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Additive manufacturing for minimally invasive endomicroscopy

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Abstract

Flexible endoscopes commonly employ coherent fiber bundles (CFB), which are indispensable in biomedicine. However, the footprint of the endoscope is limited because of the used bulky lens systems. We present a novel approach of lensless ultrathin fiber endoscopy using 3D-printed diffractive optical elements (DOE) at the fiber facet for aberration compensation. Using 2P-polymerization axial resolutions better than 20 nm can be achieved. This enables robust and cost efficient, endoscopes for biomedicine. The influence of the DOE quality especially the axial resolution towards the image quality is discussed. With a total endoscope diameter below 400 µm, novel applications for instance for in-vivo cancer diagnostics in the brain can be envisioned.

Keywords: Endoscopy, holography, 3D printing

1. Introduction

Endoscopes are used in biomedicine and industrial inspection to image hard to reach areas that are otherwise not accessible. Common flexible endoscopes employ coherent fiber bundles (CFBs) with several 10,000 fiber cores. Each fiber core enables a point-to-point intensity transmission. Coherent in the context of CFBs means, that the relative positon of individual cores remains constant along the length of the CFB. Thus, CFBs allow to transmit two-dimensional intensity profiles from the distal facet (in the specimen) to the proximal facet (at the observer) and vice versa. Typical CFBs offer core-pitches down to 3 µm and total diameters down to 300 µm, which gives the lateral resolution and image size in which the intensity distribution is sampled at the distal side. In order to increase the resolution or the field of view, or to image objects without contact, lens systems are applied at the distal fiber facet. Typically, this increases the diameter of the endoscope from a few 100 µm to above 1 mm, although miniaturized systems have been reported recently (Gissibl et al. 2016; Li et al. 2020). More importantly, such systems only allow for imaging in 2D with a low pixel number, which is given by the number of fiber cores.

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2. Holographic fiber bundles

Significant advances have recently been made to overcome the diameter limitations with lensless fiber endoscopy. Instead of the intensity only, the complex-valued information transfer is captured. It is mandatory to compensate for the path length differences between the various fiber cores, which can result from manufacturing tolerances with regard to the core diameter and the refractive index profile, but also from dynamic processes such as the bending of the fibers. The complex-valued information about the CFB is commonly measured in transmission with digital holography. Systems for in situ characterization in reflection with single sided access have also been presented (Kuschmierz et al. 2018; Warren et al. 2016). Using spatial light modulators (SLM) for digital optical phase conjugation (DOPC) enables the correction of the distorted phase profile, cf. Fig 1, meaning that the out coupled wave front equals the in coupled wave front of the total system. Adding varying Fresnel zone plates onto the SLM or introducing further adaptive optical elements such as galvanometer scanner and adaptive lenses on the proximal side of the fiber then enables 3D focus scanning or generation of arbitrary 3D light fields for instance for raster scanning microscopy, 2-photon lithography, optical trapping or cell ablation with an endoscope diameter only limited by the CFB (Kakkava et al. 2019; Moser et al. 2016; Scharf et al. 2020; Sun, Koukourakis, and Czarske 2021). As the major drawbacks such endoscopic systems are complex, sensitive to misalignment and expensive, which has hindered commercialization so far.

