

Modeling Errors Compensation With Total Least Squares for Limited Data Photoacoustic Tomography

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Abstract—The limited data photoacoustic image reconstruction problem is typically solved using either weighted or ordinary least squares (LS), with regularization term being added for stability, which account only for data imperfections (noise). Numerical modeling of acoustic wave propagation requires discretization of imaging region and is typically developed based on many assumptions, such as speed of sound being constant in the tissue, making it imperfect. In this paper, two variants of total least squares (TLS), namely ordinary TLS and Sparse TLS were developed, which account for model imperfections. The ordinary TLS is implemented in the Lanczos bidiagonalization framework to make it computationally efficient. The sparse TLS utilizes the total variation penalty to promote recovery of high frequency components in the reconstructed image. The Lanczos truncated TLS and Sparse TLS methods were compared with the recently established state-of-the-art methods, such as Lanczos Tikhonov and Exponential Filtering. The TLS methods exhibited better performance for experimental data as well as in cases where modeling errors were present, such as few acoustic detectors malfunctioning and speed of sound variations. Also, the TLS methods does not require any prior information about the errors present in the model or data, making it attractive for real-time scenarios.

Index Terms—Image reconstruction, Lanczos bidiagonalization, model errors, photoacoustic imaging, sparse total least squares, total least squares, and truncated total least squares.

I. INTRODUCTION

PHOTOACOUSTIC tomography (PAT) is a non-invasive and hybrid imaging technique combining endogenous optical contrast and high ultrasonic resolution [1]–[5]. In this, a

pulsed laser irradiates the biological tissue under investigation, the optical energy gets absorbed by the tissue, resulting in a temperature rise (in the order of milli Kelvin). Thus leading to acoustic waves generation due to thermoelastic expansion. The generated pressure waves propagate in the tissue and gets detected by the acoustic transducers placed on the boundary of the tissue. The recorded pressure information at the boundary of the tissue gets utilized in a reconstruction scheme to obtain the initial pressure rise distribution. The initial pressure rise is proportional to the product of optical fluence and absorption coefficient. The absorption coefficient is internally very sensitive to the tissue patho-physiology. So the initial pressure distribution reveals the tissue patho-physiological condition, with major applications in oncology and physiology. Moreover, PAT can be scalable to reveal structural, functional, and molecular information [6]–[10].

The important step in photoacoustic tomography is image reconstruction, which enables quantification of tissue functional properties [11]–[14]. Several reconstruction methods, including analytical and model-based, have been proposed earlier in the literature [14]. Analytical reconstruction algorithms (specifically, filtered back projection (FBP) and delay & sum) and time-reversal based algorithms have been widely used to reconstruct the initial pressure distribution [11]–[14]. These algorithms are relatively fast compared to model-based ones with a caveat that they require large data to provide much required quantification. The requirement of large data in turn solicits higher instrumentation cost and/or increased data acquisition time. The recent advances in image reconstruction have enabled utilization of model-based reconstruction schemes effectively and proven to provide quantitatively accurate results compared to analytical reconstruction algorithms in limited-data cases [14]–[16].

The photoacoustic tomographic setups that are commonly deployed records the acoustic signals over an aperture that does not enclose the object, which results in limited data (also known as incomplete data) [17]–[19] or resorts to compressed sensing approaches to accelerate data acquisition [20]. In these cases, the PA reconstruction is an ill-posed problem, necessitating the model-based algorithms to impose constraints on the solution of the inverse problem by a regularization scheme [21]–[25]. The work presented here is geared towards providing practical algorithms that can work effectively in these limited data cases (i.e., providing solution to the ill-posed problem). Most model-based algorithms assume that the model (imperfect) is known and does not minimize the imperfections in the model.

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However, model imperfections cause distortions in the image and degrade the image quality. Recently, a reconstruction algorithm to mitigate the modeling errors induced by inaccurate knowledge of transducer impulse response was proposed and shown to be effective in terms of improving the reconstructed photoacoustic image quality [26]. However, explicitly accounting for all possible model/experimental inconsistencies in a reconstruction algorithm is computationally demanding, in turn making the image reconstruction procedure not appealing in real-time.

This work introduces a scheme that was based on total least squares (TLS), which could handle modeling errors effectively. Specifically, it introduces Lanczos truncated total least squares (T-TLS) [27] as well as Sparse total least squares (Sparse TLS) [28], [29], which can simultaneously handle imperfections in the model as well as data noise. The Lanczos T-TLS was set-up in a well-established dimensionality reduction framework that uses least-squares QR (Lanczos bidiagonalization) decomposition, thus adding little to no computational complexity to perform the image reconstruction procedure. We also show that using numerical examples that Lanczos T-TLS and Sparse TLS can effectively handle acoustic detector malfunctioning and also provide more robustness to noise compared to the state-of-the-art image reconstruction methods. Similarly, another case of handling modeling errors, such as speed of sound variation, was also presented to show the effectiveness of the TLS methods. Finally, the experimental data generated from horse hair phantom was utilized to validate the effectiveness of TLS methods.

II. PHOTOACOUSTIC TOMOGRAPHY: FORWARD PROBLEM

The forward problem in PAT involves collection of pressure data on the boundary of the tissue for a given initial pressure distribution. The acoustic wave propagation in biological tissues can be modeled using the wave equation, given as

$$\nabla^2 P(d, t) - \frac{1}{c^2} \frac{\partial^2 P(d, t)}{\partial t^2} = \frac{-\beta}{C_p} \frac{\partial H(d, t)}{\partial t}, \quad (1)$$

where c is the speed of sound in the medium, β is the thermal expansion coefficient, C_p is the specific heat, and $H(d, t)$ is the absorbed energy per unit time per unit volume with spatial location indicated by d . For a stationary source, the absorbed energy can be written as $H(d, t) = H(d)H(t)$. Under the condition of stress confinement, the temporal part of the source can be approximated by a delta function $H(d, t) \approx H(d)\delta(t)$ [30]. Equation (1) with source term being $\frac{-\beta}{C_p} H(d) \frac{\partial \delta(t)}{\partial t}$ is equivalent to solving the following initial value problem [30]

$$\nabla^2 P(d, t) - \frac{1}{c^2} \frac{\partial^2 P(d, t)}{\partial t^2} = 0, \quad (2)$$

with initial conditions $P|_{t=0} = \Gamma H(d)$, where $\Gamma = \frac{c^2 \beta}{C_p}$ is the Gruneisen parameter which denotes the efficiency of conversion of absorbed energy to pressure and $\partial P / \partial t|_{t=0} = 0$.

Applying Fourier Transform to (1) gives the well-known Helmholtz equation

$$(\nabla^2 + k^2)P(d, \omega) = \frac{-j\omega\beta}{C_p} H(d, \omega), \quad (3)$$

where $k = \frac{\omega}{c}$ with ω as the angular frequency and $P(d, \omega)$ is the Fourier transform of the acoustic pressure $P(d, t)$. The solution to the above equation can be expressed using Green's function as

$$P(d, \omega) = \frac{-j\omega\beta}{C_p} H(d, \omega) G(d, \omega), \quad (4)$$

where $G(d, \omega) = \frac{-i}{4} H_0^{(1)}(k|d|)$ with $H_0^{(1)}$ being the Hankel function of the first kind of order zero [31], [32]. The impulse response for the acoustic wave equation in the time domain is obtained by applying inverse Fourier transform to (4). In this work, the above described Green's function approach was deployed to solve (1). Note that, the system matrix-based approach was utilized here to represent the forward problem as a linear system of equations [33]–[35]. The forward problem in PAT thus becomes

$$\mathbf{A}x = b, \quad (5)$$

with $\mathbf{A}$ having a dimension of $m \times n^2$ with its columns being the impulse responses of corresponding pixels, x being initial pressure distribution (in a lexicographic manner, dimension: $n^2 \times 1$, with imaging region having a size of $n \times n$) and b being the recorded photoacoustic data stacked in a single column (dimension: $m \times 1$, with m equal to the product of number of transducers and time steps used for recording the photoacoustic signal).

III. PHOTOACOUSTIC TOMOGRAPHY: INVERSE PROBLEM

The inverse problem involves the estimation of initial pressure distribution (x in (5)) from boundary measurements (b) using a reconstruction algorithm [14]. Note that $\mathbf{A}$ represents a time-variant casual system and is ill-posed due to the limited-data cases considered. Thus finding x requires the utilization of regularization to constrain the solution space and this regularization dictates characteristics of x .

The proposed method, known as the total least squares (TLS) is a generalized version of original least squares method, which seeks the solution to the equation that has perturbations both in $\mathbf{A}$ and b [27]. An efficient implementation of the same based on the Lanczos bidiagonalization was utilized in this work to provide practical utility for the proposed TLS, named as Lanczos T-TLS. The Sparse TLS method that utilizes the well known total variation (TV) penalty term was also deployed in the TLS framework. Note that for completeness, the Lanczos bidiagonalization performed in the Tikhonov framework [33], which was earlier utilized to effectively solve the PAT inverse problem, was deployed in this work as conventional/standard regularization method. The asymptotic regularization [36], based on exponential filtering of singular values, was shown as state-of-the-art method was also deployed here to compare with the TLS methods. These methods, Lanczos Tikhonov and Exponential

filtering will be discussed along with the Lanczos T-TLS and Sparse TLS methods in following subsections.

