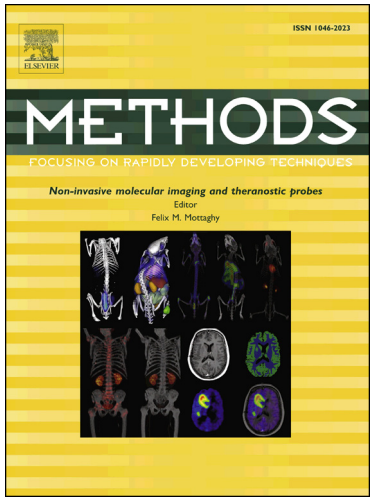

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Single pixel quantitative phase imaging with spatial frequency projections

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Abstract

We introduce a new single pixel imaging technique that automatically co-registers quantitative phase and incoherent image modalities through the simultaneous acquisition of identical object spatial frequency information. The technique consists of using a time varying groove density diffraction grating to produce a reference and scan beam. The interference between the beams produce time varying spatial frequencies in the sample. The collected light on a single pixel detector produces a time trace that allows easy recovery of coherent and incoherent contrast mechanisms. We derive theory for the quantitative phase and show excellent agreement with experimental data and numeric model. Additionally, we derive a general theory of single pixel quantitative phase theory that can be applied broadly to general methods that use a sequence of modulated light patterns for single pixel phase imaging.

Keywords: Single pixel imaging, Spatial frequency microscopy, Label-free, Microscopy, Quantitative phase imaging, Tomography
2010 MSC: 92C05, 92C55

1. Introduction

Optical imaging is a powerful technique for probing the physical organization, chemical composition, and temporal dynamics of a wide range of objects, from biological specimens to precision metrology of nanomaching. Numerous scientific endeavors rely on collecting high fidelity images of the system under study – covering microscopic and macroscopic scales. Regardless of the spatial scale involved in an optical imaging process, the light collected from an object is re-imaged to a detector and recorded. When possible, it is advantageous to record light with a segmented optical detector that serves as a camera detector chip, such as a charge-coupled device (CCD). To produce a high quality image, the light emitted by the specimen must be minimally perturbed to prevent distortions of the image incident on the detector. This limits the scope of optical microscopy with cameras to objects that are weakly scattering.

In many cases, specimens imaged in a microscope display weak absorption and small refractive index changes, rendering them nearly transparent when illuminated by visible light. Weak absorption becomes particularly problematic for thin tissue slices or cell cultures due to the small interaction volume. Fluorescent and phase contrast modalities are the most common methods to image transparent biological specimens [1–3] with high contrast. Fluorescence allows for visualization of cellular dynamics with high specificity, while phase imaging probes endogenous contrast mechanism [3, 4].

Fluorescence microscopy is a mature technology whose use in recent years has been propelled by high sensitivity detectors that allow single molecule detection. While some natively expressed biochemicals display strong autofluorescence, the introduction of exogenous or transgenic fluorescent labels has greatly expanded the impact of fluorescent microscopy by enabling particular biochemicals to be targeted and observed in biological specimens [5]. Yet fluorescent imaging is limited because not all molecules fluoresce, and the broad optical absorption and emission spectra can make it difficult to distinguish particular target molecules. In addition, fluorescent molecules are subject to photo-bleaching that can permanently degrade the ability to image a specimen for long periods of time, thus limiting the ability to perform long-term studies.

An alternative approach to fluorescence microscopy, that requires no external fluorescent probes and yields complementary information, is phase contrast microscopy. Phase contrast microscopy records spatial phase distortions of a light wave passing through a specimen due to spatial variations in optical path length (OPL). The phase accumulated by the illumination beam upon propagation through a specimen is proportional to the local index of refraction variations of the sample integrated along the direction of propagation. The vast potential of extracting information from biological specimens without adding exogenous contrast agents has motivated significant development in methods for quantitative phase imaging [6, 7].

Although optical detectors cannot directly record the rapid oscillations of the electric field, and thus fail to record optical phase, interference between two coherent fields can convert phase differences into optical intensity variations – enabling the

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