The idea is to replace natural mosquito populations with lab-engineered or transgenic cousins incapable of spreading malaria. In a major advance, a team at Case Western Reserve University in Cleveland, Ohio, showed earlier this year that it could make *An. stephensi*—a cousin of *An. gambiae*—resistant to *Plasmodium* infection by giving it an extra gene. If researchers can find a way to do the same in *An. gambiae* and also find a way to make these mosquitoes outcompete their natural counterparts, the parasite would no longer be able to propagate. "I really believe this will work one day," says Frank Collins, a proponent of transgenics at the University of Notre Dame in Indiana.

But ecologists say it's a long shot. Despite recent progress in engineering mosquitoes in the lab, many real-world questions remain unanswered. Will the designer mosquitoes be able to survive in the wild, for instance? Will they disperse, find mates, and have viable offspring—and if so, how long would it take for their parasite-resistance genes to spread? Would it help if resistant mosquitoes had fewer parasites in their saliva than wild ones, or would they have to be completely resistant? What portion of the population would have to become transgenic to actually make a dent in the rate of malaria transmission? And what's the risk that their new genetic baggage would transform them into vectors for other diseases? The only way to find out is to study natural mosquito populations, say the ecologists, many of whom are visibly irked that molecular biologists didn't involve them in planning the transgenic project. "There are lots of things they have never given much thought," says Andrew Spielman, an entomologist at Harvard School of Public Health.

"If ecologists were so eager to help, then why didn't they jump in earlier?" counter the molecular biologists.





Two worlds. Moussa Guelbeogo of the University of Notre Dame studies the mosquito in the field in Burkina Faso (*top*). Neil Lobo helped sequence the *Anopheles gambiae* genome (*bottom*).

CREDIT: (MIDDLE AND BOTTOM) CARLO COSTANTINI; MAUREEN HILLENMEYER

Ironically, some say, the controversial project might actually help bring the two sides together. Four months ago, Thomas Scott of the University of California, Davis, and Willem Takken of Wageningen Agricultural University in the Netherlands, who both study vectors in the field, assembled some two dozen of their colleagues to explore the ecological questions surrounding the transgenics plan. Only one molecular biologist was invited. Although some ecologists remained skeptical about the whole idea, most participants agreed that, because the transgenic mosquito train appears unstoppable, the best course of action is to quit griping and hop on.

Airborne

Mansonia titillans

credit: P. Lounibos/UF/FMEL

Females deposit their eggs on the underside of leaves of water hyacinths and other floating plants. An air bubble, attached to the mosquito's hydrophobic abdomen, stays behind so the eggs can breathe. Larvae and pupae attach to the roots of the plants.

Distribution: Abundant from Florida to the northern half of South America.

Breeding habitat: Ponds and other permanent bodies of water.

Feeding: Mostly mammals, including humans.

Diseases: Potential vector for Venezuelan equine encephalitis, lymphatic filariasis, and dog heartworm, which occasionally infects humans.

Mansonia titillans

They crafted a research agenda (see Scott Viewpoint on p. 117) that includes hefty doses of mosquito population genetics and studies of mating behavior, evolution, and epidemiology. Several say they have started writing grant proposals and setting up collaborations with molecular researchers.

The funding agencies appear receptive. WHO, for instance, might pay more attention to ecology. An August meeting of 50 scientists, charged with charting a scientific course for the tropical disease program for the next 5 years, recommended as a top priority field studies of malaria, dengue, lymphatic filariasis, and several other diseases.

At NIAID, vector biology director Kate Aultman says she welcomes proposals for field studies. The rift between the two sides has long frustrated her, Aultman says, and fostering collaborations has been difficult. But they are essential, she notes: "Molecular biologists, bless their hearts, don't have a clue how to catch a mosquito."

–MARTIN ENSERINK