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Expansion Microscopy

Ed Boyden

MIT, Cambridge, Massachusetts, United States

To enable the understanding, repair, and building of complex systems such as the brain, we are creating novel tools that enable molecular-resolution maps of large scale systems, as well as technologies for observing and controlling high-speed physiological dynamics in such systems. First, we have developed a method for imaging large 3-D specimens with nanoscale precision, by embedding them in a swellable polymer, homogenizing their mechanical properties, and exposing them to water – which causes them to expand isotropically manyfold. This method, which we call expansion microscopy (ExM; Science (2015) 347(6221):543-548), enables scalable, inexpensive diffraction-limited microscopes to do large-volume nanoscopy, in a multiplexed fashion – important, for example, for brain mapping. We have developed protocols for performing ExM on a variety of cell culture and tissue types, from a diversity of species; protocols are available at expansionmicroscopy.org, and over 100 preprints or peer-reviewed papers have appeared performing expansion microscopy experiments. We routinely help teach people how to perform expansion microscopy.

Running this process in reverse – which we call imposion fabrication (ImpFab; Science (2018) 362(6420):1281-1285) enables the direct assembly of 3D nanomaterials consisting of metals, semiconductors, and biomolecules arranged in virtually any 3D geometry. Second, we have developed a set of genetically-encoded reagents, known as optogenetic tools, that when expressed in specific neurons, serve as single-protein devices that enable their electrical activities to be precisely driven or silenced in response to millisecond timescale pulses of light. These templates, appropriately evolved, can be transformed into reagents that serve as fluorescent voltage indicators, enabling the imaging of fast physiological processes in 3-D with millisecond precision. In this way we aim to enable the systematic mapping, control, and dynamical observation of complex biological systems like the brain.

References

Wassie AT*, Zhao Y*, Boyden ES (2018) Expansion microscopy: principles and uses in biological research, Nature Methods 16(1):33-41. (*, equal contributors)