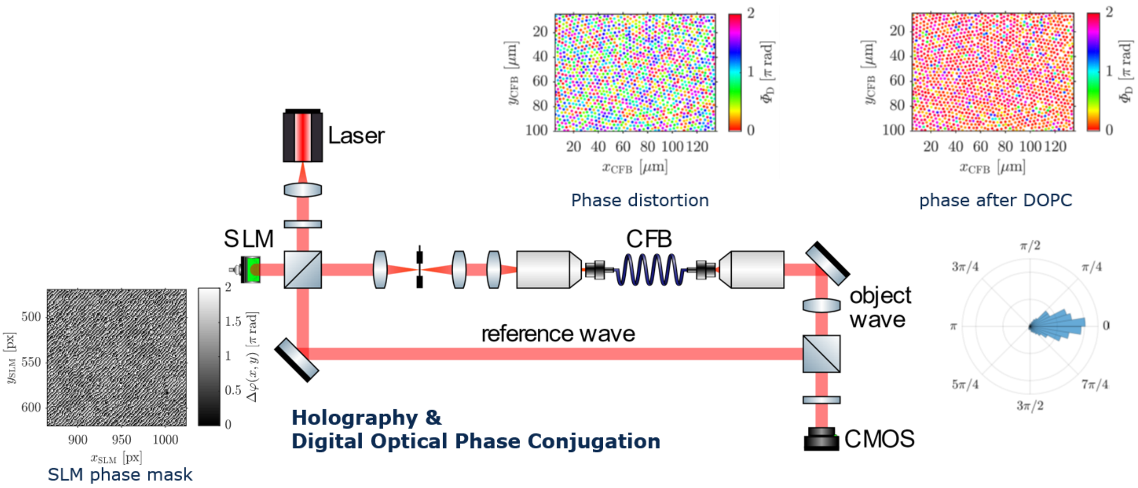

Fig. 1. Schematic of a holographic setup for characterizing and compensating the optical transfer function of a coherent fiber bundle. On the top the phase distortion before and after DOPC.

3. Static DOEs for phase compensation

In order to circumvent the above issues we investigate the use of static phase elements for optical phase conjugation. This requires the phase distortion to be static, however. Therefor the influence of fiber bending to the phase distortion was investigated first. For this purpose, a commercial CFB (Sumita, HDIG) was measured holographically and the transfer function was compensated with the above setup. Additionally, a

Fresnel lens was added to the SLM in order to achieve a focus in the far field of the distal fiber facet. The fiber was bend in increments of 1° and the far field was investigated, cf. Fig. 2.

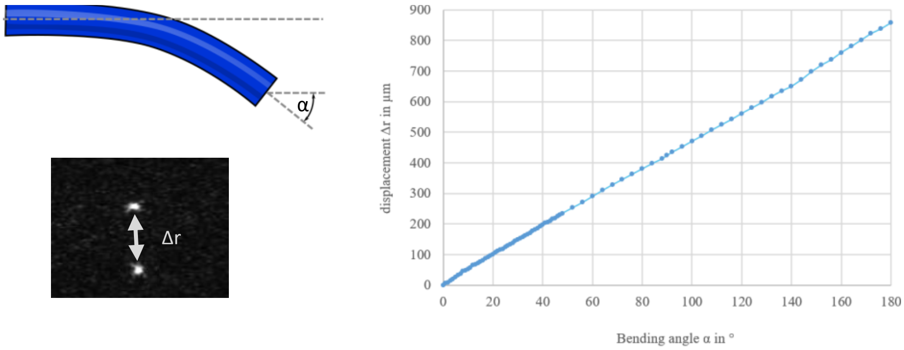

Fig. 2. Fiber bending by angle α results in lateral shift Δr of focus. Linear relationship.

The measurement shows, that a bending of the CFB results in a tilt of the transmitted wave front and a shift in the far field of the fiber. Such distortions result in a lateral shift of the acquired volume, which is often acceptable and can be compensated by measuring the distortion in reflection. Therefore, a static phase mask or DOE is sufficient for compensating the phase distortions of the CFB.

Conventionally DOEs are manufactured by photolithography. This process enables cheap production at large volumes. It is ill suited here however, since the required mask is distinct for each CFB. However, with the advancement of 2-Photon lithography an alternative process is available which enables affordable and rapid manufacturing of single DOEs with high spatial resolution. In order to test this approach, a DOE was printed onto a glass cover slice according to the acquired hologram, using a two-photon lithography system (Photonic Professional GT, Nanoscribe GmbH).

