Yale

MEDICAL INNOVATION

Secret Life of the House Sparrow

The brain of a long-maligned bird as revealed by 3D printing

CEID Fellow Max Emerson and radiology & biomedical imaging postdoctoral fellow Christine Lattin.

Since it was introduced to North America in the late 19th century, the house sparrow has received little love. "Nothing can be urged in its favor," declared an 1891 editorial in the *New York Times.* A few years later, the same newspaper deemed the birds "rats in the air." Adding insult to injury, the International Union for Conservation of Nature has long kept the house sparrow on its unceremonious list of species of "least concern."

Not all are so dismissive, though. With the help of technology and know-how at the Center for Engineering Innovation and Design (CEID), a postdoctoral fellow at the Yale University PET Center is gaining insights into the inner lives of these long-maligned birds. In many ways, it turns out, we are not so different from the house sparrow.

"There are some interesting things you can learn about birds that you can apply to humans," said Christine Lattin, a researcher in the lab of Richard Carson, professor of biomedical engineering and radiology & biomedical imaging. Working with the CEID, Lattin is currently focusing on the physiological stress response of the house sparrow.

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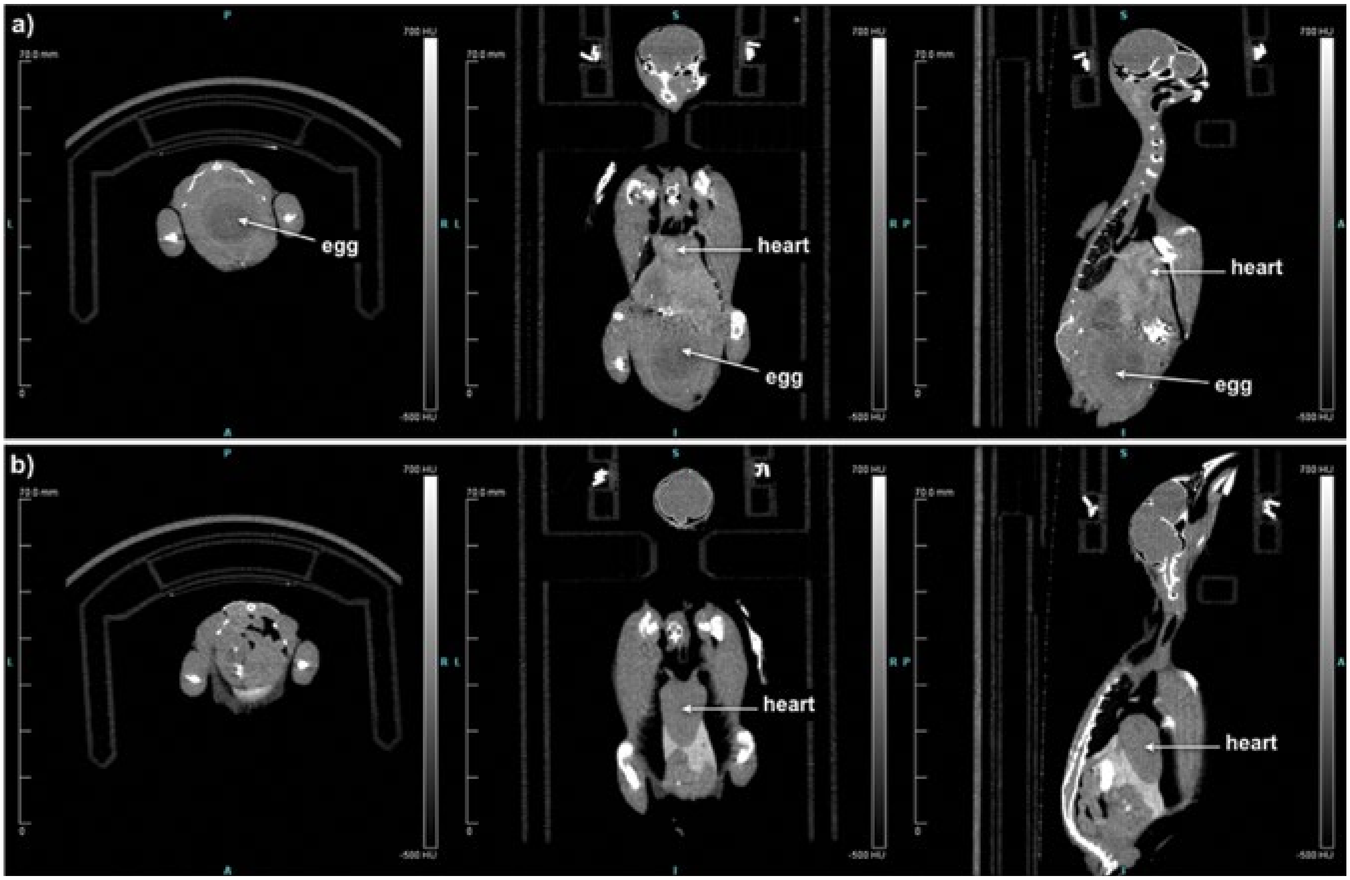
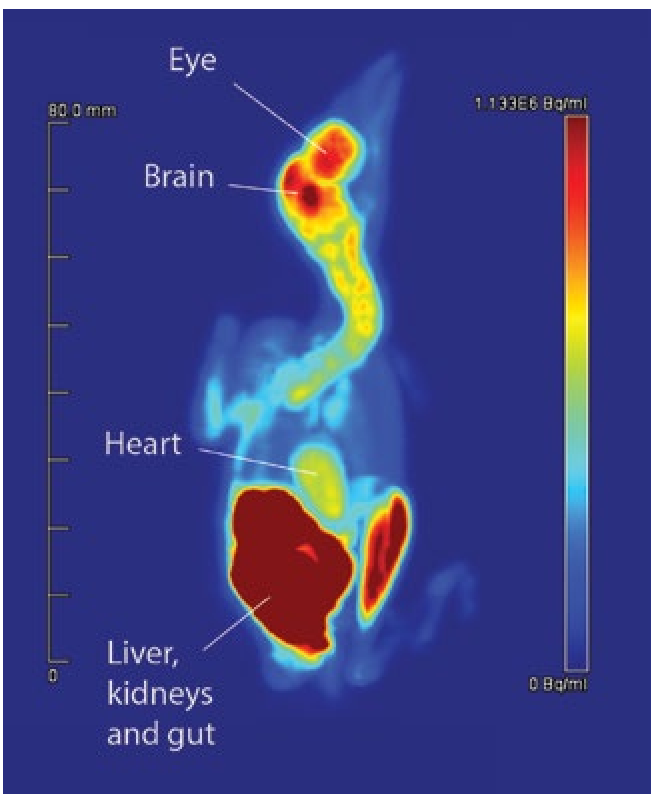


