Frontiers in Optics + Laser Science (FiO/LS) @ Optica Publishing Group 2022

Non-paraxial multiple scattering model for intensity diffraction tomography

Jiabei Zhu,[1] Hao Wang,[1] and Lei Tian[1,2,*]

[1]*Department of Electrical and Computer Engineering, Boston University, MA 02215, USA*
[2]*Department of Biomedical Engineering, Boston University, MA 02215, USA*

[*]*leitian@bu.edu*

Abstract: We propose a novel intensity diffraction tomography reconstruction algorithm based on the split-step non-paraxial model for recovering the 3D refractive index distribution of multiple-scattering biological samples.

1. Introduction

3D quantitative phase imaging (QPI) are attractive for characterizing thick biological samples by providing refractive index (RI) information of the samples. Recently, intensity diffraction tomography (IDT) has been developed [1–4]. As a phase-less technique, IDT can be easily implemented on a standard microscope using a programmable LED array. Our group has developed two strategies to push the acquisition speed enabling visualizing dynamic biological samples. The multiplexed IDT (mIDT) [4] using multiple LEDs to illuminate the sample simultaneously with a widely used LED matrix as shown in Fig.1(a). The annular IDT (aIDT) [3] using an LED ring matching the objective's numerical aperture (NA) as shown in Fig.1(b).

IDT reconstruction algorithms relying on the single scattering models [2–4] are limited to weak scattering samples, and algorithms based on multiple-scattering beam propagation method (BPM) [1] have degraded accuracy for high-resolution imaging using high-NA optics. The split-step non-paraxial (SSNP) method was recently

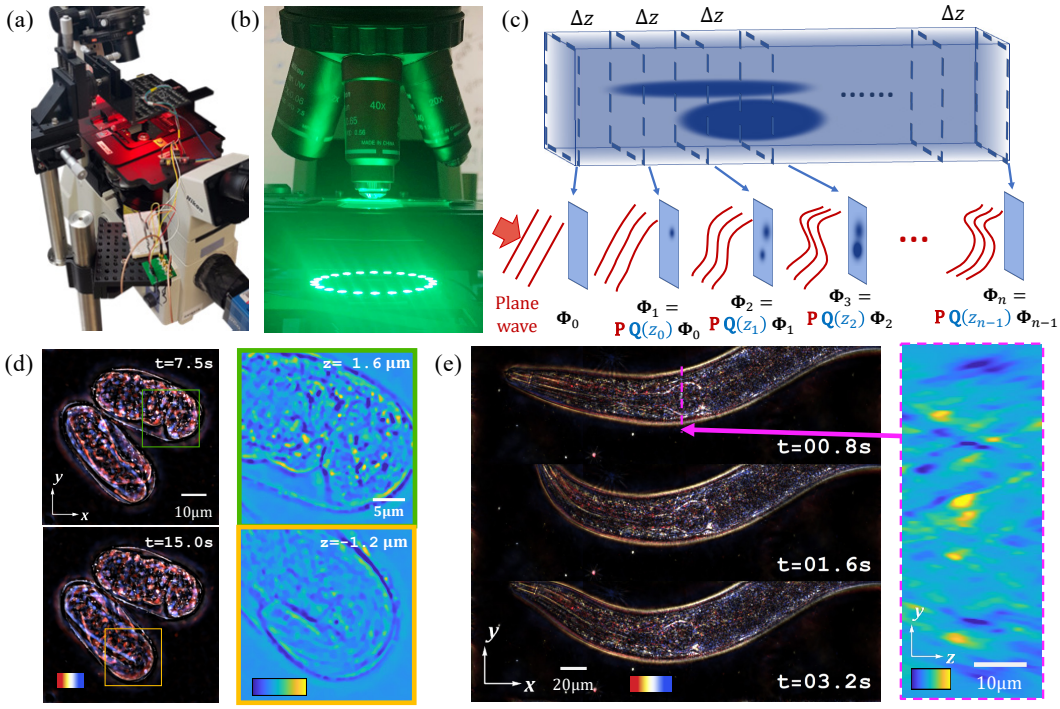

Fig. 1. (a) Our IDT/mIDT setup uses an LED matrix. (b) Our annular IDT setup uses an LED ring. (c) The SSNP model involves successive propagation to compute the scattered field. (d) Live *C. elegans* embryos reconstruction result from mIDT. (e) Live *C. elegans* worm reconstruction result from aIDT.

proposed as an alternative multiple-scattering model for ODT [5] to overcome the limitations in the first Born and BPM methods. We extended the SSNP method to IDT measurements [6] and demonstrate high-quality, large field-of-view (FOV) reconstruction results of live *C. elegans* embryos from mIDT and live *C. elegans* worm from aIDT.