A. Time Reversal Method

The k-wave time reversal is a single-step image reconstruction method, which is a standard method used for estimating the initial pressure distribution. The aim is to reconstruct the initial pressure distribution (at $t = 0$) given the measured boundary acoustic data (at time t). The k-wave time reversal was provided by an open-source k-wave toolbox [37]. It assumes that the photoacoustic solution vanishes inside the imaging region for $t > T$, where T is the longest time taken by the wave to pass through the domain [37]. A zero initial condition at $t = T$ and the boundary condition being the measured data was imposed on the wave equation to obtain the solution at $t = 0$. To improve the PA image reconstruction, the interpolated measurement vector was given as an input to the time reversal algorithm. In this work, initially this method was utilized for comparison with the proposed method.

B. Lanczos Tikhonov Regularization

The details of this method were described previously in [33], in here, it is briefly reviewed for completeness. The least-squares QR [33] based on Lanczos bidiagonalization offers a two-level regularization, one with respect to Lanczos bidiagonalization iterations and another using the reduced dimension matrices in the Tikhonov regularization framework. The Tikhonov regularization framework will minimize the following with respect to x , i.e.,

$$\Omega = \|\mathbf{A}x - b\|_2^2 + \lambda \|x\|_2^2 \quad (6)$$

with λ being the regularization parameter that dictates the reconstructed image characteristics. The l_2 -norm is represented by $\|\cdot\|_2$. The least-squares solution for this minimization is

$$x = (\mathbf{A}^T \mathbf{A} + \lambda \mathbf{I})^{-1} \mathbf{A}^T b \quad (7)$$

with $\mathbf{I}$ representing the identity matrix. Computing x using the above equation is a $\mathcal{O}(n^6)$ procedure, making it prohibitively expensive in terms of computation. The earlier work by our group utilized the Lanczos bidiagonalization to make estimation of x computationally efficient with an added advantage of enabling automatic estimation of λ [33]. In this, the system matrix $\mathbf{A}$ gets related to left and right Lanczos and bidiagonal matrices as [21]

$$\mathbf{U}_{k+1}(\beta_1 e_1) = b \quad (8)$$

$$\mathbf{A}\mathbf{V}_k = \mathbf{U}_{k+1}\mathbf{B}_k \quad (9)$$

$$\mathbf{A}^T \mathbf{U}_{k+1} = \mathbf{V}_k \mathbf{B}_k^T + \alpha_{k+1} v_{k+1} e_{k+1}^T \quad (10)$$

where $\mathbf{U}_{k+1}$ and $\mathbf{V}_k$ are left and right orthogonal Lanczos matrices of dimensions $m \times (k+1)$ and $n^2 \times k$ respectively, β_1 is the l_2 norm of b , e_k is a unit vector of dimension $k \times 1$, and $\mathbf{B}_k$ is the lower bidiagonal matrix of dimension $(k+1) \times k$ having α_k in the main diagonal and β_k in the lower subdiagonal. The Lanczos bidiagonalization was performed using the Matlab based regularization toolbox [38]. The minimization function of

the least squares problem (given by (6)) with the bidiagonalization procedure reduces to [33]

$$\bar{\Omega} = \|\mathbf{B}_k x^{(k)} - \beta_1 e_1\|_2^2 + \lambda \|x^{(k)}\|_2^2 \quad (11)$$

where $x^{(k)}$ is the dimensionality reduced version of x . The solution of (11) is

$$x_{est}^{(k)} = (\mathbf{B}_k^T \mathbf{B}_k + \lambda \mathbf{I})^{-1} \beta_1 \mathbf{B}_k^T e_1; \quad x_{est} = \mathbf{V}_k x_{est}^{(k)} \quad (12)$$

where $x_{est}^{(k)}$ is the estimated version of $x^{(k)}$. Note that for the PAT system matrix $(\mathbf{A})$, $k \ll n^2$, thus providing a computationally efficient estimation of x .

C. Exponential Filtering or Showalter Method

The Lanczos bidiagonalization was combined in the Tikhonov regularization framework to provide a computationally efficient estimate of x . Recent works, have also shown that Showalter/exponential filtering method is more generic in nature, wherein the Tikhonov regularization solution (7) becomes a special case of this [36].

In this work, a singular value decomposition (SVD) will be performed on $\mathbf{A}$ making it

$$\mathbf{A} = \mathbf{U}\mathbf{S}\mathbf{V}^T, \quad (13)$$

where $\mathbf{U}$ and $\mathbf{V}$ are left and right orthogonal matrices and $\mathbf{S}$ is a diagonal matrix containing the singular values on its diagonal with their magnitudes reducing as one moves from the first to last diagonal entries. Substituting (13) in (7), the x becomes [36]

$$x = \mathbf{V}\mathbf{S}^\dagger \mathbf{U}^T b, \quad (14)$$

where $\mathbf{S}^\dagger = \text{diag}\left(\frac{F_i}{S_i}\right)$, with F_i denoting the filter factors and S_i represents the i^{th} diagonal value of $\mathbf{S}$. For the Tikhonov case, these become [36]

$$F_i = \frac{S_i^2}{S_i^2 + \lambda} \quad (15)$$

The exponential filtering seeks to integrate the initial value problem up to a value equal to $1/\sqrt{\lambda}$, making filter factors as [36]

$$F_i = 1 - \exp\left(\frac{-S_i^2}{\lambda}\right). \quad (16)$$

This type of regularization is also known to be asymptotic regularization (making the exponential filter factors equal to Tikhonov filter factors for a case $S_i^2 \ll \lambda$). As this method performs spectral filtering with decreasing weights with decreasing in magnitude of singular values, it acts as an effective low-pass filter, thus providing better performance compared to state-of-the-art methods [36]. One major limitation of this method is that it requires a singular value decomposition of system matrix, which is a $\mathcal{O}(m * n^4)$ procedure, making it prohibitive to perform in real-time. In this work, the computation of SVD was performed using ‘*csvd*’, which is a Matlab routine in the regularization toolbox [38].

D. Lanczos Truncated Total Least Squares (Lanczos T-TLS)

The total least squares (TLS) is a method that is effective to handle $\mathbf{A}x \approx b$, where both $\mathbf{A}$ and b are subject to imperfections [27]. It provides a generalization of minimizing $\|\bar{\mathbf{A}}x - \bar{b}\|_2^2$, with ‘ $\bar{\cdot}$ ’ representing the perfect version of the entry. Note that earlier discussed methods, exponential filtering and Lanczos Tikhonov, provide an approximate solution to this minimization. The TLS seeks an approximate solution to $\|\mathbf{A}x - b\|_2^2$, where $\mathbf{A}$ and b are prone to errors. The minimization function (Γ) that needs to be minimized in this case becomes [27]

$$\Gamma = \|\mathbf{A}x - b\|_2^2 \text{ subject to } \bar{\mathbf{A}}x = \bar{b}. \quad (17)$$

Generally this problem will be solved with utilization of SVD of the augmented matrix $[\mathbf{A}, b]$ [27]. To effectively handle the noise, the smaller singular values of augmented matrix are truncated, leading to truncated TLS (T-TLS) solution [27]. The main limitation of T-TLS method is that it is computationally expensive due to the requirement to compute the SVD of the augmented matrix.

The Lanczos bidiagonalization based T-TLS provides a superior alternative to traditional T-TLS in terms of computation. The Lanczos T-TLS performs the bidiagonalization on $\mathbf{A}$. Utilization of (8)–(10) in (17) converts it to [27]

$$\bar{\Gamma} = \left\| \mathbf{U}_{k+1}^T ([\mathbf{A}, b] - [\bar{\mathbf{A}}_k, \bar{b}_k]) \begin{pmatrix} \mathbf{V}_k & 0 \\ 0 & 1 \end{pmatrix} \right\|_2^2$$

subject to $\mathbf{U}_{k+1}^T \bar{\mathbf{A}}_k \mathbf{V}_k x^{(k)} = \mathbf{U}_{k+1}^T \bar{b}_k$.

Rewriting it (similar to (11)) makes the minimization problem into [27]

$$\bar{\Gamma} = \|[\mathbf{B}_k, \beta_1 e_1] - [\bar{\mathbf{B}}_k, \bar{e}_k]\|_2^2 \text{ subject to } \bar{\mathbf{B}}_k x^{(k)} = \bar{e}_k. \quad (18)$$

where $\bar{\mathbf{B}}_k$ and $\bar{e}_k$ are full. The Lanczos T-TLS is equivalent to LSQR (without Tikhonov regularization) Algorithm-1, if $\bar{\mathbf{B}}_k = \mathbf{B}_k$. The above optimization problem can be solved using the truncated TLS algorithm, giving the Lanczos T-TLS solution.

Note that performing SVD of the augmented matrix $[\mathbf{B}_k, \beta_1 e_1]$ requires only $\mathcal{O}(k^2)$ operations with $k \ll n^2$, thus making it very efficient in terms of computation [27].

