Physics-Inspired Regularized Pulse-Echo Quantitative Ultrasound: Efficient Optimization With ADMM

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Abstract—Pulse-echo quantitative ultrasound (PEQUS), which estimates the quantitative properties of tissue microstructure, entails estimating the average attenuation and the backscatter coefficient (BSC). Growing recent research has focused on the regularized estimation of these parameters. Herein, we make two contributions to this field: first, we consider the physics of the average attenuation and backscattering to devise regularization terms accordingly. More specifically, since the average attenuation gradually alters in different parts of the tissue, while BSC can vary markedly from tissue to tissue, we apply L2 and L1 norms for the average attenuation and the BSC, respectively. Second, we multiply different frequencies and depths of the power spectra with different weights according to their noise levels. Our rationale is that the high-frequency contents of the power spectra at deep regions have a low signal-to-noise ratio (SNR). We exploit the alternating direction method of multipliers (ADMM) for optimizing the cost function. The qualitative and quantitative evaluations of bias and variance exhibit that our proposed algorithm improves the estimations of the average attenuation and the BSC up to about 100%.

Index Terms—Alternating direction method of multipliers (ADMM), L1 regularization norm, optimization, physical properties, pulse-echo quantitative ultrasound (PEQUS), weighted data term.

I. INTRODUCTION

ULTRASOUND imaging (US) has numerous medical applications [1], [2], [3]. Despite being real-time, cost-effective, and portable, it depicts a qualitative map of underlying tissue that can be affected by the settings of an ultrasound machine. As a result, its interpretation is contingent on the operator’s skills. Pulse-echo quantitative ultrasound (PEQUS) resolves the drawbacks mentioned above by revealing the quantitative properties of tissue microstructure [4], [5], [6], [7]. Fatty liver classification [8], [9], prostate cancer imaging [10], bone assessment [11], and breast cancer monitoring [12] are a few examples of clinical applications of PEQUS. PEQUS techniques are categorized into different fields [13], [14], [15], [16], [17]. In this work, we focused on spectral-based techniques [18], [19], [20], which delves into the power spectra of the radio frequency (RF) data backscattered from tissue. These techniques provide estimations of acoustic properties of tissue, which comprise attenuation [21], [22], [23], [24], backscatter coefficient (BSC) [25], and scatterer properties [26], [27], [28]. Herein, we focus on attenuation and BSC estimation.
The existing literature [29], [30], [31], [32], [33], [34] reported that regularized-based parameter estimation algorithms outperform nonregularized ones. In recent years, researchers have applied regularization to PEQUS estimation in various ways. The studies mainly differ in the type of cost functions and optimization techniques they use. A dynamic programming (DP) technique was introduced to estimate BSC with implicit compensation for the total attenuation, i.e., the attenuation produced by tissues between the transducer and the region of estimation [31], [32]. However, the MATLAB implementation of DP required more than 2000 seconds; rendering it unsuitable for immediate clinical deployment. Nevertheless, an efficient implementation of DP, especially on graphics processing unit (GPU), has the potential to provide near real-time feedback, thereby making it clinically feasible. Destrempes et al. [35] optimized a generalized least absolute shrinkage and selection operator (LASSO) problem using a Lagrangian multiplier in addition to the Bayesian information criterion for estimating attenuation and scatterer properties to improve the contrast-to-noise ratio of these features. Some of these techniques have been applied to various organs and tissues. Deeba et al. [36] focused on diagnosing liver steatosis. They presented a cost function based on total variation regularization using MATLAB’s convex optimization toolbox CVX [37] to estimate the effective scatterer diameter (ESD) and the acoustic concentration (AC). Rafati et al. [37] proposed a method to estimate the attenuation coefficient map using the attenuation coefficient slope. Accordingly, they approximated the logarithmic scale of the power spectra at each frequency as a function of depth. Consequently, the frequency where the maximum y-intercept occurred was selected for calculating the local attenuation coefficient slope. Afterward, the frequency range was limited to those where the ratio of the normalized power spectra with respect to the depths at two locations and two adjacent frequencies was within 25% of the estimated local attenuation coefficient slope. The ultimate estimate of the local attenuation coefficient slope was calculated using a linear regression on the confined frequency range. The use of L2 norms in cost functions gained popularity because of its simplicity, the L1 norm produces better results in terms of the sharpness of the estimated parameters at boundaries between structures with different attenuation and/or backscatter. Therefore, devising an efficient optimization method for penalty functions that include terms with L1 norm is crucial. ALGEBRA suffers from three major issues.