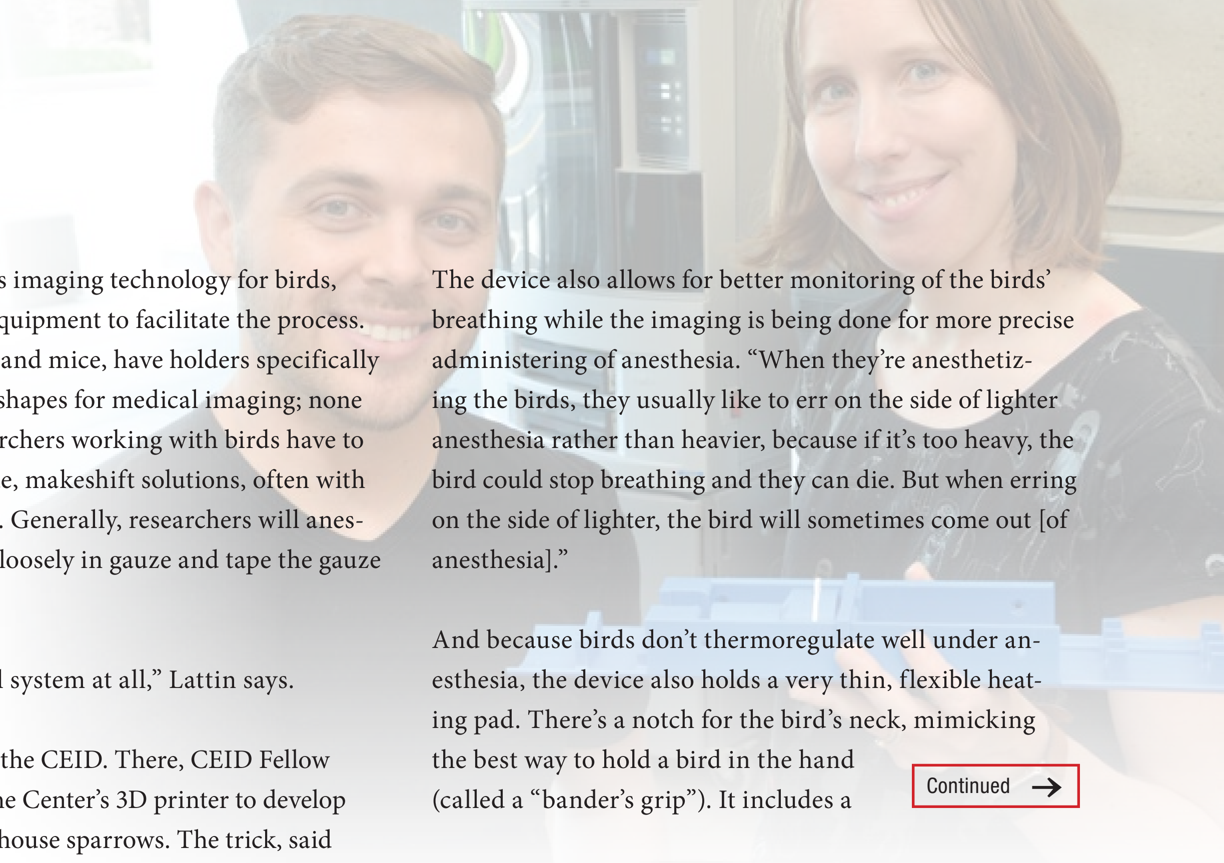
Top: *Computed tomography image from three different scans of the same female house sparrow. An egg and large masses of reproductive tissue are visible in the body cavity.* Bottom: *Positron emission tomography image of a house sparrow.*