1) *Automated Estimation of Reconstruction Parameters using Error Estimates:* All model-based reconstruction schemes performance depends on the choice of reconstruction parameters, such as λ and k , we have utilized the recently proposed error estimates [39] for an automated choice. This method was proven to be effective in terms of finding direct and iterative regularization schemes, including Lanczos Tikhonov, Exponential filtering, and non-smooth reconstruction methods. This also provides an optimal number of Lanczos iterations k . The error estimates for the norm of the error [40] is given as

$$\|e\|_2^2 \approx \eta_\nu^2 := e_o^{\nu-1} e_1^{5-2\nu} e_2^{\nu-3}, \quad \nu \in \mathbb{R} \quad (24)$$

where

$$e_o := \|r\|_2^2, \quad e_1 := \|\mathbf{A}^T r\|_2^2, \quad e_2 := \|\mathbf{A}\mathbf{A}^T r\|_2^2, \quad \text{and} \quad (25)$$

Algorithm 1: Algorithm showing main steps of Lanczos T-TLS algorithm [27].

1 Compute the Lanczos bidiagonalization of $\mathbf{A}$ for an optimal k

$$\mathbf{A}\mathbf{V}_k = \mathbf{U}_{k+1}\mathbf{B}_k \quad \text{and} \quad \beta_1 u_1 = b \quad (19)$$

2 Compute the SVD of the augmented matrix $[\mathbf{B}_k, \beta_1 e_1]$

$$(\mathbf{B}_k, \beta_1 e_1) = \tilde{\mathbf{U}}^{(k)} \tilde{\mathbf{S}}^{(k)} (\tilde{\mathbf{V}}^{(k)})^T \quad (20)$$

3 Partition the matrix $\tilde{\mathbf{V}}^{(k)}$

$$\tilde{\mathbf{V}}^{(k)} = \begin{pmatrix} \tilde{\mathbf{V}}_{11}^{(k)} & \tilde{\mathbf{V}}_{12}^{(k)} \\ \tilde{\mathbf{V}}_{21}^{(k)} & \tilde{\mathbf{V}}_{22}^{(k)} \end{pmatrix} \quad (21)$$

where $\tilde{\mathbf{V}}^{(k)} \in \mathbb{R}^{(k+1) \times (k+1)}$, $\tilde{\mathbf{V}}_{11}^{(k)} \in \mathbb{R}^{(k) \times (k)}$, and $\tilde{\mathbf{V}}_{12}^{(k)} \in \mathbb{R}^{(k) \times (1)}$

4 The TLS solution is given as

$$x_{est}^{(k)} = -\tilde{\mathbf{V}}_{12}^{(k)} (\tilde{\mathbf{V}}_{22}^{(k)})^{-1} = -\tilde{\mathbf{V}}_{12}^{(k)} (\tilde{\mathbf{V}}_{22}^{(k)})^T \|\tilde{\mathbf{V}}_{22}^{(k)}\|_2^{-2} \quad (22)$$

5 The final solution is

$$x_{est} = -\mathbf{V}_k x_{est}^{(k)} \quad (23)$$

$r = b - \mathbf{A}x$, denotes the residual vector. The error estimate for $\nu = 2$ (which was found to be optimal [40], [41]) can be expressed as

$$\eta_2 = \frac{\|r\|_2 \|\mathbf{A}^T r\|_2}{\|\mathbf{A}\mathbf{A}^T r\|_2}. \quad (26)$$

The regularization parameter λ can be obtained by minimizing (26)

$$\lambda = \arg \min_{\lambda \in \mathbb{R} > 0} \eta_2(\lambda) = \operatorname{argmin}_{\lambda \in \mathbb{R} > 0} \frac{\|r\|_2^2 \|\mathbf{A}^T r\|_2^2}{\|\mathbf{A}\mathbf{A}^T r\|_2^2}. \quad (27)$$

The required number of steps k and the regularization parameter λ was found at the iteration, where the value of η_2 becomes minimum. The detailed description of the algorithm can be found in [39].

In the case of Lanczos T-TLS, the number of Lanczos iterations k must be chosen and it plays the role of the regularization parameter. The residual vector in the case of Lanczos T-TLS can be written as

$$\|r_k\| = \|(\mathbf{B}_k, \beta_1 e_1) - (\bar{\mathbf{B}}_k, \bar{e}_k)\|. \quad (28)$$

The approach is similar to the one described in [41]. The number of steps k was obtained by performing Lanczos T-TLS for a specified fixed number of iterations (in here, it being 50) and then selecting the x_k corresponding to the minimum of $\eta_2(k)$.

E. Sparse Total Least Squares (Sparse TLS)

The TLS framework introduced till now favors the smooth solutions of x as the penalty (regularization) term is quadratic in nature. This also discourages the sharp edges in the

reconstructed initial pressure rise (x), the framework that will be introduced in this section promotes these sharp edges with an assumption that the solution is sparse in nature with the penalty term being imposed as a total variation (TV) of the expected x . This method is known as Sparse TLS [28], [29] and an alternating descent type algorithm is typically used to solve this. The algorithm involves alternate updating of unknown pressure distribution and error in the model matrix [28], [29]. The Sparse TLS will minimize the following with respect to x , i.e.,

$$\Lambda = ||[\mathbf{A}, b] - [\bar{\mathbf{A}}, \bar{b}]||_2^2 + \lambda TV(x) \text{ subject to } \bar{\mathbf{A}}x = \bar{b}, \quad (29)$$

where $TV(x) = \sum_{i=1}^{n^2} ||D_i x||_1$, with D_i representing the finite difference operator at pixel i . This optimization problem is non-convex in nature, unlike the traditional TLS, and the convergence to a global optimum is not guaranteed with a convex optimization solver [28], [29].

Typically for these type of non-convex optimization problems, the alternating descent-type algorithms were proven to be effective in terms of finding a solution. Let the error in model matrix to be denoted as Δ , which is defined as $\Delta = \mathbf{A} - \bar{\mathbf{A}}$. For a fixed model error Δ , Sparse TLS framework reduces to a Sparse LS problem and x can be computed. Similarly for a fixed x , the model error Δ can be obtained by solving a constrained Least-Squares (LS) problem. Therefore, x and Δ gets updated at every iteration of alternating descent algorithm [28], [29]. The detailed description of the algorithm is given in Algorithm-2. Note that the initial x (after first iteration) is a Sparse LS solution as the initial $\Delta = 0$. The Sparse LS problem in step-2 can be solved using any total variation solver, and the method used in this work can be found in [39], [42]–[44].

Algorithm 2: Algorithm for solving Sparse TLS.

1 Initialize: Iteration number $j = 0$ and $\Delta(j) = 0$

2 Minimize Λ_1 for $x(j)$

$$\Lambda_1 = ||b - \bar{b}||_2^2 + \lambda TV(x) \text{ subject to } [\mathbf{A} + \Delta(j)]x = \bar{b} \quad (30)$$

3 Define

$$\Lambda_2 = ||\Delta||_2^2 + ||b - \mathbf{A}x(j) - \Delta x(j)||_2^2 \quad (31)$$

Minimize Λ_2 for $\Delta(j+1)$ by making the first derivative equal to zero

$$\Delta(j+1) = [b - \mathbf{A}x(j)]x^T(j)[I + x(j)x^T(j)]^{-1} \quad (32)$$

Equivalently, using Sherman-Morrison identity

$$\Delta(j+1) = [b - \mathbf{A}x(j)]x^T(j) \left[I - \frac{x(j)x^T(j)}{1 + x^T(j)x(j)} \right] \quad (33)$$

4 if $\Delta(j+1) - \Delta(j) < 10^{-3}$ then

stop

else

update $j = j + 1$ and go to step-2

F. Figures of Merit

The efficiency of reconstruction methods was evaluated using the following metrics.

1) *Pearson correlation (PC)*: Pearson correlation (PC) was used to measure the correlation between the expected (target) and the reconstructed image. It is a quantitative metric, widely used in statistical analysis and image processing. It is given as [45]

$$PC(x, x_{est}) = \frac{cov(x, x_{est})}{\sigma(x)\sigma(x_{est})}, \quad (34)$$

where x is the expected initial pressure distribution, x_{est} is the reconstructed initial pressure distribution, σ denotes the standard deviation, and cov is the covariance. It can have values ranging from -1 to 1 . Higher value of PC indicates the higher degree of correlation between the target and the reconstructed image.

2) *Contrast to noise ratio (CNR)*: Contrast to noise ratio (CNR) was another quantitative metric used to measure the image quality of the reconstructed image. It can be defined as [45]

$$CNR = \frac{\mu_{roi} - \mu_{back}}{(\sigma_{roi}^2 a_{roi} + \sigma_{back}^2 a_{back})^{1/2}}, \quad (35)$$

where μ denotes the mean and σ represents the standard deviation. The ‘roi’ and ‘back’ represent the region of interest and the background correspondingly in the reconstructed image. The $a_{roi} = \frac{A_{roi}}{A_{total}}$ and $a_{back} = \frac{A_{back}}{A_{total}}$ represents the area ratio, where A_{roi} indicates the number of pixels with non-zero initial pressure distribution in the target, A_{total} denotes the total number of pixels in the reconstructed domain, and A_{back} is the number of pixels with zero initial pressure rise in the target phantom. Higher value of CNR indicates better differentiability of the region of interest with respect to background.