1) ALGEBRA considers L2 norm regularization for both the average attenuation from intervening tissues (henceforth referred to as $\alpha_{avg}$) and the BSC. Nonetheless, according to the physics, $\alpha_{avg}$ and BSC have different rates of spatial variations (due to the averaging effect in $\alpha_{avg}$ and the different physical mechanisms underlying absorption and scattering). In general, BSC can change from tissue to tissue, while $\alpha_{avg}$, presents more gradual changes.

2) ALGEBRA considers equal involvement for power spectra at each frequency and depth in parameter estimation. However, different frequency components of the power spectrum present varying levels of signal-to-noise ratio (SNR) as a function of depth. A maximum likelihood estimator should put less trust in low SNR data.

3) The performance of ALGEBRA in the presence of specular reflectors has not been evaluated. Specular reflectors are commonly found above or within the regions where the PEQUS features are estimated and can originate from tissue boundaries, blood vessels, or fibers of connective tissue, such as Cooper’s ligaments in the breast [39], [40]. Despite their ubiquity in ultrasound images, their presence can bias PEQUS feature estimation because of the lack of compliance with the assumption of incoherent scattering in the estimation of attenuation and backscatter [39], [41].

To overcome the drawbacks mentioned above, we utilize the L2 norm for the average attenuation and the L1 norm for the BSC in the regularization part of the cost function.
To optimize the proposed cost function efficiently, we employ the alternating direction method of multipliers or ADMM. ADMM has been previously used by Coila and Lavarello [42] for the regularization of local attenuation estimation. However, the authors did not parameterize BSC through the power-law model. We also introduce a criterion to define weights that vary with depth and frequency. Finally, we analyzed the performance of the newly proposed method in the presence of specular scatterers, in addition to other tests, including inclusions with different scattering levels with respect to the background.

In this report, we make the following contributions to the field of regularized PEQUS: 1) we incorporate physics-based regularization norms for attenuation and BSC; 2) we apply ADMM to penalize the cost function instead of the CVX toolbox in MATLAB used by Deeba et al. [36] and [43]; 3) we assign SNR-based weights that vary with depth and frequency to the echo signal power spectrum; and 4) in contrast to [36], we estimate \( \alpha_{\text{avg}} \) and BSC instead of ESD and AC.

Our proposed method is explained in Section II. Section III presents the results, followed by a discussion part in Section IV. Conclusions are laid out in Section V.

II. METHODS

A. Approach

Similar to [29], [31], and [44], we start with the reference phantom method (RPM) [45], a well-known approach employed to cancel system dependencies. In the RPM, the power spectra of a sample (phantom or tissue) \( s \) with unknown PEQUS parameters \( \alpha_{\text{avg}} \) and BSC, represented by \( \beta_r \), are normalized by the power spectra of a calibrated reference phantom \( r \). Both phantoms are scanned with the same transducer, sound speed, and machine setting:

\[
\frac{S_s(f; z, x)}{S_r(f; z)} = \frac{\sigma_b(f; z)A_r(f; z)}{\sigma_b(f; x)A_r(f; x)} \tag{1}
\]

where \( \sigma_b(f; z) \) and \( A(f; z) \) entitle BSC and total attenuation are defined through a power-law parametrization and an exponential function, respectively

\[
\sigma_b(f; z) = \beta(z) f^{-\nu(z)} \tag{2}
\]

\[
A(f; z) = \exp(-4\pi f \alpha_{\text{avg}} z) \tag{3}
\]

where \( f \) and \( z \) refer to the frequency and depth, respectively. More information can be found in [29]. Taking the natural log from both sides of (1) and applying \( \sigma_b(f; z) \) and \( A(f; z) \) in (2) and (3) for sample and reference phantom, a linear equation is obtained as

\[
X(f; z) = -4a(z) f z + b(z) + n(z) \ln f \tag{4}
\]

where

\[
a(z) = a_{\text{avg}}(z) - a_{0,r}
\]

\[
b(z) = \ln \beta_z(z) - \ln \beta_r
\]

\[
n(z) = v_y(z) - v_r.
\]

Our proposed method is based on minimizing a cost function \( C \) composed of a data term \( D \) and a regularization term \( R \). Herein, the data term is formulated as presented in [29]. The regularization term will be presented in the next part

\[
C = D + R \tag{5}
\]

\[
D = \sum_{i=1}^{N_G} \sum_{i=1}^{N_G} (X(f_i, z_i) - b_i - n_i \ln(f_i) + 4a_i f_i z_i)^2 \tag{6}
\]

where \( N_G \) and \( N_F \) refer to the number of axial lines and frequency bins, respectively.

