

FOR THE GOOD OF GATORS - AND HUMANKIND

The thrill of the chase and the challenge of the classroom keep alligator expert and HHMI professor Louis Guillette's instincts and insights sharp.

BY JOSEPH KAYS

photographs by Minnich Photo



STUDYING ALLIGATORS IS NOT FOR THE FAINT OF HEART.

Even the smallest of these prehistoric reptiles are powerful bundles of muscle and teeth, and catching them involves cruising Florida's mosquito-infested lakes in the middle of the night, ever alert for the critters' 800-pound brethren lurking nearby.

So why has University of Florida (UF) zoologist Louis J. Guillette made hundreds of these expeditions and handled more than half a million alligators, from eggs to adults, over the last two decades?

"You're on an airboat, in a swamp, at night, hunting an alligator," Guillette says. "That's why you go on thrill rides. That's why we watch *Shark Week* on TV."

The adrenaline rush isn't his only motivation, however. Dedicated to the welfare of *Alligator mississippiensis*, Guillette has become the patron saint of alligators, so to speak, working to ensure their reproductive health and preserve their rightful place in the ecology of Florida's waterways. And now he's beginning to extend his studies on the impact of pollutants on alligator reproduction to mammals, whose hormonal systems are remarkably similar to those of reptiles. In the process, he's also introducing a host of students to the rewards of practicing hands-on science.

Through an HHMI professorship awarded in April 2006, Guillette is developing a mentoring program that promotes collaboration among graduate students, undergraduates, and area high schoolers (see sidebar, page 30). And the mentoring isn't limited to the classroom and lab; Guillette regularly takes crews of students on his collecting trips.

Guillette first started plucking alligators out of Florida's lakes in the mid-1980s. State game officials wanted to understand the reptiles' reproduction so they could better manage permits for alligator farmers to harvest eggs and animals, and at the time Guillette was UF's resident expert on alligator reproduction.

Over the next few years, Guillette's team gathered data from lakes all over Florida.

"We started out doing some basic reproductive biology, partly because the alligator farmers wanted data," Guillette says. "As we went along, we realized things didn't add up. It was like we were trying to put a square peg in a round hole, and it just didn't fit."

FAILURE TO THRIVE

This was especially true for Lake Apopka, near Orlando, one of Florida's largest freshwater lakes and one of its most polluted. In some years, as few as 5 percent of its alligator eggs hatched, compared with 70 to 80 percent of eggs from a nearby lake. In the lab, half the animals that did hatch died within weeks, a mortality rate many times the norm.

Much of alligator development depends on nest variables such as temperature and moisture. But after Guillette and his team eliminated those variables as sources of the reproductive problems, they refocused on the lake water and soil. The researchers suspected that pollutant toxins, possibly stemming in part from a large pesticide spill at Lake Apopka in 1980, might be affecting the newborn alligators' hormone levels and contributing to their failure to thrive.

When the scientists analyzed blood from young alligators, they found estrogen and testosterone levels that were totally out of balance. "When you see males with hormone levels that look like those of females, that's not normal and that's what we were seeing in Lake Apopka," says Guillette. These imbalances persisted as the alligators matured. Juveniles, male and female, looked like "super-females," and when they reached adolescence, the males were still demasculinized and the females had become defeminized.

Given the abnormal hormone levels, the researchers needed to look for physical manifestations, such as effects on the animals' genitalia. Sure enough, they found that male alligators in Lake Apopka had penises that were 25 to 30 percent smaller than those of their counterparts in other lakes.

"Penis measurements have always been a tool; if this one marker is disrupted, I'm assuming others are disrupted," he says.

“Alligators are a charismatic species that people care about. Plus, if you know that alligators are having problems in the lake, you can assume that all the other species there, many of which people really don't care about, are also having problems.”

—LOUIS GUILLETTE



ALLIGATORS ARE FREQUENT VISITORS TO LOU GUILLETTE'S UNIVERSITY OF FLORIDA CLASSROOM.

