MICROBUBBLES: TOOLS FOR VESICLE BIOMECHANICS

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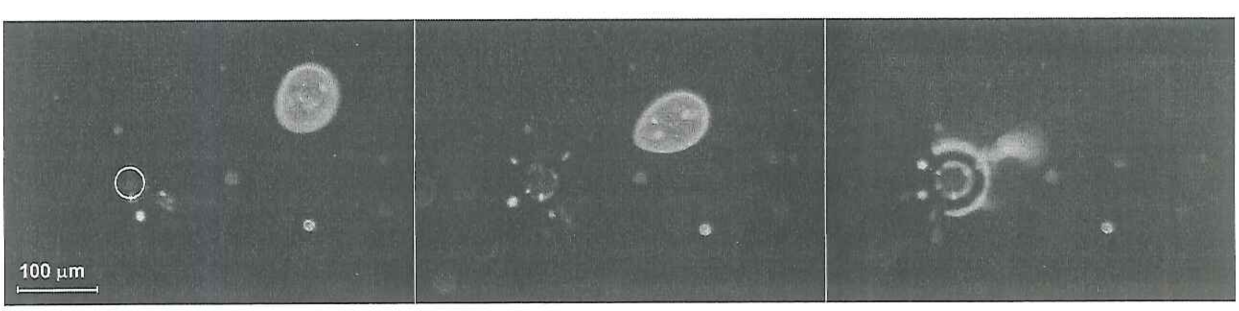
When subjected to ultrasound, micron-sized bubbles oscillate, giving rise to significant ultrasound scattering and increased echographic contrast. It has been reported that this excitation can also alter nearby cell membranes [D. L. Miller and J. Quddus, Ultrasound in Med. & Biol. 26, 661-667 (2000)], and increase the cell wall permeability for drug delivery or gene transfection purposes in various therapeutic applications. Many physical processes could be behind this phenomenon, all related to the concentration of acoustic energy onto small scales that is characteristic of small bubbles. It is unknown which process is dominant under which experimental conditions, and extremely difficult to control the collapse of strongly driven bubbles in those experiments.

We have therefore developed a new line of experiments to elucidate the possible mechanisms of ultrasound-driven cell wall permeation (sonoporation) in a well-controlled setup. Micron-sized bubbles attached to a wall are excited in a liquid containing lipid vesicles. These vesicles are commonly used to mimic cell membranes, with the advantage that their mechanical properties are well-known. In contrast to previous experiments, we observe the motion and deformation of *single* vesicles directly, rather than *a posteriori*.

The effect looks dramatic under the microscope: the vesicles are periodically accelerated towards and repelled from the bubble. In this "bouncing" motion the vesicle is subjected to a shear stress that is reflected in its elongated shape. As this deformation increases (upon increasing driving pressure or adjusting material parameters) the break-up of vesicles is also observed (see figure).



Lipid vesicle deformation and rupture (the vesicle membrane is fluorescence-marked) in the acoustic streaming flow generated by the bubble (white circle).

We interpret the motion as acoustic streaming induced by the bubble oscillations, a nonlinear effect creating a steady flow with closed streamlines from periodic driving. A quantitative theory of acoustic streaming is available, enabling us to directly model the streaming flow, vesicle transport, and vesicle deformation. Moreover, because the bubble oscillation amplitudes are actually small, it is possible to control these processes with great accuracy, and improve vastly on current methods relying on inertially collapsing bubbles.