

Correlative three-dimensional fluorescence and refractive index tomography

KYOOHYUN KIM, SEUNGWOO SHIN, AND YONGKEUN PARK

Department of Physics

Korea Advanced Institute of Science and Technology (KAIST)

Daejeon 305-701, Republic of Korea

E-mail : yk.park@kaist.ac.kr

KEY WORDS: optical diffraction tomography, quantitative phase imaging, living Cells, 4D imaging

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. Utilizing 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.

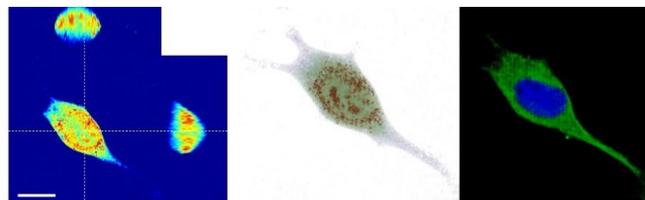


Figure 1: Cross-correlative analysis of 3D RI and 3D fluorescence images of an NIH-3T3 cell. (left) The cross-sectional slices and (middle) the 3D rendered map of reconstructed 3D RI distribution of the samples. Scale bar indicates 20 μm . (right) The 3D deconvoluted fluorescence images of the samples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

- [1] V. Lauer, New approach to optical diffraction tomography yielding a vector equation of diffraction tomography and a novel tomographic microscope, *Journal of Microscopy*, 205 (2002) 165-176.
- [2] K. Kim, H. Yoon, M. Diez-Silva, M. Dao, R.R. Dasari, Y. Park, High-resolution three-dimensional imaging of red blood cells parasitized by *Plasmodium falciparum* and in situ hemozoin crystals using optical diffraction tomography, *Journal of biomedical optics*, 19 (2014) 011005-011005.
- [3] K. Lee, K. Kim, J. Jung, J.H. Heo, S. Cho, S. Lee, G. Chang, Y.J. Jo, H. Park, Y.K. Park, Quantitative Phase Imaging Techniques for the Study of Cell Pathophysiology: From Principles to Applications, *Sensors*, 13 (2013) 4170-4191.
- [4] S. Shin, K. Kim, J. Yoon, Y. Park, Active illumination using a digital micromirror device for quantitative phase imaging, *Optics Letters*, 40 (2015) 5407-5410.
- [5] K. Kim, W. Park, S. Na, S. Kim, T. Kim, W.D. Heo, Y.K. Park, Correlative three-dimensional fluorescence and refractive index tomography: bridging the gap between molecular specificity and quantitative bioimaging, *Biomedical Optics Express*, 8(12), 5688-5697 (2017)
- [6] S. Shin, D. Kim, K. Kim, Y.K. Park, Super-resolution three-dimensional fluorescence and optical diffraction tomography of live cells using structured illumination generated by a digital micromirror device, arXiv:1801.00854