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A method to study cellular injuries using optical trapping combined with laser-induced shockwaves under quantitative phase microscope

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ABSTRACT

There is a need for new methodologies to investigate cell apoptosis and recovery, cell adhesion, and cell-cell interactions in cellular biology and neurobiology. Such systems should be able to induce localized cell injuries and measure damage responses from single cells. In this regard, pulsed lasers can be used to produce Laser-Induced Shockwaves (LIS), which can cause cell detachments and induce cellular membrane injuries, by applying shear force in order of μN. Furthermore, since the resulting shear force can increase membrane permeability, chemicals and markers can then be transferred into cells non-invasively. Continuous-wave lasers can be used as Optical Tweezers (OT), to apply non-contact delicate forces, as low as $0.1fN$, and deliver materials into cells, and also move the cells to different locations. In this paper, we introduce a combination of modalities to apply variable forces, from femto to micro newtons, to cells. Our system consists of a 1060nm continuous laser light source for OT and a 1030nm femtosecond pulsed laser for generating LIS. To have a direct measurement of changes in the cellular thickness and membrane dynamics, the cells are imaged under a Quantitative Phase Microscope (QPM). Our microscope is capable of Differential-Interference Microscopy (DIC) and Phase-Contrast microscopy (PhC) and fluorescent microscopy, making it a unique system for studying cell injuries.

Keywords: Laser-induced shockwave, LIS, Optical trapping, Optical tweezers, Quantitative Phase Microscopy, QPM

1. INTRODUCTION

Biophotonic equipment that uses focused lasers, such as laser tweezers and/or scissor and laser-induced shockwaves (LIS) are profound improvements for future cell biology research, as they enable single-cell manipulation, which is becoming increasingly prominent in biological research for studying cell features such cell adhesion, cell interactions, and DNA damage studies.[1–4] In our developed setup, we have introduced optical trapping and laser-induced shockwave setup to a quantitative phase microscope (QPM). Our laser setup provides us with the ability to apply various degrees of forces to cells. Furthermore, QPM enables imaging and quantification of transparent characteristics in cells, as well as the measurement of organelle movements and cellular dynamics such as membrane motility, in response to the forces.[5,6]

2. SETUP

The schematic of the LIS and optical trapping setup can be seen in Fig. 1. The detailed information on our QPM and LIS setup can be found in our previous publications.[7] Continuous laser light ($\lambda = 1064$ nm) passes a half-wave plate and a beam expander. Using a gimbal mirror, the beam is guided through the 4f imaging system that enables us to focus the laser light in different locations on the imaging dish.[8] Then, through a polarized beam splitter, the continuous laser light is reflected to a Beam splitter and shares the optical path with the pulsed laser light for the LIS setup.

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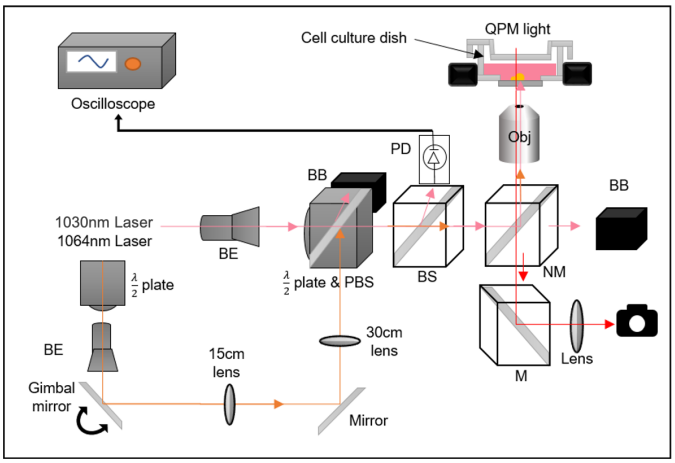

Figure 1. The schematic of laser-induced shockwave and optical trapping setup. Obj: Objective lens, BB: BeamBlocker, BS: Beam Splitter, BE: Beam Expander, NM: NIR Mirror, M: Mirror, PD: Photodiode, $\frac{\lambda}{2}$ plate: half-wave plate, PBS: Polarized Beam Splitter.

