Dual-window approach offers unprecedented view of brain dynamics

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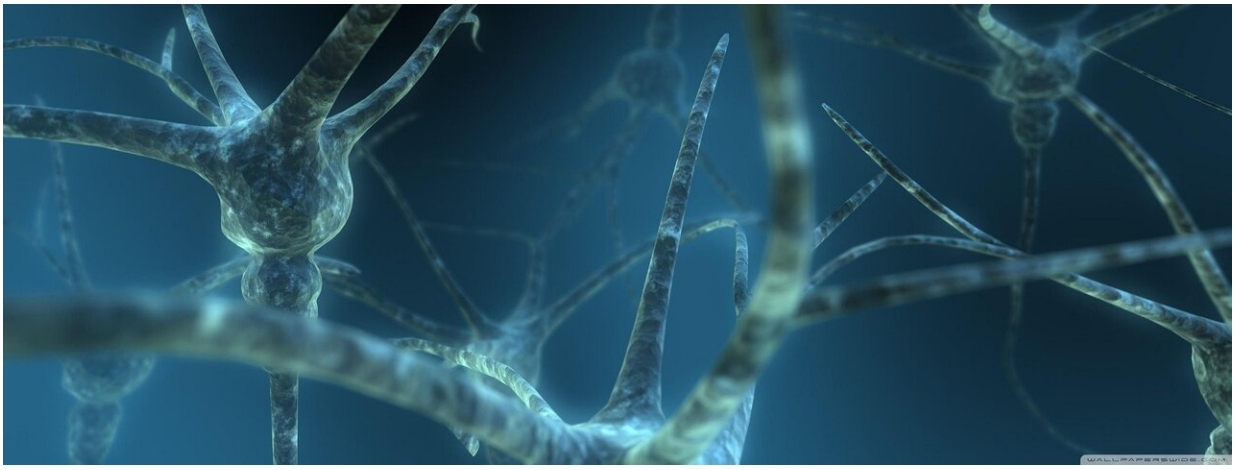

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Technologies for imaging the brains of living animals have enabled important scientific advances in recent years. Now, researchers for the first time report an approach that allows simultaneous imaging of multiple areas of the brain at different depths through glass windows implanted in the heads of living mice.

Since brain processes often span multiple regions of the brain, researchers say the new approach could lead to a more complete understanding of how the brain works in health and disease.

Many brain works and neurological diseases are associated different brain regions. For instance, the memory mechanism involves interaction of the cortex and hippocampus. Besides, spontaneous epileptiform activity occurs spreading from the lesion site to the whole cortex and even to the hippocampus in several seconds.

Chaowei Zhuang from Tsinghua University in Beijing will present the research at the virtual OSA Imaging and Applied Optics Congress and Optical Sensors and Sensing Congress to be held 19-23 July.

"The method achieves simultaneously imaging the superficial cortex and deep brain regions with brain-wide field of view, video-rate acquisition and cellular resolution, which is satisfied with the requirements of these issues," said Zhuang. "We think this method could promote research of the brain and diseases and bring great discoveries."

In the new work, researchers demonstrate the ability to take detailed, simultaneous images of structures up to 1 millimeter deep with a field of view 1 millimeter across in the brains of living mice. They accomplished this by removing part of the skull and implanting two separate windows into the brain. The first was a glass plug 2 mm across and 0.9 mm tall. The second was a microprism in the shape of a cube 1 mm across. While both windows can be used to image at different depths, the glass plug provides more detailed view of structures near two horizontal surfaces while the microprism reflects more longitudinal structures of deeper brain tissues with greater clarity.

The key advantage of the method is simultaneously observing near-whole superficial cortex and horizontally or longitudinally monitoring the deep brain tissue, with brain-wide field of view, video-rate acquisition and cellular resolution. Besides that, implanting glass cranial windows is low-cost compared to Grin lens, and is compatible with other wide-field microscopes.

To acquire images of brain structures through these windows, the researchers used Real-time Ultra-large Scale imaging,high-resolution macroscpy (RUSH) that offers 1 centimeter field of view, video-rate acquisition and 800 nm resolution. While wide-field microscopes are frequently used for brain imaging, they typically can image to a depth of 200-300 microns. The researchers used their custom-built cranial windows to overcome this limitation and allow simultaneous imaging of deep structures and those near the surface.

The researchers tested their approach by using it to image microglia cells (a type of immune cell found in the brain and central nervous system) in the superficial cortex and hippocampus of living mice. The resulting images show fine details and cellular structures in both regions, even though the cells in the hippocampus are about 0.9 millimeters deeper than those in the superficial cortex by implanting the glass plug. Both images also have a wide field of view, at least 1 millimeter across. And implanting the microprism provides the longitudinal view of the cortex from the depth from 0 to 1mm. Furthermore, the researchers will demonstrate the functional imaging results of neurons in mouse brains in the presentation.

"Our lab has focused on cortex-wide single-cell imaging since the development of RUSH," Zhaung added. "In future work, we will continue to develop new neural imaging techniques with higher throughput, higher SNR, and lower cost. Secondly, explore new algorithms to understand the insight behind the observed cortex-wide neural dynamics. Finally, we will introduce the method to a wide range of biomedical applications, which requires simultaneous observation of cellular dynamics at different depth, such as the study of epilepsy."

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