NONLINEAR PROPAGATION IN ULTRASOUND CONTRAST AGENT

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ABSTRACT : An analytical model for second harmonic propagation in ultrasound contrast agent is proposed in the parabolic and quasilinear approximations. This model takes into consideration attenuation, diffraction and nonlinear effects together with dispersion and additional nonlinearity due to bubbles. The fundamental and second harmonic ultrasonic fields radiated by a plane piston source are calculated as the superposition of Gaussian beams.
Axial evolutions of fundamental and harmonic are investigated for various frequencies. For particular frequencies, fundamental and second harmonic rapidly vanish with range. From harmonic evolution, we investigate the balance between nonlinearity and dispersion.

INTRODUCTION

With the appearance of harmonic imaging in echographic imaging, there have been more and more investigations in the field of nonlinear propagation of finite amplitude waves. The performances of this method depend on the importance of the nonlinearity of the propagating medium. In the particular case of ultrasound contrast agent, this nonlinearity may be dramatically increase. In addition to dispersion, the presence of bubbles creates indeed an additional nonlinearity coming from bubbles oscillations that exceed the one due to liquid alone.

This works presents an analytical model that calculates spatial evolutions of fundamental and second harmonic in ultrasound contrast agent in the quasilinear approximation. The model is based on a KZK equation where are integrated diffraction, attenuation and nonlinearity together with dispersion due to bubbles.

In a first stage, the nonlinear propagation equation is presented for dispersive medium such as bubbly liquids. An analytical model is presented that expresses harmonic fields in ultrasound contrast agent as the superposition of Gaussian beams. The axial evolutions of fundamental and second harmonic components are presented for various ultrasonic frequencies. Second harmonic generation is analysed in detail, and the contributions of both dispersion and nonlinearity are specially discussed.

PROPAGATION EQUATION IN BUBBLY LIQUID

Non Bubbly Liquid:

In case of non dispersive medium, the well-known KZK equation is the simplest nonlinear equation taking into account the combined effects of attenuation, diffraction and nonlinearity. It can be expressed, for a beam propagating in the *z* direction, as [1]:

$$\frac{\partial^2 p}{\partial z \partial \tau} = \frac{c_0}{2}\nabla_\perp^2 p + \frac{\delta}{2c_0^3}\frac{\partial^3 p}{\partial \tau^3} + \frac{\beta}{2\rho_0 c_0^3}\frac{\partial^2 p^2}{\partial \tau^2}, \tag{1}$$

where $\tau = t - z/c_0$ is the retarded time, $\nabla_\perp^2 = \partial^2/\partial x^2 + \partial^2/\partial y^2$ is the transverse Laplacian, $\beta = 1 + B/2A$, with B/A the nonlinear parameter, while δ, c_0 and ρ_0 are respectively the diffusivity of sound, the sound velocity and the density of the medium.

Bubbly Liquid :

The previous KZK equation has been generalised and extended to the case of dispersive medium such as bubbly liquid by Hamilton and al. [2,3].

$$\frac{\partial^2 p}{\partial z \partial \tau} = \frac{c_0}{2}\nabla_\perp^2 p + \frac{\partial D(p)}{\partial \tau} + \frac{\beta_2}{2\rho_0 c_0^3}\frac{\partial^2 p^2}{\partial \tau^2}. \tag{2}$$

It has been introduced an operator *D(p)* to take into account dispersion effects [2]:

$$D(p_n) = -\alpha'_n q_n e^{jn\omega\tau}, \tag{3}$$

with the complex attenuation coefficient at frequency $n\omega$:

$$\alpha'_n = \alpha_n + j\left(k_n - n\omega/c_0\right), \tag{4}$$

where α_n is the attenuation coefficient, and $k_n = n\omega/c_n$ the wave number at frequency $n\omega$.

For particular case of bubbly liquids, the presence of bubbles is not only synonymous with dispersion, but also with an additional source of nonlinearity coming from the dynamic nonlinearity of the bubbles oscillations [4]. This nonlinearity arising from bubbles is expressed in propagation equation (Eq.2) with a coefficient of nonlinearity β_2 instead of β for water only.

