

3D phase imaging from intensity measurements with non-paraxial multiple scattering model

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Abstract: We propose a novel algorithm based on the split-step non-paraxial model for different intensity diffraction tomography setups to recover the 3D refractive index distribution of multiple-scattering biological samples. © 2023 The Author(s)

1. Introduction

3D quantitative phase imaging (QPI) is attractive for characterizing thick biological samples by providing refractive index (RI) information of the samples. Recently, intensity diffraction tomography (IDT) has been developed as a phase-less technique that can be easily implemented on a standard microscope using a programmable LED array [1–3]. Our group has developed two strategies to push the acquisition speed enabling visualizing dynamic biological samples. The annular IDT (aIDT) [2] using an LED ring matching the objective's numerical aperture (NA) as shown in Fig. 1(a). The multiplexed IDT (mIDT) [3] using multiple LEDs to illuminate the sample simultaneously with a widely used LED matrix as shown in Fig. 1(b).

However, some of the previous IDT reconstruction algorithms relying on the single scattering models [2, 3] are limited to weak scattering samples. Others based on the multiple-scattering beam propagation method (BPM) [1] have degraded accuracy for high-resolution imaging using high-NA optics. In this abstract, we proposed a high-

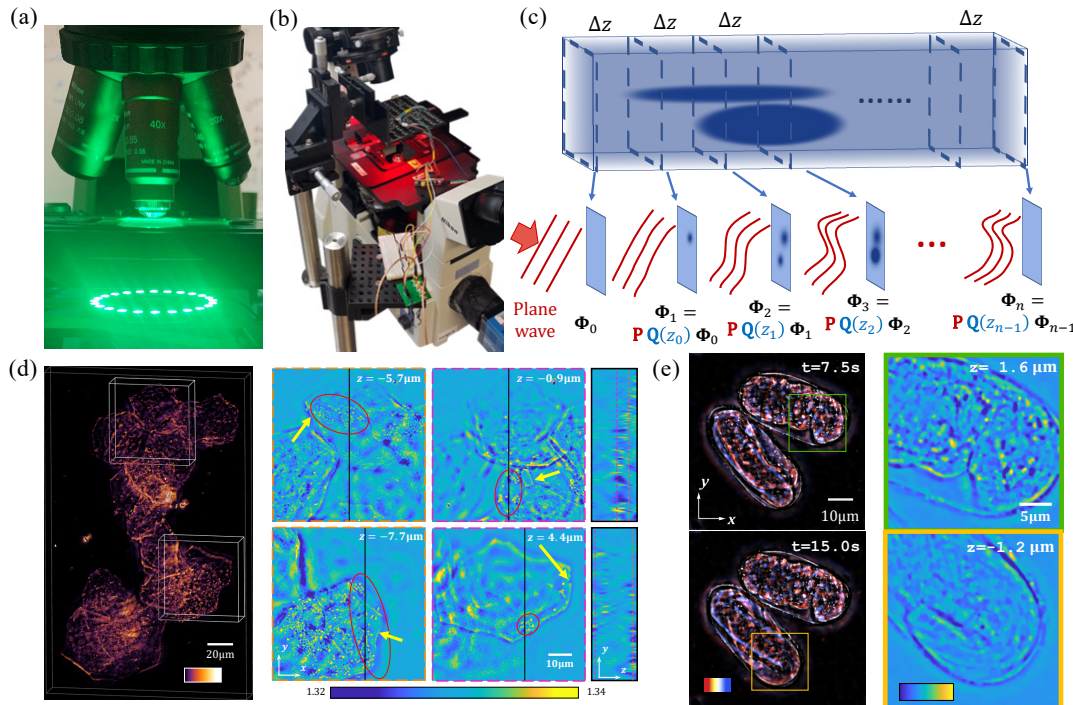


Fig. 1. (a) Our aIDT setup uses an LED ring. (b) Our IDT/mIDT setup uses an LED matrix. (c) The SSNP model involves successive propagation to compute the scattered field. (d) Unstained buccal epithelial cells reconstruction result from aIDT. (e) Live *C. elegans* embryos reconstruction result from mIDT.

NA-compatible multiple scattering model for IDT based on the split-step non-paraxial (SSNP) method. The SSNP method was recently proposed as an alternative multiple-scattering model for ODT [4] to overcome similar limitations. We extended the SSNP method to IDT measurements [5] and demonstrate high-quality, large field-of-view (FOV) reconstruction results of buccal epithelial cells from aIDT and live *C. elegans* embryos from mIDT.

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:

$$S\{\Phi_{xy}(z_0)\} = \left| \mathbf{F} \mathcal{P}_{\text{NA}} \mathbf{P}_{\Delta z_f} \mathbf{PQ}(z_{n-1}) \dots \mathbf{PQ}(z_1) \mathbf{PQ}(z_0) \Phi_{xy}(z_0) \right|^2, \quad (1)$$

where $\Phi_{xy}(z_0)$ 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; $\mathcal{P}_{\text{NA}}$ 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:

$$I_{\text{seq}}^l = S\{\Phi_{xy}^l(z_0)\}, \quad I_{\text{mul}}^l = \sum_{m=1}^M S\{\Phi_{xy}^{l,m}(z_0)\} \quad (2)$$

where I_{seq}^l and I_{mul}^l denotes the l th intensity for aIDT and mIDT respectively, and $\Phi_{xy}^{l,m}(z_0)$ specifies the illumination field from the m th LED in the l th pattern.

2.2. Inverse problem of SSNP-based IDT model

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

$$\hat{n}_r = \underset{n_r \in \Theta}{\operatorname{argmin}} \left\{ \sum_{l=1}^L \|I_{\text{SSNP}}^l - I_{\text{meas}}^l\|_2^2 + \tau R_{\text{TV}}(n_r) \right\} \quad (3)$$

where I_{SSNP}^l denotes the l th intensity estimation from SSNP-based aIDT and mIDT model; I_{meas}^l denotes the l th 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 the buccal epithelial sample from aIDT. In Fig. 1(d), the left figure shows a 3D rendering of the reconstructed RI distribution of the entire cell cluster volume. The colorbars shows RI ranging from 1.33 to 1.34. The figures on the right show the XY and XZ cross-sections of the reconstructed 3D volume. The 3D reconstruction allows easily discriminating cells at different depths. Besides, our SSNP algorithm successfully reconstructs high-resolution cell boundaries, membrane, and native bacteria around the cells.

We then apply our algorithm to a thick multi-scattering sample of live *C. elegans* embryos. In Fig. 1(e), the colorbars shows depth ranging from $-9.7 \mu\text{m}$ to $9.7 \mu\text{m}$ 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.

References

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