QUANTIFYING PHASE SENSITIVITY IN PTYCHOGRAPHY TOWARDS MULTIMODAL STUDIES OF CHROMATIN-DNA ORGANISATION

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KEY WORDS: Ptychography, phase, cellular imaging, label-free imaging.

The demand for approaches that can explore the function of biological systems without the need for sample treatments, or the addition of fluorescent tags, is steadily emerging. The development of so called 'label free' microscopies is important for the exploration of the natural state of biological systems, without alteration and without potentially effecting the processes being explored mainly related with photodamage [1]. Label free techniques utilize contrast from novel processes to provide a means of imaging without external modification. In the framework of fluorescence microscopy multiphoton excitation allows the formation of images related to intrinsic fluorescence, or higher-order harmonics [2, 3]. Phase contrast and Mueller matrix microscopy are two examples of imaging exploiting molecular properties of the sample, i.e. refractive-index variations [4]. However, the imaging of weakly interacting samples is not trivial and has required significant development or modification of current techniques to produce suitable resolution and contrast. Ptychography is a diffractive imaging technique that uses multiple diffractograms collected from spatially overlapping regions of a sample to retrieve a samples' complex transmission function, providing images of its amplitude and phase. This overlap aides not only in the unambiguous retrieval of the transmission function, but can also be used to recover the quantitative phase, with great potential as a contrast mechanism for cellular imaging including biomechanics [5, 6].

Here we explore the sensitivity of ptychographically retrieved phase information to controlled variations in refractive index and sample thickness to identify the minimum resolvable phase variation. Additionally we discuss our approach to imaging isolated nuclei by correlating the quantitative phase information from ptychography with the circular dichroism signal from circular intensity differential scattering (CIDS) scanning microscopy.

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