Finite element modeling of acoustic scattering from an encapsulated microbubble near rigid boundary*

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This article proposes a finite element model (FEM) for predicting the acoustic scattering from an encapsulated microbubble near rigid boundary. The validity of the model is first examined by comparing the acoustic nonlinear response of a free microbubble with that obtained by the Church model. Then this model is used to investigate the effect of the rigid boundary on acoustic scattering signals from microbubble. The results indicate that the resonance frequency decreases while the oscillation amplitude increases as the microbubble approaches the rigid boundary. In addition, the fundamental component of the acoustic scattering signal is enhanced compared with that of the free microbubble.

Keywords: bound encapsulated microbubble, acoustic scattering, finite element model
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1. Introduction

Since the first report on the use of ultrasound contrast agents (UCAs) in the 1960s, the echo contrast effect of microbubbles has attracted strong interest in the field of medical ultrasound.[1] These microbubbles have diameters on the order of 1–10 μm, and are filled with air or low water-soluble gas such as perfluorocarbon. The stiff (denatured albumin) or relatively flexible (phospholipids) microbubble shell is designed to reduce diffusion into the blood. The unique echo properties of the microbubbles enable ultrasound contrast imaging to be implemented not only in linear mode, but also in nonlinear harmonic modes.[2,3] More recently, the applications of UCAs have expanded to targeted imaging, thrombolysis, and drug and gene delivery.[4,5] In a targeted imaging system, microbubbles are coated with a shell that supports peptide- or antibody-based targeting ligands, where these ligands will bind to receptors on a blood vessel wall. This technique provides the potential for earlier detection and characterization of disease. However, only 20% or less of the microbubbles are adherent to the target site, thus their signal could be easily masked by the background from freely circulating agents and surrounding tissues.[5] Sensitive detection techniques are required to be developed to distinguish the signal of the adherent microbubbles from that of the free microbubbles. For this purpose, it is important to understand the acoustic responses from the adherent and free microbubbles. Efforts in modeling the acoustic response from free microbubbles have largely been focused on using various modified Rayleigh–Plesset (RP) equations.[6−8] Particularly, the modified model proposed by Church has been widely cited.[6] In these studies, a microbubble is assumed to be immersed in an infinite liquid and remains spherical during oscillation. However, the oscillation of adherent microbubbles was observed to be asymmetrical and the echo intensity at the fundamental frequency was significantly increased.[5,9]

Considering the fact that the previous analytical solutions are not flexible enough to be extended to acoustic responses from bound microbubble which is irregularly shaped and inhomogeneous, we aim to develop a numerical model for better understanding the difference in acoustic response between the bound and the free microbubbles. In the targeted imaging, microbubbles are limited in an elastic blood vessel. In this study, the vessel wall is assumed to be rigid for simplicity, and a preliminary finite element model (FEM) is proposed to describe acoustic re-

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sponses from an encapsulated microbubble near a rigid boundary. The validity of this model is examined by a comparison of acoustic behaviour of free encapsulated microbubble between the FEM and the Church model.[6,7] The acoustic scattering from an encapsulated microbubble near a rigid boundary is investigated based on this FEM, and compared with the reported measured results.

2. Theoretical models

2.1. Analytical model

Microbubble dynamics in an incompressible liquid has been studied widely by using various types of Rayleigh–Plesset (RP) equations. The Church model gives a theoretical description of the oscillation of a microbubble encapsulated by a thin viscoelastic solid shell.[6,7]

$$\begin{aligned}&\rho_{\mathrm{L}}\left(R^{''}R+\frac{3}{2}\left(R'\right)^2\right)\\&=p_0\left(\left(\frac{R_0}{R}\right)^{3\kappa}-1\right)-p_i\left(t\right)-4\eta_{\mathrm{L}}\frac{R'}{R}\\&\quad-12\mu_{\mathrm{S}}\frac{d_{\mathrm{S}}R_0^2}{R^3}\frac{R'}{R}-12G_{\mathrm{S}}\frac{d_{\mathrm{S}}R_0^2}{R^3}\left(1-\frac{R_0}{R}\right),\end{aligned}\tag{1}$$

