

## Physico-mathematical model of nonlinear acoustic properties of ultrasound contrast bubbles encapsulated by anisotropic shell

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### 1. Introduction

Image resolution is improved when microbubbles are used as a contrast agent in ultrasound diagnosis. The microbubbles are covered with a thin shell (or membrane) composed of lipids and other substances. Church<sup>1)</sup> and Hoff et al.<sup>2)</sup> proposed mathematical models from a mechanical point of view, assuming the shell to be a visco-elastic body (i.e., continuum), and established a pioneering theory of nonlinear oscillations of ultrasound contrast agent. However, as a disadvantage of previous models including Refs. [1,2], only single contrast agent is considered. The acoustic properties of multiple contrast agents are necessary because the large number of contrast agent are utilized in a clinical practice. Recently, our group proposed a mathematical model<sup>3)</sup> that can represent the nonlinear acoustic properties of many contrast agents based on mathematical model for a single contrast agent<sup>1,2)</sup>.

In general, the shell is composed of various materials such as polymers and phospholipids, which are distributed in a layered, an anisotropy thus naturally occurs and contributes to acoustic properties of bubble oscillation and ultrasound. However, all previous models (e.g., Refs. (1-3)) have assumed shell as isotropic material for simplicity. Last year, up-date equation of motion describing the oscillation of a single bubble with shell anisotropy is proposed, and the contribution of shell anisotropy to the oscillations was pointed out<sup>5)</sup>. The purpose of this study is to extend the equation of motion for a single contrast agent incorporating shell anisotropy<sup>5)</sup> to the case of multiple contrast agents and to clarify how shell anisotropy affects the ultrasound propagation.

### 2. Problem statement

The bubble is encapsulated by a purely elastic shell. An anisotropy of the shell<sup>5)</sup> is newly incorporated. As shown in Fig. 1 (b), the material

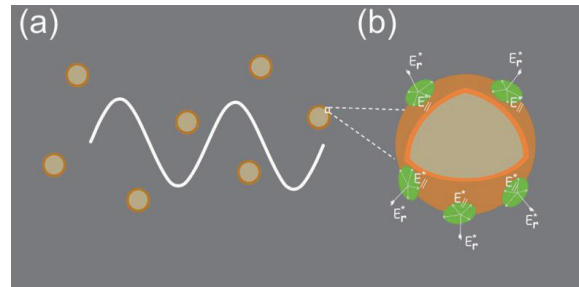


Fig. 1 (a): Ultrasound propagation in liquid containing multiple ultrasound contrast agents. (b): Schematic illustration of anisotropy of shell encapsulating bubble<sup>5)</sup>. Transverse anisotropic case is considered where radial Young's modulus  $E_r$  is different from the in-plane Young's modulus  $E_{||}$ <sup>6)</sup>.

properties are assumed to be different in the radial and orthoradial directions.

We theoretically investigate the nonlinear propagation properties of ultrasound in a liquid containing many bubbles encapsulated by the anisotropic purely elastic shell. Initially, the bubbly liquid is at rest and the bubbles are uniformly distributed. The gas inside bubbles is composed of only non-condensable ideal gas. The bubbles do not coalesce, break up, appear, and extinct.

### 3. Basic equations

The equation of motion for a bubble encapsulated by an anisotropic shell<sup>5)</sup> is used:

$$\begin{aligned} & \rho_{L0}^* R^* \frac{D_G^2 R^*}{Dt^{*2}} + \frac{3}{2} \rho_{L0}^* \left( \frac{D_G R^*}{Dt^*} \right)^2 \\ & = -4\mu_L^* \frac{1}{R^*} \frac{D_G R^*}{Dt^*} - p_L^* - \frac{2\sigma_2^*}{R^*} + p_G^* - \frac{2\sigma_1^*}{R^* - d_0^*} \\ & \quad - U^{*2} \rho_{L0}^* K_{ani} \left( 1 - \frac{R_0^*}{R^*} \right), \end{aligned}$$

where  $t^*$  is the time,  $p^*$  pressure,  $R^*$  bubble radius,  $\rho^*$  density,  $d_0^*$  initial shell thickness,  $U^*$  typical propagation speed of the wave,  $\mu^*$  viscosity,  $\sigma_1^*$  and  $\sigma_2^*$  are surface tensions at the internal and external boundaries of the shell, respectively; the subscripts G and L denote volume-averaged variables in gas and liquid phases, respectively, the

