

Experimental Validation of a Convolution-Based Ultrasound Image Formation Model using a Planar Arrangement of Micrometer-Scale Scatterers

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Experimental Validation of a Convolution-Based Ultrasound Image Formation Model using a Planar Arrangement of Micrometer-Scale Scatterers

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Abstract— The shift-invariant convolution model of ultrasound is widely used in the literature, for instance to generate fast simulations of ultrasound images. However, comparison of the resulting simulations with experiments is either qualitative or based on aggregate descriptors such as envelope statistics or spectral components. In the current work, a planar arrangement of 49 μm polystyrene microspheres was imaged using macrophotography and a 4.7 MHz ultrasound linear array. The macrophotograph allowed estimation of the scattering function (SF) necessary for simulations. Using the coefficient of determination R^2 between real and simulated ultrasound images, different estimates of the SF and point spread function (PSF) were tested. All estimates of the SF performed similarly, while the best estimate of the PSF was obtained by Hanning-windowing the deconvolution of the real ultrasound image with the SF: this yielded $R^2=0.43$ for the raw simulated image and $R^2=0.65$ for the envelope-detected ultrasound image. R^2 was highly dependent on microsphere concentration, with values of up to 0.99 for regions with scatterers. The results validate the use of the shift-invariant convolution model, although care needs to be taken in experiments to reduce the relative effects of other sources of scattering such as from multiple reflections, either by increasing the concentration of imaged scatterers or by more careful experimental design.

Index Terms—ultrasonic imaging, shift-invariant convolution, image simulation

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I. INTRODUCTION

Models of ultrasound image formation describe the forward process of how an ultrasound image is formed from an acoustic medium. Such models can be used to generate simulated ultrasound images or to obtain quantitative descriptors of the medium from real ultrasound images. A relatively simple and widely used model of image formation treats the ultrasound image (prior to envelope detection and compression) as the shift-invariant convolution of the imaging system point spread function (PSF) with the scattering function (SF) of the medium [1]. In the following paragraphs, the uses of this model are briefly reviewed in order to provide the context for the current work.

In one of the earlier applications of the shift-invariant convolution model, Bamber and Dickinson [2] generated random SFs by assuming an exponential or a Gaussian autocorrelation function. Each SF was convolved with a Gaussian-modulated sinusoid PSF and the resulting ultrasound images were found to be qualitatively similar to real ultrasound images of a sponge. The simulations were also able to predict a so-called “banding” feature visible in ultrasound images in cases where the correlation length of the SF was shorter than one of the beam dimensions. Other authors employed different SF models to generate ultrasound images. Using a so-called marked regularity model to place point scatterers in the SF, Cramblitt and Parker [3] convolved the SFs with a gated cosine PSF and found that a wide range of envelope distributions (Rayleigh, Rician, homodyned-K) could be generated that are commonly observed in experimental data. Jacobs and Thijssen [4] used structural as well as diffuse components in the SF to make predictions about first- and second-order statistics that would be observed from ultrasound images of the liver.

The shift-invariant convolution model has also been used to simulate ultrasound images using biologically-derived SFs. Waag et al. [5] used images of pig liver lobules to investigate the relationship between backscattered spectra in 1-D, 2-D and 3-D. Lizzi et al. [6] used acoustic microscope data to estimate speed of sound maps of tissue, which were used to generate simulations of conventional-frequency ultrasound images. The use of histology to estimate SF is also receiving increased attention:

Mamou et al. [7] generated 3-D acoustic impedance maps from 3-D volumes of H&E-stained histology, which was then used to estimate quantitative acoustic parameters [8]; Daoud and Lacefield [9] used histology images to derive spatial statistics of the SF. Gyöngy et al. [10] performed simulations using SFs derived from histology images and compared the first-order statistics of these images with those of corresponding real ultrasound images.

Increasingly, there has been a trend towards generating fast simulations of ultrasound images. Considering the issue of computational speed, shift-invariant convolution is an appropriate choice, since the operation is equivalent to multiplication in the Fourier domain. In the work of Hergum et al. [11], cardiac images were simulated and their appearance was found to be qualitatively similar to images simulated using a shift-variant convolution model. Gao et al. [12] also simulated cardiac images but with shift-variance in the axial direction. Burger et al. [13] combined shift-invariance with ray tracing in order to generate simulated images of phantoms and tissue volumes.

As can be observed from the above representative review, the shift-invariant convolution model is widely used in the literature yet the comparison of the resulting simulations with experiments is either qualitative or based on aggregate descriptors such as envelope statistics or spectral components. This is due to the lack of an experimental setup where the scattering distribution of an acoustic medium and the corresponding ultrasound image can be simultaneously recorded. In the current work, macrophotographs of micrometer-scale spherical scatterers were used to derive the SF of a medium that was also simultaneously imaged with an ultrasound system. Using the shift-invariant convolution model and estimates of the PSF, the one-to-one spatial correspondence between ultrasound simulations and experiment was quantitatively compared. Such quantitative comparisons allowed a validation of the shift-invariant convolution model, first by investigating what the best simulation accuracy is using different estimates of the SF and PSF, and then by considering the extent of different sources of error in the simulation.

II. THEORY

The first sub-section of this section describes how an ultrasound image can be modelled as the shift-invariant convolution of a scattering function SF and point spread function PSF . Then, the theoretical background for estimating SF and PSF is given, so that the model can be used to generate simulated ultrasound images. Next, the coefficient of determination R^2 is described, which allows the accuracy of the ultrasound simulations to be evaluated. Finally, possible sources of error between the real and simulated ultrasound images are provided. These theoretical considerations provide the basis for the research methods described in the next section.