where R is the instantaneous radius of the oscillating microbubble, the first and second time derivatives of the instantaneous radius R' and R'' denote the microbubble wall velocity and acceleration respectively, R_0 is the initial radius of the microbubble at equilibrium, ρ_{L} is the density of the liquid, η_{L} is the bulk viscosity of the liquid, p_0 is the hydrostatic pressure. κ is the polytropic exponent of the gas, $p_i(t)$ is the applied acoustic pressure, G_{S} and μ_{S} are the shear modulus and the shear viscosity of the shell, and d_{S} is the shell thickness.

The scattered acoustic pressure from the microbubble at a distance D from the centre of microbubble is given as

$$p_{\mathrm{sc}}\left(D\right)=\rho_{\mathrm{L}}\frac{R}{D}\left(2\left(R'\right)^2+RR''\right).\tag{2}$$

However, Church model can be used only for the description of free microbubble.

2.2. Finite element modeling of encapsulated microbubble

In this study, we use ABAQUS (Dassault Systèmes SIMULIA, version 6.7) to describe the acoustic responses from the encapsulated microbubble.[10] The contents of the microbubble are assumed to be ideal gas and the thermodynamic processes are assumed to be adiabatic with constant κ. The relation between pressure p and volume V is modeled as

$$p=p_0\left(\frac{V_0}{V}\right)^{\kappa},\tag{3}$$

where V_0 is the volume of the microbubble in equilibrium. The equilibrium equation for small motion of a compressible, adiabatic fluid with velocity-dependent momentum losses is taken to be

$$\frac{\partial p}{\partial x}+\gamma u_{\mathrm{L}}'+\rho_{\mathrm{L}}u_{\mathrm{L}}''=0,\tag{4}$$

where x is the spatial position of the fluid particle, u_{L}' is the fluid particle velocity, u_{L}'' is the fluid particle acceleration, ρ_{L} is the density of the fluid, and γ is the volumetric drag (force per unit volume per velocity). Furthermore, if the constitutive behaviour of the fluid is assumed to be inviscid and linear, then the pressure in the fluid can be written as

$$p=-K_{\mathrm{L}}\frac{\partial}{\partial x}\cdot u_{\mathrm{L}},\tag{5}$$

where K_{L} is the bulk modulus of the fluid. Then we obtain the equation of fluid motion only in terms of the fluid pressure

$$\frac{1}{K_{\mathrm{L}}}p''+\frac{\gamma}{\rho_{\mathrm{L}}K_{\mathrm{L}}}p'-\frac{\partial}{\partial x}\left(\frac{1}{\rho_{\mathrm{L}}}\frac{\partial p}{\partial x}\right)=0,\tag{6}$$

where p' and p'' are the first and second time derivatives of the pressure in the fluid.

The Kelvin–Voigt constitutive equation is used to describe the microbubble shell as a viscoelastic solid[11]

$$\tau_{\mathrm{s}}=2G_{\mathrm{S}}\frac{\partial u}{\partial r}+2\mu_{\mathrm{S}}\frac{\partial v}{\partial r},\tag{7}$$

where τ_{s} is the radial component of the shear stress tensor, u is the radial displacement in the shell, v is the radial velocity in the shell, G_{S} is the shear modulus of the shell and μ_{S} is the shear viscosity of the shell. The shear modulus and viscosity are in general frequency dependent.

The incident ultrasound wave in the fluid acts as the pressure at the surfaces of the viscoelastic shell and can be expressed as

$$F=-pn_{\mathrm{S}},\tag{8}$$

where n_{S} is the outward-pointing unit vector observed from the inside of the shell, and p is the applied acoustic pressure, $p=p_{\mathrm{a}}\sin(2\pi ft)$, with f being the frequency, and p_{a} the amplitude.

