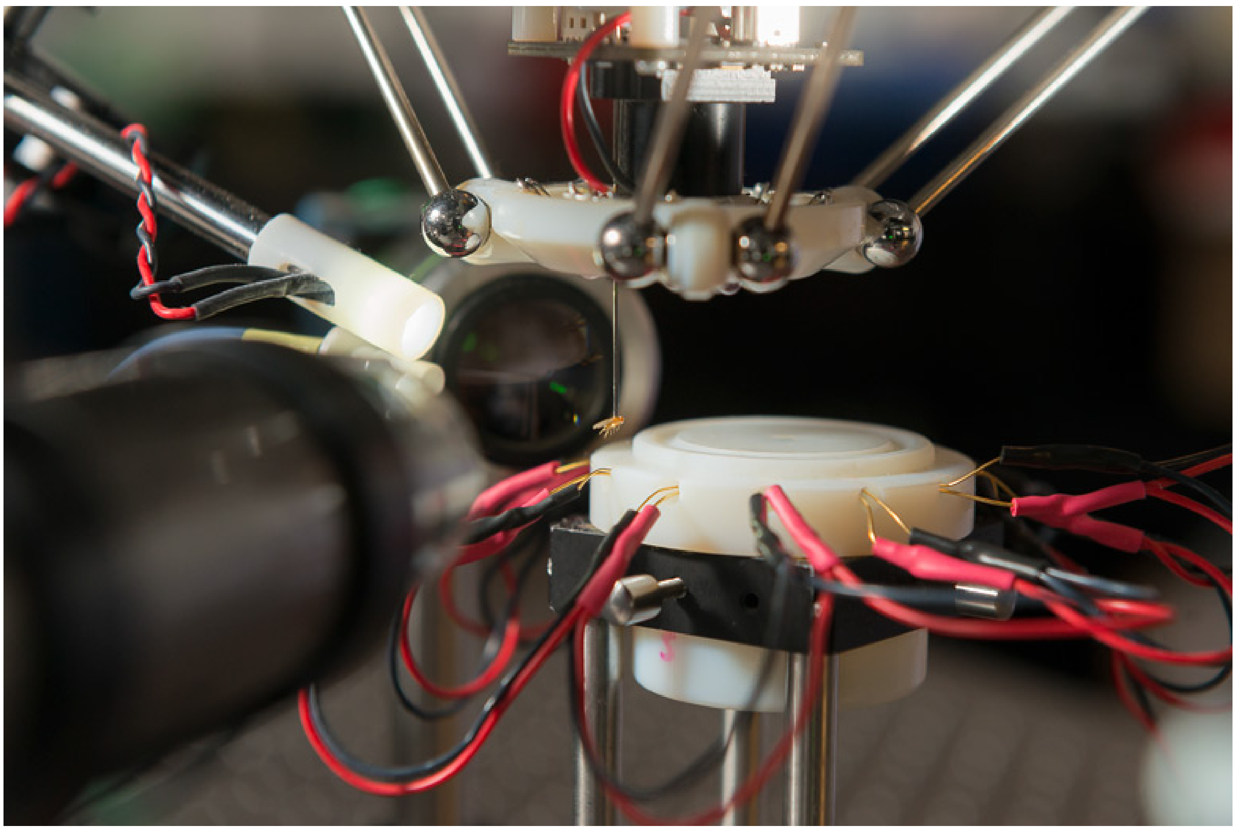
Fly-catching robot expands the scope of biomedical research

May 27 2015, by Amy Adams



A fruit fly hangs unharmed at the end of the robot's suction tube. The robot uses machine vision to inspect and analyze the captured fly. Credit: L.A. Cicero

Since the early 20th century, an unheralded star of genetics research has been a small and essentially very annoying creature: the fruit fly.

Underlying every significant discovery from fruit fly research – and there have been many, relating to almost every aspect of our own biology – is daily, monotonous time spent by scientists toiling over plastic dishes of conked-out flies.

Now a team led by Mark Schnitzer, an associate professor of biology and of applied physics, has introduced a solution to the tedium: a robot that can visually inspect awake flies and, even better, carry out behavioral experiments that were impossible with anesthetized flies. The work is described May 25 in the journal *Nature Methods*.

"Robotic technology offers a new prospect for automated experiments and enables fly researchers to do several things they couldn't do previously," Schnitzer said. "For example, it can do studies with large numbers of flies inspected in very precise ways." The group did one study of 1,000 flies in 10 hours, a task that would have taken much longer for even a highly skilled human.

The robot's fly-snatching apparatus looks like nothing so much as a miniature UFO hovering over a plate of unsuspecting flies. When it's ready to grab a fly, it flashes a brief infrared blast of light that is invisible to the flies and reflects off the animals' thoraxes, indicating the location of each inhabitant. The robot can recognize each individual fly by its reflection pattern. Then, a tiny, narrow suction tube strikes one of the illuminated thoraxes, painlessly sucking onto the fly and lifting it up.

Once the fly is attached, the robot uses machine vision to analyze the fly's physical attributes, sort the flies by male and female, and even carry out a microdissection to reveal the fly's minuscule brain. In one experiment, the robot's machine vision was able to differentiate between two strains of flies so similar they are indistinguishable to the human eye.

Speeding disease research

All this is good news to the legion of graduate students who still spend hours a day looking at flies under a microscope as part of work that continues to uncover mechanisms in human aging, cancer, diabetes and a range of other diseases.

Although flies and humans have obvious differences, in many cases our cells and organs behave in similar ways and it is easier to study those processes in flies than in humans. The earliest information about how radiation causes gene mutations came from fruit flies, as did an understanding of our daily sleep/waking rhythms. And many of the molecules that are now famous for their roles in regulating how cells communicate were originally discovered by scientists hunched over microscopes staring at the unmoving bodies of anesthetized flies.

Now that list of fruit fly contributions can be expended to include behavioral studies as well, previously impossible because the humans carrying out the analysis can neither see fly behaviors clearly nor distinguish between individuals.

In their paper, Schnitzer and his team had the robot pick up a fly and carry it to a trackball. Once there, they exposed the fly to different smells and could record how the fly behaved – racing along the trackball to get closer or attempting to turn away.

Fruit flies, also known as Drosophila, aren't the only tiny organism contributing to our understanding of human biology. A tiny worm and a transparent fish are also both widely used. Because these live in aquatic environments, it has been much easier to develop robots to automate the work of screening physical characteristics as the animals float past cameras.

What made the flies such a challenge to catch – in the laboratory setting as in the kitchen – is their air speed.

Seeing the light

Joan Savall, a senior scientist at the Howard Hughes Medical Institute, was visiting Stanford when he heard about the robotics project in Schnitzer's lab. "At the beginning we were thinking it wouldn't work," said Savall, who was first author on the paper. "It's not just picking the flies up, it's keeping them alive," he said.

In addition to not squashing the flies, the robot needed to be able to distinguish between the flies it had observed to prevent analyzing the same fly repeatedly. "The key was flashing an infrared light," Savall said. That light, which is invisible to the flies, didn't disrupt their behavior and provided a visual pattern the robot could use to distinguish between individuals.

Savall says freeing graduate students to do science rather than toiling in the fly room is one benefit of the robot, but even more important is the range of new experiments that will be possible. "In the end you can really push many fields at the same time," he said.

More information: "Dexterous robotic manipulation of alert adult Drosophila for high-content experimentation." *Nature Methods* (2015) DOI: 10.1038/nmeth.3410

Provided by Stanford University