4. Results and discussion

Fig. 3 (bottom, left) shows a section of the acquired hologram of the CFB after signal treatment. The hologram is first filtered spatially, a constant phase was assigned to each fiber core and applied to circular elements with a 2.5 µm diameter. A Fresnel phase mask was added onto the hologram in order to achieve a focus. An image of the printed DOE is shown in Fig. 3 (bottom, center-left). A holographic analysis shows, that the printed DOE has a high quantization noise of 3 steps, which causes an error of $\pm \pi/3$. This reduces the peak-to-background ratio (PBR), which is defined by the ratio of mean intensity inside the focus and the mean intensity outside the focus, to around 25, limiting the achievable image contrast. The PBR was reduced furthermore, due to alignment and scaling deviations between CFB and DOE. However, 2-photon polymerization with an axial resolution better than 20 nm is possible in principle, which would increase the PBR and image contrast significantly. Numerical simulations show, that with more than 20 quantization steps a PBR of 10,000 can be achieved. The DOE was placed in front of the proximal fiber facet, cf. Fig. 3 (top). The focus on the distal side was imaged with a microscope, cf. Fig 3 (bottom, center right). A lateral FWHM of around 1 µm was achieved. A 2-axis galvanometer scanner on the proximal side was used to tilt the illumination of the CFB, which results in a lateral focus scan. For validating the imaging capability, a USAF 1951 test target was placed in the focal distal plane and scanned in transmission.

In summary, the possibility of the 2-photon polymerization printing process holds great promise for endoscopes with sub-millimeter diameter and 3D imaging capability. The system becomes significantly more economical as no SLM is needed. We demonstrated that static phase distortions in CFBs can be compensated by 3D printed phase mask, in principle. For an application, a higher axial printing resolution is required. Furthermore, printing directly onto the CFB is desired to realize a mechanically robust system and avoid misalignment.

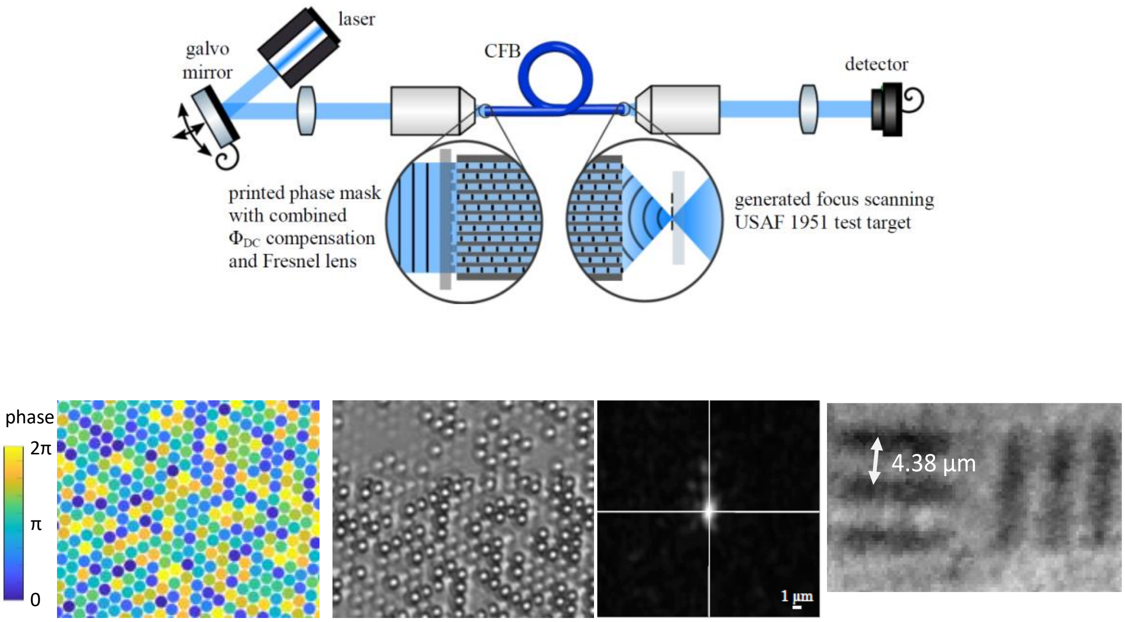

Fig. 3. Top: System for 2D raster scanning endomicroscopy without distal optics. Bottom: measured hologram (left), printed phase mask (center left), achieved focus (center right), 2D raster scan of USAF test chart, group +7, element 6 (right).

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