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A Physico-mathematical Model for Nonlinear Acoustics of Multiple Ultrasound Contrast Agents with Buckling and Rupture of Membrane

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1. Introduction

As one of the second-generation ultrasound contrast agents (UCAs), phospholipid-shell ultrasound contrast agents have promising potential for various medical applications such as echocardiography, drug and gene delivery, sonoporation, and then has received much attention. Previous studies on the interaction between phospholipid-shell encapsulated microbubbles and ultrasound focused on the behavior of a single phospholipid-shell encapsulated microbubble. A better understanding of the propagation of the ultrasound in liquid containing multiple encapsulated microbubbles has been required to thoroughly utilize and apply UCAs.

The novelty of this study is the inclusion of buckling and rupture of the phospholipid membrane [1] by incorporating the Marmottant-Gompertz model [2] into the multiple scale analysis based on two-phase flow model. As a result, a KdVB (Korteweg-de Vries-Burgers) equation as a weakly nonlinear wave equation for one-dimensional ultrasound in phospholipid-shell encapsulated bubbly liquid is successfully derived. Furthermore, the effect of bucking and rupture of phospholipid membrane on ultrasound propagation is investigated in detail. The result shows that, the characteristics of ultrasound propagation change with the initial surface tension, particularly near the transition of buckled-linear regime and the linear-ruptured regime of phospholipid-shell, where the first-order derivative and the second-order derivative of initial surface tension (i.e., surface elasticity and its first derivative) change rapidly.

2. Problem statement

Nonlinear propagation of an ultrasound in liquid containing multiple phospholipid-shell encapsulated microbubbles, which is characterized by buckling and rupture phenomenon, is investigated theoretically. The main assumptions are summarized as follows: (i) The liquid is slightly compressible; (ii) The initial flow velocities of gas and liquid phases are negligible; (iii) The number of bubbles is constant; (iv) Initially, bubble distribution are spatially uniform; (v) Bubble-bubble interaction, the mass transport across the bubble-liquid interface, the translation of bubbles, and drag force acting on bubbles, are neglected; (vi) The surface tension of shell obeys the Marmottant–Gompertz model [2].

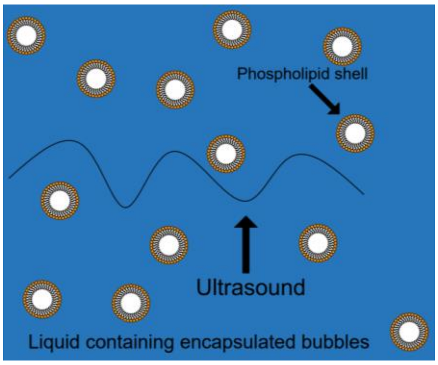

Fig. 1 Schematic of the model.

3. Basic equations

The Marmottant–Gompertz model [2] is used to incorporate the behavior of the surface tension of the phospholipid-shell:

$$\sigma^* = \sigma_{\mathrm{c}}^* \mathrm{e}^{\ln\left(\frac{\sigma_0^*}{\sigma_{\mathrm{c}}^*}\right) \mathrm{e}^{\frac{2\chi^* \mathrm{e}}{\sigma_{\mathrm{c}}^*} \sqrt{1+\frac{\sigma_{\mathrm{c}}^*}{2\chi^*}} \left(\frac{R_0^*}{R_{\mathrm{buck}}^*} - \frac{R^*}{R_{\mathrm{buck}}^*}\right)}}, \tag{1}$$

where σ^* is the surface tension, σ_c^* is the surface tension for bare interface between air and liquid phase (e.g., $\sigma_c^* = 0.072\,[\mathrm{N/m}]$ for air-water interface), σ_0^* initial surface tension, χ^* shell elasticity, R^* bubble radius, R_0^* the initial radius, and R_{buck}^* radius where the shell begins to buckle. Further, equation for balance of normal stresses across the bubble-liquid interface, modified by Marmottant et al. [1]:

$$p_{\mathrm{G}}^* - (p_{\mathrm{L}}^* + P^*) = \frac{2\sigma^*(R^*)}{R^*} + \frac{4\mu^*}{R^*}\frac{\mathrm{D_G} R^*}{\mathrm{D}t^*} + \frac{4\kappa_{\mathrm{s}}^*}{R^{*2}}\frac{\mathrm{D_G} R^*}{\mathrm{D}t^*}, \tag{2}$$

where, μ^* is the liquid viscosity while κ_{s}^* is the shell dilatational viscosity derived for shells with a small but finite and constant thickness.