HORMONAL IMPOSTERS

Although the data kept pointing to hormonal imbalances, Guillette says he didn't put all the pieces together until his "academic grandfather"—zoologist Howard Bern of the University of California, Berkeley—visited his lab and made a presentation about the impact of the synthetic estrogen called DES (diethylstilbestrol) on the ovaries of mice and women. "During his talk, a slide came up that showed the pathology of an ovary with multi-oocytic follicles," Guillette says, referring to follicles, or sacs, with more than one egg in them. "When I realized that the alligators I was working on had the same weird follicles, it was an 'Aha!' moment."

As Guillette later said in "Fooling with Nature," a 1998 *Frontline* documentary, "It was one of these incredible experiences when suddenly everything adds up. I realized, 'I have hormonal abnormalities. I have a contaminated lake. I have a top predator that accumulates contaminants.' It all just kind of came together as a hypothesis."

Once Guillette realized that he might be dealing with endocrine disrupters, he focused his research accordingly. "We had been taught, and had taught our students, that in the endocrine system the receptor was so specific it could be described as a lock, with the hormone being the key," says Guillette. "Now we realize, after an



GIVING STUDENTS RESPONSIBILITY

Lou Guillette vividly remembers the first time his undergraduate mentor gave him the keys to the lab and asked him to prepare some growth medium for an experiment the next day. >> "That was a telling moment in my professional career," says Guillette. "Not only was he trusting me with thousands of dollars of equipment, he was also trusting me to mix this stuff up correctly. Otherwise, the whole experiment would be blown. >> "I can remember working in the lab that night, thinking 'I'm a scientist. This is the real thing.' It was like I'd psychologically jumped some monster hurdle. Not only did I want to do it, I *could* do it." >> That experience has inspired Guillette to provide as many similar opportunities to UF undergraduates as possible. His teaching mantra is "Scholarship, not studentship," and he practices what he preaches. Over the last decade, more than 150 undergraduates have benefited from Guillette's hands-on, directed-research mentoring. Now, through a \$1 million, four-year grant from HHMI, Guillette has created the Group Advantaged Training of Research, or G.A.T.O.R., program to fine-tune that approach for a larger audience. >> "Everyone has to be a student for a certain period of time, but at some point you have to transition to the pursuit of knowledge yourself," he

says. "The undergraduate students in my laboratory are exposed to our research in a way few students experience. They help capture alligators, turtles, frogs, and fish. In the lab, they assist in all aspects of sample analysis." Guillette manages as many as 15 undergraduates at a time through a system that relies heavily on his graduate students. "If each graduate student is responsible for several undergraduates, I can accommodate a lot more undergraduates in my lab and the graduate students can gain valuable experience in mentoring," Guillette says. >> Postdoctoral researcher Thea Edwards, who oversees the G.A.T.O.R. program, is clearly proud of the students she mentored while pursuing her Ph.D. with Guillette. "These students were amazing and I would not have been able to complete my research without them," she says. "Of the 20, five went on to graduate school and five to medical or dental school." >> Although he easily delegates authority, Guillette's door is always open. Ed Orlando, now an assistant professor at Florida Atlantic University, says that he and other of Guillette's UF graduate students knew they could call on him any time. "He was available almost seven days a week, 24 hours a day to answer questions and offer advice," says Orlando. "He never said no and I expect that 25 years from

now he will be doing the same." >> One of Guillette's goals with the G.A.T.O.R. program is to make his teaching philosophy and strategy "exportable." >> "Does it work effectively only in my lab under my research conditions, or can other labs in other disciplines run this way also? We want to optimize this mentoring for any given research setting," he says. >> Guillette also puts a high premium on scientific communication, especially with graduate students. "Some of our students have a tough time explaining what they do, even to their parents." >> He has developed a new class, "Communicating Complexity in Science," which focuses on everything from creating effective scientific posters to dealing with the media to making science come alive for high schoolers. During the semester, he brings in prominent scientists, journalists, and policymakers to meet with students. "I think one of the reasons we're having such intense debates in our society about scientific questions like stem cells, global warming, and evolution is that we in the scientific community are expecting somebody else to interpret all of our data." In other words, it's as if the scientists—even though they understand the phenomena best—are unable or unwilling to do the interpreting themselves. —JK

awful lot of science, that yes, the estrogen receptor is exquisitely able to recognize estrogens, but really what it was designed to do was to distinguish between estrogens and androgens, like testosterone. It wasn't necessarily designed to preclude all other keys."

