Sonoporation based on nanodroplet vaporization

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Background, Motivation, Hypothesis/Goal, and Objectives

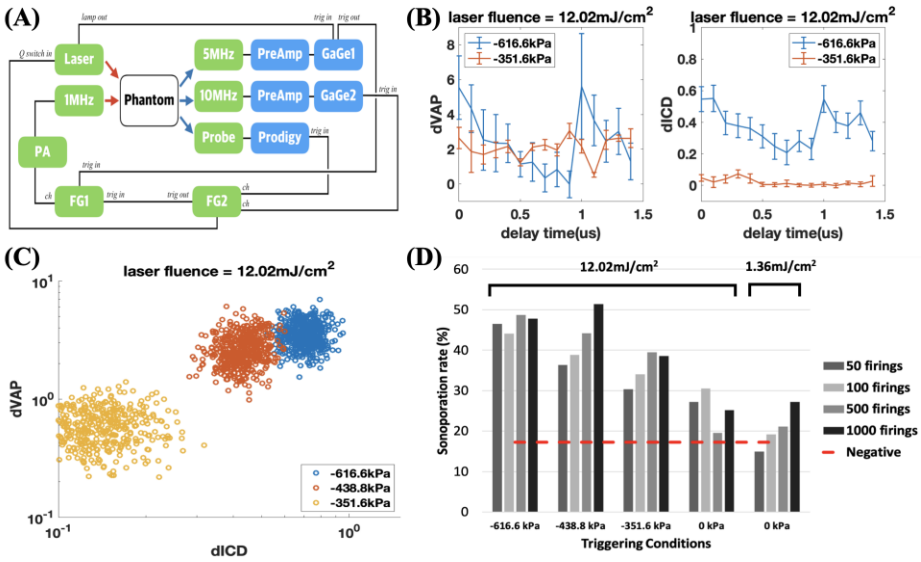
Sonoporation refers to the temporary enhancement of cell membrane permeability by exploiting acoustic cavitational effects. Microbubbles are commonly used for sonoporation. Recently, nanodroplets have also been adopted for further enhancing the sonoporation effectiveness relative to that using conventional microbubbles. Two processes are involved when nanodroplets are used. One is vaporization (i.e., the phase change from liquid to gas) and the other is inertial cavitation (i.e., microbubble destruction). To further understand the mechanism of nanodroplets-based sonoporation, we hypothesize that vaporization itself can effectively induce sonoporation. Under this hypothesis, one can further envision a new sonoporation method based on controllable and repeatable induction of vaporization and recondensation of nanodroplets and microbubbles.

Statement of Contribution/Methods

Figure A shows the schematic setup. Gold nanodroplets (AuNDs) were used. They consisted of perfluorocarbon core, human serum albumin shells and gold nanorods with a peak absorbance wavelength at 808 nm. To trigger vaporization, both acoustic droplet vaporization (ADV) and optical droplet vaporization (ODV) were applied. In addition, the pulsed wave laser used for ODV was synchronized with the 1 MHz ultrasound wave for ADV with a varying time delay within the range of 1 μs (i.e., the period at 1 MHz). Differential (i.e., background subtracted) signals at different frequency bands were used to quantify vaporization (2-4 MHz, dVAP) and cavitation (9.5-10.5 MHz, dICD). For cell experiments, conjugated AuNDs with anti-CD54 antibody were used and incubated with BNL cells. Fluorescence images were captured to evaluate the sonoporation rate.

Results, Discussion and Conclusions

When the laser fluence of 12.02mJ/cm^2 was used for ODV and the peak negative pressure (PNP) of -616.6kPa was used for ADV, we found both dICD and dVAP demonstrated 1 μs periodicity as the laser delay time changed (figure B). By reducing the PNP to -351.6kPa, the dVAP kept at a relatively similar level but the dICD reduced to around the baseline (figure C), suggesting that this particular triggering condition mainly only induced vaporization but not inertial cavitation. We also observed that the sonoporation rate did not change with the number of triggers in the former case, but it increased with the number of triggers in the latter case (figure D). Therefore, the latter case demonstrated that vaporization itself can be the primary mechanism for effective sonoporation.



(A) System setup. (B) The dVAP and dICD at relative laser delay time under different PNPs. (C) The dICD-dVAP scatter plot. (D) Sonoporation rate under different triggering conditions.