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The influence of bubble-bubble interactions on contrast agent microbubble-jetting during initial exposure to 200 kHz focused ultrasound

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***Abstract*—The initial response of contrast agent microbubbles to a burst of 200 kHz focused ultrasound with 1.5 MPa peak-negative pressure amplitude is studied. Directed jetting along the axis of propagation of the ultrasound is observed and the influence of the pressure-gradients on the bubble dynamics evidenced. Furthermore, the influence of nearby bubbles on the jetting behavior is investigated. Bubbles tend to jet towards other bubbles and to be influenced in their dynamics. Moreover, the more bubbles share the same volume, the weaker the jets become.**

***Keywords*—ultrasound contrast agent, microbubble, jetting**

I. Introduction

Microbubble-cavitation in response to focused ultrasound exposure at sub-MHz frequencies, is of significant interest for emerging applications in transcranial therapy of the brain, where frequencies of several $100\,\mathrm{kHz}$ are employed for sufficient transmission across the skull. Although a sizeable volume of literature exists on high-speed imaging of microbubbles under conventional medical ultrasound frequencies, response to such sub-resonant driving at relevant pressure amplitudes, is notably under-studied. In the present paper we study the cavitation dynamics of single microbubbles, and the interaction of several close-by microbubbles when exposed to $200\,\mathrm{kHz}$ ultrasound bursts.

II. Materials And Methods

A schematic representation of the experimental setup is given in Fig. 1. It was fully described in [1] and some more specifications were given in [2]. Briefly, we used SonoVue (Bracco, Milan Italy) contrast agent diluted by a factor of $\sim$ 1:80,000 in de-ioinsed water. A syringe pump flowed samples through a polycarbonate capillary of $500\,\mu\mathrm{m}$ internal diameter and $25\,\mu\mathrm{m}$ wall thickness (Paradigm Optics, Vancouver, WA USA) at $\sim 11\,\mathrm{mL/h}$. The capillary was positioned in the focal region at $45°$ to the propagation axis of a focused ultrasound transducer. The transducer (H-149, Sonic Concepts, Bothell, WA USA), mounted on an xyz-manipulator, geometrically focuses to $68\,\mathrm{mm}$ from the front face, in the x-direction, Fig. 1, within a custom-made tank measuring $420 \times 438 \times 220\,\mathrm{mm}^3$ filled with degassed, de-ionised water.

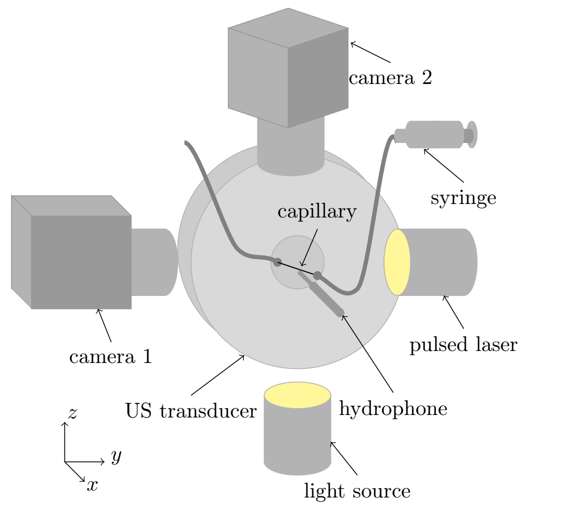

Fig. 1. Experimental setup.