ATTENUATION, PHASE SPEED AND NONLIEARITY PARAMETER IN CONTRAST AGENT

Let consider a liquid (sound velocity c_0, density ρ_0, nonlinear parameter β and hydrostatic pressure P_0) contain encapsulated bubbles (surface tension coefficient σ, polytropic exponent coefficient of the gas K, shell elasticity parameter S_p). The distribution of bubbles is supposed to be polydisperse [5] (*i.e.* with $N(R_0)dR_0$ bubbles per unit volume having equilibrium radius between R_0 and $R_0 + dR_0$).

Previous studies [1,6] on bubbly liquids have defined the expressions of complex celerity (Eq.5) and nonlinearity parameter (Eq.6) by identification with classical nondispersive nonlinear acoustics.

$$\frac{1}{\tilde{C}_n^2} = \frac{1}{c_0^2} + 4\pi\int_0^\infty \frac{N(R_0)R_0\,dR_0}{\omega_0^2 + \omega_1^2 - (n\omega)^2 + jn\omega^2\delta}, \tag{5}$$

$$\beta_2(\omega) = \beta + (4\pi)^2 c_0^4 \int_0^\infty \frac{(a + d - 3b\omega^2 + 2j\delta\omega^2)N(R_0)R_0^2 dR_0}{(\omega_0^2 + \omega_1^2 - \omega^2 + j\omega^2\delta)(\omega_0^2 + \omega_1^2 - 4\omega^2 + 2j\omega^2\delta)}, \tag{6}$$

with resonance frequency for free bubbles $\omega_0^2 = 3K(P_0 - P_g + 2\sigma / R_0)/ \rho_0 R_0^2$, additional stiffness due to encapsulation $\omega_1^2 = 2(S_p - \sigma)/ \rho_0 R_0^3$, and terms $b = (8\pi R_0^3)^{-1}$, $a = 3b(K+1)\omega_0^2$, $d = 4b\omega_1^2$. The total damping coefficient $\delta = \delta_{vis} + \delta_{rad} + \delta_{th} + \delta_{elas}$ includes viscous, re-radiation, thermal and elastic contributions [7,8,9] for encapsulated bubbles.

Phase speed c_n and attenuation coefficient α_n can be deduced from complex celerity $\tilde{C}_n$ (Eq.6) setting [1]:

$$c_n = Re^{-1}(\tilde{C}_n^{-1}), \text{ and } \alpha_n = -n\omega \,\mathrm{Im}(\tilde{C}_n^{-1}). \tag{7}$$

CALCULATION OF PRESSURE BEAMS

General analysis:

To obtain the expressions of fundamental and second harmonic, for an axisymmetric source, pressure p is defined in quasilinear theory using the method of successive approximations as :

$$p = \frac{1}{2}\left\{q_1(r,z)e^{j\omega t} + q_2(r,z)e^{j2\omega t}\right\} + cc, \tag{8}$$

where p_1 is linear solution, p_2 second order correction term ($|p_2| << |p_1|$) and cc denotes complex conjugate term [1].

Substituting. (Eq.8) into (Eq.2) yields for fundamental (Eq.9) and second harmonic (Eq.10):

$$\frac{\partial q_1}{\partial z} + \frac{j}{2k_1}\nabla_\perp^2 q_1 + \alpha'_1 q_1 = 0, \tag{9}$$

$$\frac{\partial q_2}{\partial z} + \frac{j}{2k_2}\nabla_\perp^2 q_2 + \alpha'_2 q_2 = \frac{\beta_2 k_1}{2\rho_0 c_0^2} q_1^2. \tag{10}$$

Solutions of these equations can be constructed with Green's functions G_n [1]:

$$q_1(r,z) = 2\pi \int_0^\infty q_1(r',0) G_1(r,z|r',z') r' dr' \tag{11}$$

$$q_2(r,z) = \frac{\pi \beta_2 k}{\rho_0 c_0^2} \int_0^z \int_0^\infty q_1^2(r',z') G_2(r,z|r',z') r' dr' dz', \tag{12}$$

with

$$G_n(r,z|r',z') = \frac{jnk}{2\pi(z-z')} J_0\left(\frac{nkrr'}{z-z'}\right) \exp\left[-\alpha'_n(z-z') - \frac{jnk(r^2 + r'^2)}{2(z-z')}\right]. \tag{13}$$

Once (Eq.9) solved for a known source function $q_1(r,0)$, the expression of fundamental is thus determined and injected in (Eq.10) to obtain second harmonic component.

