Near-common-path quantitative phase microscopy

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Technology Overview

Quantitative phase imaging (QPI) is a technique for accurately measuring the structure and function of transparent biological samples without requiring exogenous contrast agents (1,2). In the last few years, QPI has gained acceptance as a label-free tool to quantify pathophysiological processes at single cell level (3). The MIT-Laser Biomedical Research Center (LBRC) has been responsible for several major technological advances in the field of quantitative phase microscopy over the past decade. These techniques provide high precision measurements of optical path delay in the biological samples in a label-free manner. One such technique is diffraction phase microscopy that offers wide-field single shot quantitative phase images of relatively transparent biological samples (4).

Figure 1 shows the latest quantitative phase microscope developed in our lab. This near-common-path phase microscopy entails samples and reference beams side-by-side to ensure minimal system phase noise required for measuring nanometer scale motion. In this setup, the ability of a dove prism to "flip" an image is used to remove the need for spatial filtering commonly used in QPM setups such as in Ref (4). This leads to a stable microscope that could be easily used by non-experts and biologist obviating the need for re-alignments and maintenance for a long time. Figures 3(d),(e) illustrate single-shot quantitative phase imaging of relatively small (RKO human colon cancer cell) to very large samples (drosophila embryo) without any setup modifications.

Biomedical Application Potential

Capabilities of quantitative phase microscope (QPM) have been demonstrated in a variety of biological studies such as cell growth dynamics (5), and dynamics of pathogen infection (6). One major limitation of the QPM of the transmission type is the fact that optical path length represents the information on both the optical properties and morphology that cannot always be decoupled. However, if the biological sample is optically homogenous such as the case of the red blood cell, one can measure the cell morphology with nanometer accuracy in a single shot of the camera. Through high-speed measurement of the morphology, dynamics of the membrane thermal fluctuation may be quantified. This dynamic has been used extensively to monitor erythrocytes mechanics in health and disease condition (7,8).

Ongoing Projects

a. Studying dynamics of the erythrocyte in sickle cell anemia
b. Red blood cell mechanics affected by transgenic malaria parasites

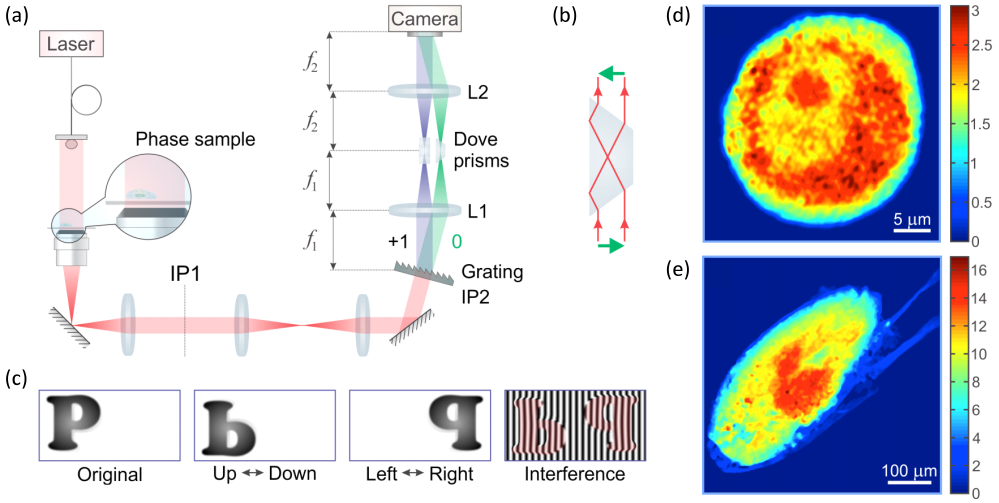

Figure 1. (a) Self-reference quantitative phase microscope; (b) Inversion of an image pattern on propagation through dove prism; (c) Original, inverted images, and the interference pattern. (d,e) Quantitative phase images of an RKO human colon cancer cell and drosophila embryo, respectively. Color bars in radians.

Background Publications

1. Popescu G. Quantitative phase imaging of cells and tissues. McGraw Hill Professional; 2011.

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5. Mir M, Wang Z, Shen Z, Bednarz M, Bashir R, Golding I, et al. Optical measurement of cycle-dependent cell growth. Proc Natl Acad Sci. 2011;108(32):13124–9.

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8. Park Y, Diez-Silva M, Popescu G, Lykotrafitis G, Choi W, Feld MS, et al. Refractive index maps and membrane dynamics of human red blood cells parasitized by Plasmodium falciparum. Proc Natl Acad Sci. 2008;105(37):13730–5.

Representative Center Publications

1. Hillman TR, Lue N, Sung Y, Dasari RR, Yaqoob Z. Near-Common-Path Self-Reference Quantitative Phase Microscopy. Photonics Technol Lett IEEE. 2012;24(20):1812–4.

2. Popescu G, Ikeda T, Dasari RR, Feld MS. Diffraction phase microscopy for quantifying cell structure and dynamics. Opt Lett. 2006;31(6):775–7.

3. Fu D, Oh S, Choi W, Yamauchi T, Dorn A, Yaqoob Z, et al. Quantitative DIC microscopy using an off-axis self-interference approach. Opt Lett. 2010;35(14):2370–2.

4. Ikeda T, Popescu G, Dasari RR, Feld MS. Hilbert phase microscopy for investigating fast dynamics in transparent systems. Opt Lett. 2005;30(10):1165–7.

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6. Yaqoob Z, Yamauchi T, Choi W, Fu D, Dasari RR, Feld MS. Single-shot full-field reflection phase microscopy. Opt Express. 2011;19(8):7587–95.

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