Flashing neurons in worms reveal how the brain generates behavior

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Saul Kato, PhD, is using a new high-resolution whole-brain imaging technique to see the neurons in the worm C. elegans. This technique allows Kato to see how the nervous system of the worm works together to generate behavior. Credit: Noah Berger

The 100 billion neurons of the human brain control our behavior, but so far there is no way to keep track of all that activity, cell by cell. Whole-brain imaging techniques like fMRI offer only a blurry view of the action, with each pixel representing tens of thousands of neurons.

To help get a clearer picture of how behavior arises from a biological neural network, UC San Francisco researcher Saul Kato, PhD, is using an animal with a much simpler brain.

Tiny, see-through worms called C. elegans, which are less than a millimeter long, engage in a wide range of complex behaviors: escaping from danger, moving toward food, sensing temperature, light and chemicals in their environment, and finding mates.

"They do everything all animals do, but they do it with only 302 neurons – and now we can watch nearly all of them at the same time," said Kato, assistant professor of neurology at the UCSF Weill Institute for Neurosciences.

Kato is using a new high-resolution whole-brain imaging technique to see how the entire nervous system of C. elegans works together to generate behavior.

The worm may be the first multicellular animal for which such a complete and detailed picture of neural activity has been visualized.

Because electrical activity in neurons corresponds to changes in calcium ion concentration, Kato's team adds a fluorescent calcium sensor to every neuron of the worm brain. Looking through a microscope, they can then see and record, at single-cell resolution, a flashing chorus of neural activity. The researchers identify patterns of activity that correspond to specific behaviors such as dorsal and ventral turns (the worms lie on their sides), and forward and backward crawling.

Parsing the flashing activity neuron by neuron is the most laborious part of the approach, says Kato, and they are now developing machine learning technologies to speed up this process.

The flashing patterns are consistent from worm to worm, like a code for worm behavior. Kato can decode a worm's behavior by looking at a readout of its neural activity.

"Even when the worm is trapped, we can tell you what the worm is trying to do just by reading its brain activity," Kato said

Earlier imaging technology could track at most a few neurons at a time, which led people to attribute specific behaviors to specific neurons. But the ability to watch the entire worm brain at work has revealed that even simple behaviors involve the whole brain. Kato likens this global activity to a chorus, where every neuron sings along to the same song but with slightly different parts.

"This chorus was a surprising finding," said Kato. "We surmise that it is a signal telling each neuron what the body is trying to do so they can contribute meaningfully to the whole animal's function, like sailors on a submarine. It's a way for the neurons to communicate with each other."

Next, Kato hopes to study how disruptions to the chorus affect behavior and underlie motor and psychiatric disorders.

"Perturbations of this healthy system cause disease," said Kato. "Now we can watch in great detail how these dysfunctional motor patterns emerge."

Provided by University of California, San Francisco

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