# Controlling the light distribution through turbid media with wavefront shaping based on volumetric optoacoustic feedback

X. Luís Deán-Ben, Héctor Estrada, Ali Özbek and Daniel Razansky*

Institute for Biological and Medical Imaging, Technical University of Munich and Helmholtz Center Munich, Ingolstädter Landstraße 1, 85764 Neuherberg, Germany.

## ABSTRACT

Wavefront shaping based on optoacoustic (photoacoustic) feedback has recently emerged as a promising tool to control the light distribution in optically-scattering media. In this approach, the phase of a short-pulsed light beam is spatially-modulated to create constructive light interference (focusing) at specific locations in the speckle pattern of the scattered wavefield. The optoacoustic signals generated by light absorption provide a convenient feedback mechanism to optimize the phase mask of the spatial light modulator in order to achieve the desired light intensity distribution. The optimization procedure can be done by directly considering the acquired signals or the reconstructed images of the light absorption distribution. Recently, our group has introduced a volumetric (three-dimensional) optoacoustic wavefront shaping platform that enables monitoring the distribution of light absorption in an entire volume with frame rates of tens of Hz. With this approach, it is possible to simultaneously control the volumetric light distribution through turbid media. Experiments performed with absorbing microparticles distributed in a three-dimensional region showcase the feasibility of enhancing the light intensity at specific points, where the size of particles is also essential to maximize the signal enhancement. The advantages provided by optoacoustic imaging in terms of spatial and temporal resolution anticipate new capabilities of wavefront shaping techniques in biomedical optics.

**Keywords:** Optoacoustic imaging, photoacoustic imaging, wavefront shaping, light focusing, turbid media.

## 1. INTRODUCTION

Light scattering in nanoscale heterogeneities is responsible for the opacity of many relevant biological and technological materials.[1] Indeed, although photons can generally penetrate scattering objects, progressive changes in the propagation direction impede tracing the location of light sources and hence seeing through this type of samples. The light intensity distribution caused by photon interference is however not random but determined by the type and location of optical scatterers, which leads to a characteristic speckle pattern. By controlling the shape of the incident light beam, it is then possible that photons propagating along multiple paths positively interfere at specific locations, so that focusing through scattering objects is enabled. Based on this principle, wavefront shaping techniques have recently emerged as a promising tool to image beyond strongly scattering samples, with unprecedented applications foreseen in imaging, photodynamic therapy and optogenetics.[2]

Of particular importance is the possibility to control the light distribution deep into biological tissues, where scattering limits the penetration of optical microscopy to a few hundred microns.[3] Diffuse light on the other hand can reach several centimeters in the so-called near-infrared window,[3] so that wavefront shaping techniques can potentially operate at these depths, ultimately limited by light absorption. Wavefront shaping techniques are based on the spatial modulation of the phase of the light wavefront being incident on a scattering object, which is generally done by means of a spatial light modulator (SLM). The optimum phase mask at the SLM is determined from readings of the light intensity at the desired point(s), for which a feedback mechanism capable to resolve the light intensity distribution is needed.[2]

The feasibility to focus through scattering objects with wavefront shaping techniques was first demonstrated by using the two-dimensional image acquired with a camera as a feedback means to measure the light energy distribution.[4] Optical feedback is however not suitable to focus light inside a scattering object as very low

*E-mail: dr@tum.de

Adaptive Optics and Wavefront Control for Biological Systems II, edited by Thomas G. Bifano, Joel Kubby, Sylvain Gigan,
Proc. of SPIE Vol. 9717, 97171L · © 2016 SPIE · CCC code: 1605-7422/16/$18 · doi: 10.1117/12.2213490

