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# Biological Imaging at High Spatiotemporal Resolution

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I will discuss our latest attempts to improve fluorescence microscopy techniques for following live biological phenomena at high spatiotemporal resolution. Emphasis will be given to structured illumination microscopy (SIM) and light-sheet microscopy (LSFM) techniques.

SIM[1] doubles the spatial resolution of light microscopy, requiring lower light intensities and acquisition times than other super-resolution techniques. I will present SIM implementations that enable resolution doubling in live volumes > 10-20x thicker[2-4] than possible with conventional SIM, as well as hardware modifications that enable effectively 'instant' SIM[3,5] imaging at rates 10-100x faster than other SIM. New applications of instant SIM, including combination with total internal reflection (TIRF) and with adaptive optics[6] will also be discussed.

The second half of the talk will focus on the development of inverted selective plane illumination microscopy (iSPIM), and subsequent application to the noninvasive study of neurodevelopment in nematodes[7]. I will discuss progress that quadruples the axial resolution of iSPIM by utilizing a second specimen view, thus enabling imaging with isotropic spatial resolution (dual-view iSPIM, or diSPIM[8,9]). Newer multiview results with more objectives[10] and more views[11], further improving spatial resolution, will also be shown. Applications of these technologies will be presented, including computational methods for untwisting worm embryos[12], with the goal of building a neurodevelopmental atlas with subcellular resolution[13].

Time permitting, I will also discuss 3 new and unpublished research projects in my lab: (1) rapid, sensor-less adaptive optics for use in SIM and LSFM; (2) 3D orientation sensing via multi-view fluorescence polarization; (3) structured illumination microcopy with ~5-fold improvement in axial resolution.

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