Unlike rats or mice, house sparrows are not conditioned to captivity (Lattin finds the birds in the wild, catching them herself), which is important if you want to measure their stress response to captivity. "I think captivity is potentially a really powerful kind of model for chronic stress," Lattin says. "A bird brought into captivity is in some ways not that different from a person who's suddenly thrown into a totally alien and stressful environment, like a soldier in combat or a child taken to a foster family. It's an alien environment, and it's highly stressful. That's one reason I'm interested in using the birds."

Medical imaging suits Lattin's work well because it allows for multiple scans of the same animals, which give researchers a better way to study variation in an individual subject, including before- and after-treatment results. Without it, Lattin said, most brain studies on animals require euthanizing the animals involved and slicing the brains.

Positron emission tomography (PET), which uses a special scanner and a radioactive drug known as a tracer to identify different types of activity in the body and brain, is the type of imaging most useful for Lattin's research. But making a PET scan of a bird isn't easy. Only a few other



labs in the world use this imaging technology for birds, so there's no universal equipment to facilitate the process. Other animals, like rats and mice, have holders specifically designed for their body shapes for medical imaging; none exists for birds. So researchers working with birds have to make do with homemade, makeshift solutions, often with less-than-perfect results. Generally, researchers will anesthetize the bird, wrap it loosely in gauze and tape the gauze to the scanner.

"I mean, it's not an ideal system at all," Lattin says.

So Lattin reached out to the CEID. There, CEID Fellow Max Emerson is using the Center's 3D printer to develop a holder customized for house sparrows. The trick, said Emerson, is designing it in such a way that the birds stay in a uniform position. Because the birds' brains are so small, even the slightest twitches can significantly diminish the quality of PET images.

"The goal was to make a standardized position for the bird," Emerson said. "Then, the researchers can look at a lot of studies without having to do too much post-processing of the data. It minimizes head movement without restricting their abdomen, so they can breathe while they're under anesthesia."