B. ADMM for L1 Norm Regularization in QUS

We consider two different regularization functions \( R_1 \) and \( R_2 \) as follows. In \( R_1 \), we use the L1 norm regularization for all the parameters

\[
R_1 = \sum_{i=2}^{N_G} w_a \cdot |a_i - a_{i-1}| + w_b \cdot |b_i - b_{i-1}| + w_n \cdot |n_i - n_{i-1}|| \tag{7}
\]

where \( w_a, w_b, \) and \( w_n \) refer to the regularization weights for each parameter. In \( R_2 \), we use the L2 norm for the average attenuation and L1 for the BSC-related terms

\[
R_2 = \sum_{i=2}^{N_G} w_a (a_i - a_{i-1})^2 + w_b \cdot |b_i - b_{i-1}| + w_n \cdot |n_i - n_{i-1}| \tag{8}
\]

Here, the issue is that the L1 norm is not analytically differentiable. To solve this, we minimize instead the following constrained cost function:

\[
C = D(x) + R(s), \quad \text{s.t.} \quad Kx + Ls = m \tag{9}
\]

where \( K \) and \( L \) are known matrices, \( m \) is a given vector, and \( x \) and \( s \) are separable variables. The augmented Lagrangian function solves the unconstrained version of the above constrained cost function as follows:

\[
\begin{align*}
L_o(x, s, y) &= D(x) + R(s) + y^T (Kx + Ls - m) \\
&\quad + \rho \left(\frac{1}{2} \|Kx + Ls - m\|_2^2\right) \tag{10}
\end{align*}
\]

where \( y \) is the Lagrange multiplier and \( \rho > 0 \) weights the constraint. ADMM solves (9) iteratively as follows:

\[
\begin{align*}
\begin{cases}
x^{k+1} &= \arg \min_x L_o(x, s^k, y^k) \\
s^{k+1} &= \arg \min_s L_o(x^{k+1}, s, y^k) \\
y^{k+1} &= y^k + \rho (Kx^{k+1} + Ls^{k+1} - m)
\end{cases}
\end{align*}
\]

where \( k \) shows the iteration number.

Therefore, as ADMM’s name implies, it penalizes each component of the cost function sequentially (alternative direction). This feature is favorable when an identical optimization procedure is not applicable for both data and regularization terms.

Herein, we start by rewriting (6) in the matrix format and express the equation as \( Qx = Y \), where \( x = [a_1 a_2, \ldots, a_{N_x} b_1, \ldots, b_{N_y} n_1, \ldots, n_{N_y}]^T \). \( Q \) is a matrix containing depth and frequency, and \( Y \) is a vector. We multiply...
both sides of this equation by $Q^T$, name $Q^TQ = H$ and $Q^TY = t$, and minimize the following cost function:

$$C = \frac{1}{2} \| Hx - t \|_2^2 + \lambda \|s\|_1,$$

s.t. $Kx - s = 0$ (12)

where $s$ denotes the regularization term and $H$ is given as follows:

$$H = \begin{bmatrix} H_1 & H_2 & H_3 \\ H_2 & H_4 & H_5 \\ H_3 & H_5 & H_6 \end{bmatrix}$$ (13)

and $H_j$, $j = 1, \ldots, 6$ are $N_x \times N_R$ diagonal matrices

$$H_1 = \left( 16 \sum_{i=1}^{N_x} f_i^2 \right) \mathbf{Z}_2, \quad H_2 = \left( -4 \sum_{i=1}^{N_x} f_i \right) \mathbf{Z}_1$$

$$H_3 = \left( -4 \sum_{i=1}^{N_x} f_i \ln f_i \right) \mathbf{Z}_1, \quad H_4 = (N_F) \mathbf{I}$$

$$H_5 = \left( \sum_{i=1}^{N_x} \ln f_i \right) \mathbf{I}, \quad H_6 = \left( \sum_{i=1}^{N_x} (\ln f_i)^2 \right)$$ (14)

where $\mathbf{I}$ is the $N_R \times N_R$ identity matrix and

$$Z_1 = \begin{bmatrix} z_1 & 0 & \cdots & 0 \\ 0 & z_2 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & z_{N_R} \end{bmatrix}$$

$$Z_2 = \begin{bmatrix} z_1^2 & 0 & \cdots & 0 \\ 0 & z_2^2 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & z_{N_R}^2 \end{bmatrix}$$

and $t$ is defined as follows:

$$t = \begin{bmatrix} t_1 \\ t_2 \\ t_3 \end{bmatrix}$$ (15)

where its $i$th term is given as follows:

$$t_1 = -4z_i \sum_{i=1}^{N_x} X(f_i, z_i) f_i$$

$$t_2 = \sum_{i=1}^{N_x} X(f_i, z_i)$$

$$t_3 = \sum_{i=1}^{N_x} X(f_i, z_i) \ln f_i$$

and $K$ is given as follows:

$$K = \begin{bmatrix} K_a & O & O \\ O & K_b & O \\ O & O & K_n \end{bmatrix}$$

and

$$K_j = w_j B$$ (16)

where $j$ can be $a$, $b$, and $n$; $w_j$ denotes the regularization weights for the corresponding parameter, and $B$ is given as follows:

$$B = \begin{bmatrix} 1 & -1 & 0 & 0 & \cdots & 0 \\ 0 & 1 & -1 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & 1 & -1 \end{bmatrix}$$ (17)

Now, to update $x$, $s$, and $y$, we exploit (10) and (11), where $D(x)$ and $R(s)$ are $(1/2)\|Hx - t\|_2^2$ and $\lambda \|s\|_1$, respectively. Accordingly, we obtain

$$x^{k+1} := (H^TH + \rho K^TK)^{-1} H^Tt + \rho K^T (s^k - y^k)$$

and to update $s$, the following equation is obtained with respect to the shrinkage function $S_{\lambda/\rho}$:

$$s^{k+1} = \arg \min_{s} \lambda \|s\|_1 - y + \frac{\rho}{2} \|Kx^{k+1} - s\|_2$$

which performs a soft thresholding

$$S_{\lambda/\rho} = \text{sgn}(\cdot) \max\left( |\cdot| - \frac{\lambda}{\rho}, 0 \right).$$

Consequently, we have

$$s^{k+1} := S_{\lambda/\rho} \left( Kx^{k+1} + y^k \right)$$

$$y^{k+1} = y^k + Kx^{k+1} - s^{k+1}.$$ (18)

In contrast to the BSC, which can vary abruptly between different tissue regions, the average attenuation varies moderately. To be consistent with this physical property, we employ the L2 norm for the average attenuation and the L1 norm for the BSC in the regularization part instead of incorporating the same norms for all the parameters. Accordingly, we split the vector $x$ into two parts for the average attenuation $x_1$ and the BSC $x_2$. Consequently, the corresponding elements of $s$ and $y$ are called $s_1$, $s_2$, $y_1$, and $y_2$. Therefore, the algorithm is modified as follows:

$$C = \frac{1}{2} \| Hx - t \|_2^2 + \lambda_1 \|s_1\|_2^2 + \lambda_2 \|s_2\|_1$$

s.t. $K_1x_1 - s_1 = 0$, $K_2x_2 - s_2 = 0$. (19)

Updating $x$ and $y$ is the same as (18), but $s$ is updated by $s_1$ and $s_2$ as follows:

$$x^{k+1} := (H^TH + \rho K^TK)^{-1} H^Tt + \rho K^T (s^k - y^k)$$

$$s_1^{k+1} := S_{\lambda/\rho} \left( (K_1x_1^{k+1} + y^k_1) / (\rho + \lambda_1) \right)$$

$$s_2^{k+1} := S_{\lambda/\rho} \left( K_2x_2^{k+1} + y^k_2 \right)$$

$$y^{k+1} = y^k + Kx^{k+1} - s^{k+1}.$$ (20)

where $H$ and $K$ are the same as (13) and (16), and $K_1$, $K_2$, $x_1$, and $x_2$ are given as follows:

$$K_1 = K_a, \quad K_2 = \begin{bmatrix} K_b & O \\ O & K_n \end{bmatrix}$$ (21)

$$x_1 = [a_1 \ a_2 \ \cdots \ \ a_{N_a}]^T, \quad x_2 = [b_1 \ \cdots \ \ b_{N_a} \ \ \ n_1 \ \cdots \ \ n_{N_a}]^T.$$ (22)
C. Computational and Experimental Phantoms

1) Computational Phantoms: RF data from a sample phantom and reference phantom were simulated in Field II using a linear transducer geometry (192 elements, 12.833 μm kerf) with a center frequency of 6 MHz and 80% bandwidth. The method in [46] allowed the addition of frequency-dependent backscatter to each set of simulated data. The average attenuation of the sample and reference phantoms is 0.7 dB cm⁻¹ MHz⁻¹ and 0.5 dB cm⁻¹ MHz⁻¹, respectively, and the BSC parameters are \( b = 1.63 \times 10^{-3} \) MHz⁻² cm⁻¹ sr⁻¹; \( n = 2.368 \) for the sample and \( b = 4.602 \times 10^{-3} \) MHz⁻² cm⁻¹ sr⁻¹; and \( n = 2.746 \) for the reference phantoms obtained by a power-law fit around the frequency range.

