Multimodal imaging of biological samples combining quantitative phase and fluorescence imaging by using a single camera

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Quadriwave lateral shearing interferometry (QWLSI) is a well-established quantitative phase imaging (QPI) technique based on the analysis of interference patterns of four diffraction orders by an optical grating set in front of an array detector [1]. As a QPI modality, this is a non-invasive imaging technique which allow to measure the optical path difference (OPD) of semi-transparent samples.

We present a system enabling QWLSI with high-performance sCMOS cameras [2] and apply it to perform high-speed imaging, low noise as well as multimodal imaging. This modified QWLSI system contains a versatile optomechanical device which images the optical grating near the detector plane. Such a device can be coupled with multiple cameras by varying its magnification. In this paper, we study the use of a sCMOS Zyla5.5 camera from Andor along with our modified QWLSI system.

The OPD signal measured by QPI modalities provides a morphologic information of the cells and reveals nuclei, membranes and organelles within the cells. The structural and density information extracted from the OPD signal is therefore complementary to the specific and localized fluorescence signal [2]. In addition, QPI detects cells even when the fluorophore is not expressed. This is very useful to follow a protein expression with time.
The 10 µm spatial resolution of our modified QWLSI associated to the high sensitivity of the Zyla5.5 enabling to perform high quality fluorescence imaging. Besides, since our system is able to perform phase imaging as well as fluorescence imaging with the same camera, this ensures a very simple and accurate superposition of the two images acquired sequentially. We will present multimodal images revealing fine structures cells, like actin filaments, merged with the morphological information of the phase.

[1] P. Bon, G. Maucort, B. Wattellier, and S. Monneret, "Quadriwave lateral shearing interferometry for quantitative phase microscopy of living cells," Opt. Express, vol. 17, pp. 13080–13094, 2009.

[2] P. Bon, S. Lécart, E. Fort and S. Lévêque-Fort, "Fast label-free cytoskeletal network imaging in living mammalian cells," Biophysical journal, 106(8), pp. 1588-1595, 2014