

THE AUTHOR FILE

Hang Lu

Practical microsystems are used to monitor flies and worms.

Hang Lu, an engineer at the Georgia Institute of Technology, creates tiny contraptions to answer biological questions. Lu approaches biology with an outsider's perspective: she started graduate school planning to work on semiconductor chips for computers,



but when her advisor shifted to microfluidics, she found that biological applications intrigued her. Two of her papers published in this issue of *Nature Methods* describe devices for very different applications, but both began as conversations with biologists who wanted to design more-quantitative experiments.

One device makes roundworms dance

to pulses of light. Putting worms into yoga positions or making them crawl in triangles is fun, says Lu, but the system has a serious purpose. Developed with coauthor Alexander Gottschalk at Johann Wolfgang Goethe University, it was designed to study *Caenorhabditis elegans* genetically modified so that certain neurons respond to light. The system precisely tracks and illuminates freely moving worms, ensuring that only a subset of the light-sensitive neurons are manipulated at precise times. This, in turn, provides an easy, noninvasive way to monitor behavior when particular neurons are stimulated or silenced¹.

One challenge was designing practical hardware, software and wetware that worked together. Instead of specialized optical equipment, for example, the researchers used a multicolor LCD projector. "You can always upgrade to the fastest everything, but then the cost might not be worth it," says Lu. "We were thinking about what would be reasonable for every lab to purchase."

The second paper began with a friendly challenge. Imaging concentric layers of skin, nervous systems and other organs forming in *Drosophila* embryos requires that the rice-shaped 500-micrometer-long embryos stand on end. Coauthor Stanislav Shvartsman at Princeton University asked Lu whether she could make a device that could automatically arrange embryos so scientists no longer needed to

manually position each one. The result of that request is an array that can, in just a few minutes, position hundreds of embryos for close-ups².

As part of the project, Shvartsman and Lu each sent a graduate student to the other's laboratory for a few days. In fact, Lu frequently sends graduate students to collaborators' labs so they can see how biologists' routines work and gauge their comfort with and access to microfluidics equipment. Lead author Kwanghun Chung returned to Athens, Georgia, USA determined to make biologists' lives easier. Lu, who completed her postdoc in a *C. elegans* lab, often tells her students that doing biology means working with lots of worms on plate after plate. "It doesn't register until they try a traditional assay and see how it's done," she says. "Then they go, 'wow, this is hard'"

Not all researchers have the instrumentation of a microfluidics lab, and one insight from Chung's visit was that researchers should be able to load the positioning array with equipment found in any laboratory. "We wanted to give it to biologists so that they could take it to whatever microscope setup they have," says Lu. Also, microscope stations are already crowded, so using the array could not require anything bulky.

In the end, Lu and colleagues created a device the same size and shape as a microscope slide that can be loaded with embryos by hand using a simple syringe.

The researchers set up a series of switchbacking channels that allow embryos to move through in any orientation. The flow pattern guides embryos toward 'traps' and into the correct orientation. Lu predicts that the design can be readily modified for other kinds of embryos as well as a variety of cells.

Most biologists, she thinks, will be able to find a collaborator or service provider who can manufacture an embryo-trapping array from the published design. Such arrays, she hopes, will let researchers go from collecting anecdotal evidence on a few embryos to performing robust statistical analysis. Shvartsman called Lu shortly after putting the embryo-loaded array under the microscope. He told her his student had done more experiments in one afternoon than in the last 3 years combined. "That's a motivating thing," says Lu.

Monya Baker

**"The way biologists do things is just so hard."
—Hang Lu**

1. Stirman, J.N. *et al.* Real-time multimodal optical control of neurons and muscles in freely behaving *Caenorhabditis elegans*. *Nat. Methods* **8**, 153–158 (2011).
2. Chung, K. *et al.* A microfluidic array for large-scale ordering and orientation of embryos. *Nat. Methods* **8**, 171–176 (2011).