The device also allows for better monitoring of the birds' breathing while the imaging is being done for more precise administering of anesthesia. "When they're anesthetizing the birds, they usually like to err on the side of lighter anesthesia rather than heavier, because if it's too heavy, the bird could stop breathing and they can die. But when erring on the side of lighter, the bird will sometimes come out [of anesthesia]."

And because birds don't thermoregulate well under anesthesia, the device also holds a very thin, flexible heating pad. There's a notch for the bird's neck, mimicking the best way to hold a bird in the hand (called a "bander's grip"). It includes a

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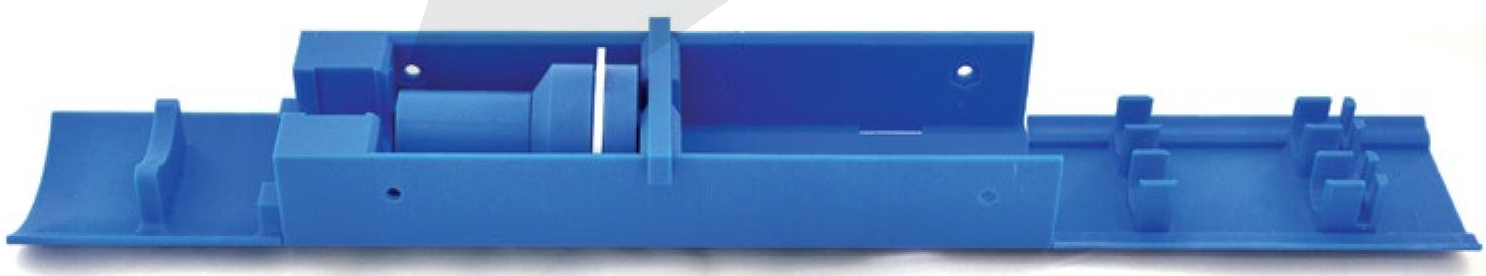
Recent iteration of the 3D-printed bird holder.



The Mystery of Monkey Bones

What A 3D Printer Could Reveal About Evolution

A bird-holding device may be a one-of-a-kind product, but one-of-a-kind creations are not uncommon for the 3D printer at the Center for Engineering Innovation & Design (CEID). Replicas of everything from ancient sculptures to skulls, neurons and greatly magnified molecules are just a few of the products to have come from it.

However wide-ranging or esoteric the subject, CEID Assistant Dr. Joseph Zinter said, it makes sense for researchers to want a permanent object that they can pick up and study. It's one thing, he said, to see images of an object on the page or computer screen. But being able to hold it or turn it around and feel the texture of the object is its own distinctive learning experience.

So it's no great surprise then, that the laboratory of Dr. Robert Wyman, professor of molecular, cellular and developmental biology, recently took advantage of the CEID printer to make replicas of monkey bones. Specifically, Wyman's lab is getting 3D prints of the bones of extant specimens of the cercopithecoid primates — also known as the Old World monkeys — which include baboons and macaques. The bone replicas will be used for comparisons to fossils and apply what are known as morphometric techniques to study the degree of variations between the bones.

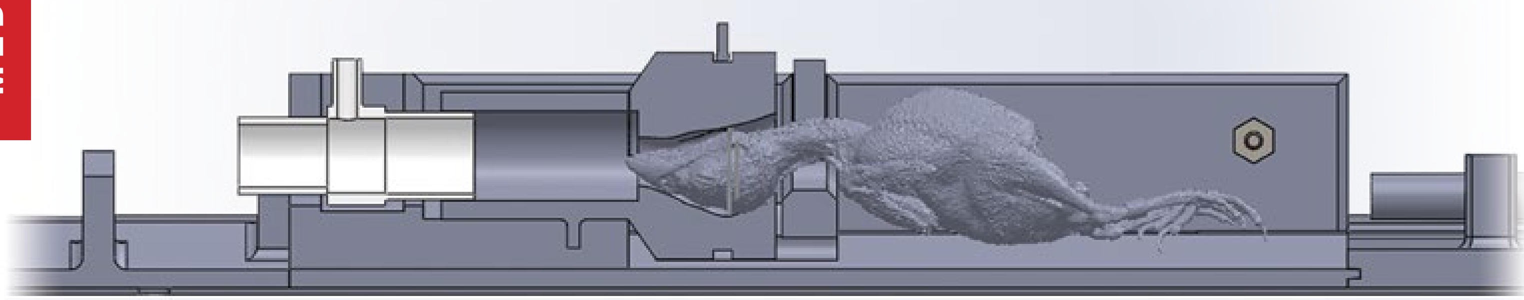
"The 3D scanning allows us to quantify joint surfaces in a manner that we were previously unable to measure," Wyman said.

