Simultaneous suppression of aberration and scattering for high-resolution optical coherence imaging deep within biological tissues

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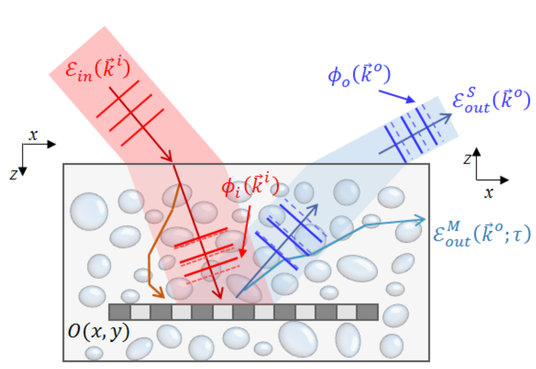
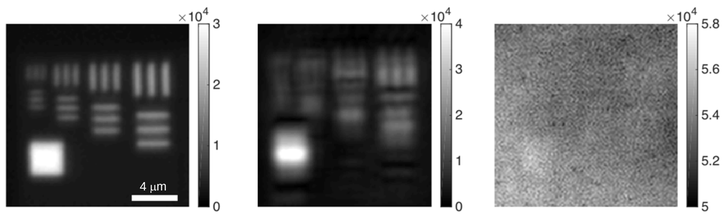
Abstract

Thick biological tissues give rise to not only the multiple scattering of incoming light waves, but also the aberrations of remaining signal waves. Due to the inability of existing optical microscopy to overcome both problems simultaneously, imaging depth warranting the sub-micron spatial resolution has remained extremely shallow. Here we present optical coherence imaging method that can identify aberrations of waves incident to and reflected from the samples separately, and eliminate such aberrations even in the presence of strong multiple light scattering. The proposed method records the time-gated complex-field maps of backscattered waves over various illumination channels, and performs closed-loop optimization of signal waves for both forward and phase-conjugation processes. We demonstrated the enhancement of Strehl ratio by more than 1,000 times, two orders of magnitude improvement over conventional adaptive optics, and achieved the spatial resolution of 600 nm up to the unprecedented imaging depth of 7 scattering mean free paths.

Introduction



- Multiple light scattering attenuates the total intensity of the single-scattered waves taken for each plane wave illumination
- Aberration undermines the proper accumulation of single-scattered waves
- Both scattering and aberration cause the reduction in the signal to noise ratio



Ideal Target image | Under aberrating layer | Under aberrating, and scattering layers

Scale bar : 4um

Theory

$$\mathcal{E}(\vec{k}^o;\vec{k}^i) = \sqrt{\gamma}P_o^a(\vec{k}^i+\Delta\vec{k})\mathcal{O}(\Delta\vec{k})P_i^a(\vec{k}^i) + \sqrt{\beta}\mathcal{E}_o^M(\vec{k}^i+\Delta\vec{k};\tau_0)$$

$$P_i^a(\vec{k}^i) = P(\vec{k}^i)\cdot\exp[-i\phi_i(\vec{k}^i)]$$
$$P_o^a(\vec{k}) = P(\vec{k}^o)\exp[-i\phi_o(\vec{k}^o)]$$

$$\mathcal{E}_{CASS}(\Delta\vec{k}) = \sum_{\vec{k}^i}\mathcal{E}_o(\vec{k}^i+\Delta\vec{k})$$
$$= \sqrt{\gamma}\mathcal{O}(\Delta\vec{k})\cdot\sum_{\vec{k}^i}P_i^a(\vec{k}^i)P_o^a(\vec{k}^i+\Delta\vec{k}) + \sqrt{\beta}\sum_{\vec{k}^i}\mathcal{E}_o^M(\vec{k}^i+\Delta\vec{k})$$

Due to aberration, the intensity of single-scattered waves is not properly accumulated

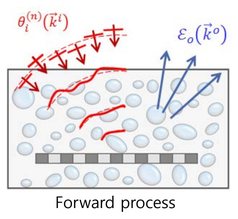
$$\left|\sum_{\vec{k}^i}P_i^a(\vec{k}^i)P_o^a(\vec{k}^i+\Delta\vec{k})\right| \le \left|\sum_{\vec{k}^i}P(\vec{k}^i)P(\vec{k}^i+\Delta\vec{k})\right|$$

$$\text{or}\quad \eta = \frac{\left\|\sum_{\vec{k}^i}P_i^a(\vec{k}^i)P_o^a(\vec{k}^i+\Delta\vec{k})\right\|^2_{\Delta\vec{k}}}{\left\|\sum_{\vec{k}^i}P(\vec{k}^i)P(\vec{k}^i+\Delta\vec{k})\right\|^2_{\Delta\vec{k}}} \le 1$$

