

From digital holographic microscopy to optical coherence tomography – separate past and a common goal

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Abstract—In this paper we briefly present the history and outlook on the development of two seemingly distant techniques which may be brought close together with a unified theoretical model described as common k-space theory. This theory also known as the Fourier diffraction theorem is much less common in optical coherence tomography than its traditional mathematical model, but it has been extensively studied in digital holography and, more importantly, optical diffraction tomography. As demonstrated with several examples, this link is one of the important factors for future development of both techniques.

Sixty years after Leith and Upatnieks published their paper describing off-axis holography [1], the technique is widely used in its digital version. The most common and interesting area of digital holography (DH) application is microscopy and biomedicine [2]. The integrated phase of the measured object provides valuable, label-free information which is directly related to e.g. dry mass in cells. In many cases the technique allows to replace fluorescence and due to its quantitative nature provides a plethora of new methods for cell characterization based on measurement and not just observation.

Optical coherence tomography (OCT), on the other hand, is a thirty years younger technique, which uses low-coherence interferometry to produce a qualitative two-dimensional image of refractive index gradient in tissue microstructures [3–4]. It is suitable to *in vivo* measurement configuration and its use in tomographic imaging of the retina was a milestone in ophthalmology [5].

When we look at the initial development of both techniques, it might seem that the link was distant at best, especially when we compare an analog holographic measurement process to point scanning time-domain OCT [4]. However, both techniques are in fact related through the same theory which links the K-space of the specimens scattering potential to object projections acquired in transmission or reflection configuration [6–7]. In this paper we show that holographic imaging in the microscopic scale and the OCT measurement are much closer to one another than it is often thought of and the techniques may be brought down to a common mathematical model to benefit from each other's

developments. We will start with a description of holographic microscopy.

As it has been described in works by Wolf [8–9], information about an analysed sample can be encoded in a complex amplitude of the plane wave that propagates through the specimen. After passing through the object, this wave can be decomposed into a sum of two waves: un-scattered wave U_0 , which is the same as the illuminating beam, and the U_s wave, scattered by the object. Both waves are summed in the hologram plane and are coded with the plane reference wave U_r .

According to the Huygens–Fresnel principle, once the plane wave from a single illumination direction interacts with a sample, each scatterer in the specimen generates a scattered spherical wave that propagates in every direction. In the case of digital holographic microscopy (DHM), only a portion of this wave is recorded with an optical system. The scattered wave (U_s) corresponds to a part of the Fourier spectrum of the scattering potential $F(R)$ of the measured object (Eq. 1).

$$F(R) = -k_0^2(n^2(R) - n_m^2) \quad (1)$$

The 2D information from the hologram may be mapped in the Fourier space onto the Ewald sphere (Fig. 1a) which represents a full scattered wave with the radius of curvature $k_0 = 2\pi/\lambda$. The information captured by the DHM from a single direction of illumination fills only a part of this sphere i.e. a single arc in 2D – (its extent is limited by the numerical aperture (NA) of the imaging system) and for this reason the retrieval of the refractive index with this method is highly inaccurate and DHM is generally considered a 2½D technique. Nevertheless, a simple measurement system (as illustrated in Fig. 2a) makes the technique highly accessible and practical [10]. However, should a series of different viewing perspectives of the object be acquired, the Fourier space becomes filled with data and depending on the projection acquisition scenario, the information is sufficient for a valid refractive index reconstruction. Such an approach is commonly known as optical diffraction tomography (ODT). Illuminating the stationary sample with a tilted beam allows to collect a larger part of the scattered wave without increasing the NA of the imaging objective [11]. To reconstruct the refractive index with this approach,

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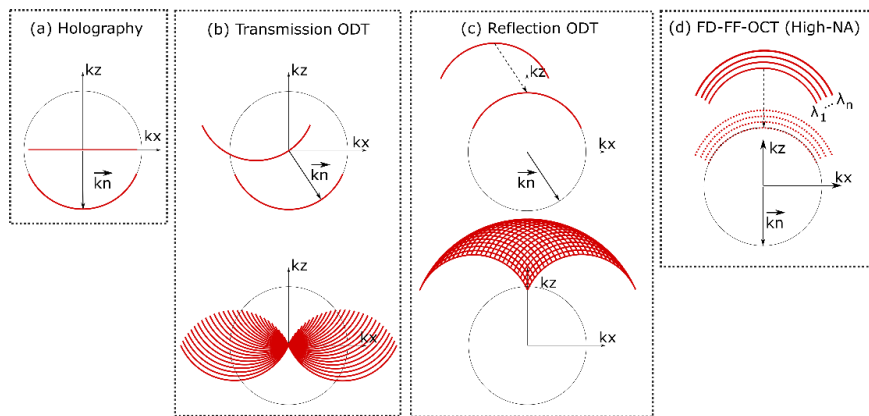


Fig. 1. Fourier space mapping based on different projection acquisition scenarios: a) simple holography, b) limited angle optical diffraction tomography, c) reflection ODT and d) Fourier domain full field optical coherence tomography realized with high numerical aperture (NA).

one must shift each part of the retrieved scattered wave to its origin described by the illumination vector \mathbf{kn} (Fig. 1b). The measurement system in this case is more complicated as an additional scanning element is required in the illumination part of the object beam such as a galvanometer mirror and an optical system to image the mirror in the sample plane, as indicated in Fig. 2b [11].