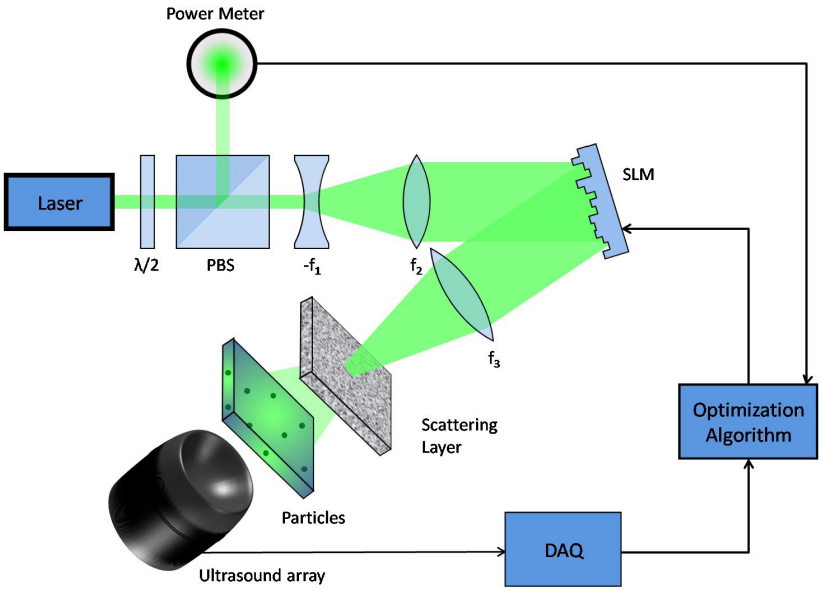


Figure 1. Lay-out of the volumetric optoacoustic wavefront shaping set-up.

resolution is rendered in the diffuse regime.[3] Indeed, the light enhancement at the target point(s) is inversely proportional to the number of speckle grains contained in the resolved volume.[5] A more promising approach based on optoacoustic feedback (optoacoustic wavefront shaping) was recently suggested, which offers important advantages to control the scattered light distribution. For example, optoacoustic signals can be collected at a rate ultimately limited by ultrasound propagation, and hence provide a very fast feedback mechanism to optimize the SLM mask. Acquisition of signals with transducer arrays and graphics processing unit (GPU)-based reconstruction procedures further enable very fast imaging rates.[6,7] Thereby, both single-element transducers and transducer arrays have been suggested for optoacoustic wavefront shaping.[8–11] Moreover, the high optoacoustic resolution potentially enables a high light intensity enhancement at the target point(s). Finally, taking into account that any substance absorbing light can generate an optoacoustic signal, the optoacoustic contrast versatility is arguably higher than in any other imaging modality.

Herein, we make use of a real-time three-dimensional optoacoustic system recently developed by our group as a wavefront shaping feedback mechanism that enables monitoring the distribution of light absorption in an entire volume with frame rates of tens of Hz.[12,13] With this approach, it is possible to simultaneously control the volumetric light distribution through turbid media.[14] Experiments performed with absorbing microparticles distributed in a three-dimensional region showcase the feasibility of enhancing the light intensity at specific points, where the size of particles is also essential to maximize the signal enhancement.[15] The advantages provided by optoacoustic imaging in terms of spatial and temporal resolution anticipate new capabilities of wavefront shaping techniques in biomedical optics.

## 2. MATERIALS AND METHODS

### 2.1 Experimental setup

A volumetric (three-dimensional) optoacoustic wavefront shaping platform was used for the experiments. A lay-out of the system is depicted in Fig. 1. It is described in detail in Ref. 14. A phase only SLM (PLUTO-BB II, Holoeye Photonics AG) consisting of a liquid crystal on Silicon (LCoS) microdisplay with 1920x1080 pixels (8 $\mu$m pixel pitch) was used to spatially modulate a light beam incident on a ground glass diffuser (Thorlabs DG10-120). The sample was placed after the diffuser. A frequency-doubled Q-switch Nd:YAG laser (Lab-190-30, Spectral physics) operating at 15 pulses per second was used for optoacoustic excitation. The laser beam was collimated and horizontally polarized before being directed to the SLM. The excited optoacoustic