A. Shift-Invariant Convolution Model

The shift-invariant convolution model is a simplification of the shift-variant convolution model, which itself depends on a number of assumptions [14,15]. Namely, wave propagation should be linear, non-attenuative, and non-dispersive, while variations in the acoustic properties of the medium should be small enough that only the incident wave is scattered (known as the Born approximation). Using such assumptions, the RF image I is modelled to arise from the convolution of a scattering function SF with a point spread function PSF . Further assuming a spatially invariant PSF leads to the shift-invariant convolution model:

$$I = SF * PSF, \quad (1)$$

where $*$ is the spatially invariant convolution operator. Taking the envelope of I yields the B-mode image B . According to the Fourier theorem, (1) can be rewritten in the Fourier domain as

$$\mathcal{F}\{I\} = \mathcal{F}\{SF\}\mathcal{F}\{PSF\}, \quad (2)$$

where $\mathcal{F}\{\cdot\}$ represents the 2-D Fourier transform operator.

B. Estimation of the scattering function SF

The scattering function SF originates from deviations of the acoustic properties of the medium from some mean. Based on differing assumptions, various expressions exist for SF : for instance, as a combination of fractional changes in density and speed of sound [14]; as fractional changes in bulk modulus [16]; or as fractional changes in acoustic impedance [15]. In the case of homogeneous scatterers placed in a homogeneous background, it is correct (up to a scaling factor) to set the estimated scattering function SF_{est} to 1 where there is a scatterer, and set it to 0 where there is background [17]. For a spherical scatterer in the plane of a linear array, SF_{est} may be treated as a circular cross-section or as the projection of the sphere function onto the 2-D plane (in similar vein to [5,17]). Alternatively, for acoustically compact spherical scatterers, SF_{est} may be set to a collection of discrete points. These estimates will later be referred to as threshold-based, projection-based, and point-based estimates, respectively.

C. Estimation of the point spread function PSF

The point spread function PSF of the imaging system arises from the combination of the incident pressure field transmitted by the transducer and the spatiotemporal response of the transducer and receive beamformer to the scattered field. One method of estimating PSF [12] is using the spatial impulse response approach at a particular depth [14], using a package such as Field II [18,19]. Alternatively, for a region where only one point scatterer is present, SF may be treated as a Dirac delta function. Thus, if the resulting image I_{real} is available, then according to (1), PSF may be estimated from it. Lastly, if SF consists of a distribution of scatterers, then using (2), an estimate PSF_{est} can be obtained as follows:

$$PSF_{est} = \mathcal{F}^{-1} \left\{ \frac{\mathcal{F}\{I_{real}\}}{\mathcal{F}\{SF_{est}\}} \right\}, \quad (3)$$

where $\mathcal{F}^{-1}\{.\}$ denotes the inverse Fourier transform. The above estimates will later be referred to as Field II-based, data-based, and deconvolution-based estimates, respectively.

D. Evaluation of simulation accuracy

When generating a simulated image I_{sim} from estimates SF_{est} and PSF_{est} , I_{sim} and the real ultrasound image I_{real} will differ by an additive error term E :

$$I_{real} = I_{sim} + E, \quad (4)$$

$$I_{sim} = aSF_{est} * PSF_{est}, \quad (5)$$

where a is an unknown scaling term arising from the scale-unknown estimates SF_{est} , PSF_{est} ; this term needs to be estimated using linear regression. Due to the partitioning of variance [20, pp. 21-23], the coefficient of determination R_I^2 can be defined as [20, pp. 92,166]

$$R_I^2 = 1 - \frac{\sigma_E^2}{\sigma_{I_{real}}^2} = \frac{a^2 \sigma_{I_{sim}}^2}{\sigma_{I_{real}}^2}, \quad (6)$$

where σ_u^2 denotes the variance of a variable u over space. The above equation leads to an interpretation of R_I^2 as the proportion of variance (or “signal power”) in the real ultrasound image that can be explained by the simulated image [21]. In similar vein, R_B^2 considers the proportion of variance in the real B-mode image B_{real} that is accounted for by the simulated B-mode image B_{sim} . One method of computing the coefficient of determination is taking the square of the Pearson correlation coefficient [21].

E. Sources of error

The source of simulation error E can be several. Firstly, the estimates SF_{est} and PSF_{est} may be inaccurate. In the case of SF_{est} , the term may wrongly estimate the scattering function from some dominant scatterers under consideration, and may further neglect scattering from other sources (hereon termed background scattering). In addition to the above, the shift-invariant convolution model may itself be inaccurate: there may be electrical noise on the image, or the PSF may be spatially varying. Lastly, the strength and concentration of scatterers may be high enough that multiple scattering becomes significant and the imaging process can no longer be described by a single convolution, even one that is spatially varying [14].

III. METHODS

This Section first presents an experimental setup that allows a real ultrasound image to be generated and corresponding scattering functions to be estimated. The different methods for estimating the point spread function are then presented. Lastly, the methods for generating the simulated images are presented, including the evaluation of simulation accuracy and the role of different sources of error.

A. Generation of Co-Aligned Ultrasound Image and Scatterer Function SF

1) General experimental setup

Figure 1 shows a schematic of the experimental setup. A water tank with deionized water was used to acoustically couple the diagnostic ultrasound linear array (LA522E, Esaote, Genoa, Italy) with the 49- μm diameter polystyrene microspheres (Chromosphere BK050, Thermo Scientific, Waltham, MA) under investigation. The density and bulk modulus of polystyrene are 1.04 kg m^{-3} and 6.2 MPa , compared to 1.00 kg m^{-3} and 2.2 MPa for water [22], so that scattering is expected to be primarily from the compressibility contrast.

The microspheres had been suspended in deionized water and then placed on top of a flat 1% aqueous agar gel using a micropipette. The spatial distribution of the microspheres was imaged using a digital camera (SP-820UZ, Olympus, Tokyo, Japan) on super macro setting (1 cm focus). The agar concentration of 1% was chosen to make the gel acoustically transparent so that the microspheres appeared to “float” in the imaging plane of the ultrasound transducer. An acoustic absorber made of graphite-loaded PDMS and placed at an angle to the transducer surface was used to reduce multiple reflections in the ultrasound image.