The constraint boundary condition of tie type is imposed on the gas–shell interface and the shell–liquid interface to ensure the continuity of the normal acceleration at the surface of the shell

$$n\left(\frac{1}{\rho}\nabla p\right) = -(n\cdot u)\,\omega^2, \tag{9}$$

where u is the harmonic radial displacement vector in the shell. The non-reflecting absorbing boundary condition is placed at the outer surface of the water for ensuring the minimum reflection when the backscattered acoustic wave leaves the computational domain. The absorbing boundary condition used in ABAQUS is the first-order condition of Bayliss, Gunzberger, and Turkel, i.e.[10]

$$\nabla p\cdot n = \mathrm{i}\,kp, \tag{10}$$

where k is the wave number. On the surface of the fixed rigid boundary, we have

$$\frac{\partial\phi}{\partial n} = 0, \tag{11}$$

where ϕ is the velocity potential.[12,13]

3. Results and discussions

3.1. Acoustic response of a free encapsulated microbubble

To examine the validity of this FEM, we calculate the acoustic responses from a free encapsulated microbubble, and compare them with the results obtained by the Church model. The gas filled in the microbubble and the surrounding liquid are assumed to be air and water respectively. An encapsulated microbubble with the initial radius (R_0) 2 μm is located in the centre of the liquid cube whose side length is 100 μm. The shell of the encapsulated microbubble is defined as incompressible homogeneous isotropic viscoelastic solid that behaves as rubber-like material. The shear viscosity of the shell is 1.8 Pa·s and the shell thickness is 20 nm. The densities and the speeds of sound of the materials used in the numerical calculation are listed in Table 1.

Table 1. Material parameters used in the calculation.

medium	gas	water	shell
density/(kg/m^3)	1.225	1000	1100
speed of sound/(m/s)	340	1500	1600

Mesh generation is important in the finite element analysis. Appropriate element types should be chosen for each part of the model and the numbers of the elements and nodes should be sufficient to meet the accuracy of the analysis. In order to achieve satisfactory results, all the elements in this study are set to be less than 0.4 μm to ensure at least 10 elements per wavelength.

Figure 1 shows the axisymmetric planar mesh for the FEM of the free encapsulated microbubble (left) and part of the same mesh with an axisymmetric sweep angle of 180° (right). The element type of the surrounding water is ACAX4 with pressure freedom only, which is the 4-node axisymmetric quadrilateral acoustic element. 19981 ACAX4 elements and 20287 nodes are used for the water. The element type SAX1 with structural freedom is applied to the shell. SAX1 is the 2-node axisymmetric stress element for thin or thick shell modeling. The encapsulation is discretized by 64 SAX1 elements and 65 nodes.

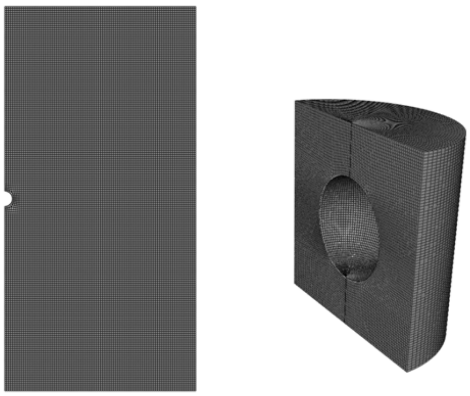


Fig. 1. Axisymmetric planar mesh for FEM and partial mesh in swept display.

The FEM is first used to predict the resonance frequency of the free microbubble. Figure 2 shows the linear frequency responses of the encapsulated microbubble predicted by FEM, where the values of shear modulus (Gs) of the shell are 10, 20 and 30 MPa.

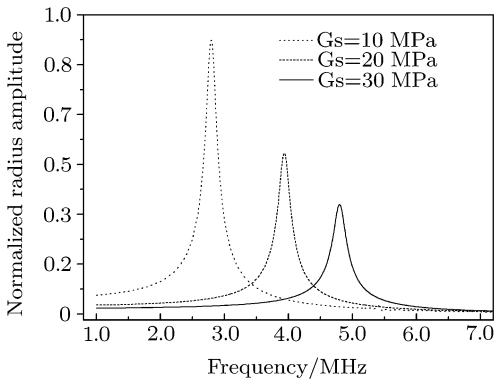


Fig. 2. Effect of shear modulus on acoustic response from a free encapsulated microbubble.