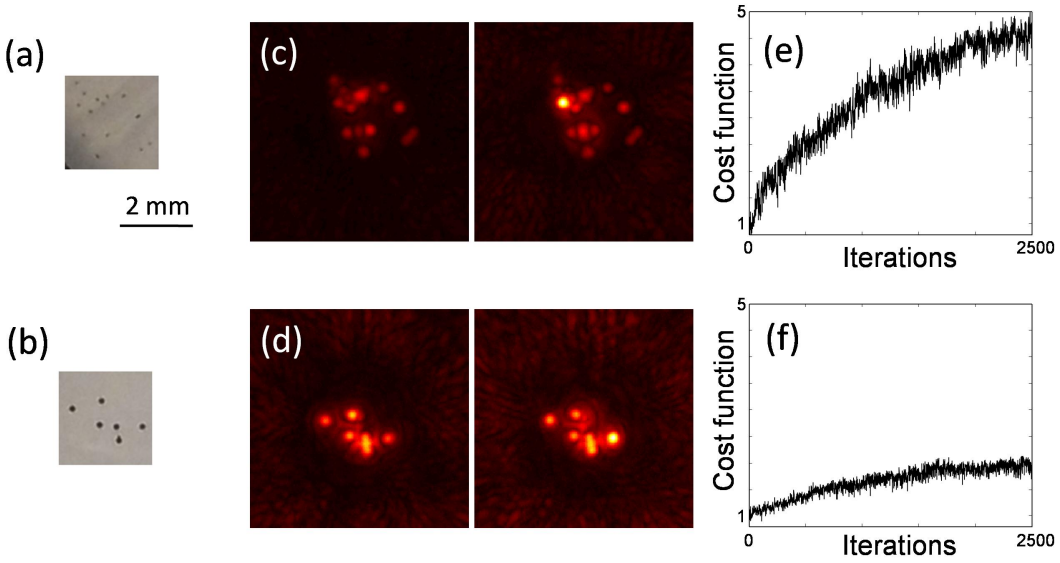


Figure 2. Focusing light into absorbing microspheres with volumetric optoacoustic wavefront shaping. (a)-(b) Actual photographs of the phantoms containing the microspheres. (c)-(d) Maximum intensity projections of the volumetric optoacoustic images for the first and last iterations in the genetic algorithm. (e)-(f) Value of the cost function as a function of the number of iterations in the genetic algorithm.

signals were simultaneously collected with a spherical array of piezoelectric transducers, and graphics processing unit (GPU)-based reconstruction was performed to render a three-dimensional optoacoustic image representing the light absorption distribution for each laser pulse.[7] This image was used to provide feedback for a genetic algorithm that iteratively optimizes the phase at the pixels of the SLM based on the maximization of a defined cost function.[16]

### 2.2 Experiment description

The experiments were designed to compare the performance of the suggested approach with absorbers of different sizes as described in Ref. 15. Polyethylene microparticles with approximate diameters 100 $\mu$m and 200 $\mu$m were embedded in agar phantoms and imaged with the volumetric wavefront shaping platform described above. In the experiments, a mask of 20x20 phase values was optimized by grouping the SLM pixels accordingly. The speckle diameter was set to approximately 27 $\mu$m, where the elongation of the speckle is larger than the size of the spheres. The cost function was defined as the maximum in a volume of interest (VOI) of the reconstructed image enclosing a microsphere, in a way that the genetic algorithm converges to an SLM mask that focuses light at this absorber.

## 3. RESULTS

Actual photographs of the phantoms are depicted in Figs. 2a and 2b for microspheres with diameters 100 and 200 $\mu$m respectively. The maximum intensity projections (MIP) along the depth direction of the corresponding reconstructed images are shown in Figs. 2c and 2d for the first and last iterations of the maximization of the cost function with the genetic algorithm. The MIPs for the first instant were obtained by setting a constant phase value in the SLM, which represents the initial iteration of the genetic algorithm. The evolution of the cost function (maximum signal intensity) as a function of the number of iterations in the genetic algorithm for the two measurements is displayed in Figs. 2e and 2f respectively. As expected, it is shown that signal enhancement is higher for smaller particles containing a lower number of speckles.

## 4. DISCUSSION AND CONCLUSIONS

The results showcased illustrate the performance of volumetric optoacoustic wavefront shaping and indicate the importance of the dimensions of the absorbing particles, which can determine the focusing feasibility of this approach. The maximum signal enhancement achieved is of particular relevance when aiming to focus light within scattering samples, e.g. biological tissues, for which volumetric wavefront shaping offers promising prospects. The speckles at depths beyond the light diffusion limit are expected to have a characteristic length converging to $\lambda/2$. On the other hand, the optoacoustic resolution scales with the imaging depth due to acoustic heterogeneities and attenuation in the medium.[17,18] In biological tissues, the optoacoustic resolution is estimated to be approximately 1/200 of the imaging depth.[19] The potential light intensity enhancement achieved for optoacoustic signals generated by absorbing molecules is then limited. The feasibility of volumetric wavefront shaping to focus light within biological tissues then appears to be affected by proper selection of efficiently absorbing particles enclosing a relatively low number of light speckle grains, which can also improve image quality in limited-view scenarios.[20] Focusing light inside biological tissues remains in any case strongly hampered by millisecond-level speckle decorrelation times as well as by the selection of coherent pulsed light beams for near-infrared wavelengths, where light penetration is optimal.[3] Overall, the size of light absorbing particles is meant to play an essential role in volumetric wavefront shaping.

## ACKNOWLEDGMENTS

D.R. acknowledges the support from the European Union under Grant Agreement No. ERC-2010-StG-260991.

## REFERENCES

[1] Mosk, A. P., Lagendijk, A., Lerosey, G., and Fink, M., "Controlling waves in space and time for imaging and focusing in complex media," *Nature photonics* **6**(5), 283–292 (2012).