3) *Signal to noise ratio (SNR)*: Signal to noise in dB was computed using the expression

$$SNR(dB) = 20 \times \log_{10} \left(\frac{M}{n} \right), \quad (36)$$

where M denotes the peak-to-peak signal amplitude and n indicates the standard deviation of the noise. Note that this figure of merit was used for the experimental data, where the target initial pressure was unknown.

IV. NUMERICAL AND EXPERIMENTAL SIMULATIONS

A. Numerical Experiments

To prove the efficacy of the TLS methods, in this work four numerical phantoms were considered as shown in Fig. 1. These phantoms mimic spatial features that will be typically encountered in photoacoustic imaging, starting from blood vessel network (Fig. 1(a)), varying sizes of objects (Fig. 1(b)), and sharp edges (Fig. 1(c)), all having only binary initial pressure distributions. The fourth phantom represents a numerical breast phantom created from contrast-enhanced magnetic resonance imaging data [46], [47]. One slice of this numerical breast

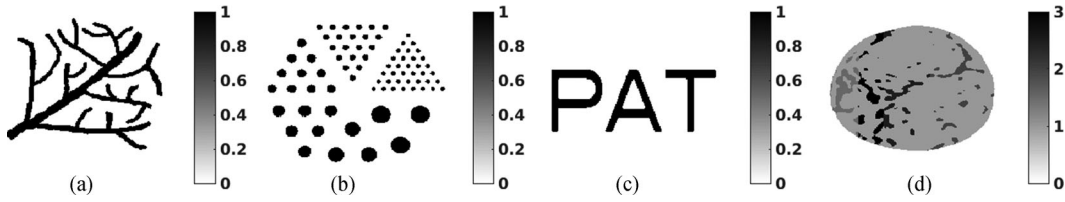


Fig. 1. Target phantoms used in this work (a). Blood Vessel phantom, (b). Derenzo phantom, (c). PAT phantom, and (d). Realistic Breast phantom.

phantom was considered here, having varying initial pressure distribution from 0 to 3 (Fig. 1(d)).

These original objects have a size of 401×401 spanning $20.1 \text{ mm} \times 20.1 \text{ mm}$ imaging region. The imaging set-up has been discussed in [34], [36] with only difference is that the experimental data was generated using higher dimensional (401×401) object and the reconstructions were performed on a lower dimensional (201×201) grid. The data generated using the higher dimensional (401×401) object was added with white gaussian noise to result in the required signal-to-noise ratio (SNR), varied from 60 dB to 10 dB, to serve as experimental data.

Sixty detectors were placed around the tissue surface equidistantly on a circle of radius 22 mm. The detectors were considered to be point detectors having a center frequency of 2.25 MHz and 70% bandwidth. The time step of 50 ns with a total of 512 time steps were chosen to record the forward and experimental data. The medium was assumed to be homogeneous with no absorption and dispersion of sound. For all cases discussed here, the speed of sound was assumed to be having a uniform value of 1500 m/s. A Linux workstation with 16 cores of Intel Xeon processor having a speed of 2.3 GHz with 256 GB RAM was utilized for performing all computations presented in this work.

As discussed earlier, the system matrix approach was utilized, with impulse responses being recorded using analytical Green's function approach (as explained earlier in Section II). For the reconstruction, the system matrix $\mathbf{A}$ was built on a 201×201 computational grid, thereby introducing discretization errors (the data was generated on 401×401 grid). The time taken to record the response of a single pixel using the Green's function approach was around 2.67 milli seconds. Therefore, building the whole system matrix (having a dimension of 30720×40401 , making $m = 30720$ and $n = 201$) took 107.51 seconds. Note that this system matrix needs to be built only once for each detection geometry and considered to be part of the problem setting. Also, the experimental data (b) for all cases was generated using the pseudo-spectral method (k-wave toolbox [37]), which also has the capability to model the speed of sound variations. Note that the photoacoustic data was filtered prior to the reconstruction to realistically simulate the effect of finite bandwidth of acoustic transducers.

To show the effectiveness of the TLS methods, we have considered a case where two out of the sixty detectors were malfunctioning when the imaging object was Derenzo phantom (Fig. 1(b)). This was mimicked by making the recorded data corresponding to these detectors have a SNR of 5 dB and rest detectors have a SNR of 60 dB. The position of the detectors

that were malfunctioning was at 8 o'clock position, assuming that the object was centered around origin.

To further validate the TLS methods, speed of sound variation was considered to include the modeling errors. The phantom used for this study was Derenzo phantom (Fig. 1(b)), with a speed of sound of 1540 m/s where the initial pressure is one and rest (background) with 1500 m/s. The generated experimental data was also corrupted with noise to result in SNR of 60 dB. Note that the system matrix ($\mathbf{A}$) was constructed assuming that speed of sound is 1500 m/s throughout the domain, thus explicitly introducing modeling errors.

B. Horse Hair Phantom Experiment

The PAT imaging system used for conducting experiments is shown in [48, Fig. 1(e)]. A Q-switched Nd:YAG laser was used for delivering 532 nm wavelength pulsed laser of 5 ns duration at 10 Hz repetition rate. Four right-angle uncoated prisms (PS911, Thorlabs) and one uncoated Plano-concave lens L1 (LC1715, Thorlabs) were used to deliver the laser pulses to the sample. The laser energy density on the phantom was $\sim 9 \text{ mJ/cm}^2$ ($< 20 \text{ mJ/cm}^2$: ANSI safety limit [49]). A triangular shaped horse hair phantom was utilized to evaluate the TLS methods. The side-length and diameter of hair are $\sim 10 \text{ mm}$ and 0.15 mm , respectively. The hair phantom was glued to the pipette tips adhered on acrylic slab [50]. The photoacoustic data was collected using a 2.25 MHz flat ultrasound transducer (Olympus NDT, V306-SU) with 13 mm diameter active area and $\sim 70\%$ nominal bandwidth. The ultrasound transducer acquires the data continuously around the hair phantom in full 360 degree for an acquisition time of 240 sec with a rotational speed of 1.5 deg/sec, which corresponds to 2400 A-lines averaged over 6 times resulting in 400 detected signals. The phantom and the ultrasound transducer are immersed in water to enable ultrasound coupling. The acquired PA signals were first amplified and filtered using a pulse amplifier (Olympus-NDT, 5072PR) and then recorded using a data acquisition (DAQ) card (GaGe, 112 compuscope 4227) inside a desktop (Intel Xeon 3.7 GHz 64-bit processor, 16 GB RAM, running windows 10 operating system). All PA data was acquired with sampling frequency of 25 MHz and simulations were performed at a rate of 12.5 MHz (as the original signal was subsampled to 512 time points keeping only alternative signal values of total 1024 time samples). Synchronization of data acquisition with laser illumination was achieved using a sync signal from laser. The reconstructed photoacoustic imaging region has a size of $40 \text{ mm} \times 40 \text{ mm}$ containing 200×200 pixels. The system matrix built for this detection geometry has a

