Coming Events

2015

MSC-SMC Annual Meeting
May 26–29, 2015
Hamilton, Ontario, Canada
www.bimr.ca/events/msc-smc-annual-meeting-2015

Inter/Micro 2015
June 8–12, 2015
Chicago, IL
www.mcri.org

SCAMDEM2015
June 9–11, 2015
Jyväskylä, Finland
www.jyu.fi/en/congress/scandem2015

Live-Cell Imaging
June 23–25, 2015
Norwich, UK
www.physoc.org/live-cell-imaging-23-25- june-2015

Microscience Microscopy Conference
June 29–July 2, 2015
Manchester, United Kingdom
www.mmc2015.org.uk

Stereology & Image Analysis
July 6–10, 2015
Liege, Belgium
www.14icsia.com

Semicon West, 2015
July 14–16, 2015
San Francisco, CA
www.semiconwest2015.org

Microscopy & Microanalysis 2015
August 2–6, 2015
Portland, OR
www.microscopy.org

2016

Microscopy & Microanalysis 2016
July 24–28, 2016
Columbus, OH
www.microscopy.org

2017

Microscopy & Microanalysis 2017
July 23–27, 2017
St. Louis, MO
www.microscopy.org

2018

Microscopy & Microanalysis 2018
August 5–9, 2018
Baltimore, MD
www.microscopy.org

2019

Microscopy & Microanalysis 2019
August 4–8, 2019
Portland, OR
www.microscopy.org

More Meetings and Courses
Check the complete calendar near the back of this magazine.

Carmichael's Concise Review

A New Approach to Super-Resolution Microscopy

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The Nobel Prize in Chemistry was awarded last year for the development of super-resolved fluorescence microscopy, which is now an established method in the armamentarium of microscopists. However the specialized microscopes for super-resolution remain expensive and complicated to use. Fei Chen, Paul Tillberg, and Edward Boyden have developed an entirely new approach to super-resolution [1]. Instead of using an instrument that can resolve objects smaller than the diffraction limit described by Ernst Abbe, Chen et al. decided to make the object of study larger so that a diffraction-limited microscope can image a structure that could only be otherwise imaged by electron microscopy or super-resolution microscopy.

Chen et al. discovered that by synthesizing a swellable polymer network within a specimen, it can be expanded, resulting in a physical magnification of four- to five-fold. The other key was the development of specific labels that could be applied to the specimen and then covalently anchored to the polymer network. These labels (for example, anti-tubulin to label microtubules) originally would be spaced below the diffraction limit, but they are then isotropically separated when the polymer network swells and can be optically resolved with a diffraction-limited microscope.

Chen et al. first set out to see whether a well-known property of polyelectrolyte gels—namely that dialyzing them in water causes expansion of the polymer network into extended confirmations—could be performed in a biological sample. They infused sodium acrylate, a monomer used to produce superabsorbent materials, along with other monomers, cross-linkers, and an accelerant into chemically fixed and permeabilized specimens that had been labeled. The specimen-polymer composite was treated with protease to digest the specimen but left the labels bound to the polymer. Dialysis with water then resulted in a 4.5-times linear expansion. Quantitative measurements and statistical analysis determined that the spatial error was less than 1%. They also determined that the fluorescent label targeted to a biomolecule of interest remained

