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An iterative fullwave simulation approach to multiple scattering in media with randomly distributed microbubbles

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Abstract

Ultrasound contrast agents (UCA), such as microbubbles, enhance the scattering properties of blood, which is otherwise hypoechoic. The multiple scattering interactions of the acoustic field with UCA are poorly understood due to the complexity of the multiple scattering theories and the nonlinear microbubble response. The majority of bubble models describe the behavior of UCA as single, isolated microbubbles suspended in infinite medium. Multiple scattering models such as the independent scattering approximation can approximate phase velocity and attenuation for low scatterer volume fractions. However, all current models and simulation approaches only describe multiple scattering and nonlinear bubble dynamics separately. Here we present an approach that combines two existing models: (1) a full-wave model that describes nonlinear propagation and scattering interactions in a heterogeneous attenuating medium and (2) a Paul–Sarkar model that describes the nonlinear interactions between an acoustic field and microbubbles. These two models were solved numerically and combined with an iterative approach. The convergence of this combined model was explored *in silico* for 0.5×10^6 microbubbles ml^{-1} , 1% and 2% bubble concentration by volume. The backscattering predicted by our modeling approach was verified experimentally with water tank measurements performed with a 128-element linear array transducer. An excellent agreement in terms of the fundamental and harmonic acoustic fields is shown. Additionally, our model correctly predicts the phase velocity and attenuation measured using through transmission and predicted by the independent scattering approximation.

Keywords

multiple scattering; contrast agent microbubbles; full-wave equation; finite difference time domain (FDTD)

Introduction

The ability of microbubbles to increase the intensity of backscattered signal from blood was first reported in 1968 (Gramiak 1968) during cardiac catheterization when contrast

phenomena in the aorta were observed due to the formation of gas cavities from the injection of saline solution. Over the past five decades there have been significant advances in application of ultrasound contrast agents (UCA). Encapsulated gas microbubbles, are widely used in diagnostic ultrasound to enhance blood-tissue contrast (Becher *et al* 2000, Goldberg 2001, Szabo 2004). They are also employed in therapy as an activator of drug incorporation or extravasation (Klibanov 2006). These microbubbles have a typical diameter on the order of a few micrometers and are enclosed in a shell of albumin, polymer, or lipid to stabilize them and prevent fast dissolution and coalescence. Many advances and efforts in the past decade have been concentrated around modeling the response and behavior of microbubbles when they are insonified with ultrasound pulses. These models have their origins in the Rayleigh–Plesset–Noltingk–Neppiras–Poritsky (RPNNP) equation, (Rayleigh 1917, Plesset 1949, Neppiras and Noltingk 1951, Noltingk *et al* 1950, Leighton 1994) which models the radial oscillations of an ideal gas bubble in an infinite incompressible liquid subjected to an acoustic field. Since the RPNNP model is based on the assumption that the surrounding liquid is incompressible, radiation damping is neglected in this model.

Subsequent models proposed by Herring (1941) and Trilling (1952), Keller–Miksis (Keller *et al* 1956, Keller and Miksis 1980) and Prosperetti (1994) account for radiation damping. De Jong’s model (de Jong *et al* 1992, 1994a, 1994b, de Jong and Hoff 1993) and Church’s model (Crum *et al* 1992, Church 1995) are two fundamental models that account for the effects of encapsulation. De Jong’s model assumes infinitesimal shell thickness whereas Church’s model was derived to account for variations in shell thickness. Both these models assume that the liquid surrounding the bubble is incompressible. Recent models which includes model by Morgan *et al* (2000), Hoff *et al* (2000), Marmottant *et al* (2005) and Doinikov *et al* (2007), consider the surrounding liquid as slightly compressible. A model proposed by Morgan *et al* was the first model to require experimental determinations of unknown shell parameters. The Chatterjee–Sarkar model (Chatterjee and Sarkar 2003) predicts the response of lipid shelled microbubbles to low amplitude acoustic pulses.