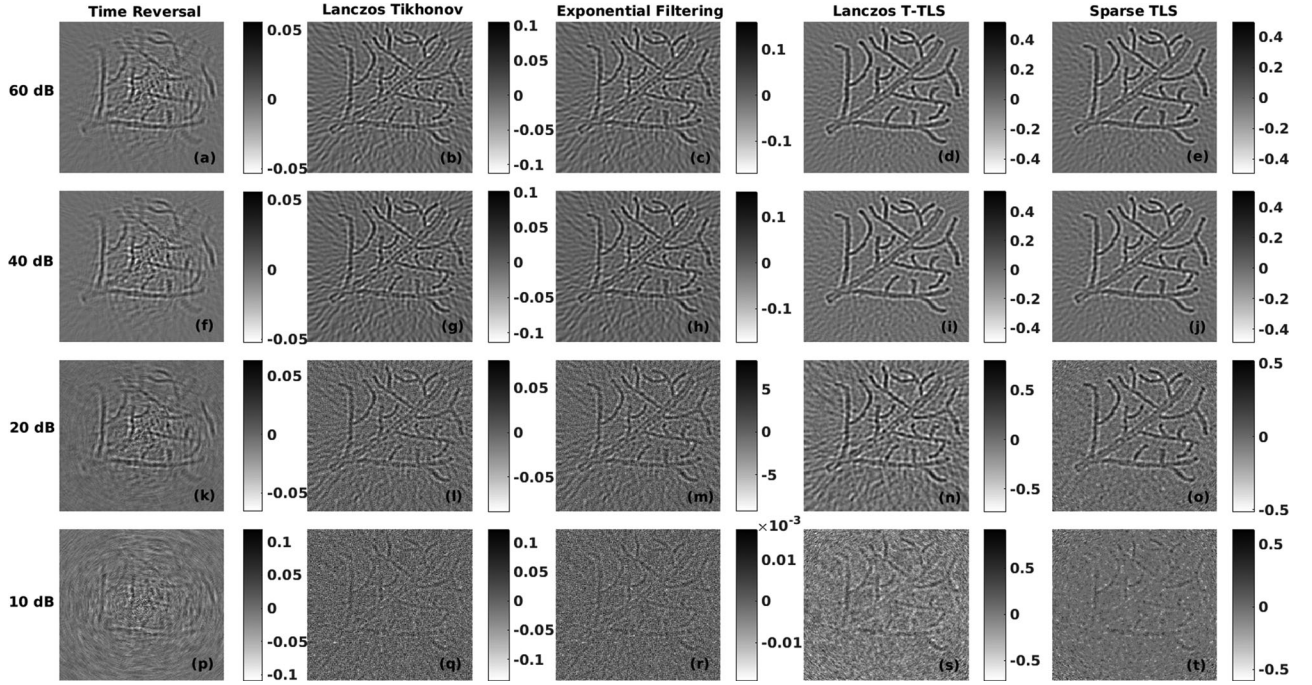


Fig. 2. Reconstructed images using the discussed methods (displayed on top of each column: Lanczos Tikhonov (Section III-B), Exponential Filtering (Section III-C), Lanczos T-TLS (Section III-D), and Sparse TLS method (Section III-E)) for varying SNR (displayed against each row: 60 dB, 40 dB, 20 dB, and 10 dB) in the data. The corresponding target image is given in Fig. 1(a). The figures of merit corresponding to these results are given in Fig. 8.

TABLE I
COMPUTATIONAL TIME (IN SECONDS) FOR THE RECONSTRUCTION METHODS
USED TO GENERATE THE RESULTS GIVEN IN FIGS. 2(A)–(E) AND 9(A)–(D)

Figure	SVD of $\mathbf{A}$	Time Rev.	Lanczos Tikhonov	Exp. Filtering	Lanczos T-TLS	Sparse TLS
2(a-e)	9,324	129	28.7 (28.1)	5.8 (111.2)	17.42	2313
9(a-d)	16,200	–	43.5 (96.1)	9.2 (321.5)	38.32	3624

The numbers in the parenthesis represent the computational time required for choosing the regularization parameter automatically. The computational time taken for the SVD of the system matrix for these results has been indicated in the second column.

dimension of 51200×40000 (51200: 512 time samples for 100 detector positions and 40000: 200×200 reconstruction grid). Note that only 100 detectors (down sampled by 4 times) were considered to represent the limited data case. In these experimental scenario, it is very hard to determine the initial pressure rise (target values).

V. RESULTS

The reconstruction results pertaining to methods discussed in this work, including TLS methods, for the blood vessel phantom (Fig. 1(a)) were given in Fig. 2. Note that the fourth column gives the Lanczos T-TLS and last column gives the Sparse TLS method results with first, second, and third columns corresponding to Time reversal, Lanczos Tikhonov, and Exponential filtering. Each row in Fig. 2 corresponds to particular SNR of the data, in here varied from 60 dB to 10 dB, as indicated against each row. The figures of merit, namely PC and CNR, for these results had been reported in Fig. 8. It is evident from these results that

TABLE II
THE COMPUTED RECONSTRUCTION PARAMETERS FOR OBTAINING THE
RESULTS PRESENTED IN THIS WORK

Figure	Sub Fig.	SNR in data	Lanczos Tikhonov (λ, k)	Exponential Filtering λ	Lanczos T-TLS k	Sparse TLS j
2	b-e	60 dB	(0.0564,49)	0.0043	45	14
	g-j	40 dB	(0.0710,44)	0.0179	43	14
	l-o	20 dB	(0.5380,31)	0.1316	26	35
	q-t	10 dB	(0.7617,17)	0.3383	14	49
3	a-d	60 dB	(0.0634,49)	0.0034	46	14
	e-h	10 dB	(0.6905,17)	0.2414	15	49
4	a-d	60 dB	(0.0564,49)	0.0050	47	12
	e-h	10 dB	(0.7617,17)	0.3523	15	48
5	b-e	40 dB	(0.0123,47)	0.0022	45	12
	g-j	40 dB	(0.0127,59)	0.0029	57	14
6	a-d	40 dB	(0.4794,35)	0.0747	29	17
7	a-d	40 dB	(0.0602,45)	0.0118	43	21
9	a-d	–	(0.0220,43)	0.0081	41	16

Note that these were found in an automated fashion using the error estimates [39].

the performance of Lanczos T-TLS and Sparse TLS methods are better compared to the discussed methods and the improvement is appreciable for the low SNR cases (where noise is more). More importantly, the recovered contrast from the TLS methods was at least 4 times more compared to Lanczos Tikhonov and Exponential filtering. From the presented results (Figs. 2 and 8), it is evident that the performance of the time reversal method is poor compared to all other methods discussed as the data available is limited. For the rest of the work, time reversal method

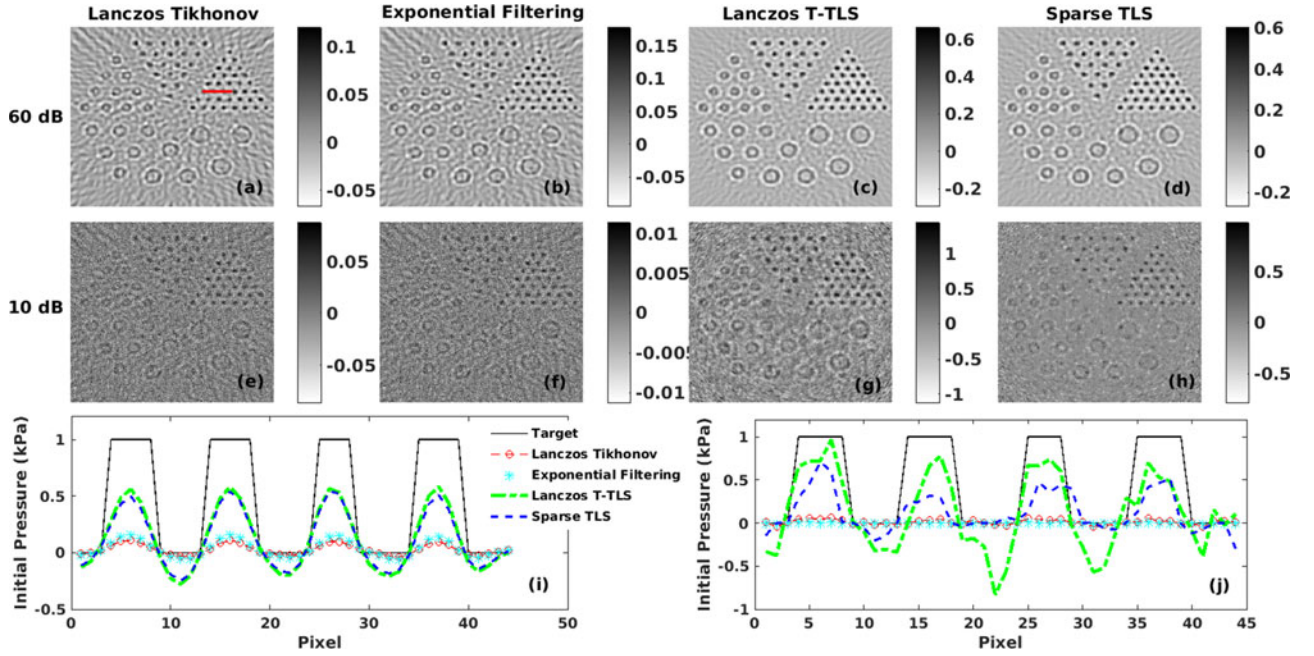


Fig. 3. Reconstructed images using the discussed methods (displayed on top of each column: Lanczos Tikhonov (Section III-B), Exponential Filtering (Section III-C), Lanczos T-TLS (Section III-D), and Sparse TLS method (Section III-E)) for highest (60 dB) and lowest (10 dB) SNR (displayed against each row) in the data. The corresponding target image is given in Fig. 1(b). The figures of merit corresponding to these results are given in Fig. 8. The one-dimensional profile plot along the red-line, as shown in (a), for all results presented in this figure for 60 dB (a)–(d) was given in (i) and 10 dB (e)–(h) was given in (j).