Therefore, the maximization of CASS intensity will lead to the elimination of aberrations

Theory

- Correction of input aberration



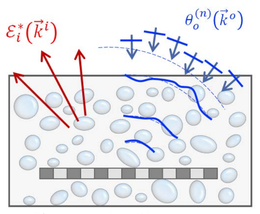
Forward process

$$\mathcal{E}^{(1)}_{CLASS}(\Delta\vec{k}) = \sum_{\vec{k}^i}\mathcal{E}(\vec{k}^i+\Delta\vec{k};\vec{k}^i)\,e^{i\theta_i^{(1)}(\vec{k}^i)}$$
$$= \sqrt{\gamma}\mathcal{O}(\Delta\vec{k})\cdot\sum_{\vec{k}^i}P_i^a(\vec{k}^i)P_o^a(\vec{k}^i+\Delta\vec{k})e^{i\theta_i^{(1)}(\vec{k}^i)} + \sqrt{\beta}\sum_{\vec{k}^i}\mathcal{E}_o^M(\vec{k}^i+\Delta\vec{k})e^{i\theta_i^{(1)}(\vec{k}^i)}$$

Find $\theta_i^{(1)}(\vec{k}^i)$ that maximizes the CLASS intensity

: $\max_{\theta_i^{(1)}(\vec{k}^i)}\sum_{\Delta\vec{k}}\left|\mathcal{E}^{(1)}_{CLASS}(\Delta\vec{k})\right|^2$

- Correction of output aberration



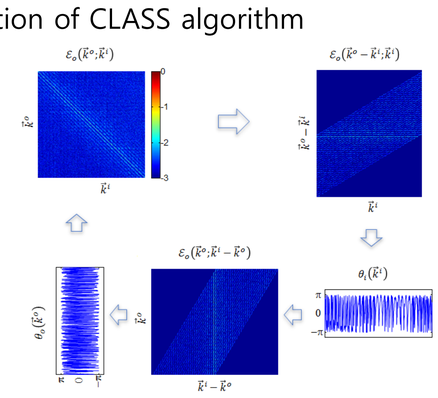
Phase-conjugation process

$$\mathcal{E}^{pc}_{CLASS}(\Delta\vec{k})$$
$$= \sqrt{\gamma}\mathcal{O}^{-1}(\Delta\vec{k})\cdot\sum_{\vec{k}^o}P_o^a(\vec{k}^o)^*\,P_i^{(1)}(\vec{k}^o-\Delta\vec{k})^*\exp i\theta_o^{(1)}(\vec{k}^o)$$
$$+\sqrt{\beta}\sum_{\vec{k}^o}\mathcal{E}_o^M(\vec{k}^o-\Delta\vec{k})^*\exp\left[i\theta_i^{(1)}(\vec{k}^i)\right]\exp i\theta_o^{(1)}(\vec{k}^o),$$

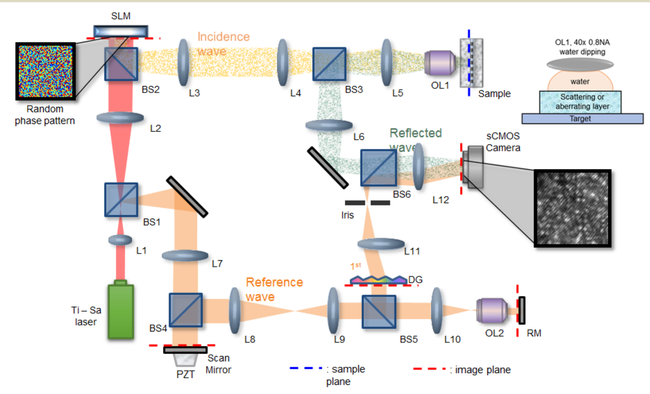
Find $\theta_i^{(1)}(\vec{k}^o)$ that maximizes the CLASS intensity

$$\max_{\theta_o^{(1)}(\vec{k}^o)}\sum_{\Delta\vec{k}}\left|\mathcal{E}^{pc}_{CLASS}(\Delta\vec{k})\right|^2.$$

