

# TAILORING MICROBUBBLE SHELL COMPOSITION FOR THERAPEUTIC ULTRASOUND APPLICATIONS

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## OBJECTIVES

Microbubbles typically serve as ultrasound contrast agents. Consequently, their performance under therapeutic ultrasound exposures is less well-known. Here, we investigated the cavitation emissions and temporal stability of lipid-shelled microbubbles with varying shell composition exposed to a 1-ms-long therapeutic pulse.

## METHODS

C<sub>4</sub>F<sub>10</sub> microbubbles with 15:1, 9:1 and 5:1 molar ratios of 1,2-distearoyl-sn-glycerol-3-phosphocholine (DSPC) and 1,2-distearoyl-sn-glycero-phosphoethanolamine-PEG<sub>2000</sub> (DSPE-PEG<sub>2000</sub>) were manufactured in-house. Lipid amounts were also decreased by 5x and 10x, maintaining the DSPC:DSPE-PEG<sub>2000</sub> 9:1 ratio. Microbubbles within a 4-mm vessel of a 5%-gelatin phantom were exposed to 10 therapeutic pulses (0.5MHz, 500 cycles, 400kPa<sub>pk-neg</sub>; n=5 batches). Acoustic emissions were recorded with a 7.5MHz passive cavitation detector.

## RESULTS

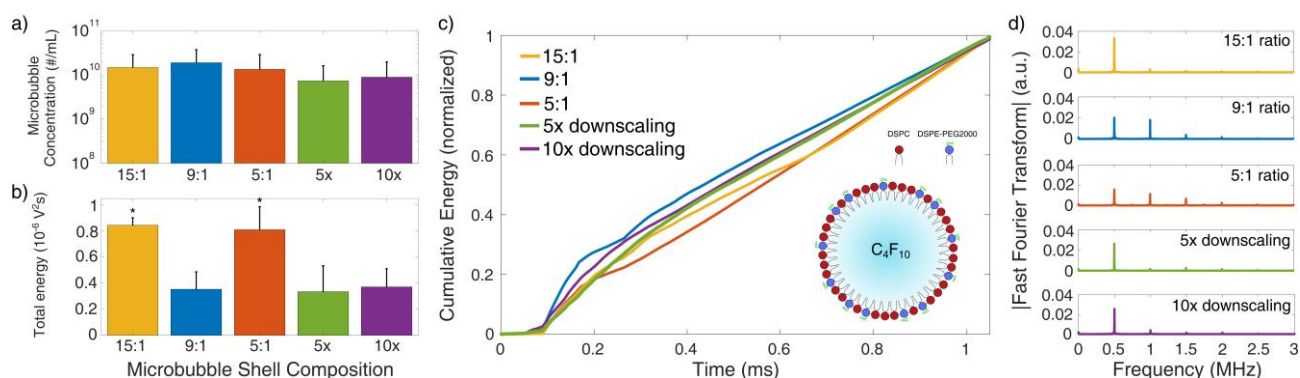
Although microbubble concentration was not significantly different, 15:1 and 5:1 ratios produced acoustic emissions with higher energy than the 9:1. Higher energy was correlated with increased temporal stability during the 1-ms pulse, as indicated by the cumulative energy evolution. Lipid decrease did not affect acoustic emissions or temporal stability. The amplitude of higher harmonics increased with reduced lipid ratio and decreased with lipid downscaling.

## CONCLUSIONS

Microbubbles with lipid shells composed at 15:1 or 5:1 ratio may be more suitable for therapeutic applications such as blood-brain barrier opening. Decrease of the lipid amount did not affect microbubble response but may lower manufacturing cost.

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**CAPTION:** a) Microbubble concentration did not change with different shell compositions. b) Acoustic energy was significantly higher for the 15:1 and 5:1 ratio. c) Cumulative energy during the 1-ms pulse. d) Frequency content for each microbubble formulation.