2) Phantom With Specular Reflectors: We investigated the susceptibility (in terms of bias and variance) of regularized PEQUIS methods to the presence of specular reflectors in the estimation of QUS parameters. Five uncorrelated frames of RF data were collected from a Gammex 410 SCG phantom (Gammex-Nuclear, Middleton, WI, USA) with an L11-5v transducer operated at 8 MHz. To get the nylon filaments to produce specular reflection, they were scanned by aligning the transducer aperture with the long axis of the fibers. In addition, reference data were collected from the background of the same phantom. The BSC of the background of the phantom was obtained from a similar phantom from the same manufacturer \((s/n 802259-28880-5)\). The background has the following properties:

1) \( \alpha_{avg} = 0.6035 \) dB cm⁻¹ MHz⁻¹
2) \( \beta_i = 2.9966 \times 10^{-6} \) cm⁻¹ MHz⁻¹
3) \( \nu_n = 3.4281 \)
4) \( \sigma_{b,r}(8 \) MHz \) = \( 3.74 \times 10^{-3} \) cm⁻¹ sr⁻¹.

3) Phantom With Inclusions—Scanner A: In order to evaluate the performance of the proposed algorithm for the characterization of localized targets, we scanned a region of the same Gammex 410 SCG phantom with three cylindrical inclusions with +12 dB, +6 dB, and −6 dB scattering with respect to the background. \( \alpha_{avg} \) and the BSC of this region is the same as the background region in the frames with specular reflectors.

4) Phantom With Inclusions—Scanner B: In order to evaluate the generalizability of the observations in the phantom with inclusion to other phantom, transducers, and scanners, we obtained ten frames of RF data from the Sono404 phantom using Siemens S3000 (Healthineers, Issaquah, WA, USA) ultrasound machine with 18L6 transducer operated at 9 MHz. The physical properties of this phantom are \( a = 0.5412 \) dB cm⁻¹ MHz⁻¹; \( b = 1.8450 \times 10^{-6} \) MHz⁻² cm⁻¹ sr⁻¹, and \( n = 3.8846 \) for the sample and the reference phantoms.

D. Weighted Frequency

We use a weighted frequency scheme to give the power spectra a score (weight) at each frequency and depth depending on the available power versus noise. To do so, the data term is multiplied by a spatially and frequency-varying weight \( w_d \).

Thus, the data term formulation is adapted as follows:

\[
D = \sum_{i=1}^{N_x} \sum_{j=1}^{N_y} w_d(i, j)(X(f_i, z_i) - b_i - n_i \ln(f_i) + 4a_i f_i z_i)^2.
\]

In the ALGEBRA method, we selected the bandwidth based on the assessment of bias and variance of BSC and average attenuation. However, herein, to select the bandwidth, we plot the logarithmic scale of the lateral average of the power spectra of sample and reference phantoms and determine the corresponding frequency range where higher power is amassed. The black dashed lines in Figs. 1 and 2 illustrate this range for power spectra obtained from a sample phantom and a reference phantom described in Section II-B, which are the corresponding frequencies for 80% of the maximum logarithmic power spectra. To calculate \( w_d \), we propose using contour level sets shown in Figs. 3 and 4, and to carry this out, we form the following equations to compute \( w_s \) and \( w_r \) for the sample and reference phantoms separately

\[
w_s = \begin{cases}
1, & S_r > T_1, \\
S_r - T_2, & T_1 > S_r > T_2, \\
T_1 - T_2, & T_1 > T_2 \\
0, & S_r < T_2,
\end{cases}
\]

\[
w_r = \begin{cases}
1, & S_r > T_1, \\
S_r - T_2, & T_1 > S_r > T_2, \\
T_1 - T_2, & T_1 > T_2 \\
0, & S_r < T_2,
\end{cases}
\]

where \( S \) is the logarithmic scale of the power spectra shown in Figs. 1 and 2, and \( T_1 \) and \( T_2 \) express the upper level and lower level of contours shown in Figs. 3 and 4 with yellow and purple colors, respectively. Since two thresholds (upper and lower levels), \( T_1 \) and \( T_2 \), are in the formulation of \( w_d \), three regions in the power spectra should be defined based on the amount of power concentration. For this purpose, we select the lower level of contours in the boundaries of the low-to-medium region and the upper level in the boundaries of the medium-to-high regions, which corresponds to 90% of the maximum and 167% of the minimum of the power spectra. In the end, the intersection of \( w_s \) and \( w_r \) computed using
Fig. 2. Lateral average of the power spectra of (a) sample phantom and (b) reference phantom in the logarithmic scale for the phantom with inclusions—scanner A.