2) *Generation of ultrasound images*

The 192-element linear array (LA522-E, Esaote, Genoa, Italy) had a 3-6 MHz response, 47 mm aperture, a 20 mm elevation focus depth, and was connected to an ULA-OP Research US system (MSD Lab, University of Florence, Florence, Italy) [23]. Due to multiplexing, 64 elements (or 15.7 mm) of the aperture were active at any time. The imaging system allows recording of pre-beamformed data that can be used later to generate ultrasound images using arbitrary receive beamforming settings. The beamformed RF images thus obtained will be denoted by I_{real} , and the envelope-detected B-mode images by B_{real} . As in Fig. 1, the transverse, elevation and axial directions in the image are denoted by x , y , z , respectively.

To help ensure the validity of the shift-invariance assumption, the imager employed a uniform delay on transmit and dynamic receive beamforming. A reference ultrasound recording was taken prior to placement of the microparticles. As is typical for linear array imaging architectures, the contiguous, 64-element active subaperture stepped through the 192-element linear array in a consecutive manner. Due to the uniform-delay transmission, this allowed averaging of the pre-beamformed RF data up to 32 times, if needed.

The imaged region ranged from a depth z of 17.2 mm to 23.7 mm, close to the elevation focus depth. Since it is linearly proportional to the receive beamwidth, one parameter of interest was the receive $F\#$, defined as the ratio of focal distance to the receive aperture. Unless otherwise stated, images were generated without dynamic receive apodization, using the maximum available aperture throughout (giving $F\#=1.1-1.5$). In the case of dynamic receive apodization, the maximum available aperture was used at the maximum imaging depth (giving $F\#=1.5$). For the calculation of beamforming delays and imaged depths z , the speed of sound was assumed to be 1482 m/s based on the temperature of the water (20 °C) [24].

3) *Estimation of the scattering function SF*

Three methods were used to estimate the scattering function, whose theory is described in Section II B. These methods corresponded to three image processing operations carried out on the macrophotograph

obtained, as illustrated in Fig. 2. After inversion of the red channel, Otsu's method [25] was employed by the MATLAB built-in function `graythresh` to obtain a suitable threshold with which to separate the polystyrene spheres from the background. This threshold was used to convert the grayscale image into a binary image, which, after removal of objects with fewer than 10 pixels, was used to generate the estimate $SF_{threshold}$. In the knowledge that the circular cross-sections represent spheres, the distance transform was applied on $SF_{threshold}$ to produce $SF_{project}$. The distance transform converts circle functions into 2-D parabolic functions that represent the projection of a sphere onto a plane [17]. Lastly, by finding local maxima in $SF_{project}$, the scattering function could be estimated as a set of point scatterers, yielding the estimate SF_{points} .

4) *Registration of ultrasound image with scattering function SF*

In order to align the ultrasound image with the scattering function, an estimate was necessary of the inter-pixel distance dx in the macrophotograph. Based on an initial estimate of 8300 nm from the dimensions of the agar gel (23.5×23.5 mm in area), the cross-correlation between $SF_{threshold}$ and the B-mode ultrasound image B_{real} was calculated for candidate values of dx in the range of 8000 nm to 8600 nm, in steps of 5 nm. To estimate dx , the value that maximized the spatial maximum of the cross-correlation function was chosen, while the location of the spatial maximum provided the spatial alignment between $SF_{threshold}$ and B_{real} .

B. *Estimation of the PSF*

As described in Section II C, three possible techniques to estimate the point spread function are the Field II-based, the deconvolution-based, and the data-based methods. In the Field II-based estimate $PSF_{Field II}$, the spatial impulse response of the transducer was estimated with Field II [18,19] using transducer element parameters provided by the manufacturer. In addition to those already mentioned, these were: 3 cycles at 4.7 MHz pulse-echo wavelet, 6 mm element height, 0.245 mm pitch, negligible

kerf. As mentioned in Section III A, imaging was only carried out using 64 of the 192 elements at any one time; this setting was also applied in the Field II simulations.

In the deconvolution-based estimate $PSF_{deconvolution}$, the ultrasound image I_{real} was deconvolved with $SF_{threshold}$ in the Fourier domain using (3). For the data-based estimate PSF_{data} , the aligned ultrasound image I_{real} and scatterer function estimate $SF_{threshold}$ (as described in the previous subsection) was used to select a region of I_{real} that contained only one scatterer.

For all three methods, the PSF estimates were cropped around a window 0.84 mm long by 2.84 mm wide, which was chosen to encompass the main lobe of the PSF. This was particularly significant in the case of $PSF_{deconvolution}$, where without cropping, the simulation would have simply returned the real ultrasound image (1,3). Such an estimate, however, would have been an artificial means of achieving a perfect simulation, while cropping the estimate around the main lobe was expected to yield a physically realistic estimate. However, it was also feared that without smooth windowing, the sudden drop in amplitude at the edges of the PSF would artificially introduce high frequency components into the PSF estimate and thus the simulated ultrasound image. Therefore, the effect of multiplying the PSF estimates by a 0.84×2.84 mm Hanning window was also investigated. From here on, the use of the rectangular or Hanning windows will be indicated by the subscripts “rect” and “Hanning”, respectively.

In order to compare the similarity between the different PSF estimates, the coefficient of determination R^2 was calculated between a reference estimate ($PSF_{Field II, rect}$) and all the other estimates. This calculation was repeated for the envelopes of the PSF estimates, to show to what extent it was the phase or the amplitude of the estimates that differed.

C. Convolution-based ultrasound simulations

1) Simulation methods

Simulations were conducted in MATLAB (Mathworks, Natick, MA). A 2-D convolution was performed between SF_{est} and PSF_{est} using a third-party FFT-based implementation [26], yielding a simulated RF image I_{sim} . The magnitude of the analytic signal gave the envelope-detected image B_{sim} .

