TOWARDS IMPROVED-RESOLUTION TOMOGRAPHIC DIFFRACTIVE MICROSCOPY

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Tomographic Diffractive Microscopy (TDM) is a technique, which permits to image unprepared specimens, by numerical recombination of measured scattered fields [1], according to the diffraction tomography theorem for weakly scattering specimens, like isolated cells, or using more sophisticated inversion procedure for more highly diffractive samples. This necessitates precise recording of both the amplitude and the phase of the light diffracted by the specimen. Using an adapted model of diffraction, a numerical reconstruction then permits to obtain an estimation of the 3-D permittivity map of the observed sample.

The improved resolution provided in TDM, compared to conventional transmission microscopy, is provided by its better high-frequency transmission, allowed by the use of coherent amplitude/phase imaging.

The improved resolution provided in TDM, compared to holographic microscopy, is provided by the variation of illumination of the sample. It is usually obtained by sample rotation [2,3], illumination rotation to numerically synthetize the use of an illumination condenser [4,5], or combining both approaches [6].

The lateral and axial extensions of the frequency support (Nyquist resolution) is given by [6]:

$$\Delta\nu_{x,y}^{Holo} = \frac{2n\sin\theta}{\lambda} \quad \Delta\nu_{z}^{Holo} = \frac{n(1-\cos\theta)}{\lambda} \qquad \Delta\nu_{x,y}^{TDM-IR} = \frac{4n\sin\theta}{\lambda} \quad \Delta\nu_{z}^{TDM-IR} = \frac{2n(1-\cos\theta)}{\lambda}$$

$$\Delta\nu_{x,z}^{TDM-SR} = \frac{4n\sin(\theta/2)}{\lambda} \quad \Delta\nu_{y}^{TDM-SR} = \frac{2n\sin\theta}{\lambda} \qquad \Delta\nu_{x,y,z}^{TDM-IRSR} = \frac{4n\sin\theta}{\lambda}$$

in holography, TDM with illumination rotation (TDM-IR), TDM with sample rotation (TDM-SR), and TDM combining both approaches (TDM-IRSR), respectively.

TDM is however an inherently diffraction-limited imaging technique. Within first-order Born approximation, lateral resolution up to λ/3.5NA has been achieved [7]. Much better resolution can be obtained if higher-order diffraction and/or if a priori information can be taken into account [8], but such approaches do not apply for weakly diffracting samples.

In such case, and in order to further increase the resolution, a possible approach would be to induce index of refraction variations within the sample, and measure induced changes in the holograms recorded for TDM reconstructions.

We explore, from a theoretical point of view, the use of specific labels, which properties, such as photochromism, would permit to take benefit in TDM of gain allowed by the structured illumination techniques, commonly used in fluorescence microscopy [9,10], in order to widen the transmitted spectrum, and improve resolution.

The drawback of such approach is that one looses the specific advantage of TDM being a label-free imaging approach. We therefore also theoretically explore other possible effects, which could be used to induce non-permanent index of refraction variations within a sample, without using labels, such as thermal effects.

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