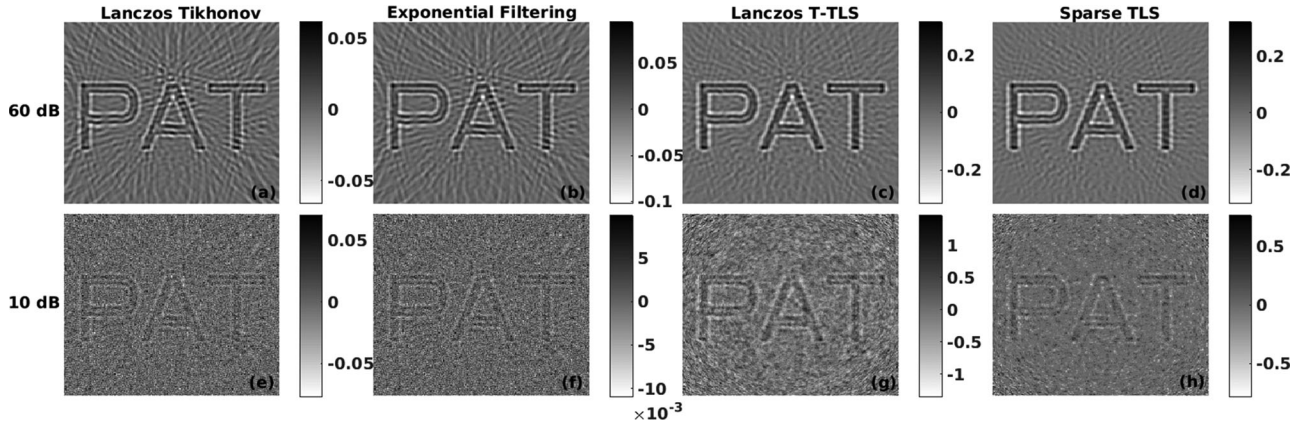


Fig. 4. Reconstructed images using the discussed methods (displayed on top of each column: Lanczos Tikhonov (Section III-B), Exponential Filtering (Section III-C), Lanczos T-TLS (Section III-D), and Sparse TLS method (Section III-E)) for highest (60 dB) and lowest (10 dB) SNR (displayed against each row) in the data. The corresponding target image is given in Fig. 1(c). The figures of merit corresponding to these results are given in Fig. 8.

was not considered as a standard method for comparison as the aim is to improve the model-based reconstruction methods that are capable of handling limited data cases effectively. The observed computational times for obtaining the reconstruction results corresponding to Fig. 2(a)–(e) were given in Table I. Note that the exponential filtering requires one time computation of SVD of A , which takes 2.59 hours of computational time. The sparse TLS method required around 160 seconds to solve step-2 of Algorithm-2 at each iteration, and around 5.16 seconds to update the model error as given in step-3 of Algorithm-2. To meet the stopping criteria, the sparse TLS required about 14

iterations. The recorded reconstruction parameters for obtaining these results were reported in Table II.

The reconstructed results for the highest (60 dB) and lowest (10 dB) SNR data corresponding to Derenzo phantom (Fig. 1(b)) were shown in Fig. 3. The figures of merit, namely PC and CNR, for these results had also been reported in Fig. 8. Again, the same trend as observed in the case of blood vessel phantom had been followed, with the TLS methods showing the best performance in terms of contrast recovery and discussed figures of merit. The reconstruction parameters for obtaining these results were reported in Table II.

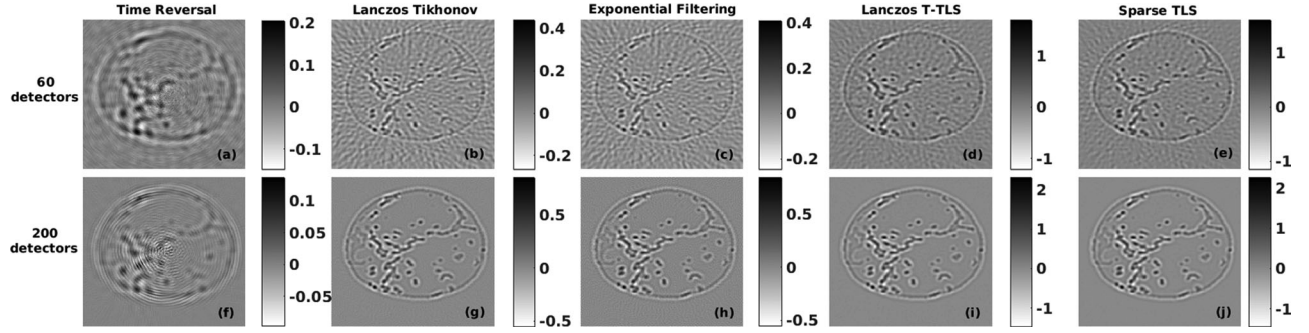


Fig. 5. Reconstructed images using the discussed methods (displayed on top of each column: Lanczos Tikhonov (Section III-B), Exponential Filtering (Section III-C), Lanczos T-TLS (Section III-D), and Sparse TLS method (Section III-E)) for detectors considered being 60 (first row) and 200 (last row) respectively. The corresponding target image is given in Fig. 1(d). The figures of merit corresponding to these results are given in Fig. 8. The computational times involved for obtaining (a)–(e) are same as the ones reported for Fig. 2(a)–(e) in Table I, similarly for (f)–(j) corresponds to last row of results reported in Table I.

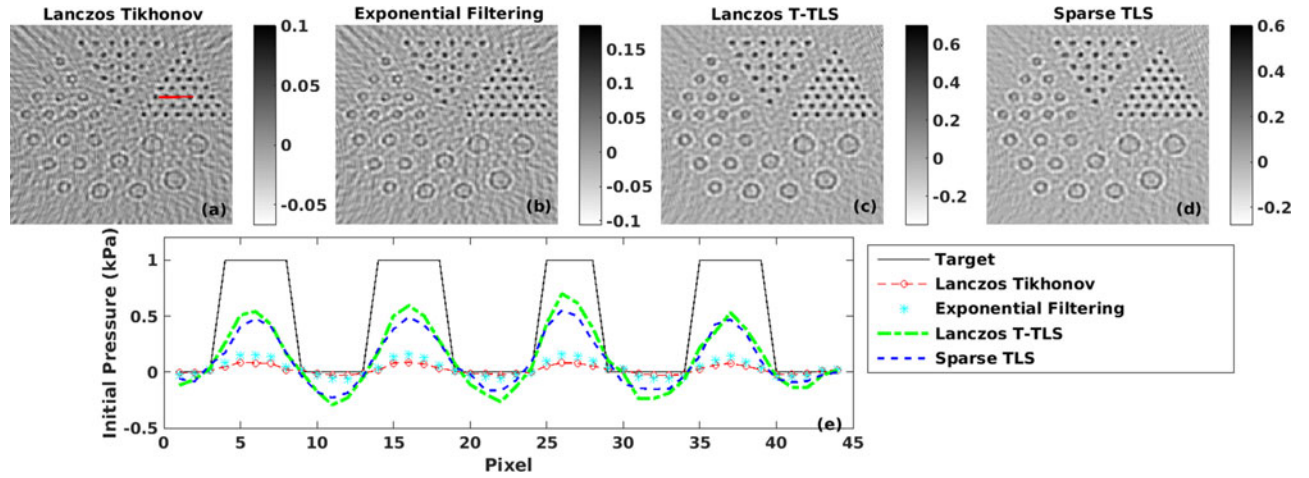


Fig. 6. Reconstructed results corresponding to mimicking the two detector malfunctioning using the discussed methods (displayed on top of each column: Lanczos Tikhonov (Section III-B), Exponential Filtering (Section III-C), Lanczos T-TLS (Section III-D), and Sparse TLS method (Section III-E)). The corresponding target image was given in Fig. 1(b). The one-dimensional profile plot along the red-line, as shown in (a), for all results presented in this figure was given in (d). The figures of merit corresponding to these results are given in Fig. 8.

The results pertaining to reconstruction of sharp boundaries pertaining to the PAT phantom (Fig. 1(c)) were presented in Fig. 4. Again, only reconstruction results corresponding to high and low SNR data were shown and figures of merit for these results were given in Fig. 8. Further, the same trend as observed earlier was also demonstrated here with the TLS methods showing better performance in terms of contrast recovery and computed figures of merit. Similar to earlier, the recorded reconstruction parameters for obtaining these results were reported in Table II.

The reconstructed results for the realistic (numerical) breast phantom (Fig. 1(d)) were shown in Fig. 5. The number of detectors used for obtaining the reconstruction results were listed against each row. The method used was listed on top of each column. The original number of time steps (512) with 200 detectors will result in system matrix size of $102,400 \times 40401$, making the problem intractable as one has to apply SVD on this matrix. So only 256 time steps with a sampling time of 100 ns (similar to the experimental conditions reported in [51]) was considered to generate the data from 200 detectors. The figures of merit,

namely PC and CNR, for these results had also been reported in Fig. 8. The computational times involved for obtaining these results were same as the ones reported in Table I with last row in the table corresponding to the last row of results (Fig. 5) and correspondingly second row in the table to first row of results shown in Fig. 5. The reconstruction parameters for obtaining these results were reported in Table II. The results indicate that even with 200 detectors, the time reversal method performance is poor compared to others. The proposed methods were able to provide better quality PA images, including improved contrast recovery, compared to its counter parts. The results obtained with 200 detectors were less prone to the streak artifacts that were observable in the case of results obtained using 60 detectors.

