'See through,' high-resolution EEG recording array gives a better glimpse of the brain

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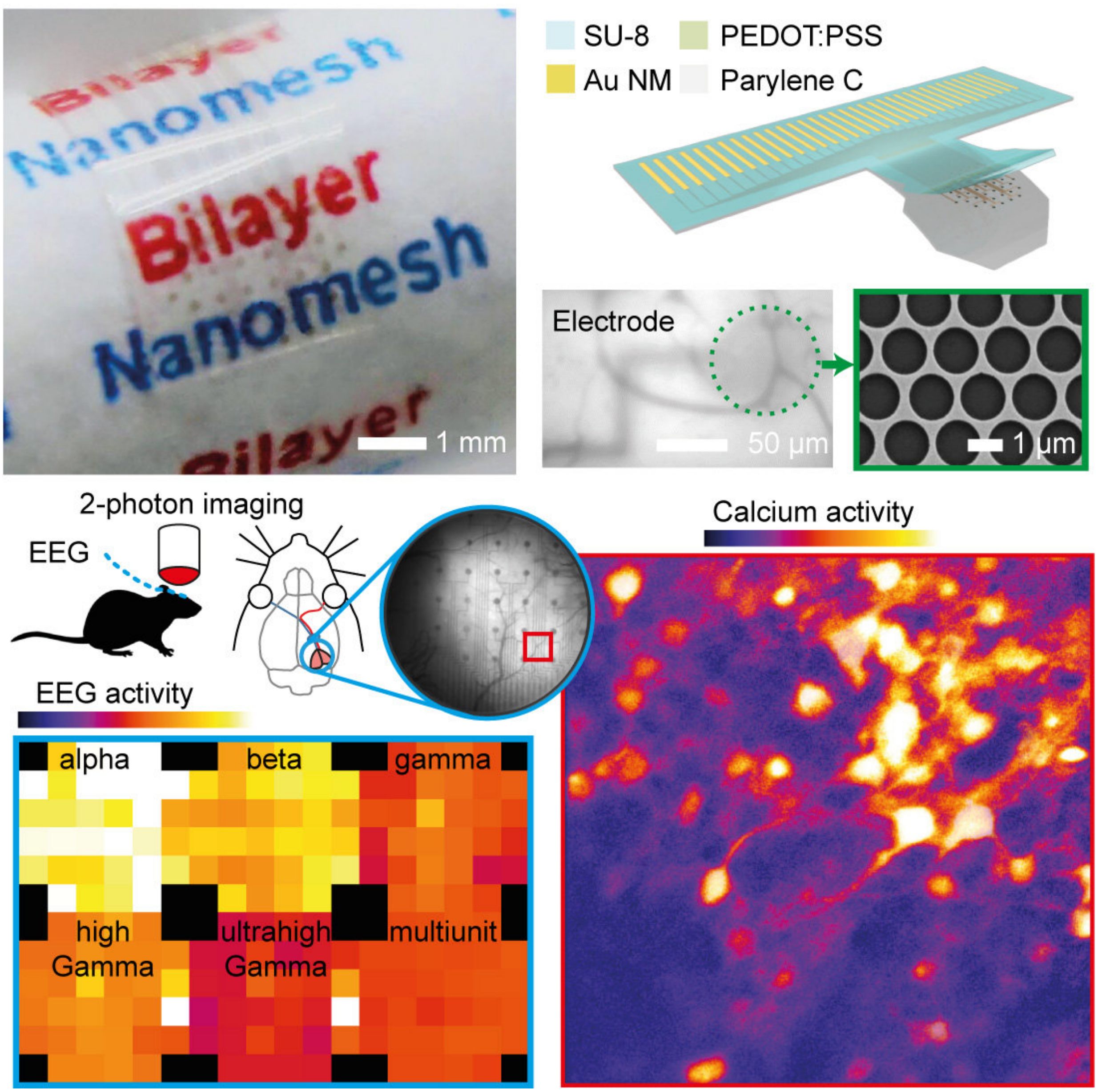

Above, the transparent bilayer nanomesh, with electrodes a few micrometers apart. Below, a schematic of EEG recording, at the single-neuron level, together with 2-photon optical imaging of calcium activity. Credit: Yi Qiang et al. Sci. Adv. 4, eaat0626 (2018).

Brain electrical discharges, measured with electroencephalograms (EEGs), have been the gold standard for measuring brain activity. But current EEGs don't have the capabilities to, say, differentiate the activity of different types of brain cells, instead averaging the signal for a whole section of the brain.

A collaboration between neuroscientist Michela Fagiolini, Ph.D. at Boston Children's Hospital with engineer Hui Fang, Ph.D. at Northeastern University has led to a highly miniaturized, "see through" EEG device, one more useful for understanding how the brain works. As they report in *Science Advances*, they placed it on the visual cortex of live, awake mice and successfully captured the electrical activity of individual neurons as they responded to visual stimuli, while simultaneously performing high-resolution optical imaging.

The new EEG microarray, designed to be placed directly on the brain, combines two key advantages. The electrodes can be placed very close together on the cortex—a-few-micrometers apart, as opposed to millimeters currently—allowing the collection of very fine-grained information. Second, the team used nanotechnologies that allow conventional electrode materials to be made transparent, allowing light to pass through the array and enabling neuroimaging to be done at the same time EEG signals are being recorded.

"This allows us to do experiments that were not possible before," says Fagiolini, who studies alterations of visual perception in Rett syndrome in Boston Children's F.M. Kirby Neurobiology Program. "In Rett syndrome, for example, we can know which specific groups of neurons are generating the abnormal EEG signals we've been observing. Or we can see how particular cell populations are impacted by abnormal electrical signaling."

The see-through nature of the electrodes also enables researchers to do optogenetics experiments (genetically altering cells using light) in conjunction with EEG. "We can then ask, if I perturb these cells, what happens to the EEG?" says Fagiolini.

Building a better microelectrode

Fang, co-senior author on the paper with Fagiolini, explains that transparent microelectrodes have been developed in the past using different materials such as graphene, but suffer from poor performance. Fang's team went back to conventional electrode materials and turned to nanotechnology, fabricating them into a fine, two-layered mesh.

"What's remarkable is that by simple nanomeshing, we show that conventional electrode materials can be made transparent, while not compromising electrode performance," says Fang, whose lab is developing novel neurotechnologies in the Electrical and Computer Engineering Department at Northeastern University.

Another helpful feature is that the microelectrode arrays are soft, flexible and more biocompatible, so they can be implanted more safely in the brain, or a section of the brain, and remain for longer periods. Unlike most current electrodes, which are rigid, they conform to the brain's curvature—a helpful feature for application to humans, whose brains are highly convoluted.

Advancing neuroscience

Fagiolini envisions using the technology to study a variety of neurologic conditions, including traumatic brain injury and spinal cord injury. Interest is spreading among neuroscientists at Boston Children's. In the future, Fagiolini plans to work with other neuroscientists to develop computational algorithms to better interpret the paired EEG and imaging data.

The team has filed a patent and plans to further refine the electrode microarray, make the system wireless and move to testing in primates and eventually humans. Patients undergoing neurosurgery for conditions such as epilepsy already have EEG arrays implanted to help identify a safe path for surgery; they could be among the first test subjects.

As a longer-term goal, the researchers hope to stimulate neurons through the electrodes to adjust their activity, rather than simply record their signals.

More information: "Transparent arrays of bilayer-nanomesh microelectrodes for simultaneous electrophysiology and two-photon imaging in the brain" *Science Advances* (2018). advances.sciencemag.org/content/4/9/eaat0626

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