2. Procedure of SSNP-based IDT model

2.1. Forward SSNP IDT model

The SSNP model discretizes a 3D sample into a series of axial (z) slices and calculates the internal field slice-by-slice (xy), as illustrated in Fig. 1(c). The scattering process of SSNP-based IDT model $S\{\cdot\}$ with single LED can be written as:

$$S\{\mathbf{\Phi}_{xy}(z_0)\} = \left|\mathbf{F}\mathscr{P}_{\mathrm{NA}}\mathbf{P}_{\Delta z_f}\mathbf{P}\mathbf{Q}(z_{n-1})\ldots\mathbf{P}\mathbf{Q}(z_1)\mathbf{P}\mathbf{Q}(z_0)\mathbf{\Phi}_{xy}(z_0)\right|^2, \tag{1}$$

where $\mathbf{\Phi}_{xy}(z_0)$ denotes the illumination field, $\mathbf{P}$ operator denotes propagation in homogeneous media, $\mathbf{Q}(z)$ operator denotes scattering of the slice at axial position z, $\mathbf{P}_{\Delta z_f}$ denotes propagation operator to the focal plane; $\mathscr{P}_{\mathrm{NA}}$ denotes low-pass filtering by the pupil function, $\mathbf{F}$ operator denotes extracting the forward-propagating field from the field vector.

For aIDT and mIDT, the estimated intensities are the combination of the scattered result calculated using SSNP algorithm from corresponding illuminations:

$$I^l_{seq} = S\{\mathbf{\Phi}^l_{xy}(z_0)\}, \quad I^l_{mul} = \sum_{m=1}^{M} S\{\mathbf{\Phi}^{l,m}_{xy}(z_0)\} \tag{2}$$

where I^l_{seq} and I^l_{mul} denotes the lth intensity for aIDT and mIDT respectively, and $\mathbf{\Phi}^{l,m}_{xy}(z_0)$ specifies the illumination field from the mth LED in the lth pattern.

2.2. Inverse problem of SSNP-based IDT model

We formulate the aIDT and mIDT reconstruction as the following optimization problem:

$$\hat{n}_r = \underset{n_r\in\Theta}{\operatorname{argmin}}\{\sum_{l=1}^{L}\|I^l_{SSNP} - I^l_{meas}\|_2^2 + \tau R_{\mathrm{TV}}(n_r)\} \tag{3}$$

where I^l_{SSNP} denotes the lth intensity estimation from SSNP-based aIDT and mIDT model; I^l_{meas} denotes the lth intensity measurement; τ is the regularization parameter, and R_{TV} is the total variation regularizer which suppresses the noise and artifacts. We perform reconstruction by iteratively refining the 3D RI estimation $n_r(x,y,z)$.

3. Results

We first apply our algorithm to a thick multi-scattering sample of live *C. elegans* embryos. In Fig. 1(d), the colorbars shows depth ranging from $-9.7\,\mu$m to $9.7\,\mu$m and RI ranging from 1.327 to 1.336. From the color-coded view (left), how the worms are folded can be clearly observed; from the single-depth cross section (right), the morphological details of the cells' outline, the buccal cavity, and the tail of the worm are reconstructed.

We also apply our algorithm to a live *C. elegans* worm sample from aIDT. In Fig. 1(d), the colorbars shows depth ranging from $-9.6\,\mu$m to $9.6\,\mu$m and RI ranging from 1.32 to 1.34. Figure 1(e) shows three consecutive volumes reconstructed by our SSNP algorithm displayed as color-coded depth projections, and a zoomed-in YZ cross-sectional views around the terminal pharyngeal bulb region.

References

1. L. Tian and L. Waller, "3D intensity and phase imaging from light field measurements in an LED array microscope," *Optica*, vol. 2, no. 2, p. 104, 2015.
2. R. Ling, W. Tahir, H.-Y. Lin, H. Lee, and L. Tian, "High-throughput intensity diffraction tomography with a computational microscope," *Biomed. Opt. Express*, vol. 9, no. 5, pp. 2130–2141, May 2018.
3. J. Li, A. Matlock, Y. Li, Q. Chen, C. Zuo, and L. Tian, "High-speed in vitro intensity diffraction tomography," *Advanced Photonics*, vol. 1, no. 6, pp. 1–13, 2019.
4. A. Matlock and L. Tian, "High-throughput, volumetric quantitative phase imaging with multiplexed intensity diffraction tomography," *Biomedical Optics Express*, vol. 10, no. 12, p. 6432, dec 2019.
5. J. Lim, A. B. Ayoub, E. E. Antoine, and D. Psaltis, "High-fidelity optical diffraction tomography of multiple scattering samples," *Light: Science & Applications*, vol. 8, no. 1, p. 82, Dec 2019.
6. J. Zhu, H. Wang, and L. Tian, "High-fidelity intensity diffraction tomography with a non-paraxial multiple-scattering model," 2022. [Online]. Available: https://arxiv.org/abs/2207.06532