Fig. 3. Contour levels of the lateral average of the power spectra of reference phantom in the logarithmic scale for the phantom with specular reflectors.

Fig. 4. Contour levels of the lateral average of the power spectra of (a) sample phantom and (b) reference phantom in the logarithmic scale for the phantom with inclusions—scanner A.

Element-wise matrix multiplication is regarded as $w_d$

$$w_d = w_s \odot w_r.$$  \hspace{1cm} (24)

Fig. 1(a) shows the power spectra of the sample phantom that were affected by the specular reflectors. Accordingly, we only consider the reference phantom to calculate $w_d$ ($w_d = w_r$). Figs. 5 and 6 show $w_d$ for the region with specular reflectors and the region with inclusions.

E. Quantitative Metrics

In this study, we report the variance and bias of the estimated features to evaluate and compare the performance of several estimation methods. To compute the variance and bias, four regions of interest (ROI) are selected for each region. Figs. 7–9 present the locations of each ROI on a B-mode image of the phantom with specular reflectors and the phantom with inclusions—scanners A and B, respectively. For the phantom with specular reflectors, the locations are selected between the fibers, and for the phantom with inclusions, they are selected at the center of the background and each inclusion. The size of ROI in Figs. 7 and 8 is $4 \times 19$ mm and $4 \times 4$ mm, respectively. Fig. 9 shows five $2.6 \times 2.6$ mm ROIs.

To report the bias and variance for each ROI, we calculate the average of the estimations across the frames, $M$, and use the following equations:

$$\text{bias}_{\alpha_{\text{avg}}} = |M_{\alpha}(\cdot) - GT_{\alpha}|$$  \hspace{1cm} (25)

$$\text{variance}_{\alpha_{\text{avg}}} = \text{var}(M_{\alpha}(\cdot))$$  \hspace{1cm} (26)

$$\text{bias}_{\text{BSC}} = 10 \log_{10}\left(\frac{M_{\text{BSC}}(\cdot)}{10^{-4}}\right) - 10 \log_{10}\left(\frac{GT_{\text{BSC}}}{10^{-4}}\right)$$  \hspace{1cm} (27)

$$\text{variance}_{\text{BSC}} = \text{var}\left(10 \log_{10}\left(\frac{M_{\text{BSC}}(\cdot)}{10^{-4}}\right)\right)$$  \hspace{1cm} (28)
where GT accounts for the ground truth. The BSC is reported at the center frequency and scaled to dB with respect to $10^{-4} \text{cm}^{-1} \text{sr}^{-1}$.

### III. RESULTS

#### A. Computational Phantoms

Figs. 10 and 11 show the bias and variance of the BSC and average attenuation estimations using different approaches on the computational phantoms, respectively. The quantitative measurements reveal that ADMM-based methods reduced the bias and variance of the BSC and average attenuation estimations up to 50%, 33.6%, 99.6%, and 95.7%. Furthermore, ALGEBRA $w_d$, ADMM $w_d$, and ADMM L1L2 $w_d$ lead to the reduction of the bias of the BSC by 1.5%, 36%, and 50% compared to the corresponding no $w_d$ methods as well as 0.5%, 32.4%, and 44.6% reductions in the bias of the average attenuation. The variance of the BSC decreased by 10.5%, 55%, and 85.5% using ALGEBRA $w_d$, ADMM $w_d$, and ADMM L1L2 $w_d$, respectively, compared to the corresponding no $w_d$ approaches, while the variance in attenuation was reduced by 9%, 3.7%, and 13.2%.

#### B. Phantom With Specular Reflectors

Figs. 12 and 13 report the bias and variance of the BSC on the decibel scale and the average attenuation, respectively. The figures demonstrate the superior performance of ADMM in terms of bias and variance compared to the performance of ALGEBRA. More precisely, comparing ADMM and ALGEBRA both without $w_d$ in regions 1–4 reveals that the bias of BSC estimation decreased 86.1%, 88.3%, 76.3%, and 83.1%, respectively, and the variance experienced 68.8%, 78.9%, 60.1%, and 77.7% reductions. Moreover, the bias of the average attenuation decreased 85.5%, 92.7%, 83%, and 93.2% in ROIs 1–4 as well as 76.5%, 84.4%, 54.1%, and 76.2% reductions in the variance. In addition, using $w_d$ in combination with different norms in the regularization term further improves the accuracy and precision of the estimates.