It is observed that there is an increase in resonance frequency and a decrease in pressure amplitude as the value of shear modulus rises. The result is in agreement with that obtained by the Church model.[6,7] Table 2 provides a comparison of resonance frequency between FEM and Church model. The relative error is less than 6.7%, which can be further improved by reducing the element size.

Table 2. Comparison of the resonance frequency of a free encapsulated microbubble between FEM and Church model.

shear modulus/MPa	FEM/MHz	Church/ MHz	relative error/%
Gs=10	2.8182	3.0239	6.7
Gs=20	3.9347	4.1380	4.91
Gs=30	4.8016	4.9721	3.43

Then the FEM is employed to investigate the nonlinear microbubble oscillation. A microbubble with the shell shear modulus 10 MPa is under the insonification of 2 MHz ultrasound. In order to compare with the Church model which is suitable for predicting bubble oscillation with small amplitude, we use a small applied acoustic pressure of 20 kPa. The microbubble vibrates nonlinearly as expected, i.e. the contraction and expansion are not symmetric. As a result, the second harmonic and higher harmonic components are observed. Figure 3 presents the nonlinear spectrum of the scattered sound wave from the microbubble. For comparison, the result obtained by the Church model is also given as a dash line. The results also show good agreement between the FEM model and the Church model, except that there is some discrepancy at the harmonic amplitude, which can also be improved by reducing the element size.

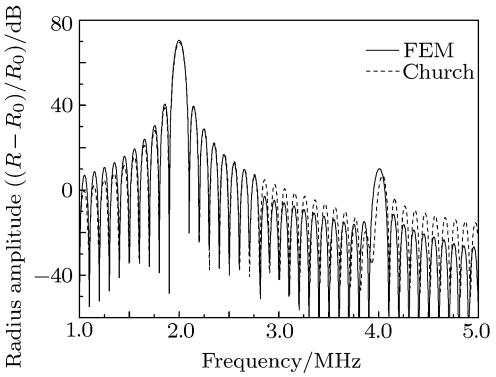


Fig. 3. Acoustic nonlinear spectrum of a free microbubble.

3.2. Acoustic response from an encapsulated microbubble near rigid boundary

Figure 4 illustrates the mesh configuration for an encapsulated microbubble near rigid boundary. 19974 acoustic elements ACAX4 and 20279 nodes are used to model the surrounding water, 64 shell elements SAX1 and 65 nodes to model the encapsulation.

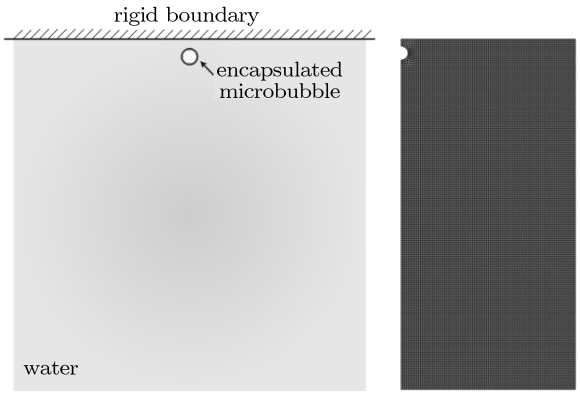


Fig. 4. A microbubble near rigid boundary and axisymmetric planar mesh.

The resonance frequency of the bound microbubble is first analysed based on this FEM and listed in Table 3. For comparison, the resonance frequency of the free microbubble is also provided in this table. The distances from the microbubble to the rigid boundary are set to be 2, 4 and 6 μm.