[2] Horstmeyer, R., Ruan, H., and Yang, C., "Guidestar-assisted wavefront-shaping methods for focusing light into biological tissue," *Nature Photonics* **9**(9), 563–571 (2015).

[3] Ntziachristos, V., "Going deeper than microscopy: the optical imaging frontier in biology," *Nature methods* **7**(8), 603–614 (2010).

[4] Vellekoop, I. M. and Mosk, A., "Focusing coherent light through opaque strongly scattering media," *Optics letters* **32**(16), 2309–2311 (2007).

[5] Popoff, S., Lerosey, G., Fink, M., Boccara, A. C., and Gigan, S., "Controlling light through optical disordered media: transmission matrix approach," *New Journal of Physics* **13**(12), 123021 (2011).

[6] Deán-Ben, X. L. and Razansky, D., "Portable spherical array probe for volumetric real-time optoacoustic imaging at centimeter-scale depths," *Optics express* **21**(23), 28062–28071 (2013).

[7] Dean-Ben, X. L., Ozbek, A., and Razansky, D., "Volumetric real-time tracking of peripheral human vasculature with gpu-accelerated three-dimensional optoacoustic tomography," *Medical Imaging, IEEE Transactions on* **32**(11), 2050–2055 (2013).

[8] Kong, F., Silverman, R. H., Liu, L., Chitnis, P. V., Lee, K. K., and Chen, Y.-C., "Photoacoustic-guided convergence of light through optically diffusive media," *Optics letters* **36**(11), 2053–2055 (2011).

[9] Caravaca-Aguirre, A. M., Conkey, D. B., Dove, J. D., Ju, H., Murray, T. W., and Piestun, R., "High contrast three-dimensional photoacoustic imaging through scattering media by localized optical fluence enhancement," *Optics express* **21**(22), 26671–26676 (2013).

[10] Chaigne, T., Katz, O., Boccara, A. C., Fink, M., Bossy, E., and Gigan, S., "Controlling light in scattering media non-invasively using the photoacoustic transmission matrix," *Nature Photonics* **8**(1), 58–64 (2014).

[11] Chaigne, T., Gateau, J., Katz, O., Bossy, E., and Gigan, S., "Light focusing and two-dimensional imaging through scattering media using the photoacoustic transmission matrix with an ultrasound array," *Optics letters* **39**(9), 2664–2667 (2014).

[12] Deán-Ben, X. L., Ford, S. J., and Razansky, D., "High-frame rate four dimensional optoacoustic tomography enables visualization of cardiovascular dynamics and mouse heart perfusion," *Scientific reports* **5** (2015).

[13] Sela, G., Lauri, A., Deán-Ben, X. L., Kneipp, M., Ntziachristos, V., Shoham, S., Westmeyer, G. G., and Razansky, D., "Functional optoacoustic neuro-tomography (font) for whole-brain monitoring of calcium indicators," *arXiv preprint arXiv:1501.02450* (2015).

[14] Deán-Ben, X. L., Estrada, H., and Razansky, D., "Shaping volumetric light distribution through turbid media using real-time three-dimensional opto-acoustic feedback," *Optics letters* **40**(4), 443–446 (2015).

[15] Deán-Ben, X. L., Estrada, H., Ozbek, A., and Razansky, D., "Influence of the absorber dimensions on wavefront shaping based on volumetric optoacoustic feedback," *Optics letters* **40**(22), 5395–5398 (2015).

[16] Conkey, D. B., Brown, A. N., Caravaca-Aguirre, A. M., and Piestun, R., "Genetic algorithm optimization for focusing through turbid media in noisy environments," *Optics express* **20**(5), 4840–4849 (2012).

[17] Deán-Ben, X. L., Ntziachristos, V., and Razansky, D., "Effects of small variations of speed of sound in optoacoustic tomographic imaging," *Medical physics* **41**(7), 073301 (2014).

[18] Deán-Ben, X. L., Razansky, D., and Ntziachristos, V., "The effects of acoustic attenuation in optoacoustic signals," *Physics in medicine and biology* **56**(18), 6129 (2011).

[19] Wang, L. V. and Hu, S., "Photoacoustic tomography: in vivo imaging from organelles to organs," *Science* **335**(6075), 1458–1462 (2012).

[20] Deán-Ben, X. L., Ding, L., and Razansky, D., "Dynamic particle enhancement in limited-view optoacoustic tomography," *arXiv preprint arXiv:1512.03289* (2015).