Subsequently, Eq. (2) is combined with conservation equations of mass and momentum [3], modified Rayleigh–Plesset equation for spherical oscillations of bubbles in slightly compressible liquid [1], equation of state, and with others. Based on the multiple scale analysis, the set of equations is reduced to simplified set by using pertubation expansion. That is, for weakly nonlinear problems, the nonlinear effect becomes apparent at a large

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distance from the sound source relative to the wavelength, denoted far-field. The far-field (i.e., the temporal and spatial scales of O($1/\epsilon$)) is described as,

$$t_1 = \epsilon t, \quad x_1 = \epsilon x, \tag{3}$$

where ϵ is a nondimensional wave amplitude with the assumption ($0 < \epsilon \ll 1$).

4. Result

The Marmottant–Gompertz surface tension is expanded as,

$$\sigma^* = \sigma_0^* \left[1 + \epsilon N_1 R_1 + \epsilon^2 (N_{22} R_2 + N_{21} R_1^2)\right], \tag{4}$$

where explicit forms of N_1, N_{22} and N_{21} are,

$$N_1 = N_{22} \equiv -ln\left(\frac{\sigma_0^*}{\sigma_c^*}\right)\frac{2\chi^* e}{\sigma_c^*}\sqrt{\left(1+\frac{\sigma_0^*}{\chi^*}\right)\left(1+\frac{\sigma_c^*}{2\chi^*}\right)}$$

$$= \frac{1}{\sigma_0^*}\frac{\partial \sigma^*}{\partial\left(\frac{R^*}{R_0^*}\right)} \quad \text{at } \frac{R^*}{R_0^*} = 1, \tag{5}$$

$$N_{21} \equiv \frac{1}{2}\frac{e^2}{\left(\frac{\sigma_c^*}{2\chi^*}\right)^2}\left(1+\frac{\sigma_0^*}{\chi^*}\right)\left(1+\frac{\sigma_c^*}{2\chi^*}\right)\left(ln\frac{\sigma_0^*}{\sigma_c^*} + ln^2\frac{\sigma_0^*}{\sigma_c^*}\right)$$

$$= \frac{1}{\sigma_0^*}\frac{\partial^2 \sigma^*}{\partial\left(\frac{R^*}{R_0^*}\right)^2} \quad \text{at } \frac{R^*}{R_0^*} = 1, \tag{6}$$

Through the linearization of modified Rayleigh-Plesset equation, the eigenfrequency of the bubble is obtained:

$$\omega_{\mathrm{B}}^* = \frac{1}{\rho_{\mathrm{L0}}^* R_0^{*2}}\left[\frac{2\sigma_0^*(N_1)}{R_0^*} + 3p_{\mathrm{G0}}^*\gamma\right], \tag{7}$$

where ρ_{L0}^*, p_{G0}^*, and γ are unperturbed liquid density, initial gas pressure, and polytropic exponent respectively.

