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Authors:	Maysamreza Chamanzar, Minyoung Huh, NINH DO, M. Reza Alam, and Michel Maharbiz
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Virtual Acousto-optic Beam Paths for Steerable Deep-tissue Optical Stimulation and Imaging

Maysamreza Chamanzar[1], Minyoung Huh[1], Ninh Hai Do[2], M. Reza Alam[2], Michel M. Maharbiz[1]
[1]Department of Electrical Engineering and Computer Science, [2]Department of Mechanical Engineering, University of California Berkeley
Chamanzar@berkeley.edu

Abstract: Here we present the first non-invasive methodology for optical delivery and steering deep inside the brain through creating reconfigurable light paths by ultrasonic waves via modulating the refractive and diffractive properties of the medium.

OCIS codes: (170.1065) Acousto-optics; (170.5120) Photoacoustic imaging; (170.6930) Tissue

1. Introduction

Optical imaging is the gold standard of non-invasive biological interrogation. Moreover, with the advent of new optical stimulation mechanisms such as optogenetics for neural stimulation, optical modality has become a topic of great recent attention both for imaging and stimulation [1]. However, two serious challenges need to be addressed for optical interrogation to be effective for deep-tissue imaging and stimulation. One is targeted delivery of light deep into the tissue (at least a few millimeters) and second is non-invasive beam steering in the tissue. The current methods of light delivery and beam steering require inserting and physically moving optical fibers, waveguides, or active light sources, which would cause a significant tissue displacement and damage to the vasculature.

As an example, in the case of optogenetic stimulation of neurons, the required minimum intensity for a channelrhodopsin to evoke action potentials is about 1mW/mm^2. Therefore to send light from the surface of the cortex from a fiber optic (200μm, NA=0.37) to excite a neuron 2 mm deep into the cortex, a very high intensity of 71.6 mW/mm^2 is required on the surface since the beam is expanded and rapidly falls below the excitation threshold of opsins. This level of required power at the output aperture of fiber can cause damage to the tissue. On the other hand, inserting such a large fiber into the brain tissue to compensate for the fast intensity drop cause severe damage to the tissue, limiting chronic optogenetic experiments. To solve this issue, we propose to send light from the surface of the tissue and then use an array of ultrasonic transducers to keep light confined and to steer its trajectory (Fi. 1a).

2. Virtual Acousto-optic Light Paths

As ultrasonic (US) pressure waves propagate through the tissue, the local refractive index of the medium is slightly modulated at the high-pressure and low-pressure regions (in any medium, refractive index is weakly pressure dependent). The key idea is that the resulting refractive index contrast along the direction of wave propagation is sufficiently large to modulate the trajectory of light. Changing the US wave patterns in the tissue can change the orientation and path of optical wave propagation. An array of these US transducers can be used to form arbitrary patterns of optical waveguides in the tissue without physically inserting light guides (Fig. 1a). To verify this idea, we performed 2D Finite Element Method (FEM) simulations in a medium modulated by ultrasonic waves. First, we modeled an ultrasonic plane wave at 15 MHz propagating in water medium (propagation along the x-axis) in the viscous regime. We consider the general form of compressible Navier-Stokes equation and assume all perturbations are small and hence neglect nonlinear terms [3]. A 15 MHz US wave has a wavelength of 100 μm and a speed of 1540 m/s in water that best represents the biological tissues in terms of the acoustic properties. The refractive index profile can be calculated from the following empirical formula [4] as a function of ultrasonic pressure:

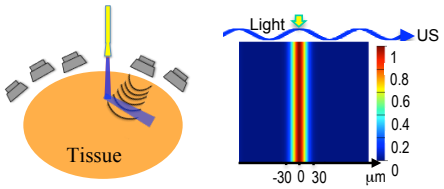

Fig. 1 (a) Schematic of optical beam steering in a tissue using ultrasonic waves. (b) FEM simulation showing the possibility of optical light waveguiding in high-pressure zone of a propagating US wave at 15MHz.

$$n = 1.332 + 1.18 \times 10^{-5} p \ , \qquad (1)$$

where p is the pressure in atmosphere and can be calculated from the local intensity of the ultrasonic waves. The maximum change of refractive index is $\Delta n = 6.75 \times 10^{-5}$ for a maximum intensity of 1.5 μm/μm^2, which is still less than the FDA safe limit for a pulsed ultrasound wave (i.e., 1.9 μm/μm^2). We used this refractive index profile in our FEM simulations to calculate the optical modes of the modulated medium. As shown in Fig. 1b, the modulated

medium supports a guided optical mode confined at the high-pressure region of the acoustic wave. The width of the waveguide is ~50 μm. Of course these virtual waveguides, turn on and off with the temporal dynamics of the ultrasonic wave propagation. However, many light sensitive biological events are slow in response and the effective integration time is much longer than the ultrasonic wave propagation. As an example, opsins response time is on the order of milliseconds, whereas the optical waveguides discussed in the example above, blink once every 67 nsec, which is at least four orders of magnitude faster than the response time of the opsins.