The interaction between a 10-cycle burst of $200\,\mathrm{kHz}$ focused ultrasound and any microbubbles in the capillary at the time of incidence, is recorded with two different cameras. A high-speed camera (Fastcam SA-Z 2100K, Photron, Bucks UK), mounted above the capillary (top-view perspective) recorded at 210,000 frames per second (fps) and a shutter time of $159\,\mathrm{ns}$. Imaging was undertaken through a $5\times$ long working distance lens (0.14 NA, Mitutoyo, Kawasaki Japan), with illumination provided by a $150\,\mathrm{W}$ halogen bulb coupled to a liquid light guide. The top-view imaging provides a general overview on the capillary ($\sim 1.5\,\mathrm{mm}$ covered) and allows only to obtain a few snapshots during the whole cavitation event. A second high-speed camera (Shimadzu HPV-X2, Kyoto Japan) imaging at 10 million fps over a duration of $25.6\,\mu\mathrm{s}$, from a side-

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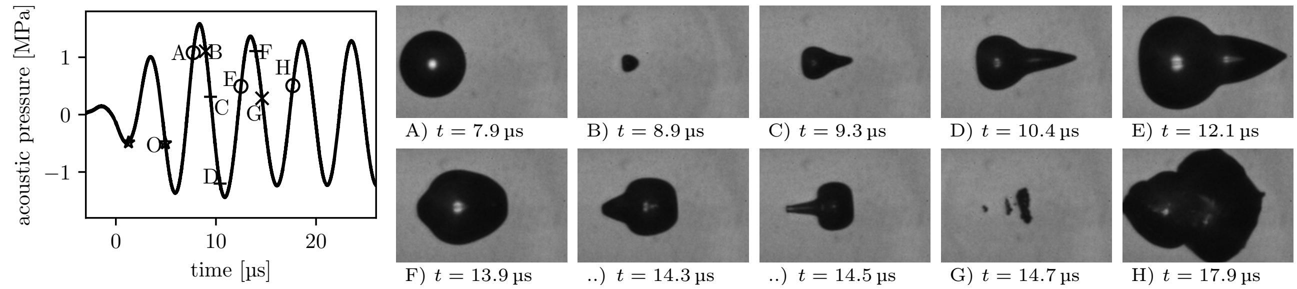

Fig. 2. Snapshot series of the jetting dynamics of a single relatively isolated bubble exposed to a $200\,\mathrm{kHz}$ ultrasound burst with a peak negative pressure of $1.5\,\mathrm{MPa}$. The different moments are indicated in the plot of the ultrasound signal shown on the left. The $*$ indicate the moments when the bubble becomes visible. Size of the frames is $210 \times 140\,\mu\mathrm{m}^2$.

view perspective, captures microbubble-cavitation response over the first 5-cycles of driving, at high temporal resolution. Illumination was achieved with synchronous (to frame capture) $10\,\mathrm{ns}$ laser pulses, coupled to a liquid light guide and a collimator lens and imaging was made through a $20\times$ long working distance objective lens (0.42 NA, Mitutoyo).

The pressure signal at the focal spot was measured prior to high speed observation (without the presence of the capillary) with a $0.2\,\mathrm{mm}$ PVdF needle hydrophone (Precisions Acoustics, Dorchester UK). The results presented below were acquired in response to a burst of pressure amplitude $\sim 1.5\,\mathrm{MPa}$. $t = 0\,\mu s$ is defined as the start of side-view capture, with transducer excitation and top-view imaging electronically triggered at $t \approx -60\,\mu s$.

III. Jetting Dynamics At High Acoustic Pressure

At a high pressure of approximately $1.5\,\mathrm{MPa}$ peak negative pressure of the $200\,\mathrm{kHz}$ pressure signal, the jetting dynamics of a single non-disturbed (isolated) bubble follows the following steps, see also Fig. 2. While the pressure signal is ringing up, a first small inflation to about $5\,\mu\mathrm{m}$ might appears (not shown in the figure). The bubble then collapses spherically and no influence on the later sequence is observed. One acoustic cycle later, the bubble starts to inflate again, it reaches its maximum radius of $\sim 45\,\mu\mathrm{m}$ at $\sim 7.9\,\mu s$, which due to inertial effects is half an acoustic period after the pressure minimum. The rapid implosion is ($\sim 9\,\mu s$) is followed by the development of a jet to the right, in the direction of the travelling ultrasound wave. At $\sim 13.2\,\mu s$ the maximum inflation is reached (corresponding to a renewed minimum pressure) and the nose of the jet starts to retract (the bubble is now exposed to an inverse pressure gradient). In the following a rebound jet to the left is formed and the bubble implodes at $\sim 14.7\,\mu s$.