All these models, including the Chatterjee–Sarkar model, are based on curve fitting of the experimental observations. They assume a Newtonian behavior of the encapsulating shell. They can accurately predict the response of a microbubble to a low amplitude perturbation. The model we have used for this work was developed by Paul *et al* (2010) and is based on the Chatterjee–Sarkar model. It describes the radial motion of the microbubble as follows:

$$R\ddot{R} + \frac{3}{2}\dot{R}^2 = \frac{1}{\rho} \left[P_{G_0} \left(\frac{R_0}{R} \right)^{3\kappa} \left(1 - \frac{3\kappa\dot{R}}{c_0} \right) - 4\eta_L \frac{\dot{R}}{R} - P_0 - P_{ac}(t) - 4\kappa_s \frac{\dot{R}}{R^2} - \frac{2\sigma(R)}{R} \right]. \quad (1)$$

Here $R(t)$ is the instantaneous radius of the bubble, ρ is the equilibrium density of the surrounding liquid, $P_{G_0} = P_0 - P_v + 2\sigma/R_0$ is the equilibrium pressure inside the bubble; R_0 is the bubble radius at rest; κ is the polytrophic exponent of the gas; P_v is the vapor pressure inside the bubble; σ is the surface tension for the liquid–gas interface; η_L is the dynamic viscosity of the liquid; P_0 is the hydrostatic pressure in the liquid; and $P_{ac}(t)$ is the driving acoustic pressure. The choice of a polytrophic exponent is based on the Peclet number to

account for thermal damping. The term $4\eta_L \frac{\dot{R}}{R}$ models damping from the viscosity of the surrounding liquid. κ_s is the dilatational viscosity that accounts for the viscosity of the polymer shell. $\sigma(R)$ is a non-linear function of the bubble radius. It is given as follows:

$$\sigma(R) = \sigma_0 + \frac{E^S(R^2 - R_E^2)}{R_E^2}. \quad (2)$$

Here E^S is the dilatational elasticity that accounts for the elastic behavior of the polymeric shell. σ_0 is the reference surface tension at unstrained position and R_E is corresponding radius. This model (henceforth referred to as the Paul–Sarkar model) accounts for compression only behavior observed with the microbubbles (Li 2013). It is valid for both small and large amplitude acoustic fields. Unlike previous models E^S was not assumed to be constant. Rather, it was assumed to be a function of the relative change in surface area $E^S = E^S(\beta)$ where $\beta = dA/A = (R^2/R_E^2) - 1$. A is the surface area of the microbubble. Two models were proposed for $E^S(\beta)$.

The quadratic elasticity model (QEM):

$$E^S(\beta) = E_0^S - E_1^S \beta \text{ for } E_0^S - E_1^S \beta > 0 \quad (3)$$

$$E^S(\beta) = 0 \text{ for } E_0^S - E_1^S \beta < 0. \quad (4)$$

The exponential elasticity model (EEM):

$$E^S(\beta) = E_0^S \exp(\alpha_s \beta). \quad (5)$$

We used the exponential elasticity model because it is continuous and differentiable and it accurately describes compression only behavior of the microbubbles at high amplitude.

Experimentally determined constants are α_s (decay constant) and E_0^S (reference dilatational elasticity) for EEM and E_0^S (reference dilatational elasticity) and E_1^S (rate of change of dilatational elasticity with respect to relative changes in surface area) for QEM. For a 10 MHz pulse, figure 1 shows the response of a 2 micron diameter microbubble. The constants used were $\sigma_0 = 0.02 \text{ N m}^{-1}$, $E_0^S = 0.07 \text{ N m}^{-1}$, $\alpha_s = 1.5$ and $\kappa_s = 7.5 \times 10^{-9} \text{ N s m}^{-1}$ and were obtained in the literature (Paul *et al* 2013).

Knowing the radial displacement and radial acceleration, one can determine the scattered pressure from the bubble surface with the relation

$$P_s(r, t) = \rho \frac{R}{r} (2\dot{R}^2 + R\ddot{R}). \quad (6)$$

These models describe the behavior of a single microbubble in an infinite homogeneous medium when subjected to an acoustic pulse. In general, the oscillations of a microbubble are non-linear in nature. It has already been demonstrated that significant multiple scattering can occur in a large population of bubbles (Stride *et al* 2005). Thus, in order to accurately simulate the wave propagation through a medium with randomly distributed microbubbles, it is necessary to account for non-linearity, multiple scattering and inhomogeneity.

