Microbubble Acoustic Signatures: Bubble Deflation

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Abstract— **Ultrasound Contrast Agents (UCAs) are used in medical imaging to enhance the visibility of structures, especially blood vessels and the liver. An example application of UCAs is the detection and classification of tumors. The most common UCA consist of microbubbles, which have pronounced non-linear acoustical scattering properties. Research on the characteristics of these microbubbles is still in progress. The project described in this paper is focussed on the classification of the microbubbles. The acoustic response of a single microbubble depends on the environment and the location of the microbubble. Three classes can be defined: Microbubbles floating freely, microbubbles in the neighborhood of a (vessel) wall, and clusters of interfering microbubbles. Many different bubble models are available and the most appropriate one must be selected to be used in the classification algorithms. Classification of these microbubbles using the characteristics of the received ultrasound signal is necessary to gain knowledge about the location and environment of the microbubble, which in turn represents properties of the tissue. In this paper, the deflation rate or aging of a microbubble is discussed. Because of the limited number of bubbles in the data-set at this moment, we are unable to define a relation between bubble size and deflation rate.**

Keywords— **Microbubbles, Acoustic signatures, Classification, Signal Analysis, Ultrasound**

I. Introduction

Microbubble contrast agents are more frequently applied in ultrasonic imaging because of the echogenic properties. The acoustic behavior is still not fully understood.

Many questions like: What are the acoustic properties of a microbubble floating freely, what is the difference compared to a microbubble near a wall and what is the effect of a neighboring bubble are still open.

To understand microbubble behavior, we are studying the signals obtained from experiments. The experimental setup is available at the University of Twente. At the time being, the setup is extended with a fully automatic bubble positioning and data acquisition system. Important issues are the processing, fitting and classification of the data.

Many mathematical models are available which characterize the acoustic response of a microbubble. These models are still under development and are difficult to verify[1]. In this paper the used model and the preliminary results of the bubble deflation rate are presented.

II. Models

In the paper of Marmottant, the deflation of a microbubble is described by using a high-speed camera. This paper shows a graph in which the bubble radius is shown after a sequence of pulses. A clear deflation of the bubble is shown. We want to observe this effect using the acoustic reflection of the microbubble. The mathematical model used by Marmottant is based on the modified Herring Equation [2] or modified Rayleigh-Plesset Equation [3], see equation (1):

$$\rho_l(R\ddot{R} + \frac{3}{2}\dot{R}^2) = P_l + \frac{R}{c}\dot{P} - (P_0 + P_{driv}(t)) \quad (1)$$

in which ρ_l is the density of the liquid, R is the bubble radius, $\dot{R}$ is the bubble wall velocity, $\ddot{R}$ is the bubble wall acceleration, P_l is the pressure in the liquid, P_0 is the hydrostatic pressure and P_{driv} is the acoustic driving pressure. $\frac{R}{c}\dot{P}$ is the Herring re-radiation term, with c the velocity of sound in the liquid and $\dot{P}$ is the first derivative of the gas pressure. In Frinking (1998)[4] the radiative losses are included as part of a total damping coefficient $-\frac{R_0\rho\omega^2}{c}R\dot{R}$. In the Herring equation these losses are described with the Herring re-radiation term.

The model used to describe our bubbles (Sonovue) is described by Marmottant [1]. He uses the Rayleigh Plesset equation and incorporated the Herring re-radiation term[5]:

$$\left(\frac{R}{c}\right)\left[\frac{dP_g(t)}{dt}\right] = \frac{R}{c}\dot{P} \quad (2)$$

The left hand side represents the notation of Marmottant and the right hand side the notation of Herring. The modified Rayleigh Plesset equation becomes: [1]:

$$\rho_l\left(R\ddot{R}+\frac{3}{2}\dot{R}^2\right)=\left[P_0+\frac{2\sigma(R_0)}{R_0}\right]\left(\frac{R}{R_0}\right)^{-3\kappa}\left(1-\frac{3\kappa}{c}\dot{R}\right)-P_0-\frac{2\sigma(R)}{R}-\frac{4\mu\dot{R}}{R}-\frac{4\kappa_s\dot{R}}{R^2}-P_{ac}(t) \tag{9}$$

$$\sigma(R)=\begin{cases}\text{Buckled state} & \sigma &= 0 & \text{if } R\leq R_{buckling}\\ \text{Elastic state} & \sigma &= \chi\left(\frac{A}{A_{buckling}}-1\right) & \text{if } R_{buckling}\leq R\leq R_{break-up}\\ \text{Ruptured state} & \sigma &= \sigma_{water} & \text{if ruptured and } R\geq R_{break-up}\end{cases} \tag{10}$$

$$\rho_l\left(R\ddot{R}^2+\tfrac{3}{2}\dot{R}^2\right) = P_l(t)-P_0-P_{driv}(t)-\left(\tfrac{R}{c}\right)\left[\tfrac{dP_g(t)}{dt}\right] \tag{3}$$

$$P_g(t)-P_l(t)=\frac{2\sigma(R)}{R}+4\mu\frac{\dot{R}}{R}+4\kappa_s\frac{\dot{R}}{R^2} \tag{4}$$