Directed jetting of gas bubbles that jet in the direction of the ultrasound field has been observed in several studies (i.e. [3], [4]), the rebound jet has however been reported only recently by [5]. In fact, the behavior of the here used contrast agents shown in Fig. 2 (a) is very similar to the one of laser induced gas bubbles reported by [5].

IV. Influence Of Other Nearby Bubbles

In [2] and in the previous section we study the jetting dynamics of contrast agent microbubbles at $200\,\mathrm{kHz}$ and a high pressure amplitude of $\sim 1.5\,\mathrm{MPa}$ under the condition that the bubble is isolated and not influenced by any other bubble or the wall, as confirmed by top-view imaging. However, in medical applications, bubbles will interact with each other as well as with biological structure such as cells and tissues. In the following we discuss the presence of other bubbles.

In Fig. 3, the same experiment as in Fig. 2 ($1.5\,\mathrm{MPa}$ peak negative pressure of the $200\,\mathrm{kHz}$) is performed, but now with two bubbles in the focal spot of the transducer. Fig. 3 (a) shows one example of two bubbles jetting towards each other. This kind of behavior can be expected as both reach a maximum size at approximately the same moment [6]. In the present case, the jet noses become so close that they interfere with each other and that the left bubble cuts through the right one (see $t = 9.7\,\mu s$ in Fig. 3 (a2)). In the following snapshots it is visible that the right bubble integrates into the left one, which keeps growing and then shows the typical characteristic of a rebound-jet. This example is however not commonly observed and most of the time, the jetting direction is influenced by both the ultrasound wave and other bubbles in its proximity. One example, where one bubble is deviated towards a second one is shown in Fig. 3 (b). Here, an influence of the bubble dynamics (with respect to the not influenced one) can be observed. The forward jet to the right develops similarly to that described for the single microbubble cavitation (splitting and nearly splitting of the jet nose has been reported in [2]). However, the collapse and development of the rebound jet (see $t = 13.9\,\mu s$ and $14.1\,\mu s$ in Fig. 3 (b2)) are altered. Instead of a clear jet to the left, the bubble seems to be elongated here.

When an increased number of bubbles are present (from reduced dilution of the contrast agent solution), not only the jetting direction and possibly the shape are influenced. As can be seen in Fig. 4 also the expansion ratio can be modified. From Fig. 4 (a) to (c) more and more bubbles are present in the field of view. Bubbles still keep jetting, their initial extension as well as their jets become however smaller and smaller. This might be an expected result as more and more bubbles are competing for the same volume during expansion