Dr. Paul Whitehead, an associate in Wyman's laboratory, said the bone replicas could shed some light on a mystery that has intrigued researchers for years. Among Whitehead's discoveries is that palm walkers make one extra motion to lower the body to be supported by the palm rather than just the fingers. That

cone designed to fit the contours of the bird's head, which is connected to a tube that pumps the anesthesia. Emerson based it on very detailed computed tomography (CT) images of the birds' skulls, which were created in collaboration with Elliott Brown, assistant professor of radiology & biomedical imaging at the Yale School of Medicine.

Emerson also created special anchors that attach the holder to the scanner bed, and a spacer to make sure it is always placed in the same location on different days they

Lattin and Emerson's device is designed to hold the bird's head firmly in place.



means they raise and lower their body more per step than their finger-walking counterparts. It's only a few inches difference per step, but add those up over millions of steps, and a lot of energy is at stake. In connection to this, the researchers want to know what the joints between the wrist bones and palm bones have to do with the maintenance of the two different hand postures and how these differences in anatomy can be related to muscle activity.

The research could even shed light on the matter of nature vs. nurture.

"How much is inborn due to genetics, how much is learned from parents, how much is the result of repetitive behavior during early development, and how much is pure randomness?" Wyman asks. "These questions have been approached many times to answer big questions like the inheritance of IQ. But that is not the way biology works. Biology works via very small tweaks to a basic program."

By focusing on the differences in walking styles, Wyman said Whitehead found a seemingly small but very compelling difference.

"Monkeys, close to our line of evolution, are extremely agile and spend a lot of time running about and climbing trees," Wyman said. "Speed is essential to escape predators, like leopards, and a high percentage of their total energy expenditure may be used up by locomotion."

Printing out the bones, Whitehead said, provides a number of benefits.

"First it's material that belongs to another institution, so we want to be able to return it," he said. "But beyond that, by scanning it and printing it out, rather than examining it solely through a microscope or magnifier, you have something that you can see more easily and something we can compare and discuss more easily. And 3D scanning allows quantification of characteristics that are more difficult to study with traditional morphometric techniques."

So if you have to be one or the other, which is better: Finger walker or palm walker?

"It depends on your circumstances," Whitehead said. "If you spend more time on the ground, it's better to be a finger walker because you're lengthening your stride every time you take a step. If you spend more time living in trees, then palm walking is advantageous because then you're lowering your center of gravity."

perform scanning. Other notches hold the syringes that deliver drugs and the radioactive tracer. Best of all, the entire device is made of lightweight, low-density plastic, which is important because very dense materials, such as metal, can cause errors and distortion in PET-CT imaging.

Previous methods for keeping the bird in place made it difficult to observe the bird during imaging. Lattin recalls one session, scheduled for an hour, which had to be stopped after 10 minutes because she couldn't monitor the bird's breathing adequately.

The final designs are still being hashed out (Emerson has produced five iterations so far). Once they get the current prototype finalized, they plan to design a two-bird holder, something that would save a lot of time and money. So far, Lattin says she's very impressed with what she's seen.

"Before, when the bird was wrapped up in gauze, I would be trying to look at their tail sticking out at the bottom, and be like 'Uh, I just saw it move, so I think it's OK,'" she says. "I haven't had to do that at all with the new bird holder because you can see their breathing so well. You can turn the anesthesia down when their breathing gets pretty slow, or you can turn it up if the breathing is faster. It's just so much better."