Gaussian Beam Expansion

The source term of a circular plane piston with a characteristic radius a, delivering a pressure P_0, is expressed as the superposition of Gaussian functions [10]:

$$q_1(r,0) = \sum_n q_{1n}(r,0) = \sum_n B_n \exp\left[-(r/a)^2\right]. \tag{14}$$

The values of n and amplitudes of Gaussian sources are selected to fit the aperture function of the transducer. The A_n and B_n coefficients are analogous to the optimised coefficients set given by Wen and Breazeale [10]:

$$A_n = \frac{a}{\sqrt{B_n^{Wen}}} \quad , \qquad \text{and } B_n = P_0 A_n^{Wen} . \tag{15}$$

From the principle of linear superposition, if an axial symmetric source is decomposed in a series of Gaussian functions, the fundamental field can also be expressed as a linear combination of the fields radiated by these Gaussian sources [10]:

$$q_1(r,z) = \sum_n q_{1n}(r,z) = \sum_n B_n \frac{e^{-\alpha'_1 z}}{1 - jz/z_0} \exp\left[-\frac{(r/a)^2}{1 - jz/z_{0n}} \right] , \tag{16}$$

with a different Rayleigh distance for each Gaussian source $z_{0n} = k_1 A_n^2 / 2$.

Substituting (Eq.14) into (Eq.7) gives for second harmonic field [6,11]:

$$q_2(r,z) = \frac{\beta_2 k_1}{2\rho_0 c_0^2} e^{-\alpha'_2 z} \sum_n \sum_{n'} B_n B_{n'} \int_0^z \bar{q}_{nn'}(z,z',r)dz' \quad , \tag{17}$$

with

$$\bar{q}_{nn'}(r,r',z) = \frac{e^{-(2\alpha'_1 - \alpha'_2)z'}}{c_{nn'}z' + d_{nn'}} \exp\left[-r^2 \left(a_{nn'}z' + b_{nn'} \right) / \left(c_{nn'}z' + d_{nn'} \right) \right] , \tag{18}$$

where $a_{nn'}, b_{nn'}, c_{nn'}, d_{nn'}$ can be expressed as functions of A_n and $A_{n'}$:

$$a_{nn'} = -\frac{4j}{kA_n^2 A_{n'}^2} , \qquad b_{nn'} = \frac{A_n^2 + A_{n'}^2}{A_n^2 A_{n'}^2} , \qquad c_{nn'} = -\frac{i}{k}(b_{nn'} + a_{nn'}z) , \qquad d_{nn'} = 1 - \frac{i}{k} b_{nn'} z . \tag{19}$$

Second harmonic is thus a linear summation of self- and cross-interaction terms of the Gaussian beams.

THERORETICAL RESULTS

Simulations have been led for Albunex® with volume fraction of gas $\eta = 10^{-5}$, and shell parameters defined by De Jong [9]: $S_p = 8 N.m^{-1}, S_f = 4.10^{-6} kg.s^{-1}$.