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subscript 0 denotes the quantities in the initial uniform state at rest, and the superscript \* denotes a dimensional quantity. Here, anisotropic factor  $K_{ani}$  is constant determined from the elastic constants of the shell, the explicit form is shown in the original paper<sup>6</sup>). Furthermore, to close the set of equations, the conservation equations of mass and momentum for bubbly liquid based on two fluid-model<sup>3,4</sup>) are used:

$$\begin{aligned} \frac{\partial}{\partial t^*}(\alpha\rho_G^*) + \frac{\partial}{\partial x^*}(\alpha\rho_G^*u_G^*) &= 0, \\ \frac{\partial}{\partial t^*}[(1-\alpha)\rho_L^*] + \frac{\partial}{\partial x^*}[(1-\alpha)\rho_L^*u_L^*] &= 0, \\ \frac{\partial}{\partial t^*}(\alpha\rho_G^*u_G^*) + \frac{\partial}{\partial x^*}(\alpha\rho_G^*u_G^{*2}) + \alpha\frac{\partial p_G^*}{\partial x^*} &= F^*, \\ \frac{\partial}{\partial t^*}[(1-\alpha)\rho_L^*u_L^*] + \frac{\partial}{\partial x^*}[(1-\alpha)\rho_L^*u_L^{*2}] \\ + (1-\alpha)\frac{\partial p_L^*}{\partial x^*} + P^*\frac{\partial\alpha}{\partial x^*} &= -F^*, \end{aligned}$$

where  $\alpha$  is the volume fraction of gas phase,  $x^*$  space coordinate,  $u^*$  fluid velocity,  $P^*$  surface-averaged pressure, and  $F^*$  interfacial momentum transport<sup>3,4</sup>).

#### 4. Results

We successfully derived the KdV-Burgers equation<sup>6</sup>) including the effect of shell anisotropy in terms of the liquid pressure perturbation  $p_L'$ :

$$\frac{\partial R_1}{\partial \tau} + \Pi_1 p_L' \frac{\partial p_L'}{\partial \xi} + \Pi_2 \frac{\partial^2 p_L'}{\partial \xi^2} + \Pi_3 \frac{\partial^3 p_L'}{\partial \xi^3} = 0,$$

$$\tau \equiv \epsilon t, \quad \xi \equiv x - (1 + \epsilon\Pi_0).$$

where  $\tau$  and  $\zeta$  are independent variables through the variable transformation, and  $\epsilon$  is the nondimensional wave amplitude. The constant coefficients  $\Pi_i$  ( $i = 0, 1, 2, 3$ ) represent advection, nonlinearity, attenuation, and dispersion of ultrasound, respectively. We here consider the following two cases of  $E_{||}$  to express shell anisotropy: (i)  $E_r = 3.8 E_{||}$ : anisotropic case 1 and (ii)  $E_r = 2E_{||}$ : anisotropic case 2. In anisotropy case 2, shell anisotropy suppresses the attenuation  $\Pi_2$  and promotes nonlinearity  $\Pi_1$  coefficients. In ultrasonic diagnosis, the attenuation of ultrasound is an important acoustic characteristic as images are formed using reflected waves. Nonlinearity generates higher harmonics of the wave, improving image resolution.

#### 5. Summary

The equation of motion for a single bubble

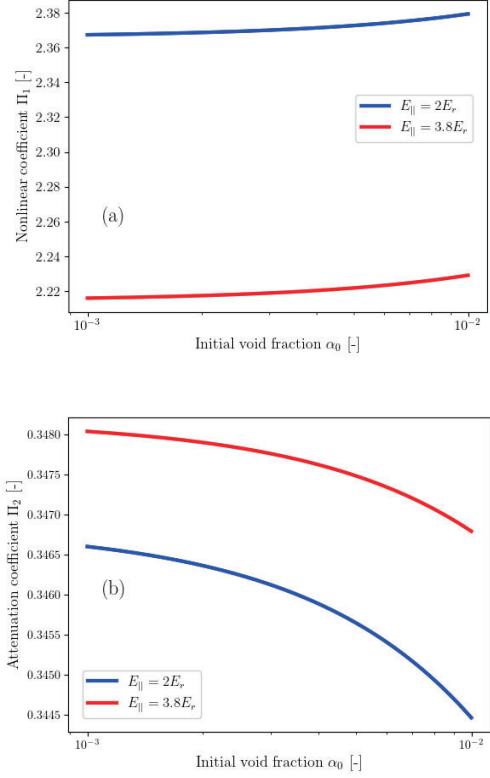


Fig. 2 Coefficients of the KdV-Burgers equation vs initial void fraction  $\alpha_0$  : (a) nonlinearity  $\Pi_1$  and (b) attenuation  $\Pi_2$ .

encapsulated by a purely elastic shell with an anisotropy<sup>5</sup>) was extended to the case of multiple bubbles, and we have derived the equation for a nonlinear propagation of ultrasound in liquid containing multiple encapsulated bubbles<sup>6</sup>).

#### Acknowledgment

This work was partially carried out with the aid of the JSPS KAKENHI (22K03898), based on results obtained from a project subsidized by the New Energy and Industrial Technology Development Organization (NEDO) (JPNP20004), the Komiya Research Grant from the Turbomachinery Society of Japan.

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