The quantitative comparison of ALGEBRA with and without $w_d$ in Fig. 10 shows that smoother estimations are achieved by incorporating $w_d$ in the cost function. Using the $w_d$ strategy in ADMM reduced the bias of BSC by 88.1%, 52.5%, and 98.9%, in regions 1–3, compared to not using $w_d$. In addition, the variance is reduced by 42.1% in region 1. Moreover, attenuation evaluation results in 86.3% and 44.6% reductions in bias in regions 1 and 3. A 52.2% lower variance is reported in region 1 when using ADMM with $w_d$ versus not using $w_d$. The MATLAB implementation of ALGEBRA shows that it is 100 times faster than ADMM for this region.

#### C. Phantom With Inclusions—Scanner A

The results of BSC estimation at the center frequency using six techniques are shown in Fig. 14. Parametric images obtained from ADMM are more similar to the ground truth compared to those obtained with ALGEBRA. From Figs. 15 and 16, it is perceived that incorporating $w_d$ in the

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Fig. 10. Comparison of (a) bias (dB) and (b) variance (dB^2) of the BSC in the computational phantom. Results are shown on a decibel scale with respect to 10^{-4} cm^{-1} sr^{-1}.

Fig. 11. Comparison of (a) bias (dB cm^{-1} MHz^{-1}) and (b) variance (dB^2 cm^{-2} MHz^{-2}) of the average attenuation in the computational phantom.

ALGEBRA cost function reduces the bias and variance of the BSC and the average attenuation estimations. Comparing the results of our proposed technique concerning ADMM without weighting the data term shows an 80.3% reduction in the bias in region 2 as well as 15.5%, 22.1%, and 1% reduction in the variance of BSC estimation in regions 1, 3, and 4, respectively. Furthermore, attenuation evaluation results in 29.4%, 88.2%, and 66.1% decline in the bias of regions 2–4, respectively, and 4.2% and 10.9% reductions in variance in regions 1 and 3, respectively. The MATLAB implementation of ALGEBRA shows that it is 18 times faster than ADMM for this region.

D. Phantom With Inclusions—Scanner B

Figs. 17 and 18 show the bias and variance of the BSC and the average attenuation, respectively. The figures illustrate that overall, lower bias and variance are obtained using ADMM L1L2 w_d compared to the other algorithms.

IV. DISCUSSION

This article presented a novel cost function consisting of L2 norm weighted data term and L1 and L2 norm regularization terms optimized using ADMM. Our method was applied to a computational phantom as well as data acquired from phantoms with cylindrical inclusions and specular reflectors with two different scanners and transducers.

Unlike [29], we carefully focused on selecting the bandwidth in the first part of our proposed technique. In [29], the frequency range was chosen based on the evaluation of the bias and variance of the BSC and the average attenuation estimations. Therefore, we observed that for the region with inclusions, the application of ALGEBRA within a wide frequency range leads to very good agreement with the ground truth values of the BSC. However, herein, our strategy for selecting the bandwidth of interest is different. Figs. 1 and 2 show that the frequency ranges were chosen based on the parametric image of the power spectra of the sample and reference phantoms. The intersection of the corresponding frequency ranges of the sample and the reference phantoms with high concentrated power is accounted for as the bandwidth of interest, which is depth-dependent as well. Our proposed approach for selecting the bandwidth of interest outperforms the method we applied in [29] because: 1) it is possible that a
wide frequency range leads to excellent results in terms of the quantitative and qualitative assessments, but the selected band may contain low power (which is the case when sample and reference phantom are the same) and 2) in clinical applications with unknown ground truth, the evaluation of bias, which leads to selecting the frequency range, is not practical. When the spectrum is corrupted by the presence of tissue boundaries or specular reflectors, the selection of the bandwidth can be done on the reference data, as shown in Fig. 5.

In the next step, we weighted the data term using the contour level sets derived from the bandwidth analysis. Weighting the data term is similar to giving scores from 0 to 1 to the least and most informative band of the echo signal power spectrum. On the other hand, considering zero weight does not make sense as there is still power on the less informative parts. Furthermore, assigning zero weights means completely ignoring the data term part of the cost function. Hence, we shifted the calculated $w_d$ and normalized it by dividing it by the maximum value of the newly calculated $w_d$. Afterward, we assigned the L2 regularization norm for attenuation and the L1 norm for BSC to be in accordance with the physics-based properties of each.

