Improved neural probe can pose precise questions without losing parts of the answers

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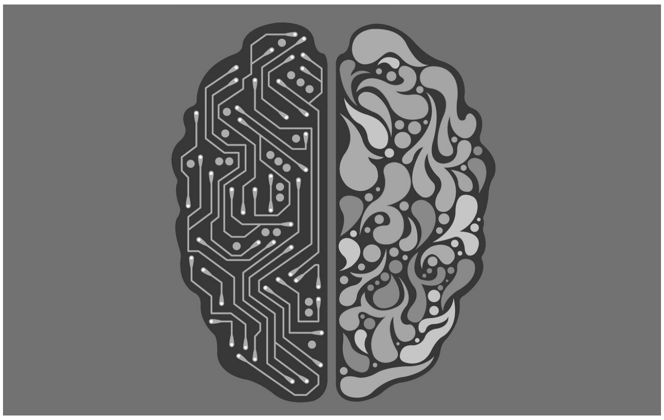

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A technique for studying individual circuits in the brains of mice has been hampered because the light needed to stimulate neural activity briefly overwhelms the electrodes "listening" for the response. Now, improved shielding within the neural probe enables those lost signals to be captured.

"Consider a conversation, in which the first few and the last few words of a sentence are omitted or distorted. In such a dialogue, not much information can be reliably deciphered. This is the same situation in our research," said György Buzsáki, the Biggs Professor of Neuroscience at New York University School of Medicine and a co-author of the new paper describing the results.

"Our dialogue with brain circuits starts with a question in the form of a light pulse. If the beginning and the end of the pulse—our 'question'—produce large artifacts, we lose the instantaneous and often very critical neuronal responses."

To address this problem, a team of engineers at the University of Michigan set out to improve their neural probe so that it could record complete answers. This enables experiments that were previously impossible.

"As an example, we can mimic a brain wave by turning on the micro-LEDs at a certain frequency and see how the neural circuit behaves. We can also implement what is called a closed-loop control and make the LEDs turn on as soon as we detect a certain brain signal," said Kanghwan Kim, first author on the new paper in *Nature Communications* and a recent Ph.D. graduate in electrical and computer engineering from U-M.

Understanding communication among brain cells is key to advancing our understanding of the brain and developing treatments for neurological diseases such as Alzheimer's Disease. One of the new experiments that the team has in mind would explore memory.

"For example, we can make neurons in the hippocampus fire in a pattern that would enhance memory consolidation and see if the memory is actually improved," said Euisik Yoon, senior author on the paper and a professor of electrical engineering and computer science at U-M.

The probe is designed for a technique called optogenetics, in which mice have been genetically modified so that their neurons can be stimulated with light. The trick is to make LEDs small enough that they can prod a single neuron, rather than the tens of them stimulated by conventional electrical pulses.

Michigan's neural probe team accomplished this five years ago with the smallest known light sources on implantable probes. But the signals that turn the LED on and off briefly overwhelm the electrodes that listen for the response.

"It is like if there is a big bang sound—like a gunshot or an explosion. You may not hear for a while until your ears recover," Yoon said.

To address this problem, Kim added a layer of electrical shielding to the design. But even the light itself can pose a problem, as it is absorbed by the silicon of the probe and converted into electrical noise sensed by the electrodes. For this, Kim added boron to the silicon. This increased the silicon's conductivity, enabling the silicon to keep the noise away from the electrodes.

"Now that the artifact is removed, we can modulate neurons in nearly any area of the brain and determine exactly where in the brain the neurons are located, and how they are influencing neighboring neurons," Yoon said.

The researchers can also turn on multiple light sources simultaneously, making it possible to study the brain's complex neural circuits at near-cellular resolution. The devices have been successfully demonstrated in mice.

More information: Kanghwan Kim et al, Artifact-free and high-temporal-resolution in vivo opto-electrophysiology with microLED optoelectrodes, *Nature Communications* (2020). DOI: 10.1038/s41467-020-15769-w

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