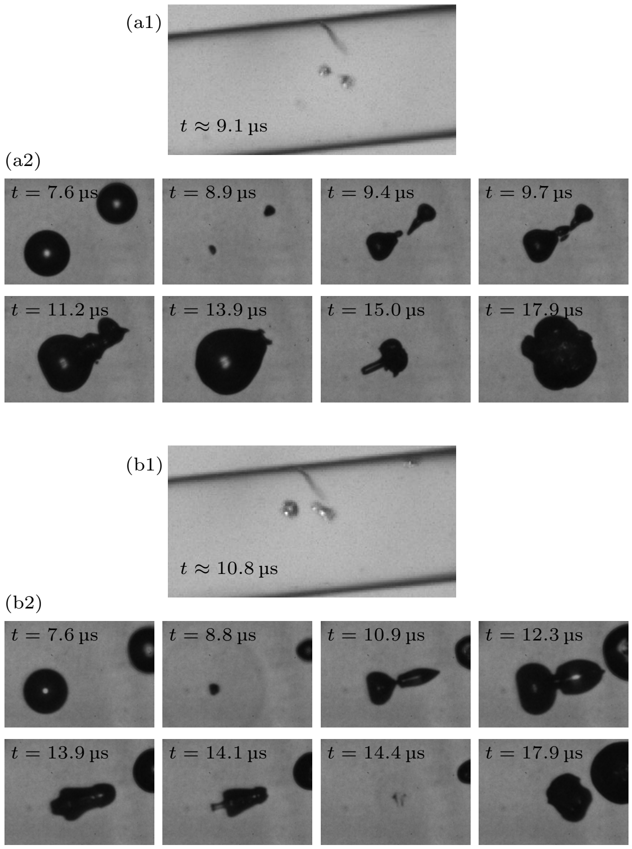

Fig. 3. Bubbles jetting in the presence of a second bubble: (a) one bubble deviated towards a second one and (b) two bubbles jetting towards each other. Parts (a1) and (b1) are top-view image showing the capillary (diameter $500\,\mu m$) and the two bubbles, parts (a2) and (b2) are side-view imaging (frame size $240 \times 180\,\mu m^2$).

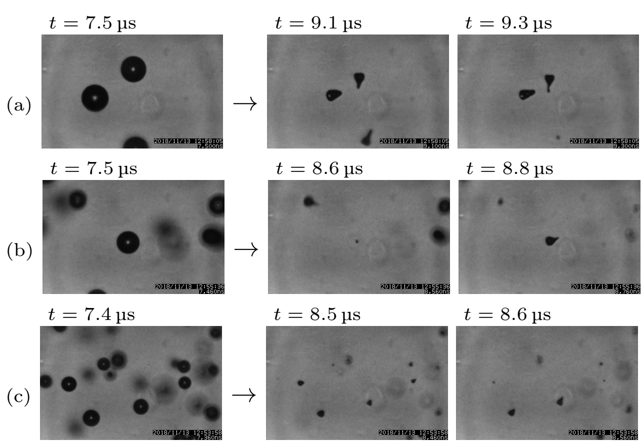

Fig. 4. Influence of an increasing number of bubbles during ultrasound exposure. All frames have the size $430 \times 260\,\mu m$.

phase. It is however important to take into account for medical applications, where bubble-bubble interaction is expected.

V. Conclusions

In the present paper we showed the bubble dynamics of single ultrasound contrast agent bubbles exposed to 200 kHz ultrasound burst. The observed jetting dynamics is comparable to those recently reported by [5]. Furthermore, we study the influence of multiple bubble-bubble interaction. Jets are deviated towards other bubbles and their shape might change. Furthermore, the expansion ratio diminishes with an increasing number of close by bubbles.

References

[1] J.H. Song, A. Moldovan and P. Prentice, “Non-linear acoustic emissions from therapeutically driven contrast agent microbubbles”, Ultrasound Med Biol, 2019, vol 45, pp.2188-2104.

[2] S. Cleve, C. Inserra and P. Prentice, “Contrast agent microbubble-jetting during initial interaction with 200 kHz focused ultrasound”, Ultrasound Med Biol, 2019 (in press).

[3] B. Gerold, P. Glynne-Jones, C. McDougall, D. McGloin, S. Cochran, A. Melzer and P. Prentice, “Directed jetting from collapsing cavities exposed to focused ultrasound”, Appl Phys Lett, 2012, vol 100, pp.024104.

[4] C.-D. Ohl, R. Ikink, “Shock-wave-induced jetting of micron sized bubbles”, Phys. Rev. Lett., 2003, vol 90, pp.214502.

[5] J.M. Rossellò, W. Lauterborn, M Koch, T Wilken, T Kurz and R Mettin, “Acoustically induced bubble jets”, Phys Fluids, 2018, vol 30, pp.122004.

[6] S.W. Fong, D. Adhikari, E. Klaseboer and B.C. Khoo, “Interactions of multiple spark-generated bubbles with phasedifferences”, Exp Fluids, 2009, vol 46, pp.705–724.