Finally, our novel cost function was minimized using ADMM. An important point that should be considered is that the expense of the computational complexity for reducing the bias and variance is worth, especially when a phantom or tissue that we attempt to characterize is similar to the region with specular reflectors, meaning that the majority part of the media is with the same QUS parameters and a small fraction of that has different parameters. In such a case, ALGEBRA completely fails, and our proposed technique is highly preferable. However, like ALGEBRA, a limitation of our method is that for calculating the local attenuation, the effective attenuation needs to be estimated first. Overall, the best results in terms of bias and variance for all experiments were achieved by weighting the data term and applying L1 and L2 norms in the regularization part of the cost function.

In general, the selection of $w_d$ needs to consider the bandwidths with available echo power in both the sample and the reference. In this work, the attenuation of the sample and reference phantoms was similar, resulting in similar bandwidths with available power. Consequently, considering...
only the reference phantom would be sufficient in this specific scenario.

In clinical examples where the true values of the attenuation and backscatter are unknown, choosing the weights can be more challenging. In such cases, one way to design the weights is to first run a nonregularized least squares (LSQ) estimator, which is equal to setting zero regularization weights for all the parameters and plotting the QUS parameters. Then, we can set
Fig. 15. Comparison of (a) bias (dB) and (b) variance (dB^2) of the BSC in four ROI in the region with inclusions. Results are shown on a decibel scale with respect to 10^{-4} cm^{-1} sr^{-1}.

Fig. 16. Comparison of (a) bias (dB cm^{-1} MHz^{-1}) and (b) variance (dB^2 cm^{-2} MHz^{-2}) of the average attenuation in four ROI in the region with inclusions.

Fig. 17. Comparison of (a) bias (dB) and (b) variance (dB^2) of the BSC in five ROIs of the Sono404 phantom. Results are shown on a decibel scale with respect to 10^{-4} cm^{-1} sr^{-1}.

the weights to the values in the range of 1e^{-1}, 1e^{1}, 1e^{2}, \ldots, 1e^{8} and plot the results. Let us assume that for the weight 1e^{3}, the results are almost identical to the LSQ. This means this weight is too small. Furthermore, if we suppose that for the weight 1e^{7}, the results are constant, it means that the chosen weight is too large. In this case, 1e^{5} can be the optimal weight. To test
this, we can double the optimal weight ($2e^5$) and plot the results. If the results are similar to those obtained with $1e^5$, then the optimal weight is $1e^5$. This implies that the results are independent of the weight.

In this work, we did not try to optimize the computational complexity of the algorithm. Instead, our goal was to introduce an approach for estimating the attenuation and BSC. By optimizing both the implementation efficiency and parallelization of the technique, it may be possible to reduce its runtime by several orders of magnitude, thereby enabling the method to be potentially suitable for clinical deployment.

Another limitation is that the algorithm proposed here is based on the use of a reference phantom. Although new reference phantom free methods have been developed, the RPM can be feasibly implemented in the clinic without having to scan a phantom after each patient. Commercial scanners can be equipped with a pretuned reference phantom or data to train a machine learning model for providing the attenuation values. However, these systems provide the BSC measurement at one frequency [14].

Altogether, incorporating $w_d$ in the data term as well as employing L1 and L2 norms in the regularization part improve the estimation. However, the percentage of the outperformance depends on the data and the size of ROI. For instance, in the region with specular reflectors and the Sono 404 phantom, the superior performance of ADMM L1L2 $w_d$ is clearer. However, since the size of ROI in the inclusion region is smaller than the specular reflector region, the parameter estimation is more sensitive to the bias–variance tradeoff.

Significant differences between our work and other groups are: 1) proposing weighting the data term and 2) taking into account physics properties of QUS parameter in the cost function. We predict using $w_d$ and combining L1 and L2 norms in the cost function can further improve the bias of estimation for the cases where sample and reference phantoms are different.

V. CONCLUSION

Here, we proposed a novel approach for estimating the average attenuation and the BSC. Our algorithm incorporates ADMM to penalize a cost function containing L2 norm weighted data term and L1 and L2 norms regularization terms to be associated with the physical properties of the BSC and the average attenuation. Visual and quantitative evaluations justify that our proposed algorithm substantially outperforms the other techniques.

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