Sheet of light

The development of fluorescent proteins as genetically encoded probes for biological specimens has been pivotal for a renaissance of fluorescence microscopy in recent years. A prime example of this progress in microscopy is a technique (first described in 1903) that uses a sheet of light to illuminate a sample instead of the commonly used full-field or point illumination. The use of a light sheet allows for fast high-resolution volumetric imaging of three-dimensional (3D) samples that can be quite large by microscope standards while keeping light dosages low. When coupled with living specimens expressing fluorescent proteins, this technique greatly minimizes phototoxicity and its compromising effects on the integrity of a living specimen. The resulting capabilities are allowing researchers to explore biology that was previously inaccessible.

In this special Collection, we are pleased to present a selection of papers published in Nature Methods, Nature Communications and Nature Reviews Molecular Cell Biology that highlight the expanding capabilities and applications of light-sheet fluorescence microscopy (LSFM).

In a Perspective (p. 7), Stelzer and colleagues discuss the problems of typical cell monolayer samples used for fluorescence microscopy and the importance of moving to more physiologically representative 3D samples. An overview and comparison of different light-sheet implementations and other optical sectioning techniques (Mertz, p. 10) helps researchers choose the microscopy method appropriate for their circumstances.

Recently there has been great interest in fast high-resolution imaging of large cleared tissue samples, particularly for mapping neurons and their connections in the whole brain. Early work (Dodd et al., p. 23) showed that LSFM is well suited for imaging cleared brain and other large fixed samples. As with point-scanning fluorescence microscopy, two-photon illumination can aid in deep imaging of living tissue, even for developing embryos (Truong et al., p. 29).

Imaging of embryo development and even faster processes in whole living organisms is probably where LSFM holds the most promise. To increase the speed of LSFM and improve resolution, multiple groups have developed implementations using four objective lenses and two light sheets (Weber and Huisken, p. 21). These systems have been used on whole living zebrafish embryos for functional imaging of nearly all brain neurons with close to one-second temporal resolution (Ahrens et al., p. 33) and for measuring endothelial cell migration patterns and tissue remodeling in the early endoderm (Schmid et al., p. 41).

The greatest challenge in LSFM now is data handling and analysis, from registration and merging of multiple views (Preibisch et al., p. 19) to the greater challenge of merging data from multiple samples (Schmid et al., p. 41). The terabyte-sized data sets generated by LSFM make data analysis across samples difficult, but without it the significance of results is unclear.

Finally, Diaspro and colleagues (p. 51) show it is possible to merge LSFM and super-resolution microscopy, potentially opening up applications beyond the reach of either technique on its own. We are pleased to acknowledge the support of Carl Zeiss Microscopy in producing this Collection. As always, Nature Publishing Group carries sole responsibility for the editorial content.

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