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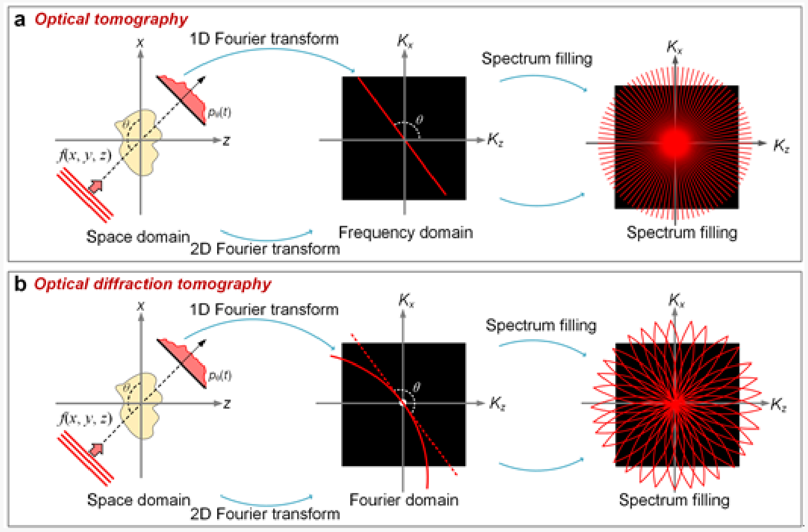
Optical diffraction tomography for 3D refractive index imaging: Techniques and applications

FAYETTEVILLE, GA, UNITED STATES, August 25, 2026 /EINPresswire.com/ -- Refractive index (RI) reflects key sample properties such as morphology, density, stress, and composition. Optical tomography (OT) and optical diffraction tomography (ODT) reconstruct 3D RI distributions from transmittance wavefronts recorded at multiple illumination angles using Fourier slicing or diffraction principles. This review summarizes the principles, implementations, and reconstruction algorithms of 3D RI imaging techniques. Further, different 3D RI imaging approaches are compared, and the current trends and future perspectives are discussed.

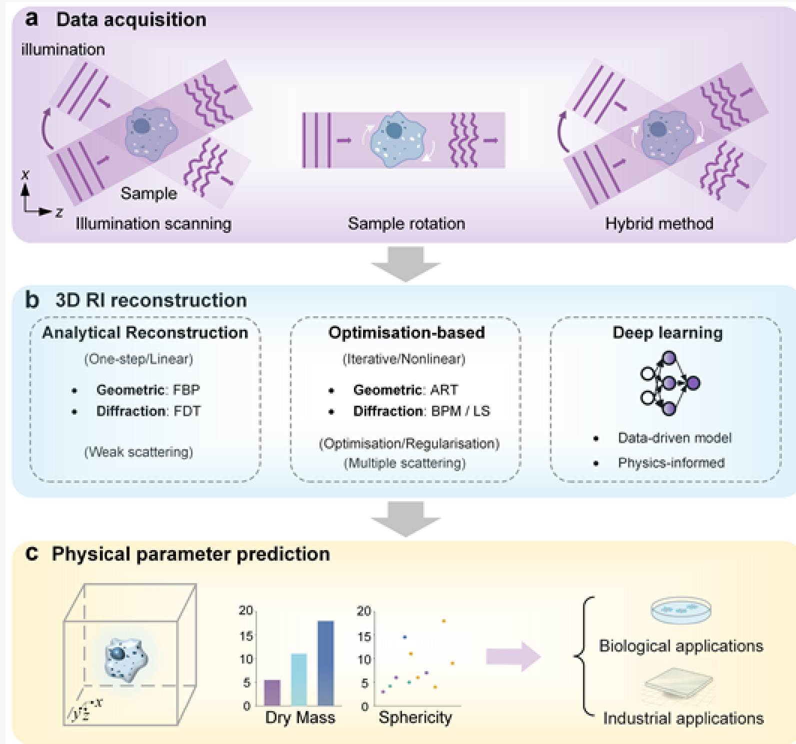


Principle and workflow of 3D RI imaging via OT or ODT.

