Digital Optical Phase Conjugation for tissue turbidity suppression

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Technology Overview

Optical imaging and spectroscopy of biological cells and tissue provide a tremendous amount of information that can be utilized for diagnostic and therapeutic purposes. However, multiple scattering effects fundamentally limit the sample depth from which the pertinent information can be successfully retrieved; the light is quickly diffused within the tissue mainly due to refractive index variations on a length scale comparable to the optical wavelength. Thus scattering is the dominant extinction process, accounting almost exclusively for the limited imaging depth range. For example, the absorption coefficient m_a of gray matter is only 0.2 cm^{-1}, yet the scattering coefficient m_s for the same tissue is equal to 77 cm^{-1} at the wavelength of 800 nm [1].

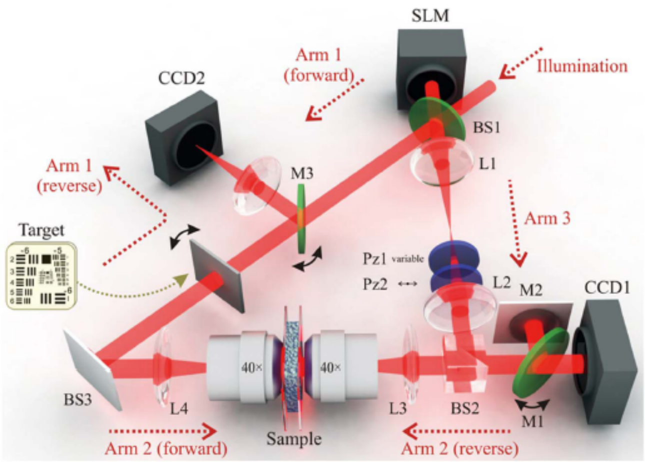
Optical phase conjugation (OPC) is an elegant technique for reversing the effects of multiple scattering. Its first demonstration of image transmission through diffusing media was performed using photorefractive crystals as the phase-conjugate mirrors [2]. LBRC researchers collaborated in using this approach to achieve turbidity suppression in biological samples [3]. A three-dimensional hologram of the light scattered from the sample was recorded in the crystal, which permitted a ‘‘time-reversed’’ version of the original scattered wave to be generated. The time-reversal property was most dramatically evidenced when the phase-conjugate reconstructed wave encountered the turbid sample, leading to the reconstruction of the original, complex sample structure.

Recent advances in OPC utilize a digital implementation of the technique for turbidity suppression in biological tissues [4, 5]. In digital optical phase conjugation (DOPC), the “phase-conjugate mirror” operation is performed by two distinct devices, a sensor and an actuator [4]. The former is used to acquire the complex-scalar transverse field distribution of the scattered light wave, and the latter, to generate the complex-conjugate, reverse-propagating reconstruction of the scattered wavefield distribution. In practice, a CCD camera is used as the sensor, upon which a digital hologram is recorded in order to obtain the original complex amplitude distribution. The actuation step is performed using a liquid-crystal based device [6], such as a spatial light modulator (SLM), which imparts a user-controllable phase distribution to the light wave reflected from it.

