Focused ultrasound-induced oscillations of microbubbles:
Influence of key parameters on cavitation dose

Background, Motivation and Objective

In ultrasound-mediated blood–brain barrier (BBB) opening procedures, intravenously administered microbubbles (MBs) — gas-filled structures stabilized by lipid or protein shells — play a key role. While their primary application is as contrast agents in ultrasound imaging, MBs have shown significant potential in modulating BBB permeability. When exposed to focused ultrasound in brain vessels, MBs oscillate, temporarily disrupting the tight junctions of endothelial cells lining cerebral blood vessels, thereby enabling the transient passage of macromolecules larger than 400 Da. This mechanism can be leveraged to enhance the delivery and efficacy of therapeutics e.g. curing Alzheimer's disease.

Statement of Contribution/Methods

This study explores how different parameters influence MBs (SonoVue, Bracco) acoustic emissions, including MBs concentration (0.0008%, 0.004%, 0.016%, 0.08%, 0.4% [V/V]), peak negative pressure (61.5 ± 8, 121 ± 15.5, 252.5 ± 33, 600 ± 80, 1300 ± 165, and 2600 ± 340 kPa), and ultrasound pulse duration (100, 200, 1000 µs). Experiments were performed in a flow setup incorporating a focused transducer (H101, Sonic Concepts, $f_0 = 1.05$ MHz) and a passive receiver. Based on the recorded acoustic signal, three cavitation metrics were calculated: stable cavitation dose from harmonics (SCD_{har}), stable cavitation dose from ultraharmonics (SCD_{ultra}), and inertial cavitation dose (ICD) from broadband signal.

Results/Discussion

Results, presented below, show that SCD_{har} generally increases with pressure, peaking at 600 kPa, and significantly declining at higher pressures. SCD_{ultra} exhibited maximal responses at MBs concentrations of 0.004% and 0.016%, whereas ICD remained consistent across concentrations, without notable differences. Significant ICD response was observed at pressures ≥ 600 kPa and reached its highest levels at the highest MBs concentration (0.4%). To date, there is no standardized method for quantifying cavitation dose, which remains an active area of research. The findings presented here identify trends in MBs responses obtained under varied conditions. The selected concentrations, negative pressures and pulse durations levels enable a comprehensive view of MBs responses within the given setup.