Acoustic measurements of resonance behavior of single ultrasound contrast agent microbubbles

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With an increased interest in more sophisticated ultrasound contrast-specific imaging techniques, scientists are investigating means to accurately and quantitatively study the behavior of ultrasound contrast agents (UCA) in an ultrasound field. Acoustical studies on populations of UCA bubbles with a known size distribution have been widely performed. Several authors have proposed to fit experimentally obtained attenuation spectra with modeled spectra [1-2]. Although these models describe single bubble responses, they predict bulk behavior of a UCA as weighted sums of contributions from different bubble sizes. Bubble-bubble interactions are thus not taken into account although this could play an important role. Furthermore, Gorce et al. [2] showed by considering fractions of the native size distribution of SonoVue, that the shell properties of the bubbles are size-dependent. Therefore, to better understand and describe the behavior of UCA, one should look at individual bubbles.
Several authors have shown that high speed optical measurements provide quantitative information on the dynamical behavior of a single microbubble in a sound field [3]. Furthermore, such measurements have revealed new phenomena, e.g. compression-only behavior [4], threshold behavior [5] and the occurrence of surface modes [6], which have never been measured acoustically. Nevertheless, high speed imaging of microbubbles has some disadvantages. Dedicated high-speed cameras are costly and of limited availability. Moreover, optical studies are limited by the resolving power of the optical system in detecting small radial responses at low acoustic pressures. Furthermore, although optical measurements give quantitative information on the amplitude of oscillation of the microbubble, they do not provide a direct quantitative measure of the sound produced by these microbubbles (which is important for diagnostic applications).
To overcome these shortcomings we present quantitative acoustic measurements on single BR-14 (Bracco Research S.A., Geneva, Switzerland) microbubbles at low acoustic driving pressures, combined with simultaneous high speed imaging of the same bubble to resolve its radial dynamics. Single ultrasound contrast agent microbubbles were insonified at different frequencies, using both chirps and a microbubble spectroscopy approach [3] to investigate their full resonance behavior. Depending on the initial bubble radius, driving pressure amplitude and frequency, either optical or acoustical methods have a better sensitivity to detect the response of a single microbubble to ultrasound. Calculating the sound emission from the measured radius time curves gives excellent quantitative agreement with the directly measured sound emission. This finding gives good confidence in using radial responses as a measure for the acoustic response, and vice versa. An excellent agreement was found between the optical and acoustical response for bubbles displaying ‘compression-only’ behavior, showing for the first time that the compression-only bubbles display strong second harmonic sound emission.

Finally, we will show how 'threshold behavior' of a microbubble can be identified in its acoustical response [5].

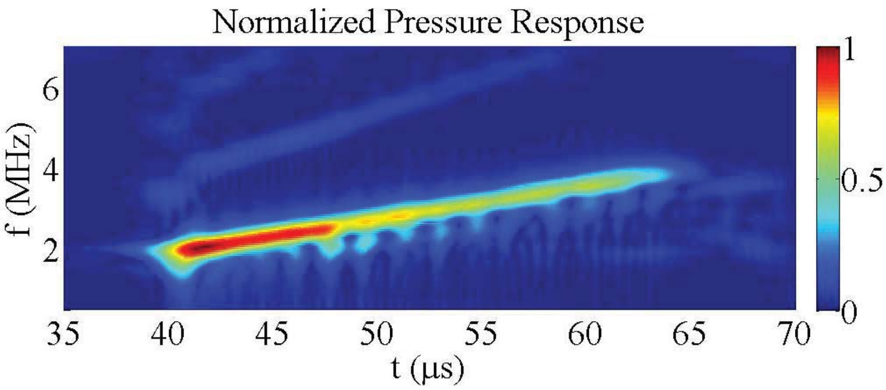

Figure: Typical acoustic response of a single microbubble with a radius of 3 µm to a 40-kPa amplitude chirp with a frequency sweep ranging from 1 to 4 MHz. Both the fundamental and the second harmonic responses are clearly visible.

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