Finite difference time domain methods have previously been used to solve 3D linear wave equations in inhomogeneous media (Mast *et al* 1997, 2002). The non-linear wave equation has also been solved with finite differences but in a retarded time form and within the paraxial approximation that assumes that the field variations in the transverse direction are very slow compared to the field variations in the axial direction (Zabolotskaya 1969). The full-wave equation does not rely on this approximation and describes the nonlinear propagation in a heterogeneous attenuating medium

$$\nabla^2 p - \frac{1}{c_0^2} \frac{\partial^2 p}{\partial t^2} + \frac{\delta}{c_0^4} \frac{\partial^3 p}{\partial t^3} + \frac{\beta}{\rho c_0^4} \frac{\partial^2 p^2}{\partial t^2} + \frac{1}{\rho} \nabla p \cdot \nabla \rho - \sum_{m=1}^v \xi_m = 0. \quad (7)$$

Here, the first two terms represent the linear wave equation and the remaining three terms account for thermoviscous diffusivity, nonlinearity and relaxation respectively. The relaxation term ξ_m should satisfy the equation

$$\dot{\xi}_m + \omega_m \xi_m = a_m \omega_m \frac{\Delta c}{c_0} \nabla^2 p. \quad (8)$$

Here, p is the acoustic pressure, c_0 is the equilibrium sound speed, ρ is the equilibrium density, δ is the acoustic diffusivity and β is the non-linearity coefficient. Relaxation equation has v peaks at frequencies ω_m . Weight a_m depends upon frequency and is also dependent upon the particular attenuation law modeled. Change in velocity c must obey the Kramers–Kronig relation to preserve causality. A detailed implementation of the relaxation term is explained by Pinton *et al* (2009). The diffusivity is a function of the absorption coefficient α and the angular frequency ω as:

$$\delta = \frac{2\alpha c_0^3}{\omega^2}. \quad (9)$$

The full-wave equation accounts for medium nonlinearity, attenuation, and all wave effects, such as multiple scattering, reflection, and refraction. The full-wave equation was solved with the finite difference time domain method by Pinton *et al* (2009) which we will refer to

as the Fullwave simulation tool. The advantage of using the full-wave equation is that it accurately describes an ultrasonic beam in the off-axis region and is valid for arbitrary scatterers in the field. Additionally, it is implemented in a way that it allows additive sources to be placed in the medium enabling any point of the domain to act as a secondary acoustic source. It has been validated for long-range propagation such as in imaging (Pinton *et al* 2011).

The proposed iterative simulation approach in this paper combines the Paul–Sarkar model describing the acoustic radiation by individual bubbles and the Fullwave simulation tool modeling the interactions between the acoustic field and microbubbles during propagation through media containing a population of randomly distributed microbubbles.

Methodology

In this simulation, we generated an acoustical map containing microbubbles randomly distributed with a controlled volume fraction. To ensure uniform distribution of microbubbles in the tubes, the computational grid was divided several sub-sections of 10×10 pixels and centers of microbubbles were randomly placed in each of these sub-sections. 1%, 2% and 0.5% distribution were generated by generating 1 microbubble per sub-section, 2 microbubbles per sub-section and 1 microbubble per 2 subsections (microbubbles were generated in 1 randomly selected subsection amongst two neighboring subsections) respectively. The homogeneous medium in which the microbubbles were distributed had the properties of water for all simulations discussed in this paper. The proposed iterative multi-step approach first treats the bubbles as conventional (linear) scatterers in the 0th iteration (shown in the figure 2). A 10 MHz 3-cycle Gaussian pulse with peak negative pressure of 600 kPa is transmitted in the medium. During this first step, the pressure at each bubble's surface is recorded. Then, using equations (3), (4) and (7) and using constants $\gamma_0 = 0.02 \text{ N m}^{-1}$, $E_0^S = 0.07 \text{ N m}^{-1}$, $\alpha = 1.5$ and $\kappa^S = 7.5 \times 10^{-9} \text{ N s m}^{-1}$, the radial displacement of each microbubble is evaluated. The radiated pressure by each microbubble is evaluated using equation (6). In the 1st iteration, these pressure signals are included as additive sources at each bubble location and ultrasound propagation is again simulated just like in the 0th iteration. Then, the pressure at each bubble's surface is recorded again. The same procedure is repeated over all the iterations to account for all multiple scattering interactions and the additive source term is modified for every subsequent iteration. The corrected radiated pressure is evaluated for every iteration following the same procedure. This iterative approach allowed us to account for multiple scattering interactions between microbubbles.

