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# MIT, Georgia Tech robot records brain cell information

By [Lori Valigra](#)

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With much still unknown about the inner workings of the brain, researchers at MIT and the Georgia Institute of Technology have discovered an automated way to record electrical activity inside neurons in the living brain, hoping it will some day help lead to new treatments for disease.

While gaining such knowledge offers information such as patterns of electrical activity, the cell's shape, and even a profile of which genes are turned on at a given moment, tapping into those cells manually has been a painstaking and slow task for human researchers.

The researchers said they have shown that an experimental robotic arm guided by a cell-detecting computer algorithm can identify and record from neurons in the living mouse brain with better accuracy and speed than a human experimenter, according to the researchers, who described their study in the May 6 issue of the journal *Nature Methods*.

The researchers recently created a startup company, [Neuromatic Devices LLC](#), based in Atlanta, Ga., to commercialize the device, which it calls the AutoPatch 1500. It includes hardware and software to identify single neurons. The company was spun out of Georgia Tech's [Precision Biosystems Laboratory](#) in January, and is based on the patent pending technology for automated whole-cell patch clamp electrophysiology of neurons in vivo.

The researchers said their new automated process eliminates months of training and provides long-sought information about living cells' activities. Using their technique, it may be possible to classify the thousands of different types of cells in the brain, map how they connect to each other, and figure out how diseased cells differ from normal cells, they added.

The project is a collaboration between the labs of Ed Boyden, associate professor of

biological engineering and brain and cognitive sciences at MIT, and Craig Forest, an assistant professor in the George W. Woodruff School of Mechanical Engineering at Georgia Tech.

"Our team has been interdisciplinary from the beginning, and this has enabled us to bring the principles of precision machine design to bear upon the study of the living brain," Forest said in a statement. His graduate student, Suhasa Kodandaramaiah, spent the past two years as a visiting student at MIT, and is the lead author of the study.

The method could be useful in studying brain disorders such as schizophrenia, Parkinson's disease, autism and epilepsy. "In all these cases, a molecular description of a cell that is integrated with [its] electrical and circuit properties ... has remained elusive," said Boyden, who is a member of MIT's Media Lab and McGovern Institute for Brain Research. "If we could really describe how diseases change molecules in specific cells within the living brain, it might enable better drug targets to be found."

Kodandaramaiah, Boyden and Forest set out to automate a 30-year-old technique known as whole-cell patch clamping, which involves bringing a tiny hollow glass pipette in contact with the cell membrane of a neuron, then opening up a small pore in the membrane to record the electrical activity within the cell, according to a press release. This skill usually takes a graduate student or postdoc several months to learn.

Kodandaramaiah spent about four months learning the manual patch-clamp technique, giving him an appreciation for its difficulty. "When I got reasonably good at it, I could sense that even though it is an art form, it can be reduced to a set of stereotyped tasks and decisions that could be executed by a robot," he said.

He and his colleagues built a robotic arm that lowers a glass pipette into the brain of an anesthetized mouse with micrometer accuracy. As it moves, the pipette monitors electrical impedance, a measure of how difficult it is for electricity to flow out of the pipette. If there are no cells around, electricity flows and impedance is low. When the tip hits a cell, electricity can't flow as well and impedance goes up.

The pipette takes two-micrometer steps, measuring impedance 10 times per second. Once it detects a cell, it can stop instantly, preventing it from poking through the membrane. "This is something a robot can do that a human can't," Boyden said.

When the pipette finds a cell, it applies suction to form a seal with the cell's membrane. Then, the electrode can break through the membrane to record the cell's internal electrical activity. The robotic system can detect cells with 90 percent accuracy, and establish a connection with the detected cells about 40 percent of the time, according to the researchers.

The researchers also showed that their method can be used to determine the shape of the cell by injecting a dye. They are now working on extracting a cell's contents to read its genetic profile.

Development of the new technology was funded primarily by the National Institutes of Health, the National Science Foundation and the MIT Media Lab.

The researchers are now working on scaling up the number of electrodes so they can record from multiple neurons at a time, potentially allowing them to determine how different parts

of the brain are connected. They are also working with collaborators to start classifying the thousands of types of neurons found in the brain.

Boyden said he believes this is just the beginning of using robotics in neuroscience to study living animals. A robot like this could potentially be used to infuse drugs at targeted points in the brain, or to deliver gene therapy vectors, he said. He hopes it will also inspire neuroscientists to pursue other kinds of robotic automation, such as in optogenetics, the use of light to perturb targeted neural circuits and determine the causal role that neurons play in brain functions.

Neuroscience is one of the few areas of biology in which robots have yet to make a big impact, Boyden added. "The genome project was done by humans and a giant set of robots that would do all the genome sequencing. In directed evolution or in synthetic biology, robots do a lot of the molecular biology," he added. "In other parts of biology, robots are essential."

He said the Neuromatic Devices robot has potential uses on many fronts. "For example, the ability to assess the state and contents of single cells in intact tissue could yield new drug targets. By enabling researchers to hone in on molecules that are prominent in an altered cell, but not a normal one, more specific drug targets might be possible," he said in written responses to questions from Mass High Tech. "Another anticipated use is for single-cell resolution analyses of tissue samples such as biopsies or tissues removed during surgery—by enabling those tissue samples to be analyzed, the robot might help inform treatments."


He added that many groups simply want to use a robot in their research. "There is commercial potential here as a research tool, because analyzing cell properties is a major aspect of biology and medical research."

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