To incorporate the stress arising from the viscosity of the liquid we use the surrounding liquid viscosity μ which is present in the second term on the right hand side of (4) and if we incorporate the surface dilatational viscosity elastic modulus of the lipid shell κ_s we obtain the third term on the right hand side for the frictions in the shell.
Inserting (4) in (3) results in:

$$\rho_l\left(R\ddot{R}+\tfrac{3}{2}\dot{R}^2\right) = P_g(t)-\tfrac{2\sigma(R)}{R}-4\mu\tfrac{\dot{R}}{R}-4\kappa_s\tfrac{\dot{R}}{R^2}- P_0-P_{ac}(t)-\left(\tfrac{R}{c}\right)\left[\tfrac{dP_g(t)}{dt}\right] \tag{5}$$

Choosing an ideal polytropic gas law:

$$P_g\propto R^{-3\kappa} \tag{6}$$

with κ the polytropic gas constant.

$$P_g(t)=\left[P_0+\frac{2\sigma(R_0)}{R_0}\right]\left(\frac{R}{R_0}\right)^{-3\kappa} \tag{7}$$

$$\frac{d}{dt}P_g(t)=\left[P_0+\frac{2\sigma(R_0)}{R_0}\right]\left(\frac{R}{R_0}\right)^{-3\kappa}\left(-\frac{3\kappa}{R}\dot{R}\right) \tag{8}$$

Substitution of (7) and (8) in (5) results in (9).
The modified Rayleigh-Plesset equation presented in this section is used for several states of the microbubble[1] designated by $\sigma(R)$ in (10), in which χ is the elastic modulus, A is the area of the bubble and $A_{buckling}$ is the buckled area of the bubble.

In the reduced model, the shell is considered only elastic. For small vibrations, the surface tension σ can be linearized around the equilibrium radius of the bubble:

$$\sigma(R_0)\approx\sigma(R_0)+2\chi\left(\frac{R}{R_0}-1\right) \tag{11}$$

This model is used at this moment to characterize our bubbles and it may require adjustment to incorporate bubble deflation or aging.

III. Experiments

The current available data set contains 109 measurements on microbubbles. Each measurement contains a sequence of 20 measurements of the response of the microbubble on an acoustic pulse. A photograph of the bubble is taken at the start and end of the measurement sequence. This is done to see if the bubble has deflated or changed position. All these measurements were done by Jeroen Sijl [6] for the initial purpose of characterization of the bubble shell parameters, which is the reason why the experiment is not perfectly conditioned for the measurement of bubble deflation.

In this experiment the deflation of the bubble is analyzed. We have measured the amplitude of the response of ten identical pulses separated by 30 ms followed by a pause of 1-3 seconds and then again ten identical pulses separated by 30 ms. Each pulse has a peak to peak amplitude of 120 kPa and consists of 5 cycles from a 2.25MHz sinusoidal signal with a Hanning window. The top-top response voltage of each pulse is measured. A detailed description of the setup can be found in Sijl (2005). On this data a 1st order polynomial is fitted from which we obtain the deflation slope. The slope is an indication of the bubble