We conducted a set of 2D simulations to model the backscattering of ultrasound by randomly distributed microbubbles in a set of acoustically transparent tubes. The simulation setup is shown in the figure 3(a). To validate the convergence of the proposed simulation approach, we carried out 20 iterations. An array of 64 elements was simulated. In each simulation, only one of the 64 elements was used to transmit an acoustic pulse with a central frequency of 10 MHz and all 64 transducer elements were used to receive the backscattered signals. All of the elements of the array were consecutively used as transmitters one by one, until a $64 \times 64 \times N$ matrix was obtained where N is the number of time points. This matrix is referred to as the inter-elemental matrix. The grid size used was 2.13 micron (90 points per

wavelength) for these simulations. The simulations were conducted for 0.5% (5×10^7 microbubbles ml^{-1}), 1% (10^8 microbubbles ml^{-1}) and 2% (2×10^8 microbubbles ml^{-1}) bubble concentration by volume. These concentrations are based on clinically relevant concentrations (Appis *et al* 2015). The width of each transducer element was 300 microns. The dimension of the medium was 19.2×4.8 mm. The width of each tube was 200 microns and the center-to-center distance between neighboring tubes was 250 microns. Perfectly matched layer (PML) boundary conditions were applied at all four boundary surfaces to avoid surface reflections. The incident acoustic pressure on one bubble in the medium, while simulating propagation of ultrasound through the medium with 1% bubble concentration, and the corresponding scattered pressure from the bubble surface for Iteration #1 and Iteration #2 are shown in figure 4. After each iteration, the scattered pressure is evaluated at each bubble surface and it is used as a source term for the next iteration. Attached video (Mm 1 (stacks.iop.org/PMB/62/4202/mmedia)) shows multiple scattering by microbubbles after 20 iterations for a simulation with 2% bubble concentration by volume when emitter no 33 is transmitting the pulse.

To evaluate the accuracy with which this model can estimate the inter-elemental matrix, we conducted an experiment that mimics the simulation setup using a set of cellulose tubes of 200 micron diameter each with neighboring tubes separated by a distance of 250 microns. As in the simulation, we used five tubes in the experiment. A 128-element linear transducer array (L11-4v, Verasonics, Seattle, WA), was used for this experiment. Bubbles were injected slowly in all tubes simultaneously using a single syringe to ensure that they were equally distributed in the tubes. The data acquisition sequence described previously for the simulations was used in the experiments to acquire and inter-elemental matrix of dimensions $128 \times 128 \times N$. The experimental setup is shown in figure 3(b).

Lipid shelled microbubbles were fabricated according to a method described by Streeter *et al* (2010). The distribution of microbubble diameters was centered at approximately 1 micron (Accusizer 780A, PSS-NICOMP, Port Richey, FL). To compare the simulation and experimental results, we only used the data transmitted and collected by the central 64 elements of the linear array. The experimental data was resampled so that both datasets had the same time step.

To further validate our simulation approach, we simulated the propagation of a plane wave through the medium to measure the phase velocity and attenuation coefficient. In a heterogeneous medium, when one of the components is highly compressible compared to the other (in this case, the microbubbles are significantly more compressible than the surrounding water), the resulting acoustic velocity is much less than the acoustic velocity in each of the individual media. This was first observed by Wood (1955) while studying the transmission of acoustic signals through curtains of bubbles in water. Using Wood's theory, the velocity in the heterogeneous medium can be predicted

$$c = \sqrt{\frac{E_f E_a}{[x E_f + (1-x) E_a] [x \rho_a + (1-x) \rho_f]}} \quad (10)$$

where c is velocity of sound, x is the volume fraction of air, ρ_a and ρ_f are densities of fluid and air respectively and E_f and E_a are bulk modulus of fluid and air respectively. However, Wood's theory does not account for dispersion. Wood's theory gives a reasonable estimate of velocity at low microbubble concentrations but is not accurate in presence of significant multiple scattering. A validated approach to predict the velocity and attenuation of ultrasound is the independent scattering approximation (ISA). To predict the velocity using the ISA, we conducted a reference simulation with no scatterers and another simulation with a single scatterer (bubble) to calculate the normalized forward scattering intensity. From this, the effective wave number for a given volume fraction of scatterers can be evaluated (Mézière *et al* 2014), which gives access to the phase velocity and attenuation.

