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Multimodal system for studying astrocyte cells, under quantitative phase microscope

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Abstract: In this study, we present a system that is able to cause shear stress on the order of micro-Newtons to 0.1 femto-Newtons and quantitatively evaluate damage responses in individual astrocyte cells.

1. Introduction

Traumatic brain injury (TBI) happens when a force is applied to the brain and interferes with its normal functioning, according to the Centers for Disease Control and Prevention. In response to this force and the resulted damage, brain cells interact throughout time in the central nervous system (CNS) to keep the brain in a healthy condition by protecting viable cells and clearing debris. Through a process known as reactive astrogliosis, astrocytes play a critical role in the response to all types of CNS disturbances [1, 2]. The critical role of astrocyte cells in TBI will be better understood with more research into how astrocytes sense and react to different degrees of mechanical stress.

To date, it has been shown that wounded brain cells release molecular stress signals as a result of TBI, which trigger astrocytes' reactive response. This has been demonstrated to affect astrocytes in a variety of ways, including morphology [2].

Quantitative phase microscopy (QPM) is one of the leading methods for studying cellular morphology. This modality enables the imaging and quantification of transparent characteristics in cells, as well as the measurement of organelle movements and cellular dynamics, such as membrane motility [3, 4].

The ability to manipulate a single cell without affecting other cells, or affecting a group of nearby cells with various degrees of force, in a cultured environment can be an effective way to study and simulate diseases that deal with cellular injuries, such as TBI. By utilizing biophotonic tools such as optical tweeezers, non-contact delicate forces can be applied to single cells, desired materials can be delivered into cells, and also cells can be placed at different locations. Laser-induced shockwaves, on the other hand, have been used to simulate TBI at the cellular level by applying exact and controllable shear stress to the cells [5].

2. Setup

By combining two different laser systems, an optical tweezers system and a laser-induced shockwave system, with a QPM, a multimodal comprehensive imaging system is presented that is able to apply various degrees of shear stress on individual astrocyte cells, and quantitatively evaluate the caused injury and the morphological changes in astrocytes resulted from the injury afterwards. Further details of the implementation can be found in [6].

3. Optical trapping

Optical tweezers can be employed in different ways to evaluate astrocytes' response to injuries. One way is to optically trap silica beads and push them towards cells to apply delicate forces as low as 0.1 femto-Newtons. Another approach is to trap dead neurons or astrocyte cells and move them near to healthy astrocyte cells. Previous studies have shown the phagocytic response of astrocyte cells to the injury of a nearby cell [7]. Our system enables the evaluation of this response at different distances from an intact astrocyte cell. Fig. 1 shows reconstructed 3D images, captured with QPM), of an optically trapped dead astrocyte that was placed at different positions relative to an intact astrocyte cell.

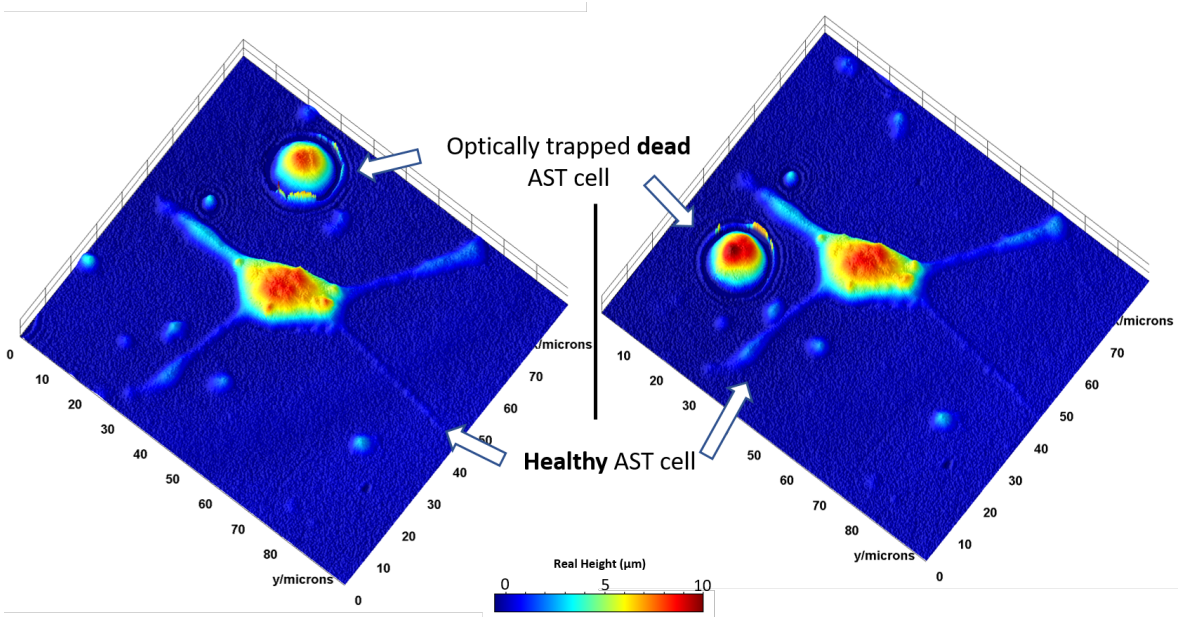

Fig. 1. Reconstructed 3D images of astrocyte cells. A dead astrocyte cell was placed at different positions relative to an intact astrocyte cell using optical tweezers.

4. Conclusion

Astrocyte cells have been found to serve an important part in maintaining normal brain function following an injury. However, how they perceive the injury, communicate, and adjust their morphology are still relevant research areas. We developed a new method for assessing astrocyte response to brain injury that allows us to apply different levels of damage while simultaneously monitoring changes in cell morphology and investigating intracellular damage and healing in real time.

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