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Robots hunt neurons to record brain activity

Devices could reveal inner workings of neurons and how they communicate with each other.

Helen Shen

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ASPEN, COLORADO

Automated assistance may soon be available to neuroscientists tackling the brain's complex circuitry, according to research presented last week at the Aspen Brain Forum in Colorado. Robots that can find and simultaneously record the activity of dozens of neurons in live animals could help researchers to reveal how connected cells interpret signals from one another and transmit information across brain areas — a task that would be impossible using single-neuron studies.

A robot that can access the internal workings of neurons could be scaled up to allow 100 cells to be studied at a time.

MIT MCGOVERN INSTITUTE/E. BOYDEN/SPUTNIK ANIMATION

The robots are designed to perform whole-cell patch-clamping, a difficult but powerful method that allows neuroscientists to access neurons' internal electrical workings, says Edward Boyden of the Massachusetts Institute of Technology in Cambridge, who is leading the work.

Manually performing the method on live animals requires extensive training to perfect and, as a result, only a handful of neurophysiologists use the technique, says Boyden, who presented at the conference. He is developing the automated tool with Craig Forest at the Georgia Institute of Technology in Atlanta and others. "We think that it helps democratize procedures that require a lot of skill," he says.

In May, the group described how a basic version of the robot can record electrical currents in single neurons in the brains of anaesthetized mice[1]. The robot finds its target on the basis of characteristic changes in the electrical environment near neurons. Then, the device nicks the cell's membrane and seals itself around the tiny hole to access the neuron's contents. On 24 August, Boyden presented results showing that a more advanced version of the robot could be used to identify and probe four neurons at once — and he says he wants to push the design further, perhaps to tap as many as 100 neurons at a time.

The researchers have also begun tweaking the robot to harvest the contents of cells, which could be tested for gene expression. Relating gene expression to neuronal activity could aid our understanding of what goes wrong in neurological disorders. “Maybe gene expression does specify electrical properties of neurons, and maybe it doesn’t. If it does, that would be fantastic to know,” says Boyden.

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Neural recordings from live animals are most often collected using electrodes inserted between cells. These external recordings detect outgoing neuronal signals, but cannot measure the roiling electrical activity within each cell that determines whether and how rapidly a neuron fires.

Recordings made inside single neurons, including those obtained from whole-cell patch-clamping, have revealed some clues about how incoming signals — observed as positive and negative electrical currents — combine to influence a neuron’s outgoing transmissions. Recordings from multiple cells could help researchers to work out which neurons talk to each other and how they silence or excite one another to affect cognition or behaviour.

Other researchers have developed tools intended to record from inside up to 12 neurons at once[2], but the technology has not yet been tested in live animals, and it still requires direct control by a human experimenter.

Computational neuroscientist Sean Hill, director of the International Neuroinformatics Coordinating Facility in Stockholm, says that Boyden’s robot could save time. But he cautions that it might also remove a crucial element of human judgement in deciding which types of neuron to record from. “The proof will be in using it and seeing how well it performs,” he says.

Prakash Kara, a neuroscientist at the Medical University of South Carolina in Charleston, says that the technique looks “extremely promising”. However, Kara notes that the technology may be difficult to scale up to allow researchers to record large numbers of neurons. Each recording element typically exerts a small amount of pressure on the brain, so on a large scale has the potential to cause damage.

Despite these technical hurdles, Kara says that even the single-channel robot offers benefits. “People who are not terribly experienced with whole-cell patch-clamping might be able to do experiments that they otherwise couldn’t,” he says.

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References

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Ed Boyden said: Just a brief note that all of this work (not just the first paper) is a joint and equal production of my lab at MIT, and of the lab of Craig Forest at Georgia Tech. Suhasa Kodandaramaiah is the Georgia Tech graduate student who, working across our groups, spearheaded the collaboration that yielded the first paper. A testimony to the power of interdisciplinary joining-forces to yield neurotechnology...

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