EDITORIAL

Microscopy breakthrough stretches confocal resolution

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Image: Professor Ed Boyden enlarges brains to reveal nanoscale detail [Dominick Reuter]

US-based researchers have unveiled a method they call expansion microscopy to image large biological specimens at nanoscale resolution using just a confocal microscope.

The technique uses an expandable polymer and water to swell tissue to around four and a half times its usual size, so that nanoscale structures, once blurry, appear within focus on an ordinary confocal microscope.

"Instead of acquiring a new microscope to take images with nanoscale resolution, you can now take the images on a regular microscope," says Professor Ed Boyden (http://bcs.mit.edu/people/boyden.html) from Massachusetts Institute of Technology (http://web.mit.edu/). "[This method] may provide a key tool for comprehensive, precise, circuit-wide brain mapping."

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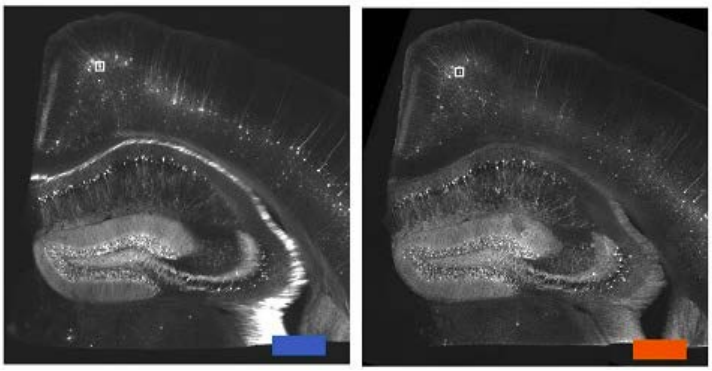
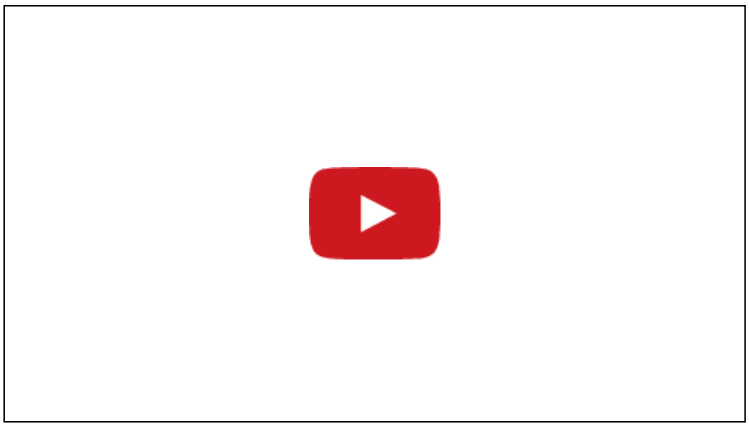


Images of a mouse brain segment enlarged (right) have greater resolution than those acquired using conventional microscopy without water expansion (left). [Ed Boyden, Fei Chen, Paul Tillberg]

As Boyden explains, sodium acrylate is first infused into chemically fixed brain tissue, with polymerisation agents then added to form a tissue-polymer composite network within the sample.

With the acrylate polymer network in place, researchers incorporate custom-designed fluorescent labels, based on a chemical fluorophore, antibody and chemical anchor, that link to the chosen targets.

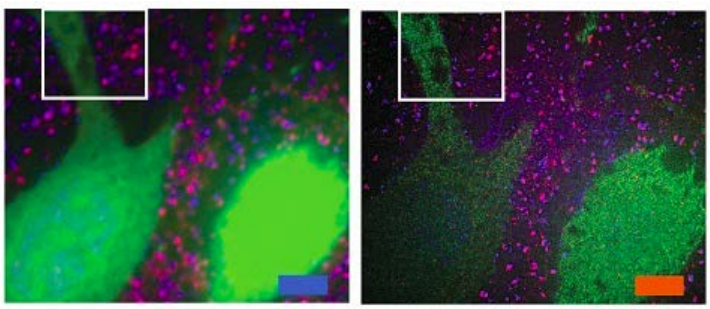
They then treat the tissue-polymer sample with protease, to homogenise its mechanical properties, and finally rinse it in water to trigger the 4.5 times linear expansion.



MIT researchers led by Ed Boyden have invented a new way to visualize the nanoscale structure of the brain and other tissues. [Boyden Lab @ MIT, Nick Moore and Julie Pryor]

"By covalently anchoring specifics label located within the specimen directly to the polymer network, labels spaced closer than the optical diffraction limit can be separated and optically resolved," says Boyden.

Testing his method on HEK 293 cells - human embryonic kidney cells - as well as 500 µm mouse brain tissue slices, the researcher used confocal laser scanning and spinning disk microscopy to resolve molecules that had been as close as 70 nm before expansion.



Expansion microscopy of dendrites in a mouse brain: nanoscale structures once blurry (left) appear sharp (right) with an ordinary confocal microscope. [Ed Boyden, Fei Chen, Paul Tillberg]

"Expansion microscopy can achieve super-resolution with standard fluorophores, and on a diffraction-limited microscope," highlights Boyden.

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"And because the expansion microscopy-processed sample is almost entirely water, eliminating scattering, [the method] may empower fast methods like light-sheet microscopy to become super-resolution methods," he adds.

Research is published in Science (http://www.sciencemag.org/content/early/2015/01/14/science.1260088).