Finally, the KdVB equation is derived :

$$\frac{\partial f}{\partial \tau} + \Pi_1 f \frac{\partial f}{\partial \xi} + \Pi_2 \frac{\partial^2 f}{\partial \xi^2} + \Pi_3 \frac{\partial^3 f}{\partial \xi^3} = 0, \tag{8}$$

where Π_1, Π_2, and Π_3 represent nonlinear effect, attenuation effect, and dispersion effect, respectively; τ is time variable and ξ is space variable from variable transformation:

$$\tau \equiv \epsilon t, \quad \xi \equiv x - \left(v_{\mathrm{p}} + \epsilon \Pi_0\right)t, \tag{9}$$

where the phase velocity v_{p} and advection effect Π_0 are given by

$$v_{\mathrm{p}} = \sqrt{\frac{3\alpha_0(1-\alpha_0+\beta_1)\gamma p_{\mathrm{G0}}/\rho_{\mathrm{L0}}^* + \beta_1(1-\alpha_0)R_0^{*2}\omega_{\mathrm{B}}^{*2}}{3\beta_1\alpha_0(1-\alpha_0)U^{*2}}}, \tag{10}$$

$$\Pi_0 = -\frac{1}{6\alpha_0}(1-\alpha_0)\frac{)R_0^{*2}\omega_{\mathrm{B}}^{*2}}{U^{*2}}, \tag{11}$$

Where α_0 is the initial void fraction, virtual mass coefficient β_1 = 0.5 is used for spherical bubble case, and U^* is typical propagation speed.

The explicit form of nonlinear coefficient is,

$$\Pi_1 = \frac{1}{6}\left[k_1 - \frac{k_2}{\alpha_0} + \frac{(1-\alpha_0+\beta_1)k_3}{\beta_1(1-\alpha_0)} + \frac{k_4}{\alpha_0(1-\alpha_0)} - \frac{R_0^{*2}\omega_{\mathrm{B}}^{*2}}{U^{*2}}\frac{2k_5}{\alpha_0}\right], \tag{12}$$

where, the expressions of k_1, k_2, k_3 and k_4 are identical with their counterparts in our previous study for uncoated bubble [3]. Since there is a shift of the eigenfrequency ω_{B}^* to higher value due to the initial elastic coefficient (i.e., $\sigma_0^* N_1$) , the values of k_1, k_2, k_3 and k_4 are different from those for free bubble case. The expression of k_5, however, is different from its counterpart and is given by

$$k_5 = \frac{U^{*2}}{R_0^{*2}\omega_{\mathrm{B}}^{*2}}\left[\frac{3\gamma(3\gamma+1)p_{\mathrm{G0}}}{2} - \left(\frac{R_0^{*2}\omega_{\mathrm{B}}^{*2}}{U^{*2}} - 3\gamma p_{\mathrm{G0}}\right) \times \frac{N_{21} - N_1^2 + 1}{N_1 - 1}\right], \tag{13}$$

where $p_{\mathrm{G0}} \equiv p_{\mathrm{G0}}^*/\left(\rho_{\mathrm{L0}}^* U^{*2}\right) \equiv O\,(1)$ is nondimensional pressure for the gas phase.

The expression of k_5 shows that there is also the contribution of N_{21}. In the transition regime of buckled state to elastic state, $\sigma_0^* N_1$ change rapidly from zero to $\chi*$ (i.e., $\sigma_0^* N_{21}$ is positive) while in the transition regime of elastic state to ruptured state, $\sigma_0^* N_1$ change rapidly from $\chi*$ back to zero (i.e., $\sigma_0^* N_{21}$ is negative). These rapid rates of change result in the dominance of $\sigma_0^* N_{21}$ in nonlinear coefficient.

5. Summary

A KdVB equation for nonlinear propagation of ultrasound in liquid containing multiple phospholipid-shell encapsulated bubbles is derived. The buckling and rupture phenomenon of the shell is incorporated into the study by using Marmottant-Gompertz surface tension model. The result shows that the buckling and rupture phenomenon affect the nonlinear coefficient through the increase of eigenfrequency caused by elastic coefficient. Moreover, the behavior of nonlinear term is also significantly affected by the rate of change of elastic coefficient. A quantitative discussion will be provided in a presentation.

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References

1. P. Marmottant et al : J. Acoust. Soc. Am. **118.6** (2005) 3499.
2. J. Gümmer, S. Schenke and F. Denner: Ultrasound Med Biol. **47(10)** (2021) 2958.
3. Kanagawa: J.Acoust. Soc. Am. **137** (2015), 2642.