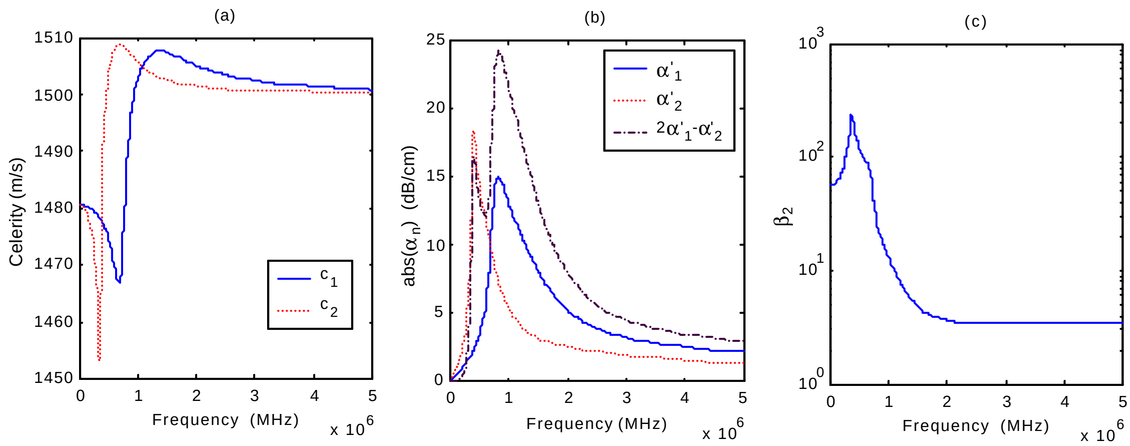

Figure 1: Evolutions with frequency of celerity (a), attenuation (b) and nonlinearity parameter (c) for Albunex® solution with a volume fraction $\eta = 10^{-5}$.

Evolutions of phase speed, attenuation and nonlinearity parameter are presented Fig.1.
As expected, celerity (Fig.1a) and attenuation (Fig.1b) show the most important variations around bubbles resonance (0.8 MHz) [6].
Nonlinear parameter b_2 presents two resonances (Fig.1c) [6]. The higher one occurs when the frequency of incident acoustic wave coincides with the bubbles resonance frequency. The lower resonance appears when second harmonic frequency matches the bubbles resonance one. It rises values of 250, greater than for pure water ($b = 3.5$).

Axial evolutions of pressure component are presented (Fig. 2) for fundamental and second harmonic for various frequencies from 0.1 (a) to 5 MHz (h).