Before any further simulations were carried out, a method was sought to validate R^2 (see Section II D) as a measure of agreement between simulations and experiment. For this, a simulated image was generated using $SF_{est} = SF_{threshold}$, $PSF_{est} = PSF_{Field II, rect}$. The real and simulated ultrasound images were circularly shifted with respect to each other in units of pixels, whereupon R^2 was calculated for all possible shifts. R^2 was calculated both between the raw RF images I_{real} and I_{sim} , and between the envelope (B-mode) images B_{real} and B_{sim} , yielding the measures R_I^2 and R_B^2 , respectively (see Section II D).

2) Evaluation of simulation accuracy for different estimates of SF, PSF

In an attempt to find the best possible simulation accuracy, R_I^2 and R_B^2 were calculated for various estimates SF_{est} and PSF_{est} . First, simulations were carried out using $SF_{threshold}$, $SF_{project}$, and SF_{points} (see Section III A) and $PSF_{Field II, rect}$ as a reference estimate of the PSF. Then, simulations were carried out using the three different estimates of the PSF, with $SF_{threshold}$ used as the estimate of the SF.

3) Identification of sources of error

A list of possible sources of simulation error have been provided in Section II E, whose relative roles were assessed by the variation in R_I^2 , R_B^2 for different simulation and imaging settings. The variation with different estimates of SF_{est} and PSF_{est} has already been addressed in the previous subsection. The role of background scattering in the simulation error was assessed by subtracting a reference ultrasound

image (taken prior to scatterer displacement) from the real ultrasound image; while that of electrical noise was assessed by temporal averaging of the pre-beamformed data 32 times (see Section III A).

The use of uniform transmit delays was expected to reduce the shift-variance of the PSF; the effect of using dynamic receive apodization to further minimize shift-variance was also investigated. In addition to the issue of shift variance, the level of error may vary with the concentration of scatterers, either due to the varying level of signal, or due to the introduction of multiple scattering from the polystyrene spheres. These effects were investigated by calculating spatial maps of R_I^2 , R_B^2 over 40×40 pixel windows (corresponding to 333×333 nm), so that the spatial variation of simulation accuracy may be observed, including for regions of low and high scatterer concentration.

IV. RESULTS AND DISCUSSION

A. Generation and registration of ultrasound image with scattering function

Figure 3 shows the estimated scattering function $SF_{threshold}$ aligned with the real ultrasound image. During the process of alignment (see Section III A), the distance dx between the macrophotograph pixels was estimated as 8325 nm. The other estimates $SF_{project}$, SF_{points} are not shown due to lack of visibility, but differences between them at a higher zoom level can be observed in Fig. 2.

B. Estimation of PSF

Figure 4 shows the various estimates of PSF (see Section III B), with values of R_I^2 , R_B^2 showing their variation in phase and amplitude compared to the reference $PSF_{Field II, rect}$. These values show that there are significant differences between the reference raw PSF and other raw PSFs. On the other hand, there is less variation between the envelopes, implying that the estimates vary less in amplitude than in phase. Hanning windowing increases the similarity with the reference $PSF_{Field II, rect}$, which means that there is considerable variation between the PSF estimates near the edges that is thereby suppressed. It is hypothesised that this variation is mostly from noise; the validity of this hypothesis will be evaluated in

the next subsection, where the accuracy of simulations will be considered.

C. Convolution-based ultrasound simulations

Figure 5 shows the variation of R_I^2 , R_B^2 as the real and simulated ultrasound images are spatially shifted with respect to each other. Both R_I^2 , R_B^2 drop to negligible levels for spatial shifts exceeding the dimensions of the PSF (Fig. 4), demonstrating their validity as measures of similarity between real and simulated images. Interestingly, R_B^2 is less spatially sensitive and shows higher values of agreement than R_I^2 . These differences are deemed to be due to the sensitivity of R_I^2 to phase mismatch, which is demonstrated by the oscillatory variation of R_I^2 with axial shift Δz .

1) Evaluation of simulation accuracy for different estimates of SF, PSF

Figure 6 compares the real ultrasound image and simulations obtained using three estimates of the scattering function: $SF_{threshold}$, $SF_{project}$, SF_{points} . $R_I^2 = 0.36$ for all three simulations, while R_B^2 is in the range 0.59–0.61, showing that there is little difference between simulation accuracy. This is likely because the polystyrene spheres are close to being point scatterers ($ka=0.49$).

In Figure 7, the real ultrasound image is compared with simulations obtained using the six different PSF estimates shown in Fig. 4. As expected, Hanning windowing the PSF estimate will suppress high-frequency components at the edges (see Section III B) and suppress noise near the edges (see Section IV C 1), thereby yielding better simulation results. Compared with the reference estimate $PSF_{Field II, rect}$, the best estimate $PSF_{deconv, Hanning}$ increases R_I^2 from 0.36 to 0.43 and R_B^2 from 0.59 to 0.65.

2) Identification of error sources

From the previous subsection, it could be seen that there was little difference in simulations when using different estimates of SF and a somewhat greater difference (a change in R_I^2 of up to 0.07) with different estimates of the PSF. However, even with the best estimates, only 43% of the signal variation in

the real raw ultrasound image could be explained by the simulation, or 65% in the case of envelope-detected images. Therefore, in addition to errors in estimating the SF and PSF, other sources of error are also likely to be significant.

Figure 8 shows the effect of temporal averaging and of subtracting a background image without polystyrene scatterers. The resulting changes in R_I^2 , R_B^2 are at most 0.01, showing that the contributions of electrical noise and background scattering are minimal. Figure 9 shows the effect of introducing dynamic receive apodization, which reduces shift-variance in the PSF. Instead of an improvement, there is a slight decrease (0.02) in R_B^2 , possibly due to a decrease in signal owing to a decrease in the receive aperture (see Section III A).