The detailed procedure to determine the velocity and attenuation using the ISA is described in Meziere *et al* (2014). As the emitted signal is a pulse centered at 10 MHz with a -6 dB bandwidth of around 100%, we limited our study to the 5–15 MHz frequency range. The transmitted signals were recorded for each simulation and experiment at various depths and by performing fast Fourier transforms (FFT) the signal was converted into the frequency domain, in which the phase velocity was calculated by unwrapping the phase angle $\varphi_\omega(z)$ of the frequency domain signal $s_\omega(z)$ as,

$$\varphi(z) = \arg(s_\omega(z)) = \varphi(0) + kz \quad (11)$$

where z is the depth at which transducer was placed. The phase velocity can be calculated as follows:

$$v(\omega) = \frac{\omega}{k(\omega)}. \quad (12)$$

The attenuation coefficient $\alpha(\omega)$ can be computed by assuming an exponential decay as follows:

$$|s(\omega)| = e^{-\alpha(\omega)z}. \quad (13)$$

Results and discussion

After completing 20 iterations of the simulation, we calculated the correlation coefficients between the scattered pressure on the surface of a particular bubble for a particular iteration with the corresponding scattered pressure after the 20th iteration. Averaging the correlation coefficients over all the bubbles for a particular iteration yields the average correlation coefficient for that particular iteration. The convergence plots for each of the simulation are shown in figure 5(a). Within eight iterations the correlation coefficient was higher than 0.99 for all simulations.

Another way of assessing the convergence of the simulation approach is to evaluate the convergence of the intensity of the pressure radiated by each bubble during a particular

iteration compared to the 20th iteration. Figure 5(b) shows the convergence plot for the intensity of the pressure radiated by the microbubbles.

The correlation coefficient between the experimentally recorded inter-elemental matrix and the computationally evaluated inter-elemental matrix using our simulation approach after each of the 20 iterations is shown in figure 6 for all bubble concentrations (0.5%, 1% and 2%).

The convergence plots shown in figure 5 show that, at low concentrations (0.5% and 1%), eight iterations are sufficient to simulate the multiple scattering interactions occurring between the micro bubbles. For a 2% concentration however, a larger number of iterations (around 12) was required to reach a correlation coefficient of 0.99. This was expected, as an increase in the micro-bubble concentration leads to an increased number of scattering interactions. These results are confirmed by the correlation between the experimental and simulation results shown in figure 6. The lower the micro-bubble concentration, the sooner the experimental and simulation results will be in agreement. For a 0.5% concentration, a correlation coefficient of 0.9 between simulation and experiments is reached after four iterations. 8 and 10 iterations are required to achieve the same agreement for 1% and 2% concentrations respectively.

Figures 7(a)–(c) show a comparison between the velocities predicted by the simulation, measured from the experiments, and predicted by the ISA. Figures 7(d)–(f) show a comparison between the attenuation predicted by the simulation and measured experimentally, and predicted by the ISA.

Figure 7 shows overall a very good agreement between the simulation results and the experimental results for all concentrations, both in terms of the velocity and the attenuation. As expected, the ISA predictions of the phase velocity and attenuation are more accurate for lower concentrations although the attenuation remains underestimated. This is due to the fact that the ISA only accounts for the first order interactions between the micro bubbles, and does not allow the wave to interact twice with the same scatterer. Wood's theory predicts the velocity of sound reasonably accurately for 0.5% bubble concentration. This is of course less and less accurate as the concentration of scatterers increases. Velocity predicted by Wood's theory for 0.5%, 1% and 2% microbubble concentration were $1.32 \text{ mm } \mu\text{s}^{-1}$, $0.94 \text{ mm } \mu\text{s}^{-1}$ and $0.68 \text{ mm } \mu\text{s}^{-1}$ respectively. It can be observed that Wood's theory can reasonably approximate the velocity of the sound at low microbubble concentrations. At 0.1% bubble concentration, the fit between the simulation and the ISA model was in much greater agreement, but the ISA model still underestimated the attenuation value predicted by the simulation model by 15%, as shown in figure 8. At 0.1% microbubble concentration, the magnitude of the velocity was $1.41 \text{ mm } \mu\text{s}^{-1}$, which was a reasonably accurate approximation.