3. LASER-INDUCED SHOCKWAVE

Laser-induced shockwaves have been found to be one of the promising biophotonic tools to study cellular injuries. For instance, it has been shown that it can be used to simulate traumatic brain injury at the cellular level.[9] With the current setup, we are able to apply LIS, while recording phase-contrast (PhC), differential interference (DIC) and quantitative phase images.[7,10] Fig. 2 displays an example of applying LIS in astrocyte cells' medium. PhC (Fig. reffig:LIS(a,b)), DIC (Fig. 2(c,d)), and QPM images (Fig. 2(e,f)) before and right after the LIS have been shown in this figure. Quantitative height changes in the membrane and the nucleus of nearby astrocytes can be measured using phase images, as we can measure the real height of the cells before and after the injury.

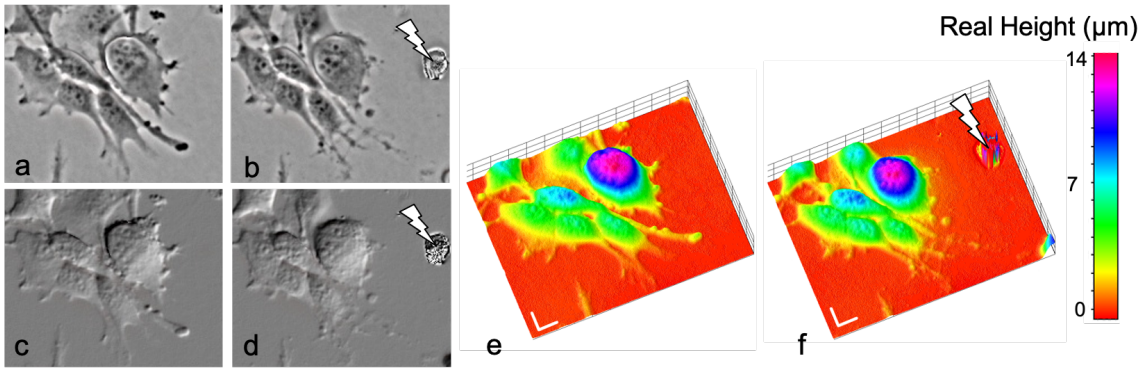

Figure 2. Laser-induced shockwave experiment in astrocyte cells' medium. **(a,b)**PhC, **(c,d)** DIC, and **(e,f)** QPM images before and right after the LIS have been displayed in this figure.

4. OPTICAL TRAPPING

The second method that is used in our system enables applying minor forces to the cells with the use of optically trapped polystyrene beads. Fig. 3 shows an example of trapping and pushing a 10um bead toward an astrocyte cell.

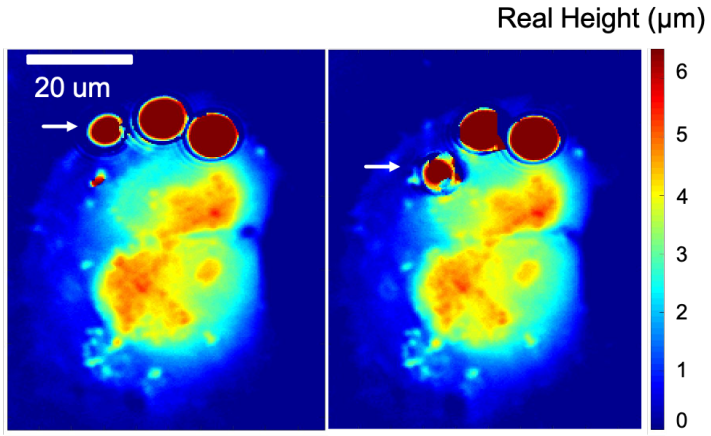

Figure 3. Quantitative phase images of trapping and pushing a 10um bead towards an astrocyte cell.

5. CONCLUSION

In this paper, we introduced a promising system that has combined multiple modalities making it a unique combination for cellular injuries. Our future studies will focus on the applications of our system, such as studying traumatic brain injury at the cellular level, by investigating the brain cells' responses, to various degrees of forces.

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