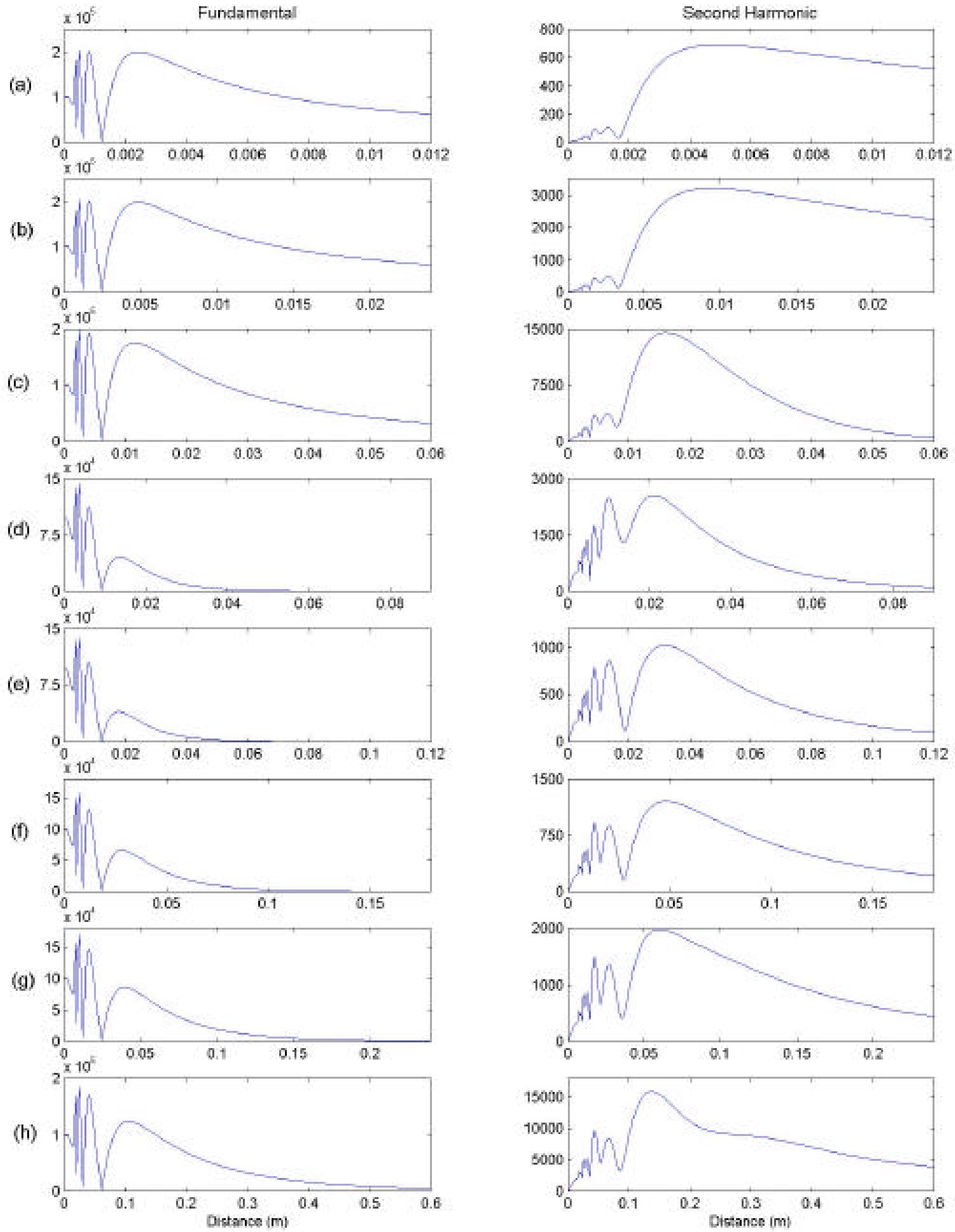

Figure 2 : Axial evolutions of pressure (Pa) for fundamental (left column) and second harmonic (right column) for Albunex solution ($\eta=10^{-5}$). These evolutions are presented for various driven acoustic frequencies: 0.1 (a), 0.2 (b), 0.5 (c), 0.75 (d), 1 (e), 1.5 (f), 2 (g), and 5 (h) MHz.

The evolution of the fundamental component of pressure is simple to analyse. For frequencies of 0.1, 0.2 and 0.5 MHz, (below the resonance frequency of contrast agent), fundamental component is not very affected by the presence of bubbles. Ultrasonic frequencies of 0.75 and 1

MHz are around resonance frequency. Dispersion effects are then maximum, and pressure level are strongly attenuated. Then, as ultrasound frequency increases (1.5 to 5 MHz), attenuation gradually decreases, and the pressure level are less affected.

For second harmonic, analysis is more complicated. The second harmonic is indeed proportional (Eq.17) to β_2, $\exp(\alpha'_2 z)$ and $\exp((2\alpha'_1 - \alpha'_2)z)$, whose evolutions are presented on (Fig.1). It is thus necessary to consider simultaneously the evolution of nonlinear parameter which governs harmonic growth, and phenomena of dispersion.
Ultrasonic frequencies of 0.1 and 0.2 MHz are far from bubbles resonance, and dispersion effects are weak. Second harmonic thus moves proportionally with β_2 (greater than for water).
For ultrasonic frequency of 0.5 MHz, its harmonic component frequency amounts to 1 MHz, close to the resonance frequency of the bubbles. β_2 is maximum and there is a strong growth of the harmonic (to 0.15 bar). However, nonlinear effect is limited to distances close to transducer, because the strong attenuation created by resonant bubbles makes pressure levels quickly fall.
Then, as ultrasound frequency increases (0.75-1MHZ), harmonic component moves from resonance. Both nonlinearity parameter and attenuation rapidly decrease. However, fundamental component coincides with bubbles resonance. The attenuation term $\exp((2\alpha'_1 - \alpha'_2)z)$ is maximum (Fig.1b). Harmonic pressure levels are then minimum.
From 1.5 MHz, second harmonic levels are not very affected by the presence of bubbles.

CONCLUSION

An analytical model, based on the superposition of Gaussian beams, has been presented to investigate nonlinear propagation in contrast agents. Dispersion and additional nonlinearity due to bubbles have been integrated and calculated considering the particularities and characteristics of ultrasound contrast agent (bubbles distribution, encapsulation …). The axial evolutions of fundamental and second harmonic component have been presented for various frequencies. It has been shown that the increase in second harmonic, due to nonlinearity is counterbalanced by a strong decrease imposed by dispersion.

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