Refractive index (RI) is an important parameter for describing the optical properties of materials and is closely related to sample morphology, density, stress, chemical composition, and other information. Three-dimensional RI imaging enables quantitative 3D characterization of the internal structures of transparent or weakly scattering samples without fluorescence labeling, showing great significance in cell biology, pathology, hematology, microbiology, materials science, and industrial inspection.

In a new review article published in Light: Advanced Manufacturing, the team of Professor Peng Gao and the team of Professor Chao Zuo have systematically reviewed the basic principles, experimental implementations, reconstruction methods, and representative applications of optical tomography (OT) and optical diffraction tomography (ODT) for three-dimensional refractive index imaging.

3D RI imaging via OT/ODT is performed by retrieving transmittance wavefronts (via holography or single-beam phase retrieval approaches) when rotating the illumination or the sample, and filling a 3D spectrum with the spectra of the wavefront projections, as shown in Fig. 1. For 3D RI reconstruction, OT (Fig. 1a) utilizes Fourier slicing theorem, approximating the measured phase as the integral of RI along the projection direction. It is computationally efficient but neglects diffraction effects. ODT (Fig.1b) is based on the Fourier diffraction theorem and can more accurately describe light-field propagation in weakly scattering samples, making it suitable for higher-precision 3D RI reconstruction.



Schematic overview of 3D RI imaging and reconstruction pipeline.

Common acquisition strategies include illumination rotation, sample rotation, and hybrid modulation. Illumination rotation causes less disturbance to live cells but is susceptible to the “missing cone” problem. Sample rotation can provide more isotropic frequency coverage but imposes higher requirements on sample morphology and mechanical stability. Hybrid modulation can further expand frequency coverage, but it also increases system complexity and acquisition time.

For complex-field acquisition, the paper classifies quantitative phase imaging methods into interference-based, refraction-based, and diffraction-based approaches. Interference-based methods, such as digital holographic microscopy, offer high phase sensitivity and are commonly used for complex-field acquisition in ODT. Refraction-based methods provide stable systems with relatively simple structures. Diffraction-based methods can recover phase from intensity images and have advantages in system simplification and coherent-noise suppression.

The reconstruction methods comprise analytical reconstruction, optimization-based reconstruction, and deep learning-based reconstruction. Analytical methods have clear physical meanings and high speed but are limited by the weak-scattering assumption. Optimization-based methods can handle more complex propagation and scattering processes but require higher computational cost. Deep learning methods show potential in missing-cone artifact suppression, resolution enhancement, and rapid reconstruction, but their generalization ability and interpretability still need improvement.

After the 3D RI distribution is reconstructed, physical parameters such as dry mass, volume, sphericity, and RI heterogeneity can be further extracted to provide quantitative descriptors for biological analysis and industrial inspection.

The key advantages of 3D RI imaging are label-free operation, quantitative measurement, and 3D visualization. In life sciences, ODT can be used for single-cell 3D RI imaging, enabling quantitative analysis of red blood cell morphology, cellular dry mass, organelle distribution, and cellular dynamics. At the subcellular scale, it can reveal the spatial distributions of nuclei, lipid droplets, nucleoli, mitochondria, filopodia, and other structures, and can complement fluorescence microscopy and structured illumination microscopy. Beyond biomedical applications, 3D RI imaging is also highly valuable in materials science and industrial inspection. The functions of many optical components and transparent materials, such as optical fibers, gradient-index lenses, microlenses, and polymer microstructures, are directly determined by their internal RI distributions. ODT can non-destructively obtain 3D RI information inside samples and be used for internal defect detection, density inhomogeneity analysis, and structural integrity evaluation.

Overall, ODT is evolving from a traditional optical measurement method into an integrated platform combining optical modulation, computational imaging, and artificial intelligence. In the future, ODT will continue to advance toward faster data acquisition, higher-precision and more isotropic 3D reconstruction, and deeper integration of physical models with deep learning. With the joint development of hardware modulation, complex-field acquisition, reconstruction algorithms, and multimodal imaging technologies, ODT is expected to become an important tool for label-free 3D microscopic imaging and precision optical inspection.

References
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Lucy Wang
BioDesign Research
email us here