Table 3. Comparison of resonance frequency between bound and free microbubble.

	bound microbubble			free microbubble
	2 μm	4 μm	6 μm	
resonance frequency	2.4546 MHz	2.5455 MHz	2.6364 MHz	2.8182 MHz

It is observed that the existence of the boundary leads to the decrease in resonance frequency, and that the resonance frequency turns smaller as the microbubble approaches the rigid boundary. In the previous experimental study,[14] an optical method (microbubble spectroscopy) was used to study the effect of a rigid wall on the resonance frequency of individual microbubble. It was indicated that the presence of the wall tended to lower the resonance frequency, which is consistent with our results.

Furthermore, the FEM is applied to the nonlinear dynamic analysis of the bound microbubble under a 15 μs excitation of 2 MHz ultrasound at an acoustic pressure of 0.02 MPa. Figure 5 illustrates the radius variations with time for the bound and free microbubbles. In the figure, the dot line, dash dot line and the short dash line correspond to microbubble with its geometry centre 2, 4 and 6 μm away from the rigid boundary respectively; while the solid line is for the free microbubble. It is obvious that the oscillation amplitude increases as the microbubble turns closer to the boundary. The maximum radius of the bound microbubble with distance 2, 4, and 6 μm from the rigid boundary is 1.39%, 0.78% and 0.56% larger than that of the free microbubble.

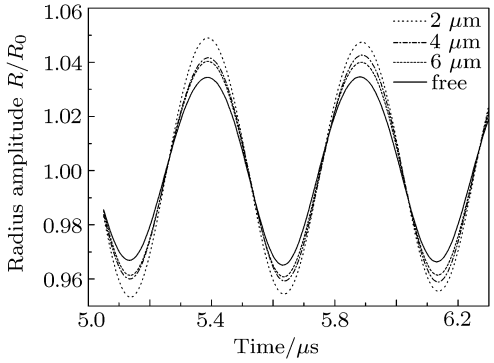


Fig. 5. Variations of radius for the bound and free microbubbles.

The spectra of the acoustic signal scattering from the bound microbubble and the free microbubble are compared in Fig. 6, where the dot line, the dash dot line and the short dash line correspond to the microbubbles whose geometric centres are 2, 4 and 6 μm away from the rigid boundary respectively; while the solid line represents the spectrum of the free microbubble.

