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Research Brief: Robots Trained in Patch-Clamp Experiments

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11 May 2012. For decades, neuroscientists have struggled to learn the precise sequence of steps necessary to perform patch-clamp electrophysiology on neurons in a living brain. Now, engineers have dumped the tedious task on a forever patient robot. In the May 6 Nature Methods online, researchers at MIT and the Georgia Institute of Technology in Atlanta report that they programmed a robot arm to slide a pipette through tissue, checking for cells near its tip along the way until it finds one to patch and analyze. The work was a collaboration between the laboratories of neuroscience expert Ed Boyden at MIT, and mechanical engineer Craig Forest at Georgia Tech.

First author Suhasa Kodandaramaiah, a student of Forest's who visited MIT for two years, spent four months learning the art of patch-clamp in living mouse brains. He then sorted out the step-by-step tasks involved, and programmed a robot to do it for him. The robotic arm lowers the patch pipette two microns at a time. To hunt for cells, it checks the electrical impedance at the pipette tip 10 times per second. Bumping up against a cell blocks electrical current, and the robot immediately stops. It then uses suction to make a seal with the cell, and generates an electrical pulse to open up the membrane for whole-cell patch-clamp.

Kodandaramaiah tested the robot with neurons in the mouse hippocampus and cortex. The robot was 90 percent accurate in detecting cells, although 10 percent of its recordings appeared to come from electrically inactive glia. It managed to obtain patch recordings during 33 percent of its attempts. For comparison, a qualified human had a hit rate of 29 percent. The robot had a good chance of success for about the first hour of attempts; after that, the authors think the patching process pushed the cell away, diminishing returns.

Boyden hopes the robot will help researchers understand the disruption of neural signaling in diseases such as Parkinson's. The technology could scale up, with one person controlling many devices at once, the authors suggested. The auto-patch robot could also prove useful for more than electrophysiology work. For example, the team used it to inject dye, and is now working to suck up a cell's genetic material. It might eventually be used to deliver drugs or gene therapy, the researchers believe. They have started a company, Neuromatic Devices, in Atlanta, to sell the equipment. —Amber Dance.

Reference:

Kodandaramaiah SB, Franzesi GT, Chow BY, Boyden ES, Forest CR. Automated whole-cell patch-clamp electrophysiology of neurons in vivo. Nature Methods. 2012 May 6. Abstract

For an auto-patching robot of your own, visit Neuromatic Devices.

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Whole-cell patch-clamp has been a mainstay neuroscience tool for decades, but is generally only performed in vitro. The few groups that have gotten this to work in vivo have completed near-heroic efforts. While the robot methodology will probably be challenging to set up the first time (like any complicated technique would be), it seems that the continued use of such an approach would be easier and less cumbersome than doing in-vivo patching manually. The ability to do several animals at one time is also appealing.

In the setting of disease models, in-vivo patch-clamp will be powerful. The Alzheimer's field has battled to understand the role that Aβ has on synaptic transmission and plasticity. A big limitation for us so far has been the lack of physiological techniques and types of Aβ. In-vivo patch-clamping will be one great way to answer some fundamental questions in the setting of intact neuronal networks and plaques. I think the possibilities here are very exciting!

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