Apart from rotating the illumination, it is common practice to also (or only) rotate the sample [12], which provides more isotropic reconstruction resolution due to more uniform Fourier space coverage [13–14]. Nevertheless, a significant portion of information, which is back-scattered by the illuminated sample is lost due to imaging in transmission and what is more, this configuration is only suitable for *in vitro* or *ex vivo* measurements. For this reason it is often beneficial to perform ODT in reflection [15] as in Fig. 1c and use a much simpler configuration of the microscope [16]. However, retrieving only high frequencies as in Fig. 1c does not, in practice, allow access to information on refractive index changes, which is mostly located in the low-frequency region. One of the directions currently pursued is to maximize the coverage of the data in the Fourier space without applying sophisticated compressed sensing-based methods or other regularization approaches. One of the possible solutions is to combine the information acquired in transmission and reflection [17–18]. However, if the backscattered information was additionally detected with two opposite reflection ODT systems, then the most complete spectrum coverage would be obtained – without even perturbing the sample with its rotation. One of the interesting solutions for this approach is to place the sample directly on the mirror and alter the illumination direction [19]. With this tool, the information backscattered is either collected directly by the system or through reflection off the mirror beneath the sample.

The one remaining strategy for data coverage increase in ODT is to use the fact that the diameter of the Ewald sphere is scaled with wavelength and thus, different

spheres may be mapped with a hyperspectral approach. Using multiple wavelengths is a desired modality since it can be used as another measure to characterize the sample [20] or to directly combine information from all wavelengths in the Fourier space [21]. In the second case the dispersion of the sample may be the source of reconstruction errors and, in general, should be compensated, especially if the wavelength range is significant for the sample measured. Accordingly, the wavelength scanning strategy may be used also in the case of reflective ODT and has been realized along with a vector-based approach to improve the axial resolution of the reconstruction result [22].

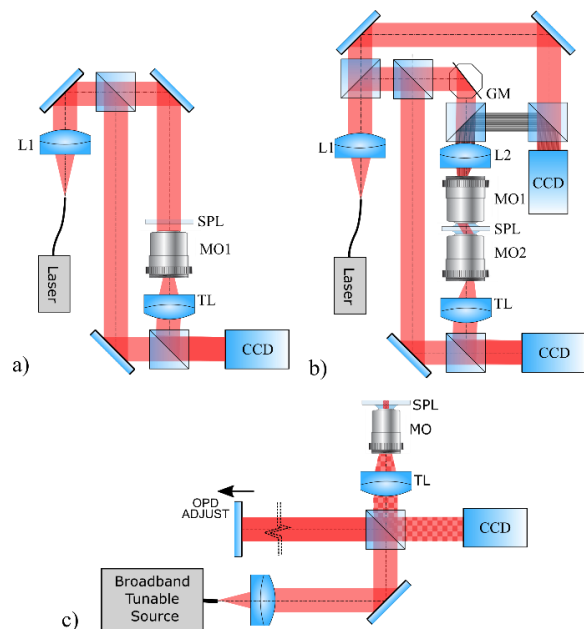


Fig. 2. Implementations of typical measurement systems for a) transmission digital holographic microscopy, b) dual-camera transmission and reflection mode optical diffraction tomography and c) Fourier domain full field optical coherence tomography. MO: microscope objective, SPL: sample plane, TL: tube lens, CCD: digital camera.

In this case, if only the wavelength scanning was to be performed at a constant illumination angle, the situation in the Fourier spectrum would be illustrated with Fig. 1d) and could be referred to as wavelength-scanning digital holography, but in fact the same spectrum coverage would be provided through Fourier domain full field optical coherence tomography (FD-FF-OCT) [6, 23]. A simplified idea of FD-FF-OCT realized with a swept-source is presented in Fig 2c.

Despite numerous implementations, all the OCT systems may be described with a unified K-space theory [6], which in this context could be also called Fourier diffraction theorem. The example of FD-FF-OCT presented in this paper is the closest implementation to DHM and ODT due to the usage of multiple wavelengths, and also one of the most dynamically developed implementations in recent years [24].

While the development of OCT was mostly based on a different theoretical model [6], it followed a direction towards quantitative phase imaging (QPI), which is a more general group of methods that includes DHM and ODT as the techniques capable of delivering reliable phase-based measurements. A few methods were developed in this pursuit, e.g. the FD-FF-OCT method was applied in transmission to retrieve the phase of the measured samples [25]. One of the interesting approaches was implementing the off-axis configuration in parallel FD-FF-OCT [26]. This solution, however, required axial scanning of the sample to perform tomography. Moving the sample – actually rotating to two angular positions was also used to assess the refractive index of the sample in FD-FF-OCT based on differences in the optical path length (sensitive to reconstruction misalignment) [27]. The method based on comparing optical path lengths of the sample to retrieve the refractive index of a layer was also possible without rotating the sample, but not without additional measurement modality – in this case OCT was supplemented with multiphoton microscopy, which unfortunately requires staining to retrieve second optical path length [28].

Recently, an interesting approach, which leans on traditional tomographic methods, has been proposed to solve the aforementioned lack of quantitative information [29]. The sample was rotated and at consecutive angular positions measured with OCT. The data was processed with a filtered back-projection algorithm and a forward model was used to optimize the 3D refractive index distribution and so far this has been the most advanced and successful proposition.

Both ODT and OCT are developed in the directions that head towards each other – ODT working in reflection mode to improve practical applicability and OCT

modified to provide quantitative information or two techniques merged together [18] that would provide new diagnostic tools in biomedicine. With a common ground – unified K-space theory we expect a multitude of new exciting systems to appear in the next few years.

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