In 1999, Guillette began collaborating with Taisen Iguchi of Japan's Okazaki National Research Institutes to sequence hundreds of alligator genes related to reproduction, particularly those related to estrogen receptors. "This allowed us to start talking about the genetic basis of the alligator, which not only gave us a powerful toolbox for understanding alligators but also for doing comparisons with mice and humans. The genetic mechanisms that turn reproductive development on and off are almost identical whether you're studying a mouse, a human, or an alligator."

The researchers also learned that even trace amounts of hormonal imposters could have an impact. "Hormones work at incredibly small concentrations," says Guillette.

While he is careful not to draw parallels between alligators and humans, Guillette says it would be naïve to dismiss the implications, considering that reproductive hormones in both species are very similar. In fact, the similarities are so great that, in 2006, the National Institute of Environmental Health Sciences (NIEHS) awarded a grant to Guillette to study ovarian development in alligators.

"At NIEHS we are not interested in alligator health, but Lou shows how understanding that can inform studies on animal models and humans," says Jerry Heindel, scientific program

administrator for the NIEHS Cellular, Organ and Systems Pathobiology Branch. "That is why we fund him. He sees the big picture and helps people connect the dots."

AN OBJECT LESSON

Although the alligator is important as an animal model for human disease, Guillette is also interested in alligator health per se. And he is committed to protecting the species.

"I want to conserve and preserve these animals and the environment they live in," Guillette says. "Alligators are a charismatic species that people care about. Plus, if you know that alligators are having problems in the lake, you can assume that all the other species there, many of which people really don't care about, are also having problems."

He points out that, because of the alligator's high profile, Florida and the federal government have purchased thousands of acres of farmland around Lake Okeechobee, a massive lake in south-central Florida where Guillette also found alligator reproductive problems, and are restoring it to a wild state. Preserving alligator habitat is also a core goal of the federally funded Everglades restoration project.

Guillette acknowledges that some may wonder why all the effort. "I've heard people say we're up to our armpits in alligators, but what we're really up to our armpits in is people," he says. "It's not that there are so many alligators. It's just that people are pushing them into smaller and smaller spaces." ■



HELPING HUMAN POPULATIONS

As the father of four grown children, Guillette was always concerned about the implications of endocrine disruptors for children. But as a zoologist he just couldn't envision studying actual human effects by himself. >>**In this case**, a suitable collaborator was already close at hand. Guillette's wife, Elizabeth, a medical anthropologist at UF, was able to identify a perfect natural laboratory in and around the Yaqui Valley of northwestern Mexico. There she found two groups of people, located about 50 miles apart, who were demographically near-identical except for their exposure to pesticides. >>**The Sonoran Mayan** people of the valley split philosophi-

cally over the use of pesticides and other modern agricultural techniques during the country's Green Revolution of the 1940s and '50s. Residents who remained in the valley embraced pesticides, herbicides, and other agricultural chemicals, while the other group moved to the foothills and stuck to organic farming. >>**Aside from that one difference**, says Elizabeth Guillette, "these groups were the same in every respect—culturally, genetically, and socioeconomically. They had the same diet, the same child-rearing practices, and the same school system." >>**But when she asked children** from the two communities to perform simple

play activities, like catching a ball or drawing stick figures, "the kids who had been exposed to pesticides lagged far behind." >>**Follow-up studies** that Elizabeth Guillette published with her husband and several other collaborators in *Environmental Health Perspectives* in 2006 showed that daughters born to women who were exposed to pesticides had significantly less mammary tissue than their counterparts in the foothills. >>**Lou Guillette says** that private agencies have translated the research results into Spanish and have done extensive outreach in the area to encourage residents to limit their exposure to chemicals. —JK