3. Experimental Results

To verify the possibility of acousto-optic beam steering in the tissue, we built an experimental setup as shown in Fig. 2a, where light from an external laser diode passes through a water tank, where it can efficiently interact with the ultrasonic waves propagating along the perpendicular direction in the water medium. We chose water as the medium to demonstrate the concept, since the impedance of water is a good first order approximation to the impedance of many biological tissues. We used a focused immersion transducer with a center frequency of 5MHz and a focal length of 1.09 cm from Olympus Scientific Solutions drived by a waveform generator (33522B, Keysight Technologies) through a 150 W power amplifier. The acoustic intensity of the transducer was measured using a hydrophone to be 20 nW/μm^2 about two orders of magnitude smaller that what we need to form a 50 μm optical waveguide. We formed a sinusoidal grating in the water medium (Fig. 2b) and could diffract light even with such a low ultrasonic wave intensity (Fig. 2c-h). As shown in Fig. 2c-e, the location of the first order diffracted beams can be changed by change of the ultrasonic wave frequency. Moreover, the angle of the diffracted beams can be controlled by changing the ultrasonic wave angle with a 1:1 ratio (Fig. 2f-h). By using an ultrasonic transducer phased array, we can essentially create arbitrary patterns of light in the medium.

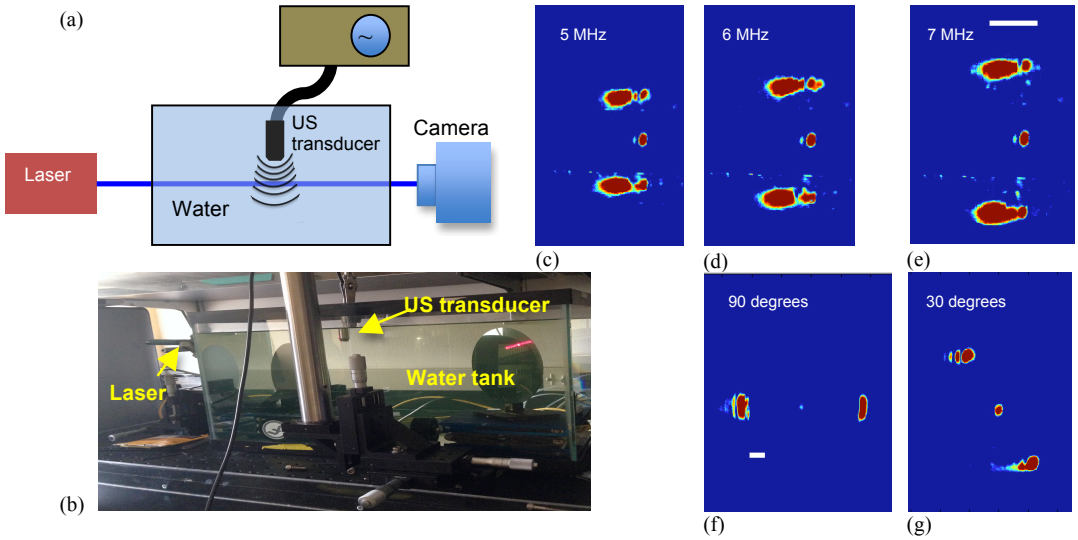

Fig. 2 (a) Schematic of the characterization setup. (b)-(d) Normalized light intensity patterns demonstrating that by changing the location of two diffracted beam patterns, we can scan a biological tissue. (e) and (f) show the effect of the angle change to steer the optical beam pattern. Scale bars are 2 mm. (c)-(e) share the same scale bar. (f)-(g) have the same scale.

In the presentation, we will discuss more details about our experiments and how we are translating this concept for deep tissue imaging (e.g., in the brain) experiments.

4. References

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