High-throughput sonoporation of cells by cavitating microbubble arrary

Xiufang Liu[1, 2], Long Meng[1*], Wenjun Zhang[1], Lisheng Xu[2], Lili Niu[1], Hairong Zheng[1]

[1] *Paul C. Lauterbur Research Center for Biomedical Imaging, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, China*

[2] *Sino-Dutch Biomedical and Information Engineering School, Northeastern University, Shenyang, Liaoning, China*

**Email:long.meng@siat.ac.cn*

Background, Motivation and Objective

Sonoporation is a targeted drug delivery technique, which employs the cavitation microbubbles to generate transient pores in cells' membrane, allowing the foreign substance passing through the pores of membranes. Compared to inertial cavitation, stable cavitation inducing sonoporation is more moderate and controllable, and thus has received an increasing attention. Typically, it is difficult to realize the sonoporation at the single cell level, particularly for suspended cells, due to the complex interaction between the microbubble and cells. In this paper, we apply stable cavitating microbubble array to achieve a high-throughput sonoporation of individual cells with high efficiency.

Statement of Contribution/Methods

By designing the rectangular channel array with the uniform size at the sidewall, monodisperse microbubble could be generated when the fluid flowed through the rectangular structure due to surface tension. As the individual microbubble had the same diameter, the oscillating amplitude of the each microbubble was almost the same, ensuring the homogeneous sonoporation with a high efficiency. A piezoelectric transducer (PZT) with the frequency of 107 kHz was placed adjacent to the polydimethylsiloxane (PDMS) microfluidic device on the same glass substrate with ultrasound coupling gel. The laser Doppler vibrometer (LDV) system, as a noninvasive method, was introduced to measure the occurrence of stable cavitation. Human breast cancer of MDA-MB-231 cell suspension with the presence of propidium iodide (PI) and Calcein-AM was injected into microchannel, which PI (red) entering cell demonstrated membrane's pore was produced and Calcein-AM (green) existing in cells represented cell was live.

Results/Discussion

When the microbubble was excited by the PZT, higher harmonic signals emitted by the oscillating microbubbles could be detected by LDV, as depicted in figure (a), indicating stable cavitation occurred. Figure (b) was a merged fluorescence image, illustrating that high reversible sonoporation efficiency of 96.6 ± 1.74 % was achieved. After 150s, the number of the sonoporated cells could reach more than 1863 ± 7.56. Furthermore, this parallel device can be served as an efficient and versatile tool to investigate the mechanism of sonoporation at single cell level.