The results corresponding to the case of two detectors malfunctioning were exhibited in Fig. 6 for all four methods discussed in this work, including TLS methods (Lanczos T-TLS and Sparse TLS). The corresponding figures of merit were plotted as a bar graph in Fig. 8 (reconstruction parameters were given in Table II). It was evident from these results that the traditional methods, such as Lanczos Tikhonov and Exponential filtering,

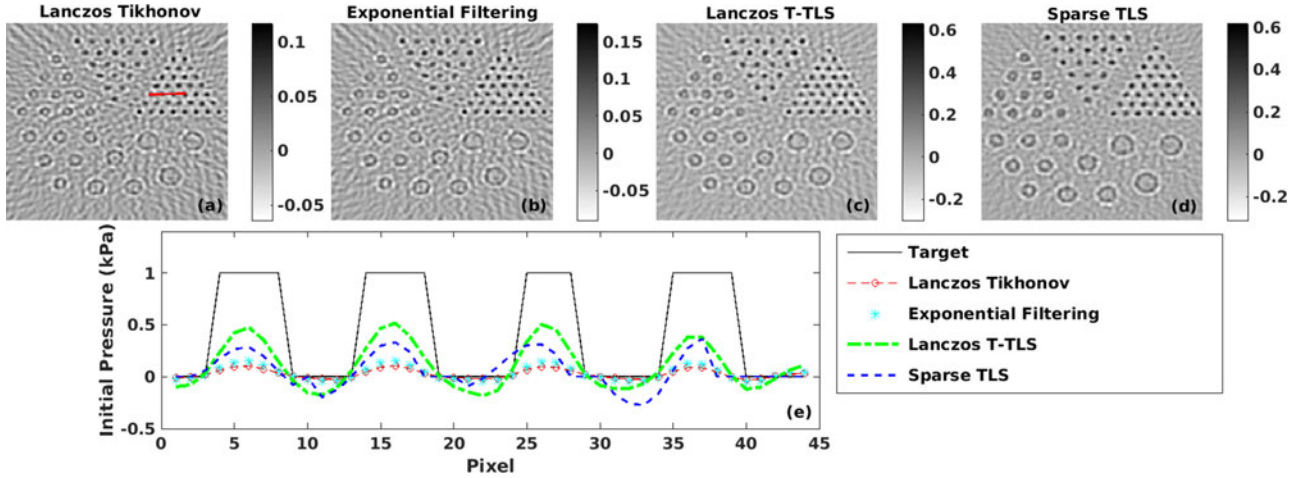


Fig. 7. Reconstructed results corresponding to speed of sound variations using the discussed methods (displayed on top of each column: Lanczos Tikhonov (Section III-B), Exponential Filtering (Section III-C), Lanczos T-TLS (Section III-D), and Sparse TLS method (Section III-E)). The corresponding target image was given in Fig. 1(b). The one-dimensional profile plot along the red-line, as shown in (a), for all results presented in this figure was given in (d). The figures of merit corresponding to these results are given in Fig. 8.

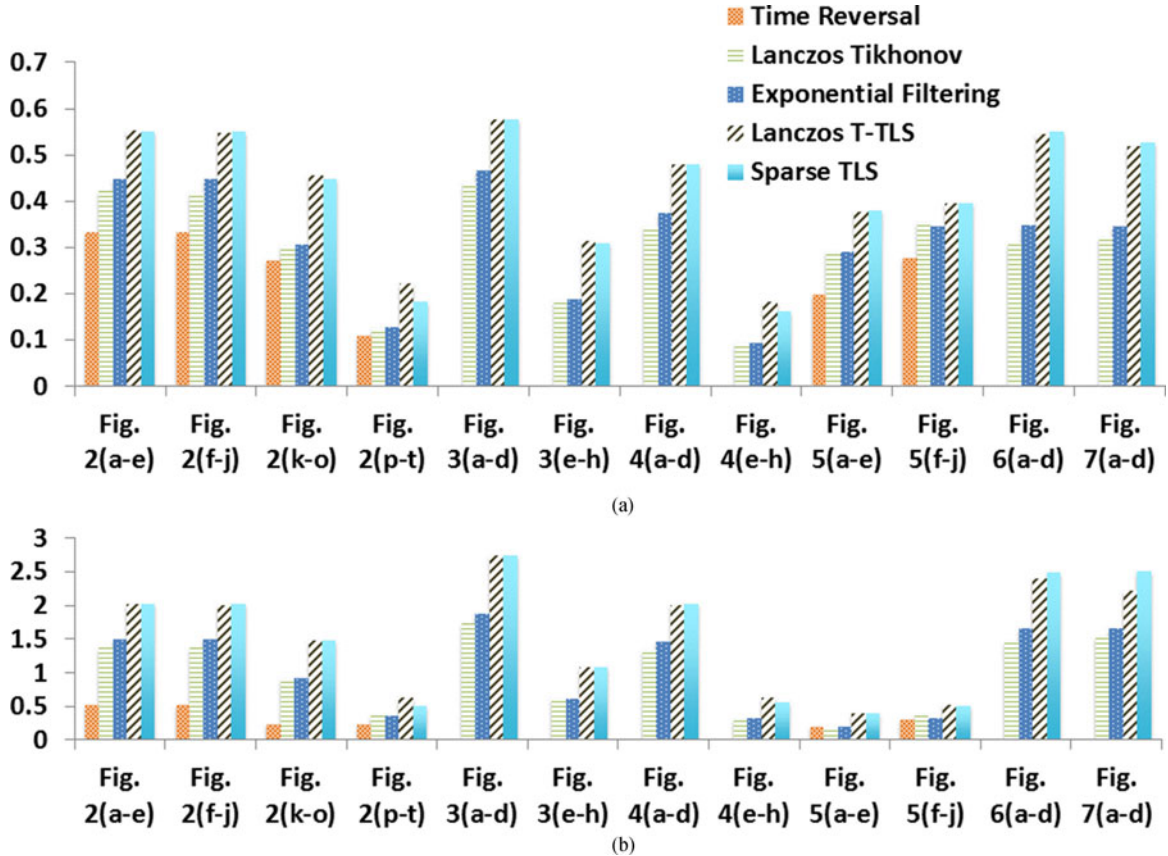


Fig. 8. Comparison of performance metrics (PC and CNR) for the reconstructed images presented in Figs. 2, 3, 4, 5, 6, and 7. (a) Pearson correlation (PC), (b) Contrast to Noise Ratio (CNR).

had streak artifacts manifested due to detectors malfunctioning. The TLS methods were more robust to these scenarios and the observed image quality is on par with the results presented for the case of 60 dB noise (first row of Fig. 3).

Finally, the reconstructed results for speed of sound variations were presented in Fig. 7. The figures of merit corresponding

to these results were shown in Fig. 8, with the reconstruction parameters given in Table II. From these results, even though the SNR of the data is 60 dB, the small variation of speed of sound (modeling error) has considerably degraded the results (comparing Fig. 3(a)–(c) with Fig. 6(a)–(c)) and the TLS methods (Lanczos T-TLS and Sparse TLS) were able to exhibit

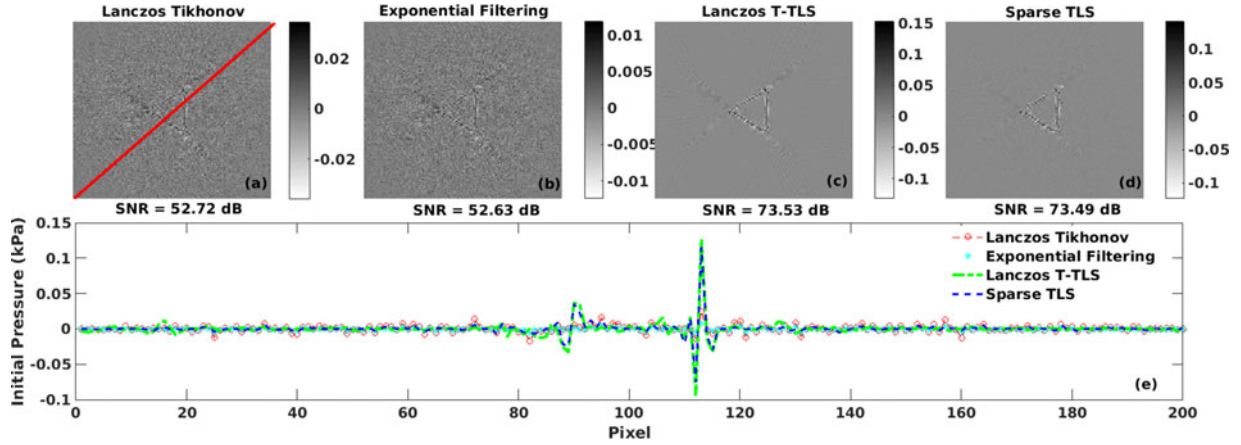


Fig. 9. Reconstructed images using the discussed methods (displayed on top of each column: Lanczos Tikhonov (Section III-B), Exponential Filtering (Section III-C), Lanczos T-TLS (Section III-D), and Sparse TLS method (Section III-E) for experimental horse hair phantom data. The one-dimensional profile plot along the red-line, as shown in (a), for all results presented in this figure was given in (d). The SNR corresponding to these results are given correspondingly at the bottom of the each image.

better performance especially in terms of Pearson correlation (Fig. 8(a)).