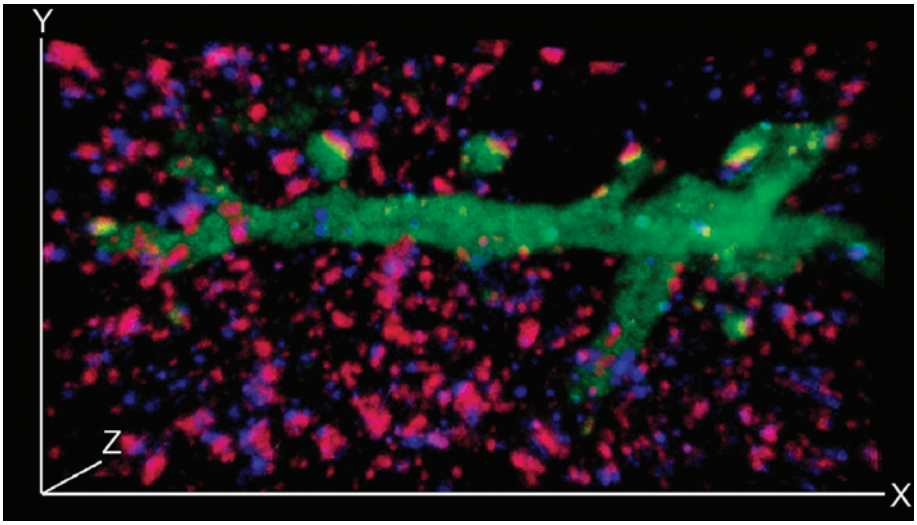

Figure 1: A volume-rendered image from CA1 layer of the mouse hippocampus showing neurons (expressing cytosolic yellow fluorescent protein in green), presynaptic elements (stained with anti-Bassoon, blue), and postsynaptic elements (stained with anti-Homer1, red). The scale bar in the X direction is 13.5μm, Y is 7.3μm, and Z is 2.8μm.

doi:10.1017/S1551929515000383

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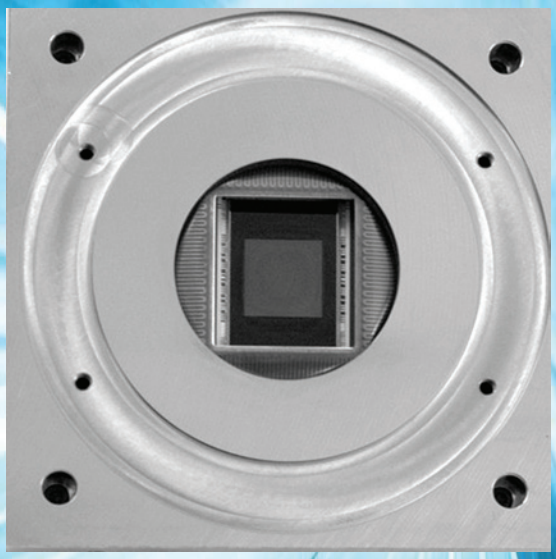
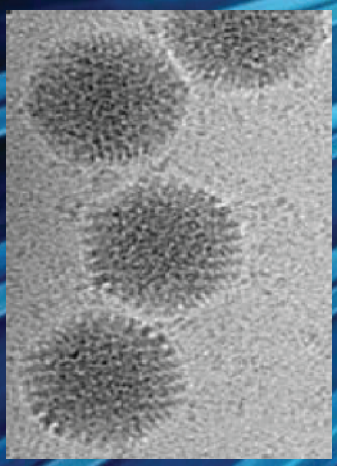
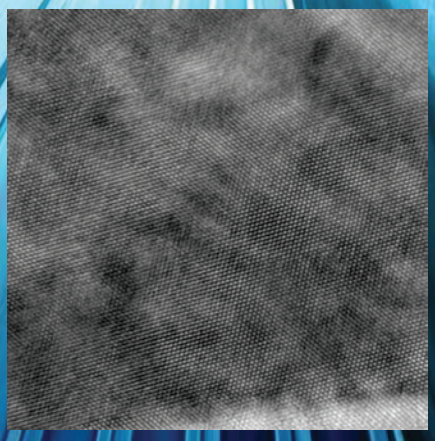




Adenovirus

Dr. Cameron Ackerley
The Hospital for Sick Children

Diffraction



Lattice

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covalently anchored to the polymer network. Because the biologic specimen had been swelled, the object was mostly water and scattering was eliminated. The entire process of labeling, gelation, digestion, expansion, and imaging is called expansion microscopy (ExM).

Chen et al. performed ExM to examine microtubules in fixed human embryonic kidney cells. With confocal laser scanning microscopy they compared pre- and post-ExM images and found them to be visually indistinguishable, suggesting that ExM caused practically no distortion. They also compared pre-ExM samples examined with a super-resolution structured illumination microscope to post-ExM specimens examined with a confocal microscope and showed that microtubule networks were more sharply resolved by ExM. They then examined mouse brain tissue (Figure 1) and found the post-ExM measurement errors were only 2 to 4%. Labeling for pre- and post-synaptic molecules showed that ExM enables multiscale imaging and visualization of nanoscale features within volumes relevant to understanding neural circuits.

This new technique offers great promise. Chen et al. suggest that by tuning the material properties of the ExM polymer, such as the density of cross-links, yet higher effective resolutions may be possible!

References

[1] F Chen et al., *Science* 347 (2015) 543–48.

[2] The author gratefully acknowledges Dr. Edward Boyden for reviewing this article.

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