To address the question of how shift variance and scatterer concentration affects simulation accuracy, Figure 10 shows the spatial variation of R_I^2 , R_B^2 . Both R_I^2 and R_B^2 display higher values in regions with scatterers, up to 0.98, 0.99, respectively. Shift-variance in the axial direction is not noticeable; however, R_I^2 seems to show phase decorrelation around the left and right edges. Stretching the estimate of SF in the transverse direction did not improve results. It is possible, however, that misalignment between the SF and real ultrasound image was more complex, such as a rotation error. Since R_I^2 has been shown to be more sensitive to alignment errors than R_B^2 , this would explain why R_B^2 retains higher values at the left and right edges.

The results of Fig. 10 show that a higher concentration of scatterers did not reduce simulation accuracy, which implies that in the current experiment, multiple scattering from polystyrene scatterers was not a significant phenomenon. On the contrary, low scatterer concentrations reduced the level of signal and therefore simulation accuracy. It is not clear, however, what source of noise is chiefly responsible for the reduction in simulation accuracy. Fig. 8 shows that the roles of electrical noise and background scattering are not dominant. One hypothesis is that reflections from the acoustic absorber behind the phantom (Fig. 1) may have caused additional scattering from the polystyrene particles. The other is that the air content of the water may have caused microbubbles to appear over time, which could

not be adequately subtracted using the reference image. One such microbubble may be at $x = -0.5$ mm, $z = 21.5$ mm (Fig. 10).

V. CONCLUSION

The present work has shown how a shift-invariant model of ultrasound image formation is able to predict ultrasound images of microparticles in the imaging plane of a linear array. Using the coefficient of determination metric allowed the calculation of the proportion of variance in the real ultrasound image that could be explained by the simulated image. The coefficient of determination was calculated both for the raw ultrasound image and the envelope-detected (B-mode image), denoted by R_I^2 , R_B^2 , respectively. After the scattering function (SF) estimate was aligned with the ultrasound image, the variation of both measures was calculated as the real and simulated images were circularly shifted with respect to each other. R_I^2 and R_B^2 exhibited clear maxima at the correct alignment, diminishing to negligible levels when the misalignment was greater than the dimensions of the point spread function (PSF). In addition, R_I^2 was shown to be more sensitive to misalignment errors than R_B^2 due to the former being sensitive to phase differences. These results underlined the validity of the coefficient of determination measure, and the differing interpretations of R_I^2 and R_B^2 .

In the next step, various estimates of SF, PSF were tested to see which yielded the best simulation. All three estimates of SF gave similar results. In the case of the PSF, deconvolution of the real image with the estimated SF, followed by Hanning windowing ($PSF_{deconv,Hanning}$) gave the best results, yielding $R_I^2 = 0.43$, $R_B^2 = 0.65$.

In the last step, the source of simulation error was explored. Regions of scatterers showed high values of R_I^2 , R_B^2 (up to 0.98, 0.99, respectively), while regions without scatterers were dominated by noise. Since the reduction of electrical noise and background (non-polystyrene) scattering from agar only changed values of R_I^2 , R_B^2 by up to 0.01, it is possible that other sources of error were more significant. For example, scattering of the polystyrene particles from multiple reflections or scattering from microbubbles could have also contributed to simulation errors. From the above observations, it is

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3 expected that by increasing the concentration of imaged scatterers or by more careful experimental
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5 design, higher overall values of R_f^2 , R_B^2 can be obtained.
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8 To the authors' knowledge, the current work presents the first example of a medium being imaged
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10 with ultrasound that has also had its scattering function estimated spatially, allowing for the validation of
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12 the shift-invariant convolution model of ultrasound image formation. The above results show that, at least
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14 for the experimental setup used in the current work, the shift-invariant convolution model describes most
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16 of the variation in a B-mode image, however care should be taken to reduce other sources of scattering
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18 such as due to multiple reflections or microbubbles. Planned extensions of this work include validating
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20 the model using other scatterer arrangements such as 3D distributions of spherical scatterers, live
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22 biological cells, and eventually tissue. In addition to validating the shift-invariant convolution model, the
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24 experimental setup herein provided allows a host of experiments to be conducted where knowledge of the
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26 scattering function is required. For instance, methods to estimate any structural descriptor may be tested
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28 in an experimental setting, including the location of individual scatterers using superresolution imaging
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30 [27].
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REFERENCES

- [1] C. R. Hill, J. C. Bamber, G. R. ter Haar (eds.), "Reflection and scattering" in *Physical Principles of Medical Ultrasonics*, 2nd ed. Chichester, UK: John Wiley and Sons, 2004, pp. 191–219.
- [2] J. Bamber, R. Dickinson, "Ultrasonic B-scanning: a computer simulation," *Phys. Med. Biol.*, vol. 25, pp. 463–479, 1980.
- [3] R. M. Cramblitt, K. J. Parker, "Generation of non-Rayleigh speckle distributions using marked regularity models," *IEEE UFFC*, vol.46, pp.867–874, 1999.
- [4] E. M. G. P. Jacobs, J. M. Thijssen, "A simulation study of echographic imaging of diffuse and structurally scattering media," *Ultrasonic Imaging*, vol 13, pp. 316–333, 1991.
- [5] R. C. Waag, J. O. Nilsson, J. P. Astheimer, "Characterization of volume scattering power spectra in isotropic media from power spectra of scattering by planes," *J. Acoust. Soc. Am.*, vol. 74, pp. 1555–1571, 1983.
- [6] F. L. Lizzi, M. C. Rorke, D. L. King, E. J. Feleppa, A. Kalisz, J. B. Sokil-Melgar, J. Nowakowski, "Simulation studies of ultrasonic backscattering and B-mode images of liver using acoustic microscopy data," *IEEE UFFC*, vol.39, pp. 212–226, 1992.
- [7] J. Mamou, M. L. Oelze, W.D. O'Brien Jr, J. F. Zachary, "Extended three-dimensional impedance map methods for identifying ultrasonic scattering sites," *J. Acoust. Soc. Am.*, vol. 123, pp. 1195–1208, 2008.
- [8] A. J. Dapore, M. R. King, J. Harter, S. Sarwate, M. L. Oelze, J. A. Zagzebski, M. N. Do, T. J. Hall, W. D. O'Brien, "Analysis of human fibroadenomas using three-dimensional impedance maps," *IEEE Trans. Med. Imaging*, vol. 30, pp. 1206–1213, 2011.
- [9] M. Daoud, J. Lacefield, "Stochastic modeling of normal and tumor tissue microstructure for high-frequency ultrasound imaging simulations," *IEEE Trans. Biomed. Eng.*, vol. 56, pp. 2806–2815, 2009.

