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Computational Laser Metrology using In Situ Calibration for Lensless Fiber Endoscopy

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Summary:
For biomedical applications, lensless holographic fiber endoscopes in needle size based on in-situ calibration have been realized. 4D imaging with cellular resolution and video rate capability is demonstrated.

Keywords: remote phased array, computational optics, calibration, brain imaging, optical tweezing

Introduction

Endoscopes with minimal invasiveness are important for translating various biophotonic techniques, such as 3D imaging, optogenetic cell stimulation, flexible optical tweezers, and to deep tissue in vivo applications. Lensless holographic fiber endoscopes, which do not require any electro-mechanical elements on the distal fiber end, allow a drastic miniaturization of the probe dimensions to only a few hundred microns. Fig.1 show schematically the comparison of the conventional and the novel lensless endoscope.

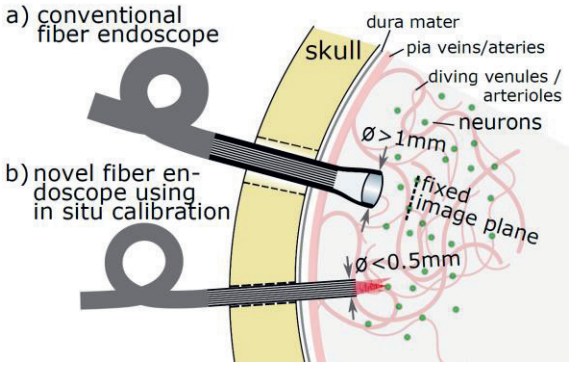

Fig. 1 Schematic comparison of the conventional (a) and the novel endoscope (b), which enables 3D imaging without using lenses.

The lensless endoscope deliver three-dimensional information by exploiting wavefront shaping. Using coherent fiber bundles (CFB) complex light fields can be defined based on remote phased arrays. The transmitted phase pattern is scrambled due to inter-core coupling and random core-to-core phase delays as well as dynamic processes such as bending of the CFB. The resulting phase distortion Φ_{CFB} has to be measured non-invasively without access to the distal fiber end.

Method: Exploiting scattering in the coherent fiber bundle (CFB) for exploring 3D objects

In order to realize an in-situ calibration, we apply a 150 µm thick glass plate onto the tip of the CFB, see Fig. 2. A guide star is generated through the CFB by illuminating only a single CFB core, which emits a Gaussian laser beam. The light is reflected back into the CFB from the glass plate surface with a predefined wavefront. The phase distortion Φ_{CFB} is recorded holographically after backpropagation through the CFB. Using a spatial light modulator (SLM) and employing digital optical phase conjugation we can now focus directly to the virtual guide star position. In previous work, we employed additional Fresnel lenses on the SLM for 3D focus scanning. In order to speed up the scanning process, phase ramps and lens functions are here added by a 2D galvo scanner for lateral scanning (1 kHz on fast axis) and a tunable lens for axial scanning (up to 50 Hz). 3D scanning with high speed is enabled. The whole diameter of the probe tip is below 500 µm.

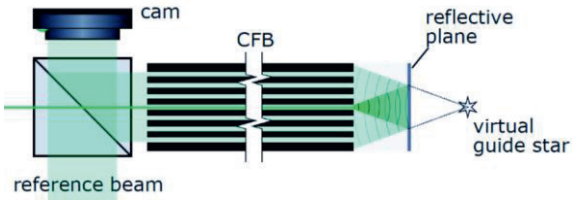

Fig. 2 Scheme of the patented novel in situ calibration method [1,2].

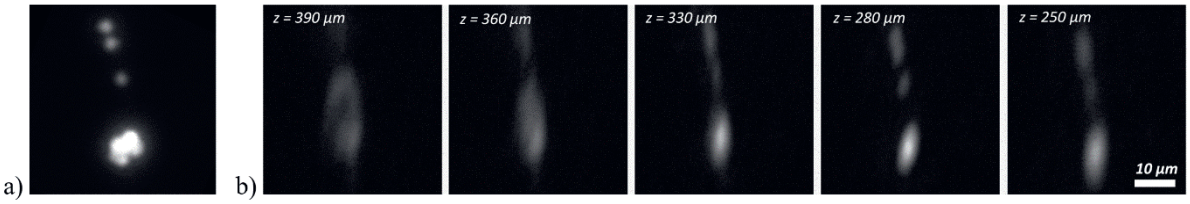

Fig 3. (a) Microscope image of fluorescent beads with 3 µm diameter (b) 3D backwards scan through the CFB

Application

To test the 3D scanning capability, fluorescent beads were applied to a cover glass (see Fig. 3a), positioned at a distance of 280 µm in front of the CFB. The arrangement of the beads in comparison to the reference image can clearly be seen. The maximum scanning speed is currently limited to about 1,000,000 voxels/s by the fluorescence light power, speed of the scanning and detector noise. A diffraction limited focus with a minimum value of 1 µm (FWHM) was determined within the volume of 150 µm x 150 µm x 1000 µm.

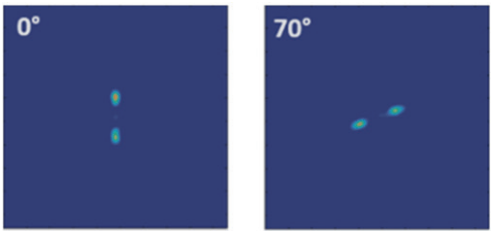

Fig. 4 Examples for rotation of a double focus

Besides optical brain imaging and optogenetic activation of neurons, versatile applications in biomedicine are being pursued. Tomographic refractive index reconstruction for instance in cancer diagnostics relies on a precise cell-rotation. This can be realized by an asymmetric double focus intensity distribution, where the rotation axis is defined by the relative focus position. To test our setup for lab-on-a-chip techniques in vivo cell-rotation we assigned the individual fiber cores randomly to two separate foci. Displaying a Fresnel lens and adequate tilts on each part of the SLM allows the two fiber parts to contribute to the related focal spot. The two main adaptively adjustable parameters of this configuration are the distance of the beam crossing (in this example at 350 µm) and the focal length (f = 500 µm), both measured from the fiber facet. Rotating the phase mask on the SLM allows rotating the two spots. Fig. 3b shows the intensity distribution at 500 µm from the fiber facet. The maximum angle deviation amounts to about 1° while the mean deviation is about 0.45°, making this a promising technique for 3D cell rotation. Fig. 4 shows examples of a double focus.

Conclusion and Outlook

Due to their small diameter, 3D capability and flexibility, holographic fiber endoscopes result in a paradigm shift for biomedicine. Minimal invasively imaging and optogenetic stimulation can be enabled in deep tissue regions. We presented a novel computational technique for in situ calibrating to correct the phase distortions within the coherent fiber bundle with only single sided access. A significant increase in imaging speed was achieved by adaptive optics. 3D fluorescent imaging and complex pattern projection for cell rotation were demonstrated.

Acknowledgement

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