It should be noted that multiple scattering in a medium constituted by a group of randomly or periodically distributed bubbles has been extensively studied for simple air bubbles embedded in a soft matrix, using Foldy's model or the ISA (Leroy *et al* 2008, 2009, Bretagne *et al* 2011, Ben Salem *et al* 2013). However, to our knowledge, no such work had

been conducted for ultrasound contrast agents, which exhibit a specific viscoelastic behavior due to their lipid shell. Additionally, the numerical model presented and validated here does not rely on intrinsic approximations on the concentration of micro bubbles, contrary to the ISA. With a large number of simulation iterations, it should be possible to accurately describe the exact behavior of wave transport in moderately concentrated populations of free ultrasound contrast agent microbubbles. However, the computational cost of performing such a large number of iterations should be taken into account. Our model in present form does not account for the microbubbles interacting with each other or with microbubbles adhering to targeted surfaces.

Conclusion

The results indicate that multiple scattering of ultrasound in a medium with randomly distributed microbubbles can be modeled using an iterative approach combining propagation modeling and microbubble modeling. This method developed for 2D simulations can be easily extended to 3D simulations because the scattering at each individual bubble surface is evaluated separately, which automatically accounts for the expected additional multiple scattering in 3D simulations. In addition, since this is a full-wave equation-based method, the ultrasound field is described for all points in space and time for the domain.

The inter-elemental matrix of a system is an extremely useful tool because the output of the system can be predicted for any input acoustic pulse. For a multiple scattering medium, important characteristics like the scattering mean free path can be determined using the inter-elemental matrix. The accurate determination of the inter-elemental matrix in a bubbly medium can open up the possibility of evaluating the micro-architectural properties of vascular networks in which contrast agent microbubbles are injected.

A limitation of this method is its computational cost. The total number of computations increases with the density of microbubbles since the pressure scattered by each bubble must be calculated for each iteration, in order to define the source terms for the next iteration. It can be observed from figures 5 and 6 that the rate of convergence decreases with an increasing number of bubbles, which is to be expected. A higher density of microbubbles will lead to a higher number of iterations, thus delaying the time required to reach convergence. Nevertheless, this is currently the first simulation method that can model the complex phenomena related to multiple scattering physics of ultrasound by ultrasound contrast agents.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Bubble response according to the Paul–Sarkar model (EEM) to a simple 10 MHz pulse.

STAGE		DETAILS	METHOD
Iteration 0	Primary interactions	Scattering of incident pulse (or incident pulse scattered from one bubble to other) by bubbles	FDTD simulation of propagation
	Primary radiation	Acoustic radiation from bubbles in response to primary interactions	Paul-Sarkar model
Iteration 1	Secondary interactions (Primary radiation as additive source)	Primary interactions + Scattering of primary radiation	FDTD simulation of propagation (with additive sources)
	Secondary radiation	Acoustic radiation from bubbles in response to secondary interactions	Paul-Sarkar model
Iteration 2	Secondary interactions (Primary & secondary radiations as additive sources)	Primary interactions + Scattering of primary radiation + Scattering of primary radiation	FDTD simulation of propagation (with additive sources)

Figure 2.
Iterative fullwave simulation method—algorithm.

Figure 3.
 (a) Simulation setup with 64 elements linear array with five tubes separated by 250 microns (center-to-center) distance with grid step 2.13 micron. (b) Experimental setup with five 200 micron cellulose tubes separated by a 250 micron center-to-center distance in which microbubbles are injected using an attached syringe.

Figure 4.

Primary and secondary interactions at one of the bubbles for backscattering simulation at 1% bubble concentration.

Figure 5.

(a) Convergence plot for radiation at bubble surface and (b) convergence plot for intensity of scattered signals.

Figure 6.

Comparison between experimentally obtained inter-elemental matrix and inter-elemental matrix produced from simulations.

Figure 7.

(a)–(c) Comparison between the phase velocity predicted by simulation and the ISA approach with experimentally measured phase velocity. (d)–(f) Comparison between predicted attenuation coefficients by simulation and the ISA approach with experimentally measured attenuation coefficient.

Figure 8.

(a) Comparison between the phase velocity predicted by simulation and the ISA approach.
 (b) Comparison between predicted attenuation coefficients by simulation with and the ISA approach.