- [10] M. Gyöngy, L. Balogh, K. Szalai, and I. Kalló, "Histology-based simulations of ultrasound imaging: Methodology," *Ultrasound Med. Biol.*, vol. 39, pp.1925–1929, 2013.
- [11] T. Hergum, S. Langeland, E. Remme, H. Torp, "Fast ultrasound imaging simulation in k-space," *IEEE UFFC*, vol. 566, pp. 1159-1167, 2009.
- [12] H. Gao, H. F. Choi, P. Claus, S. Boonen, S. Jaecques, G. H. Van Lenthe, G. Van der Perre, W. Lauriks, J. D'hooge, "A fast convolution-based methodology to simulate 2-D/3-D cardiac ultrasound images," *IEEE UFFC*, vol.56, pp. 404–409, 2009.
- [13] B. Burger, S. Bettinghausen, M. Radle, J. Hesser, "Real-Time GPU-Based Ultrasound Simulation Using Deformable Mesh Models," *IEEE Trans. Med. Imaging*, vol.32, pp.609–618, 2013.
- [14] J. A. Jensen, "A model for the propagation and scattering of ultrasound in tissue," *J. Acoust. Soc. Am.*, vol. 89, pp. 182–190, 1991.
- [15] R. J. Zemp, C. K. Abbey, M. F. Insana, "Linear system models for ultrasonic imaging: Application to signal statistics," *IEEE UFFC*, vol. 50, pp. 642–654, 2003.
- [16] J. M. Mari, T. Blu, O. B. Matar, M. Unser, and C. Cachard, "A bulk modulus dependent linear model for acoustical imaging," *J. Acoust. Soc. Am.* vol 125, pp. 2413–2419, 2009.
- [17] J. P. Kemmerer, M. Gyöngy, M. L. Oelze, "Modeling of physically large weak scatterers in the beam of a single-element transducer" submitted to *J. Acoust. Soc. Am.*, 2014.
- [18] J. A. Jensen, "Field: A program for simulating ultrasound systems," *Med. Biol. Eng. Comput.*, vol. 34, pp. 351–353, 1996.
- [19] J. A. Jensen, N. B. Svendsen, "Calculation of pressure fields from arbitrarily shaped, apodized, and excited ultrasound transducers," *IEEE Trans. Ultrason., Ferroelec., Freq. Contr.*, vol. 39, pp. 262-267, 1992.
- [20] X. Yan, X.G. Su, *Linear regression analysis: theory and computing*, Singapore: World Scientific, 2009.
- [21] S. Weisberg, *Applied Linear Regression*, third edition. Hoboken, New Jersey, USA: John Wiley & Sons, 2005, pp. 31-32.

[22] Onda Corporation, "Tables of acoustic properties of materials," Available online at http://www.ondacorp.com/tecref_acoustictable.shtml. Last visited January 17, 2015.

[23] E. Boni, L. Bassi, A. Dallai, F. Guidi, A. Ramalli, S. Ricci, J. Housden, P. Tortoli, "A reconfigurable and programmable FPGA-based system for nonstandard ultrasound methods," *IEEE UFFC*, vol. 59, pp. 1378–1385, 2012.

[24] V. Del Grosso, C. Mader, "Speed of sound in pure water," *J. Acoust. Soc. Am.*, vol. 52, pp. 1442–1446, 1972.

[25] N. Otsu, "A threshold selection method from gray-level histograms," *IEEE Trans. Syst., Man, Cybern.*, Vol. 9, No. 1, 1979, pp. 62-66.

[26] B. Luong (2009, June) FFT-based convolution. MATLAB Central File Exchange, #24504 [Online] <http://www.mathworks.com/matlabcentral/fileexchange/24504-fft-based-convolution>, last accessed June 2014.

[27] K. J. Parker, "Superresolution imaging of scatterers in ultrasound B-scan imaging," *J. Acoust. Soc. Am.*, vol. 131, pp. 4680–4689, 2012.

FIGURES AND TABLES

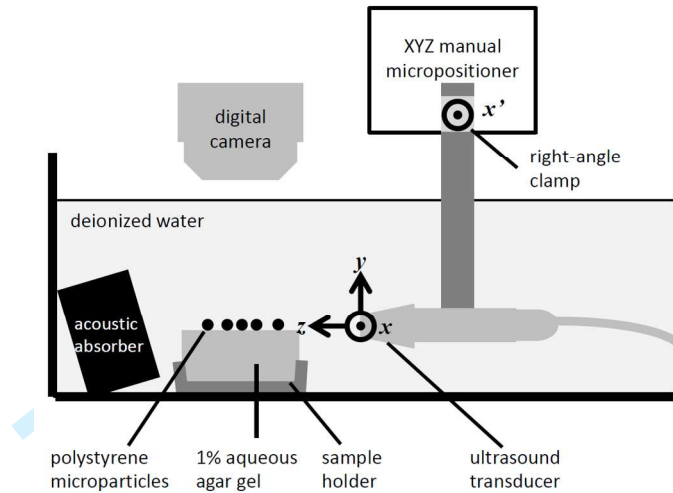


Fig. 1. Schematic of experimental setup. 49 μm diameter polystyrene microspheres are resting on the surface of a 1% agar gel. The surface is in the imaging plane of a linear array that has been aligned with an XYZ micropositioner. Alignment was achieved by successive rotations around the x' axis and movements in the y direction until the level of scattering from the polystyrene spheres, as observed on a live ultrasound B-mode image, was maximized. An acoustic absorber made of graphite-loaded PDMS and placed at an angle to the array surface is used to reduce multiple reflections. A digital camera in macro mode (1 cm focus) images the distribution of microspheres.