The experimental results obtained using horse hair phantom were shown in Fig. 9. From the reconstructions, it was evident that the Lanczos T-TLS and Sparse TLS methods have better contrast recovery compared to the state-of-the-art methods, Lanczos Tikhonov and Exponential filtering. The computational times for obtaining the reconstruction results corresponding to Fig. 9(a)–(d) were given in Table I. Note that the SVD of $\mathbf{A}$ (size being 51200×40401 , same dimensions corresponding to the results shown in Fig. 5(f)–(j)) takes 4.5 hours of computational time. As the ground truth for the experimental data is unavailable, the SNR as given in (36) was utilized to evaluate the methods. The reconstructions from Lanczos Tikhonov and Exponential filtering were dominated by noise, whereas the TLS methods were more robust in providing better SNR images.

VI. DISCUSSION

The traditional regularization methods, including Lanczos Tikhonov and Exponential Filtering, relies on the assumption that noise exists only in the data (b). As stated earlier, solving wave equation using any numerical method requires discretization of imaging domain, making it susceptible to numerical errors. Additionally, to make these numerical methods have manageable computational complexity, simplifications on the physics of the problem (example being speed of sound being constant through out the imaging domain) makes the model have imperfections. This leads to errors in the underlying model ($\mathbf{A}$) as well. In these scenarios, traditional regularization schemes may not be effective in terms of providing a good quality photoacoustic image as seen in the presented results. The total least squares (TLS) provides a generic framework to effectively handle imperfections arising in $\mathbf{A}$. The application of TLS to ultrasound inverse scattering [52], inverse problem in Electrocardiography (ECG) [53], and Phillips test problem [27] has shown its efficacy in terms of handling both geometrical and

discretization errors. The same trend was observed in here for photoacoustic imaging as well as the primary assumption of this method is that model ($\mathbf{A}$) is inaccurate. Note that traditional T-TLS uses SVD, which is computationally demanding, making it prohibitive for large scale problems like the one at hand.

In this work, Lanczos bidiagonalization was utilized to accelerate the T-TLS as the system matrix $\mathbf{A}$ for the photoacoustic tomography was sparse and structured (please see Fierro *et al.* [27]). Note that the iterative methods with a suitable preconditioner can be solved in $\mathcal{O}(Ln^4)$ operations, where L denotes the number of iterations, which in terms of computational complexity can be equivalent to Lanczos bidiagonalization. However, choosing an appropriate preconditioner is a challenging task and most often the convergence (L) depends on the preconditioner choice [54]. The Lanczos T-TLS method does not have any explicit regularization parameter, rather applies regularization in terms of number of Lanczos bidiagonalization iterations, giving an additional gain in terms of computational efficiency. However, an explicit regularization parameter can be included in the Lanczos T-TLS method, but, there is no significant improvement in the image quality. The traditional LSQR method [21] that also uses Lanczos bidiagonalization is equivalent to conjugate gradient method applied to normal equations and spurious solutions are possible when exact arithmetic was not used [27]. In addition, the traditional LSQR is also not very effective in handling large data-model misfits, such as the one experienced in detector malfunctioning (Fig. 6). The spurious solutions can be effectively handled when an explicit regularization gets deployed, as in the case of Lanczos Tikhonov, but these methods rely on inverse noise arising out of only data noise (b).

As expected, when the SNR reduces (noise increases), the regularization parameter (λ) becomes larger to effectively mitigate the noise in the data. The same trend was observed for the results presented in this work (please refer to Table II). The reverse trend needs to be observed in terms of Lanczos iterations, that is lower k representing more filtering. This was followed in presented results of Table II. Note that all these reconstruction

parameters (λ and k) were found in an automated fashion using the error estimates [39]. Even though, figures of merit such as PC can better assess the reconstructed image quality, the residual error has been commonly used to compare the quality of reconstruction algorithms in tomographic problems [55]. In addition, in practice as the initial pressure distribution is unknown, it is not plausible to use other figures of merit to determine the optimal value of k .

The TLS methods does not have any knowledge of noise in $\mathbf{A}$ and b , making it very appealing in all experimental scenarios. The results presented in this work does not commit any inverse crime [56], that is the experimental data was generated on 401×401 grid and reconstructions were performed on 201×201 computational grid.

It should also be observed from presented results, especially in terms of figures of merit (Fig. 8), the improvement observed using low SNR (high noise) data was substantial (as high as 50%) making the TLS methods very compelling to be utilized in these scenarios. However, it should be noted that for weakly ill-posed problem (such as full-data case), the method may not give an observable advantage [27], [52]. Advanced instrumentation currently allows photoacoustic tomographic scanners to acquire large amounts of data [60] and in these scenarios, proposed method will be impractical to apply given the computational complexity involved. Table I shows the computational times involved for obtaining the SVD of the system matrix ($\mathbf{A}$) and migrating from 60 to 100 detectors doubles the computational time needed. Having large system matrix (corresponding to full data case) will also be impractical as the computational complexity becomes intractable. In many practical scenarios, it is not possible to obtain the full-data [19], [61]–[65]. In these cases, the inverse problem becomes ill-posed and working with limited data necessitates the usage of regularization to constrain the solution space [18], [66]. The proposed method has a distinct advantage in terms of handling large data-model misfits without adding any additional computational burden (as evident from Table I). The major drawback of system matrix-based algorithms is the requirement to store a large model matrix. However, by exploiting the sparsity of the model matrix, the system matrix can be stored efficiently using many available efficient storage modes [57]. Even though the direct fully three-dimensional reconstruction can be challenging as it is going to be computationally demanding, in practice, one could perform slice by slice two-dimensional reconstruction and combine these slices to form a three-dimensional volume.

The speed of sound variation, especially between glandular versus fat tissues encountered in breast imaging, can be as high as 10% [58]. In here, the variation was kept at 2.67% and still the performance of the Lanczos Tikhonov and Exponential filtering methods has degraded considerably. As expected, the TLS methods were able to handle these modeling errors effectively resulting in more desirable reconstructed images (Fig. 7). It is important to note that modeling errors can be result of limitation of available information, for example even though it is possible to model the speed of sound variations, knowing the speed of sound for tissues under examination is not possible in real-time. Moreover, the estimation of speed of sound is an unstable

process especially when it is jointly estimated along with initial pressure [59]. In this work, the speed of sound variation was considered as a modeling error and the proposed method was able to handle these without effecting the reconstructed initial pressure distribution. It is important note that, the modeling errors in terms of speed of sound variations that were considered in this work are only effecting about 15% of the total imaging domain. When these errors are present in 50% of the imaging domain, the proposed method will not be able to handle these errors as the mathematical framework is capable of handling only perturbations. In most practical scenarios, the background speed of sound can be estimated quite accurately and the difficulty lies with knowing the speed of sound in the regions of interest. All the forward models that are existing in photoacoustic imaging largely assume that the speed of sound is constant throughout the domain and equal to the background region speed of sound. Thus these modeling errors invariably creep in and having a method that can handle these effectively will provide accurate reconstruction results.

It is important to note that the Sparse TLS method that utilizes the total variation (TV) penalty term provides marginal improvement over the Lanczos T-TLS, at the same time, adding atleast 130 times more computational complexity (Table I). Also, the Sparse TLS method that was presented in [28], [29] deployed ℓ_1 -norm based penalty, whereas in this work, a TV penalty was utilized. Note that the Lanczos bidiagonalization framework performs the dimensionality reduction, thus making it equivalent to a sparse recovery method. The implementation of Sparse TLS was performed in the original domain, without applying any dimensionality reduction to preserve the desired singular values. As the Sparse TLS problem is non-convex in nature [29], unlike ordinary TLS that can be globally optimized, finding the solution involves penalizing equivalent of trace norm (sum of singular values), thus truncation of singular values may lead to irregular or no convergence of the algorithm.

The TLS methods introduced in this work does not require either pre-filtering or any post-processing of the data and it can be used for any kind of model imperfections such as transducer's malfunctioning, speed of sound variations, as well as mismatch in modeling the impulse response properties of the transducers. Even though the method has been known, the proposed framework was applied and successfully shown to be effective for the reconstruction of photoacoustic images. The code along with necessary phantom images were provided as an open-source to the enthusiastic users [67].

VII. CONCLUSION

This work introduced two variants of total least squares (TLS), a Lanczos bidiagonalization based truncated total least squares (T-TLS) and Sparse TLS for effectively handling large data-model misfits and proven to be more robust to noise compared to the state-of-the-art methods in limited data photoacoustic tomography. The Lanczos T-TLS method was implemented in the Lanczos bidiagonalization framework to provide computationally efficient reconstruction results with an added advantage of being effective in handling imperfections in acoustic

wave propagation model. This method was also proven to be competent in handling experimental deficiencies, such as detector malfunctioning and speed of sound variations without adding any additional computational burden. The Sparse TLS method performance was on par with the Lanczos T-TLS, but the computational complexity involved may be a deterrent to make it appealing for real-time scenarios. The results were also validated experimentally using horse hair phantom. The traditional methods assume that the underlying forward model is perfect, thus attributing discrepancies between data-model as the noise in the data, leading to either over or under regularized solution. The TLS methods introduced here explicitly assumes that the model has imperfections and handles these discrepancies competently to provide better quality photoacoustic images.

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