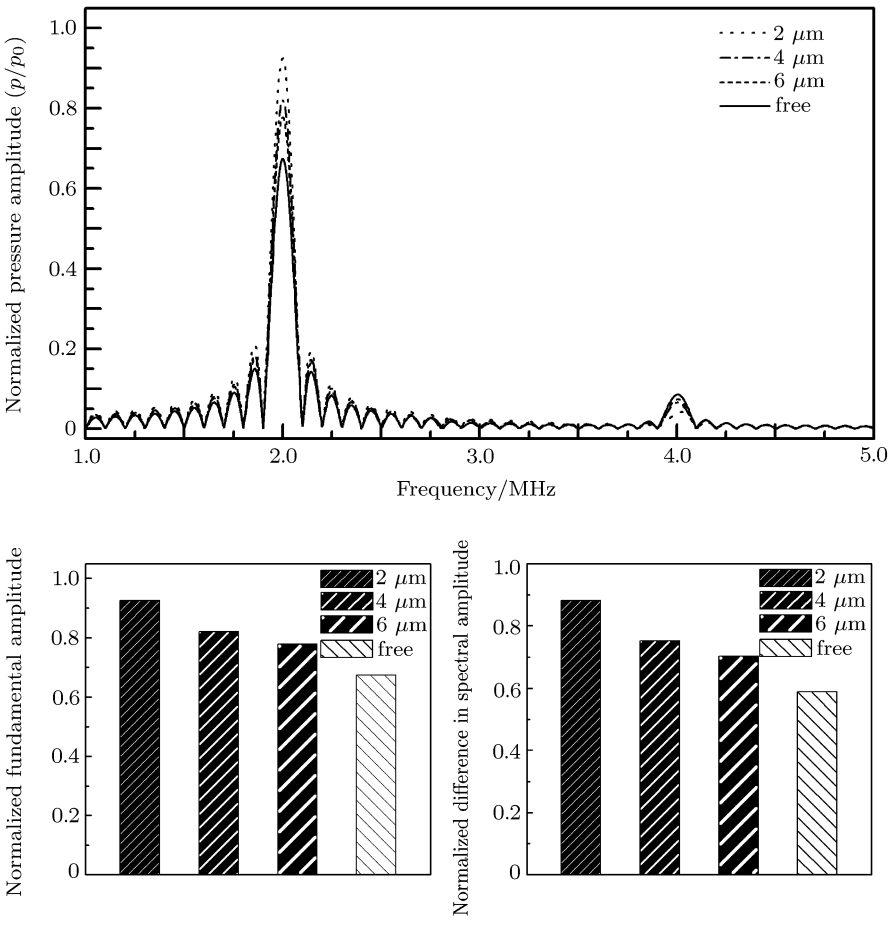


Fig. 6. Spectra of acoustic scatterings from bound and free microbubbles.

As can be seen, the fundamental component of acoustic scattering signal from the bound microbubble is enhanced (lower left) when the microbubble moves closer to the rigid boundary, and the difference between the amplitude of fundamental frequency and that of the second harmonic frequency becomes larger (lower right). Zhao *et al.* used a 200 μm micro-tube to mimic a blood vessel, where the microbubble solutions flowed through the tube at a mean velocity of 10 mm/s.[5,9] They found the fundamental spectral intensity to increase about 14–22 dB for bound microbubbles compared with free microbubbles with transmission at 2 and 4 MHz. Our numerical results confirm these previous measurements.

4. Conclusion

We develop an FEM to predict the acoustic responses from a bound microbubble. Linear resonance and acoustic nonlinear behaviours of the bound microbubble are investigated by using the FEM. Results demonstrate that the microbubble oscillates more violently when the microbubble is closer to the rigid boundary, and that the fundamental component of the acoustic scattering signal is increased while the difference in magnitude between the fundamental component and the second harmonic component turns larger. Future study will be focused on the research of the acoustic behaviour of the adherent microbubble in the elastic micro-tube.

References

[1] Frinking P J A, Bouakaz A, Kirkhorn J, Ten Cate F J and de Jong N 2000 *Ultrasound Med. Biol.* **26** 965

[2] Chen H, Li X J, Wan M X and Wang S P 2006 *Acta Acustica* **31** 523

[3] Gong YJ, Zhang D, Xi X Y, Gong X F and Liu Z 2007 *Acta Phys. Sin.* **56** 7051 (in Chinese)

[4] Hu Y, Ge Y, Zhang D, Gong X F and Zheng H R 2009 *Acta Phys. Sin.* **58** 4746 (in Chinese)

[5] Zhao S K, Kruse D E, Ferrara K W and Dayton P A 2006 *J. Acoust. Soc. Am.* **120** EL63

[6] Church C C 1995 *J. Acoust. Soc. Am.* **97** 1510

[7] Gong Y J, Zhang D, Gong X F, Tan K B and Liu Z 2006 *Chin. Phys.* **15** 1526

[8] Chen Q, Zou X Y and Cheng J C 2006 *Acta Phys. Sin.* **55** 6476 (in Chinese)

[9] Zhao S K, Ferrara K W and Dayton P A 2005 *Appl. Phys. Lett.* **87** 134103

[10] Dassault Systèmes SIMULIA 2007 *ABAQUS Theory Manual* **v6.7**

[11] Doinikov A A and Dayton P A 2006 *J. Acoust. Soc. Am.* **120** 661

[12] Blake J R, Taib B B and Doherty G 1986 *J. Fluid Mech.* **170** 479

[13] Harris P J 1992 *Inter. J. Numer. Meth. Engin.* **33** 1813

[14] van Der Meer S M, Dollet B, Voormolen M M, Chin C T, Bouakaz A, de Jong N, Versluis M and Lohse D 2007 *J. Acoust. Soc. Am.* **121** 648