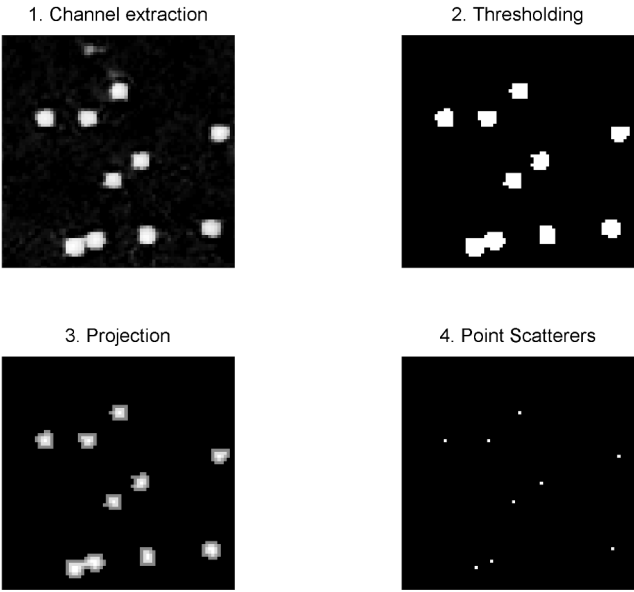


Fig. 2. Steps in estimating the scattering function SF of the polystyrene scatterers from a macrophotograph. 1. Extraction of the red channel in the RGB photograph and inversion to produce a grayscale image. 2. Thresholding of the grayscale image. 3. Projection of sphere functions onto 2-D image. 4. Reduction of scatterers to discrete points. The last three steps produce three corresponding estimates of SF , namely $SF_{threshold}$, $SF_{project}$, SF_{points} .

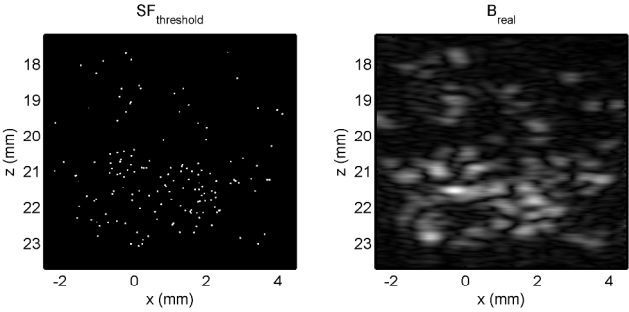


Fig. 3. Alignment of estimated scattering function with experimentally obtained B-mode image. Left: estimated scattering function $SF_{threshold}$ based on thresholded macrophotograph data (Fig. 2). Right: corresponding experimentally obtained B-mode image B_{real} .

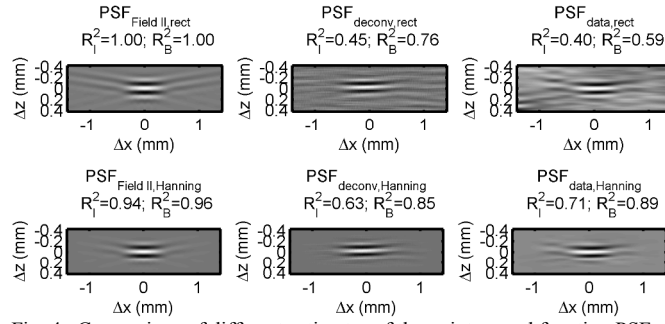


Fig. 4. Comparison of different estimates of the point spread function PSF of the imaging system. As described in Section III B, three methods were tested: the Field II-based method (left column), the deconvolution method (center column), and the data-based method (right column). The PSFs were multiplied by a rectangular window (top row) and a Hanning window (bottom row). Using $PSF_{Field II, rect}$ as a reference, values of R^2 were computed for the raw PSFs (R_I^2) as well as for their envelopes (R_B^2).

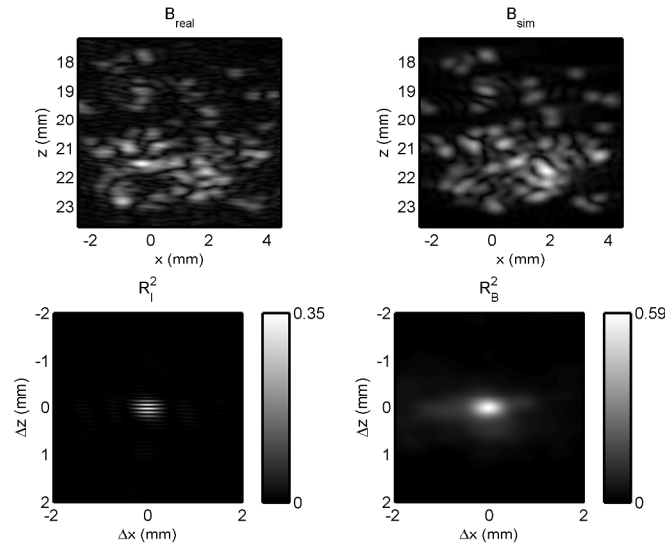


Fig. 5. Spatial sensitivity of the coefficients of determination R^2 for the raw RF and envelope (B-mode) data between real and simulated ultrasound images. Top left: real ultrasound image. Top right: simulated ultrasound image computed using $SF_{threshold}$, $PSF_{Field II, rect}$. Bottom: variation of R^2 for raw RF images (left) and envelope (B-mode) images (right) as a function of lateral and axial circular shifts Δx , Δz between real and simulated ultrasound images. Although the full range of circular shifts was computed, the figures only show a $[-2, 2]$ mm box for greater clarity. Outside the box, values of R^2 are negligible.

