Understanding Olfaction: An Interview with Elizabeth Hong

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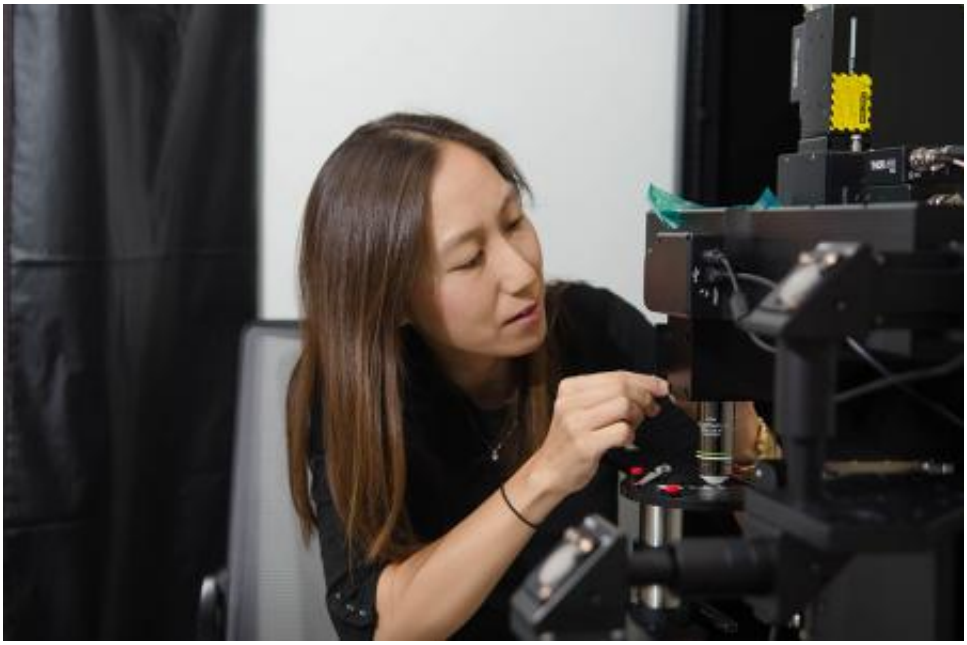

Elizabeth Hong, Assistant Professor of Neuroscience, works on the two-photon laser scanning microscope in her lab. Credit: Lance Hayashida/Caltech

You walk by a bakery, smell the scent of fresh cookies, and are immediately reminded of baking with your grandmother as a child. The seemingly simple act of learning to associate a smell with a good or bad outcome is actually quite a complicated behavior—one that can begin as a single synapse, or junction, where a signal is passed between two neurons in the brain.

Assistant Professor of Neuroscience Betty Hong is interested in how animals sense cues in their environment, process that information in the brain, and then use that information to guide behaviors. To study the processing of information from synapse to behavior, her work focuses on olfaction—or chemical sensing via smell—in fruit flies.

Hong, who received her bachelor's degree from Caltech in 2002 and her doctorate from Harvard in 2009, came from a postdoctoral position at Harvard Medical School to join the Caltech faculty in June. We spoke with her recently about her work, her life outside the laboratory, and why she is looking forward to being back at Caltech.

How did you initially become interested in your field?

It's rather circuitous. I was initially drawn to neuroscience because I was interested in disease. I had family who passed away from Alzheimer's disease, and it's clear that with the current demographic of our country, diseases associated with aging—like Alzheimer's—are going to have a large impact on society in the next 20 to 30 years. Working at the Children's Hospital Boston in graduate school, I also became increasingly interested in understanding the rise of neurodevelopmental disorders like autism.

I really wanted to understand the mechanistic basis for neurological disease. And then it became clear to me that part of the problem of trying to understand neurological disorders was that we really had no idea how the brain is supposed to work. If you were a mechanic who didn't know how cars work, how could you fix a broken car? That led me to study increasingly more basic mechanisms of how the brain functions.

Why did you decide to focus your research on

olfaction?

Although we humans have evolved to move away from olfaction—humans and primates are very visual—the whole rest of the animal kingdom relies on olfaction heavily for all of its daily survival and functions. Even the lowliest microbe relies on chemical sensing to navigate its way through the environment. We study olfaction in an invertebrate model—the fruit fly Drosophila. We do that for a couple of reasons. One is that it has a very small brain, and so its circuits are very compact, and that small size and numerical simplicity lets us get a global overview of what's happening—a view that you could never get if you're looking at a big circuit, like a mouse brain or a human brain.

The other reason is that there are versatile genetic tools and new technologies that have allowed us to make high-resolution electrical and optical recordings of neural activity in the brains of fruit flies. That very significant technical hurdle had to be crossed in order to make it a worthwhile experimental model. With electrophysiological access to the brain, and genetic tools that allow you to manipulate the circuits, you can watch brain activity as it's happening and ask what happens to neural activity when you tweak the properties of the system in specific ways. And the fly also has a robust and flexible set of behaviors that you can relate to all of this.

What are some of the behaviors that you are interested in studying?

We're very interested in understanding how flies can associate an odor with a pleasant or unpleasant outcome. So, in the same way that you might associate wonderful baking smells with something from your childhood, flies can learn to arbitrarily associate odors with different outcomes. And to know "when I smell this odor, I should run away," or

"based on what happened to me the last time I smelled this odor, this might be an indicator of food"—that's actually a fairly sophisticated behavior that is a basic building block for more complex higher-order cognitive tasks that emerge in vertebrates.

There are many animals that are inflexibly wired. In other words, they smell something, and through evolution, their circuits have evolved to tell them to move toward it or go away from it. Even if they are in an unusual environment, they can't flexibly alter that behavior. The ability to flexibly adapt our behavior to new and unfamiliar environments was a key transition in the evolution of the nervous system.

You are also a Caltech alum. What drew you back as a faculty member?

Yes, it seems like such a long time ago, but I was an undergraduate here—a biology major in Page House—from 1998 to 2002. I was also a SURF student with [Professor of Biology] Bruce Hay and later with David Baltimore [president emeritus and Robert Andrews Millikan Professor of Biology]. It's kind of wild to have as your colleagues people who were your mentors a decade ago, but I think the main reason I chose Caltech was the community of scholars here—on the level of faculty, undergraduate students, graduate students, and postdocs—that I will be able to interact with. In the end, you mainly just want to be with smart, motivated people who want to use science to make a difference in the world. And I think that encapsulates what Caltech does.

Do you have any interests or hobbies that are outside of the lab?

I used to play horn in the wind ensemble and orchestra, including the time when I was here as an undergraduate. But these days, any time that

I'm not in the office, I'm with my two young kids. Right now, we're really excited about exploring all the fun and exciting things to do outdoors in Southern California. We've done a lot of hiking and exploring the natural beauty here. The kids have gotten into fishing lately, so our latest thing has been scoping out the best places to fish. I would love to hear from members of the community what their favorite spots are!

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