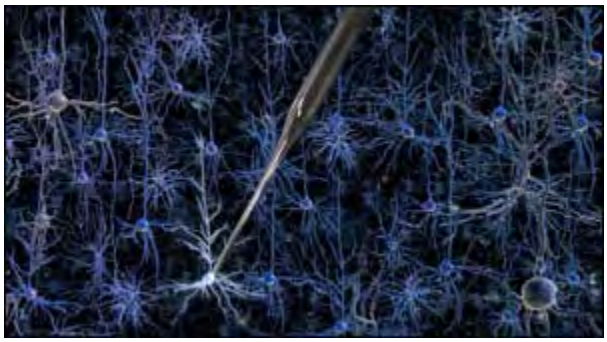
Robot Reveals Inner Workings of Brain Cells

ATLANTA, May 10, 2012 — A robotic arm guided by a cell-detecting computer algorithm analyzes and records information from neurons present in the living mouse brain with better accuracy and speed than a human experimenter. The automated method could help scientists classify various types of brain cells, map how they connect to each other and determine how diseased cells differ from normal cells.

Gaining access to the inner workings of a neuron in the living brain offers an abundance of information, including its patterns of electrical activity, its shape and a profile of which genes are turned on at a given moment. Achieving this entry, however, has proved a painstaking task that is considered an art form because of its difficulty.

That could soon change with the new automated method developed by scientists at MIT and Georgia Institute of Technology. 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, collaborated on the project. Forest's graduate student, Suhasa Kodandaramaiah, spent two years as a visiting student at MIT.



Researchers at MIT and Georgia Tech have developed an automated process, called whole-cell patch clamping, which involves bringing a tiny hollow glass pipette into 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. (Image: Sputnik Animation and MIT McGovern Institute)

"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.

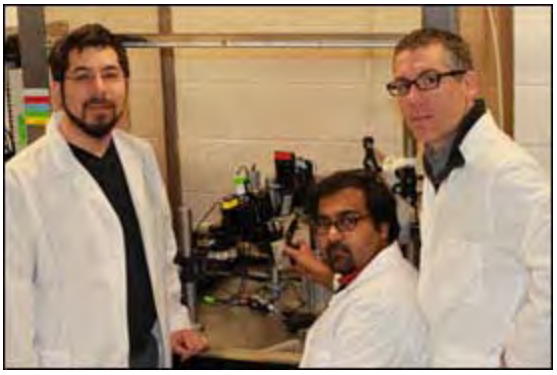
The method could prove useful in the study of brain disorders such as Parkinson's disease, autism, schizophrenia and epilepsy, Boyden said.

"In all these cases, a molecular description of a cell that is integrated with [its] electrical and circuit

specific cells within the living brain, it might enable better drug targets to be found."

The team automated a 30-year-old technique known as whole-cell patch clamping, in which a tiny hollow glass pipette is linked to the neuron's cell membrane, followed by a small pore opening within the membrane for recording the electrical activity inside the cell. This skill usually takes a graduate student or a postdoc several months to learn.

Kodandaramaiah learned the manual patch-clamp method in about four months.



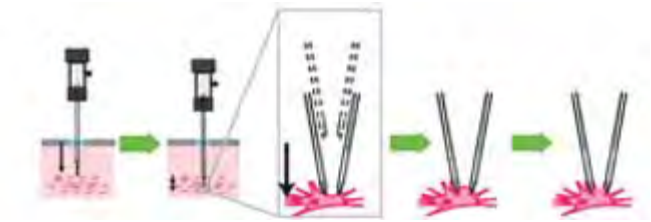
MIT researcher Ed Boyden (left) and Georgia Tech researchers Suhasa Kodandaramaia (seated) and Craig Forest have developed an automated process of finding and recording information from neurons in the living brain. (Image: MIT)

"When I was 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.

Kodandaramaiah and colleagues constructed a robotic arm that lowers a glass pipette into the brain of an anesthetized mouse with micrometer accuracy. While under motion, electrical impedance is measured. 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.

With-2 µm steps, the pipette measures impedance 10 times per second. After detecting a cell, it becomes deactivated automatically to prevent it from poking through the membrane, something that a human cannot do, Boyden noted.

Once a cell is detected, the pipette performs suction to form a seal with the cell's membrane. The electrode breaks through the membrane to record the cell's internal electrical activity with 90 percent accuracy using the robotic system. It can establish a connection with detected cells about 40 percent of the time.



MIT and Georgia Tech researchers have created a four-step process in which a robotic arm guided by a cell-detecting computer algorithm finds and records information from neurons in the living brain. A pipette is lowered to a target zone in the brain, then advanced until a neuron is detected. A seal is formed between the pipette and the cell, and a small pore is opened in the membrane to record the electrical activity within the cell. (Image: MIT and Georgia Tech)

The scientists also discovered that the method could 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.

They created a startup company, Neuromatic Devices, to commercialize the device.

The investigators are now working to scale up the number of electrodes so they can record from multiple neurons at a time to determine how different parts of the brain are connected.

Boyden believes that this is just the beginning of using robotics in neuroscience to study living animals. A robot of this caliber could be used to infuse drugs at targeted points in the brain or to deliver gene therapy vectors. He hopes that it will inspire neuroscientists to pursue other robotic automation for optogenetic

The study appeared in the May 6 issue of *Nature Methods*.

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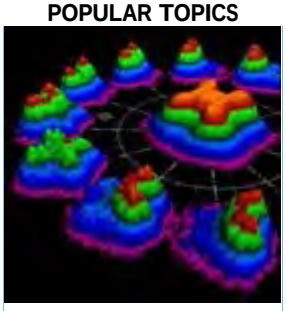

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