- Application of CLASS algorithm



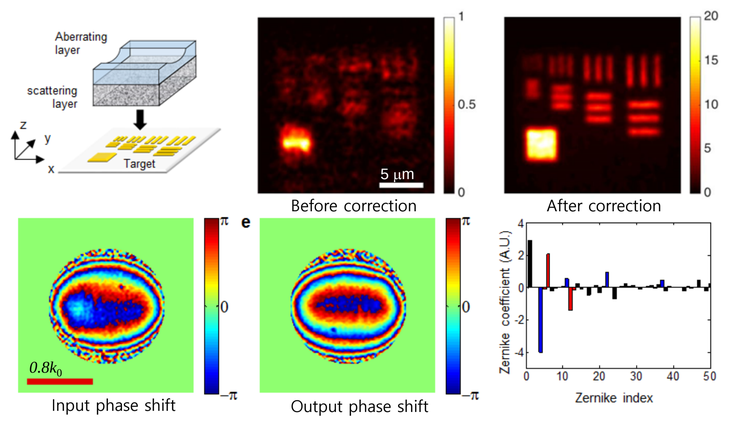
Experimental setup



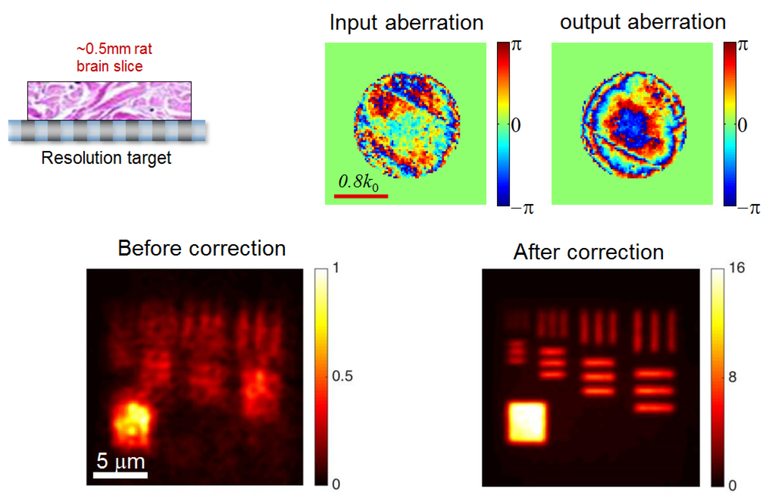
- Same as CASS, but random patterns were used for the illumination, and NA was extended to 0.8

Experimental result

- Demonstration using tissue phantom and resolution target

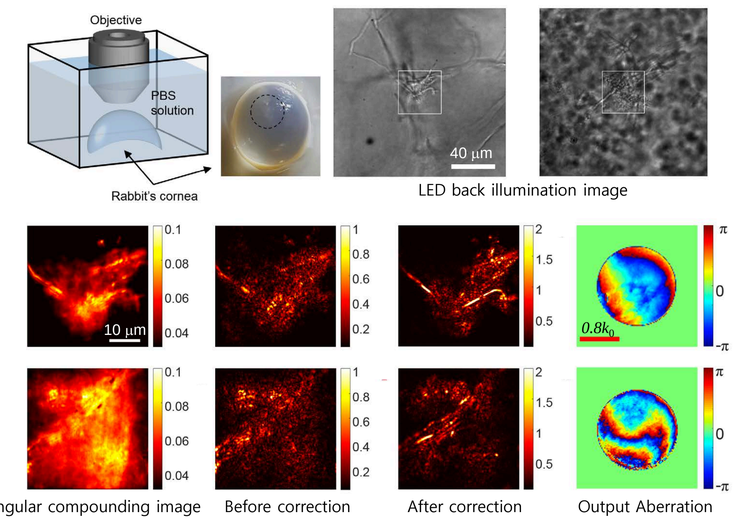


- Imaging targets under biological tissues



600 nm spatial resolution was achieved

- Imaging the hyphae of Aspergillus cells in a rabbit's cornea



Conclusion

- By combining the time-gated detection and spatial correlation of input/output angles, we could collectively accumulate the single-scattered waves from time-resolved reflection matrix.
- We developed a method that can deal with input and output aberration, respectively, in the presence of strong multiple scattering.
- We are in the middle of streamlining the instrument for biological applications.

Refference

1. Kang, S. *et al.* Imaging deep within a scattering medium using collective accumulation of single-scattered waves. *Nature Photonics* **9**, 253-258 (2015).
2. Born, M., Wolf, E. & Bhatia, A. B. *Principles of Optics: Electromagnetic Theory of Propagation, Interference and Diffraction of Light.* (Cambridge University Press, 1999)
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