TOOLBOX

'Light beads' method images activity across the mouse brain

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A **new imaging technique** captures neurons firing nearly simultaneously across big swaths of brain tissue in living mice. The method could help researchers understand how wide-ranging networks of neurons communicate and how these patterns differ between wildtype mice and mouse models of autism. According to **one theory of autism**, unusual patterns of signaling between distant regions of the brain underlie the condition's traits.

Researchers often monitor brain activity in mice by using a technique called two-photon calcium imaging, adding fluorescent protein tags to the calcium ions that flood into cells when neurons fire. They can excite the proteins with a laser and detect the fluorescence with a microscope to observe cells in action.

This method typically limits researchers to one small area for study. To image a larger portion of the brain, they often have to scan section by section, which is too slow to capture the interactions of distant neurons. Researchers can speed up the process by illuminating neighboring regions in the brain with a series of sequential laser beams, each slightly delayed from the previous one to avoid muddying signals. But splitting a laser and delaying each beam usually requires complex equipment, making it difficult to scale up. Scientists have been able to capture the activity of only 12,000 neurons using this approach.

The new method enables researchers to track the activity of more than 1 million individual neurons in about 16 cubic millimeters of mouse brain — more than 10 times the volume imaged using previous techniques. "That is definitely by far the largest volume and the largest number of neurons that anyone has captured simultaneously," says **Alipasha Vaziri**, professor of neurotechnology and biophysics at Rockefeller University in New York City. He led the new work, which is described in August in *Nature Methods*.

The technique — called light beads microscopy — involves splitting a laser beam into 30 beams,

each one exciting a spot at a slightly different depth in the brain. This split creates a column of “light beads” that measures about 500 microns in depth, enabling researchers to scan an entire block of the brain in the same time it normally takes to scan a small 2D slice with conventional approaches.