

New Technique Captures Entire Fly Brain in 3D

The method combines two approaches to reveal a high-resolution map of all 40 million synapses

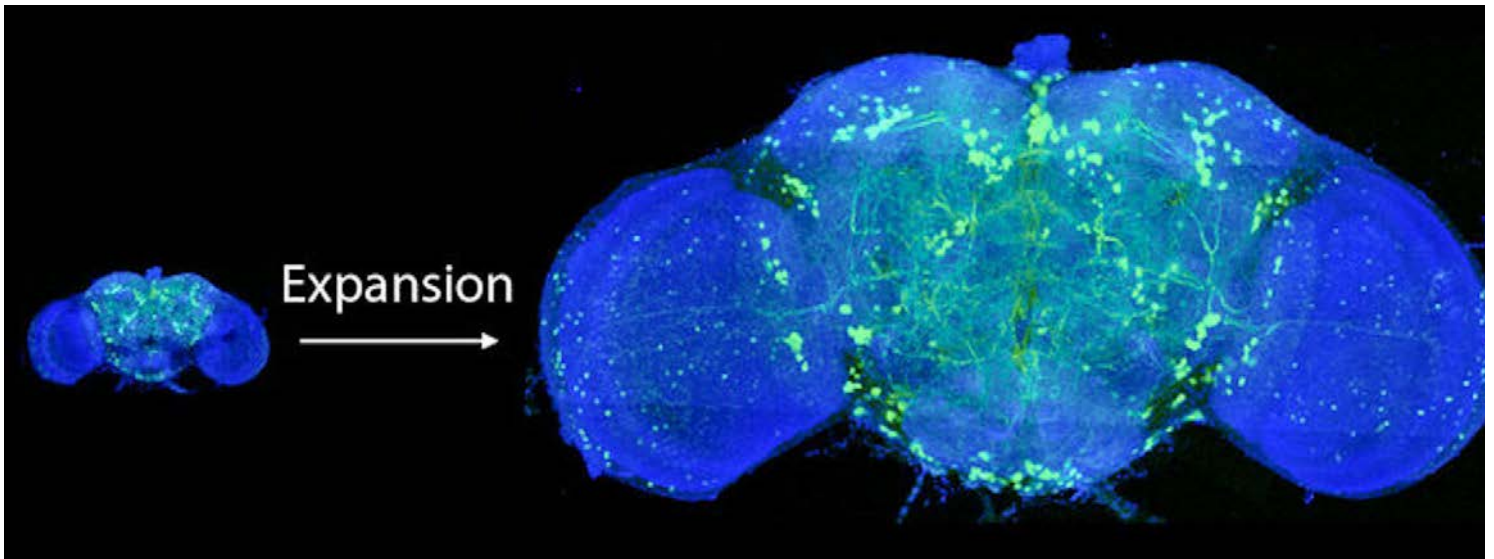
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A new technique that marries two methods, expansion microscopy and lattice light-sheet microscopy, has allowed researchers to image a fruit fly's brain in its entirety with intricate detail and in a flash, relative to other microscopy approaches, scientists reported yesterday (January 17) in *Science*.

ABOVE: A forest of dendritic spines protrude from the branches of neurons in the mouse cortex.
GAO ET AL., *SCIENCE*, 2019

Expansion microscopy "blows up" the tissue before imaging to make it easier to see details. To do this, the researchers add a swelling, water-absorbent polymer gel to preserved tissue. When transferred from a salty bath to pure water, the polymer grows, stretching out the tissue. In the case of the fly brain imaged in this work, the tissue ballooned by a factor of four.



The fruit fly brain expanded to four times its usual size.

GAO ET AL., *SCIENCE*, 2019

The imaging relies on fluorescent tags that glom onto proteins in cells and also attach to the gel. The proteins are digested to leave the fluorescent molecules in place. Then, to trace the neurons in the brain tissue, the researcher turned to a technique called lattice light-sheet microscopy, a relatively gentle imaging method that doesn't obliterate the sample.

The method sweeps an ultrathin layer of light through the tissue. By using less intense light than other microscopy techniques, the beam can linger on the sample while not "burning out" the fluorescence or obscuring some of the picture, *Science* reports.

And it's fast, too. Because lattice light-sheet microscopy illuminates a whole plane instead of one spot, researchers were able to capture the whole fly brain in roughly 62 hours. To do this type of imaging with an electron microscope could take years, according to a press release from the [Howard Hughes Medical Institute](#).

The imaging produces a mountain of 3D "cubes," which need to be stitched together by computational tools. In the end, the team was able to map all 40 million plus synapses of a fruit fly brain at nanometer resolution.

The technique yielded similar results when looking at a slice of a mouse's brain.

"This is a taste of the future. . . . We're getting these huge rich data sets and we're starting to get better tools to squeeze information from them," Joshua Vaughan, a fluorescence microscopy expert from the University of Washington who was not involved in this work, tells *STAT*.

Explore a 3D map of a fly's brain



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