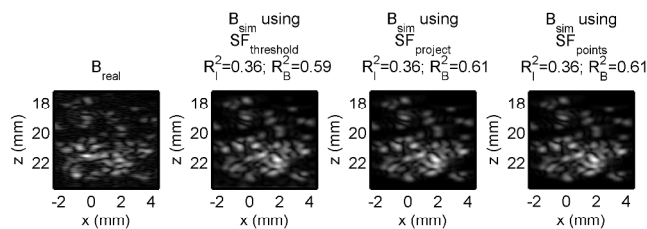


Fig. 6. Comparison between the real ultrasound (left) and simulated ultrasound images computed using three different estimates of the scattering function (Fig. 2). All three simulations used $PSF_{Field II, rect}$ (Fig. 4).

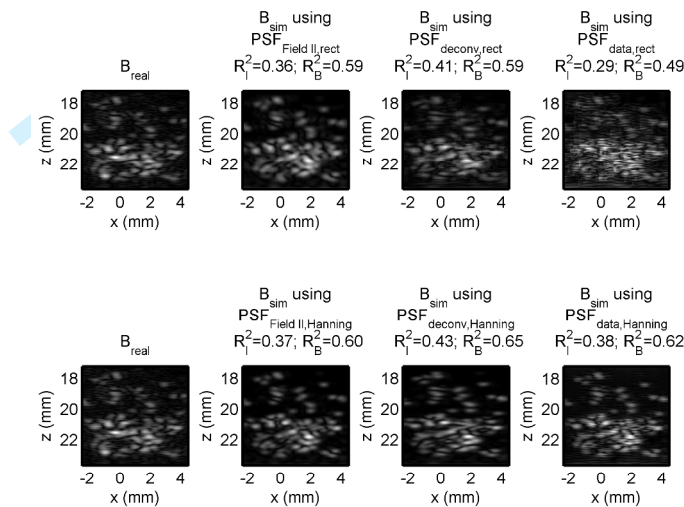


Fig. 7. Comparison between the real ultrasound image (first column) and simulated ultrasound images computed using six different estimates of the point spread function PSF (Fig. 4). For all simulations, the scattering function was estimated by $SF_{threshold}$ (Fig. 2).

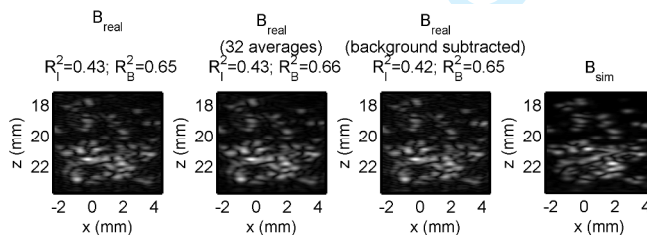


Fig. 8. Comparison between real ultrasound images and a simulated image. The real ultrasound images were generated without averaging or reference subtraction; with averaging of the pre-beamformed RF data to reduce electrical noise; and with subtraction of a reference signal prior to scatterer placement to reduce background scattering. The simulated image was generated using $SF_{threshold}$ and $PSF_{deconv, Hanning}$ (Fig. 7).

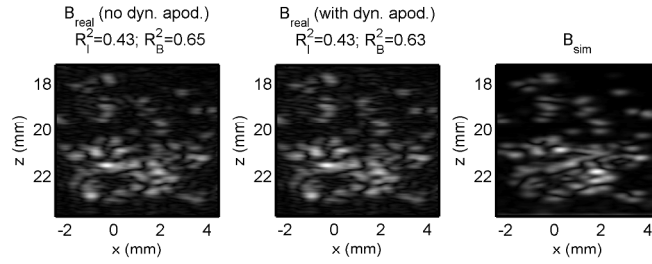


Fig. 9. Comparison of two real ultrasound images, one generated without, the other with dynamic receive apodization, with a simulated ultrasound image. The simulated image was generated using $SF_{threshold}$ and $PSF_{deconv,Hanning}$ (Fig. 7).

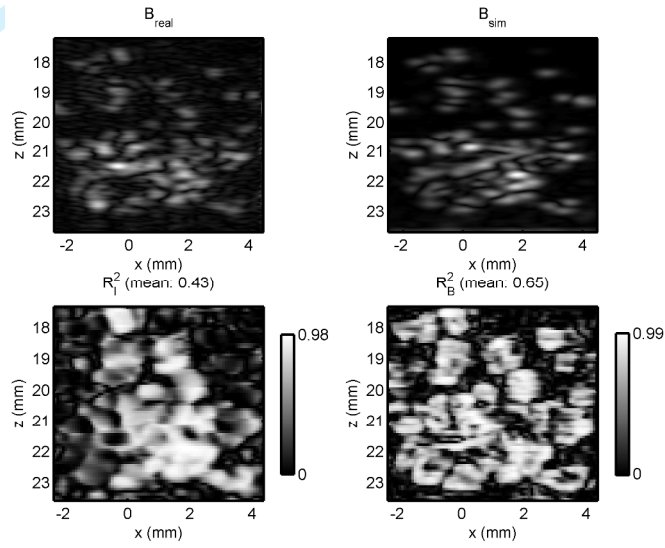


Fig. 10. Estimation of the spatial variation of the coefficients of determination R^2 for both the raw images I and B-mode images B . Top left: real ultrasound image. Top right: simulated ultrasound image, generated using $SF_{threshold}$ and $PSF_{deconv,Hanning}$ (Fig. 7). Bottom left: spatial map of R^2 between I_{real} and I_{sim} . Bottom right: spatial map of R^2 between B_{real} and B_{sim} .