Correlative three-dimensional fluorescence and refractive index tomography

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Optical diffraction tomography (ODT) provides the measurements of quantitative imaging of three-dimensional (3-D) refractive index (RI) distribution of biological cells and tissues, which provides structure and chemical information about the samples. 3-D RI distribution is reconstructed from the measured multiple 2-D optical fields diffracted by the sample from various illumination angles via the Fourier diffraction theorem [1-3].

Here, we present an optical setup combining ODT with three-channel 3D fluorescence microscopy, to enhance the molecular specificity of the 3D RI measurement. Uilizing a Mach-Zehnder interferometry equipped with a dynamic micromirror device, 3D RI maps of a sample is measured with high speed and precision. The 3D RI distribution and 3D deconvoluted fluorescence images of HeLa cells and NIH-3T3 cells are measured, and the cross-correlative analysis between RI and fluorescence of live cells are presented. In addition, the use of structured illumination microscopy was applied to achieve super resolution fluorescence imaging. Like PET/CT provides both the morphological and molecule specific imaging in medical diagnosis, the present method is an optical analogy which provides both morphological and molecular imaging of biological cells.

Figure 1: Cross-correlative analysis of 3D RI and 3D fluorescence images of an NIH-3T3 cell. (left) The cross-sectional slices and (middle) the 3D rendered map of reconstructed 3D RI distribution of the samples. Scale bar indicates 20 μm. (right) The 3D deconvoluted fluorescence images of the samples stained with Hoechst (blue) and GFP-tubulin (green).

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