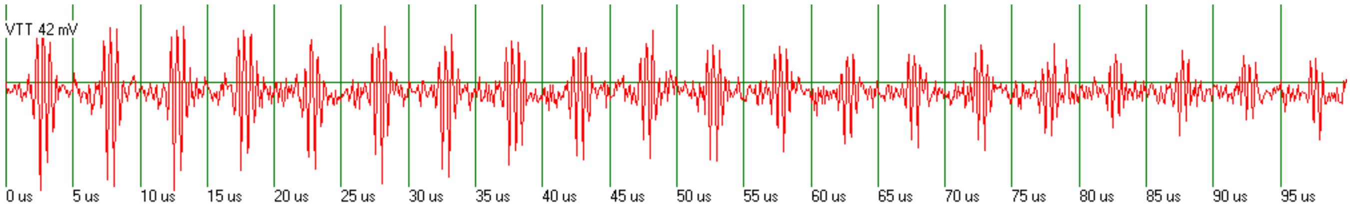

Fig. 1. Response sequence of bubble with a high deflation rate

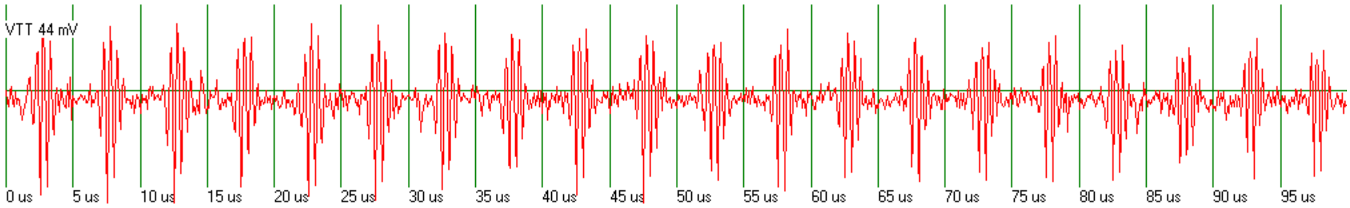

Fig. 2. Response sequence of bubble with a low deflation rate

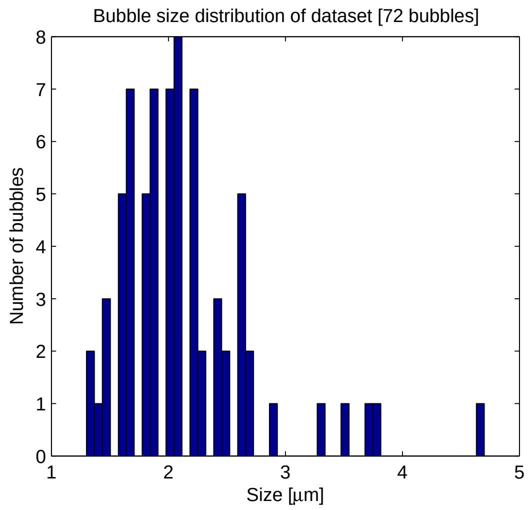

Fig. 3. Bubble-size distribution

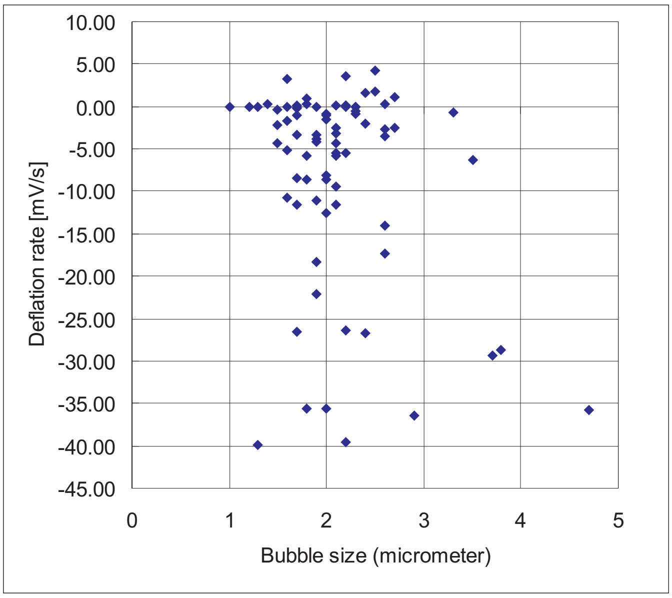

Fig. 4. Bubble-size versus deflation time

deflation-rate. Figures 1 and 2 show the concatenation of each bubble response with the bubble response in a 5 μs frame. Figure 4 shows the results of the deflation rate from the data-set consisting of a set bubbles with a distribution as shown in figure 3. From this figure we should expect to see a correlation between the bubble size and the deflation rate, but due to the limited amount of measured microbubbles we cannot draw any conclusions.

IV. Discussion

Since the timing of the triggering of the pulse has no strict interval of 30ms, we have to do these measurements again with the new setup. In this new setup we expect to get more measurements in which we may find a relation between bubble size and deflation rate. We also expect that it is possible to classify the buckled or elastic state using the acoustic signature of the bubble.

V. Conclusion

Main part of the project is the signal analysis and classification of the acoustical and optical data obtained from the bubbles. Focus will be on the non-averaged data of the acoustic bubble signature and the differences between the signals of one sequence (of 20 measurements). The point of interest in this sequence is the porosity of the microbubble, the change in echogenicity due to the porosity and the pressure sensitivity of the porosity property.

Due to the limited amount of microbubbles and the temporal variation between the measurements we are able to draw conclusions. In future experiments the new setup will be used in which full automatic data acquisition will take place. This automation results in more acoustical bubble data. We expect to see a representation of bubble properties in the acoustic signal. These properties are valuable for the adjustment and extension of the bubble model and the optimization of the physical bubble.

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