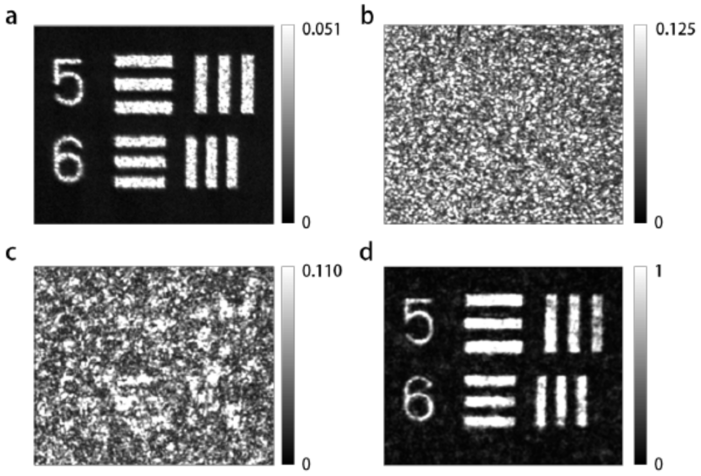
This approach has also been adopted by Cui and Yang [4]; other work by Hsieh et al. has demonstrated DOPC using the second-harmonic-generated field [5, 7]. However, full-field imaging through turbidity using DOPC has only been demonstrated in our Center. The DOPC setup employs a ring interferometer configuration as shown in the figure below. The challenging optical alignment problem of matching the forward- and reverse- propagating wavefields has effectively been solved. The SLM used as the phase conjugate-mirror “actuator” was capable of being directly imaged onto the CCD used as “sensor” in the ring interferometer, the key to the sub-wavelength accuracy attained in the optical alignment. Finally, we have successfully delivered and reconstructed a wide-field image through a highly turbid medium using digitally controlled, “time-reversed” light.

Biomedical Application Potential

DOPC has a number of advantages over non-digital approaches. A stored digital hologram is a permanent record of the scattered light wave, and it is not limited by the recording efficiency or recording lifetime of a photorefractive crystal. Additionally, the ability to digitally control the reconstruction wavefront provides the flexibility to modify it, in order to achieve an enhanced reconstruction, or to scan a focused spot over a limited range [11]. Recently, DOPC in combination with ultrasonic modulation has enabled high-resolution deep-tissue fluorescent imaging [8, 9] and it has been shown that DOPC can be performed with respect to a fluorescence signal from turbid media [10]. We plan to combine our wide-field DOPC approach with ultrasound (as guide-star) to perform functional imaging in thick turbid tissue samples.



Optical schematic for ring-interferometric DOPC approach. BS: beam-splitter; CCD: charge-coupled device camera; L: lens; Pz: polarizer; SLM: spatial light modulator. The double-headed back arrows at M1, M3 and the target indicate flip stages. Horizontally polarized illumination enters from the top-right.



Detected intensity reconstruction in the image plane. (a) target object image without a turbid medium. (b) No SLM control. (c) Optimized SLM control in the absence of “fine-tuning”. (d) Optimized, fine-tuned SLM control.

Background Publications

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3. Yaqoob, Z., Psaltis, D., Feld, M. & Yang, C. Optical phase conjugation for turbidity suppression in biological samples. *Nature photonics* **2**, 110 (2008).
4. Cui, M. & Yang, C. Implementation of a digital optical phase conjugation system and its application to study the robustness of turbidity suppression by phase conjugation. *Optics Express* **18**, 3444-3455 (2010).
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8. Yang, Y. M., Judkewitz, B., A, D. C. & Yang, C. Deep-tissue focal fluorescence imaging with digitally time-reversed ultrasound-encoded light. *Nature Communications* **3**, 8 (2012).
9. Si, K., Fiolka, R. & Cui, M. Fluorescence imaging beyond the ballistic regime by ultrasound-pulse-guided digital phase conjugation. *Nature Photonics* (2012).
10. Vellekoop, I. M., Cui, M. & Yang, C. Digital optics phase conjugation of fluorescence in turbid tissue. *Appl. Phys. Lett.* **101**, 081108-081108-081104 (2012).

Center Publications [Will be linked to data base]

1. Yaqoob, Z., Psaltis, D., Feld, M. & Yang, C. Optical phase conjugation for turbidity suppression in biological samples. *Nature photonics* **2**, 110 (2008).
2. Hillman, T. R., Yamauchi, T., Choi, W., Dasari, R. R., Feld, M. S., Park, Y. & Yaqoob, Z. Digital optical phase conjugation for delivering two-dimensional images through turbid media. *Scientific Reports* **3**, 1090 (2013).

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