Quantitative Phase Imaging and Artificial Intelligence: Label-Free 3D Imaging and Analysis of Individual Live Cells

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We present a rapid and label-free method for single cell analysis, utilizing quantitative phase imaging (QPI) and machine learning. Holotomography (HT), one of the 3D QPI techniques, uses laser interferometry to measure 3-D refractive index (RI) distribution. HT serves as a powerful tool for imaging small transparent objects, such as biological cells and tissues. HT is an optical analogous to X-ray computed tomography (CT); HT measured multiple 2-D holograms of a sample with various illumination angles, from which a 3-D RI distribution of the sample is reconstructed by inversely solving the wave equation. Unlike conventional fluorescence-based imaging techniques, HT provides label-free 3-D imaging capability. Without any fixation or labeling, 3-D images of live cells can be obtained with high spatial resolution (down to 110 nm) and high temporal resolution (several 3D tomogram measurements per second). Furthermore, HT provides quantitative imaging capability: RI maps of a cell are precisely and quantitative measured, from which various cellular analysis can be followed. Employing HT, we address various biological and medical problems by phenotyping cell types from the measured 3-D RI tomograms of individual cells and training deep learning algorithms to rapidly and precisely classify cell types. We present applications in hematology, cell biology, and immunology. In particular, we will discuss the potentials of the present approach for single cell analysis.