Author's response to reviews

Title: Estimating view parameters from random projections for Tomography using spherical MDS

Authors:

Yi Fang (fang4@purdue.edu)
Sundar Murugappan (smurugap@purdue.edu)
Karthik Ramani (ramani@purdue.edu)

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Author's response to reviews: see over
Response to Reviewers

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Authors: Yi Fang, Sundar Murugappan and Karthik Ramani

Contact E-mail: fang4@purdue.edu

- General answer to the reviewers is given on the Page 2
- Answers to Reviewer 1 are given on the Page: 3-7
- Answers to Reviewer 2 are given on the Page: 8-15

Please note: In the revised manuscript, we highlight the new added content using red color, highlight the deleted content using blue color with strikethrough. The grammar corrections are not highlighted in the revised manuscript.
General Answer to Reviewers’ Comments

We thank all reviewers for providing valuable and constructive comments and suggestions. The major concerns arise from the two following aspects:

1. The applicability of the described method for MRI imaging and 4DCT

2. The language and flow of the paper.

We are sorry that we didn’t address those two parts clearly. We over claimed the applicability of our proposed method in the original manuscript. We have addressed those problems in the revised manuscript.
Answers to Reviewer 1's Comments

(Notations: Ci: the ith comment; Ai: answer to the ith comment.)

C1: This is a very interesting paper with many applications, particularly in CT. I applaud the authors including links to source code.

A1: Thank you for your comments.

The source code is updated so that it is not dependent with the dijkstra.dll. The source code can now be run under Linux OS.

C2: The paper needs to add some quantitative measures of reconstruction performance. I realize that you cannot just subtract the original and reconstructed images since there is an arbitrary rotation, but the rotation could be removed by registration and a reconstruction difference image and error metric computed. This is essential to determining the performance of the method.

A2: Thank you for your valuable suggestion.

As per your suggestion, we registered the original and final images and compared the two to evaluate the performance of our method. The results are included in the revised manuscript. We designed the experiment in the following way. We registered the two images by a global rotation which can be referred from the correspondence between the original projections and re-ordered projections. As we know the ground truth of original projections, we can easily refer the global rotation angle by finding the position difference between the corresponding projections. We provide the measure of quality of reconstruction by using peak signal-to-noise ratio (PSNR) and mean squared error (MSE). They are computed by the following equations:

\[
MSE = \frac{1}{mn} \sum_{i=0}^{m-1} \sum_{j=0}^{n-1} [I(i,j) - K(i,j)]^2
\]

\[
PSNR = 20 \times \log_{10}(\frac{MAX(I)}{MSE})
\]

Where I is the original image and K is the reconstructed image and m, n are the size of the images respectively.

The Figure 1 below displays the three images – the original, reconstructed and the registered from left to right. The middle image is reconstructed from 512 projections. The image on the right is the registered image by a global rotation for the image in the
middle. As per the experiment we conducted, the MSE and PSNR between the image on the right and left are 0.0037 and 24.2804 respectively. Please note that this new experiment is added in the Section 3.2 in the revised MS, starting with “We further verify …”.

![Image](Image URL)

Figure 1: Original Image, Reconstructed Image and Registered Image

Furthermore, we provide another measure for the accuracy of the recovered angles. We calculated the difference between the estimated view angles and original angles after a global registration.

\[
\text{AngDif} = \sum_{i=1}^{L} [\text{EAng}_i - \text{OAng}_i]^2
\]

Where \( L \) is the number of the projections, \( \text{EAng} \) denotes the estimated angle for the projection and \( \text{OAng} \) denotes the original angle. In the above test, AngDif is 0 when there is no noise added to the images.

C3: The relationship between the work and that of references 10, 11, and 18 is unclear. What are the potential advantages of the sMDS approach over those already published? The work in reference 10 is very close to that presented with similar results. Could a direct experimental comparison be done?

A3: Thank you for pointing out the issue.

The major difference between the work described in the above references and ours is two fold:

a) Our method is a global manifold learning method while the methods in the references are local. Both the local and global methods have pros and cons. The local method is faster, but sensitive to noise as for every point only a small neighborhood is considered for calculating the distance metric. On the other hand, our global method first propagates the local metric to a global distance measure and then uses it for global manifold learning, where all the points are considered
instead of just a small neighborhood. This propagation is comparatively slower of \( O(n) \), but is robust to noise. The differences between the two types of approaches are summarized in the following table [1,2].

<table>
<thead>
<tr>
<th>Criteria</th>
<th>References (10, 11 and 18)</th>
<th>ISOMAP (our method)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approach</td>
<td>Local</td>
<td>Global</td>
</tr>
<tr>
<td>Isometry</td>
<td>Most of the time, covariance distortion</td>
<td>Yes</td>
</tr>
<tr>
<td>Robustness to Noise</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Speed</td>
<td>( O(N^2) )</td>
<td>( O(N^3) )</td>
</tr>
</tbody>
</table>

b) In our method, the similarity between two lines is measured in the Fourier domain, where as in the references, it is computed directly on the space domain. Performing the computations on the Fourier domain helps us to handle noise better, by allowing us to choose a proper subset range of frequency instead of the complete range. The figure below shows the plot (Figure 2) between ‘magnitude of noise’ and ‘magnitude of signal’ along different frequencies. As it can be seen, when the noise is kept constant across different frequencies, the signal decays rapidly. The optimal range of the frequency is in the low frequency area.

Figure 2: The logarithmic value of the magnitude of signal and noise as a function of frequency. X-axis denotes the frequency range from 0 to 0.5 (0.5 denotes Nyquist frequency), Y-axis denotes logarithmic value of the magnitude of the Fourier transform of signal and noise. (SNR=1 in the Figure)


C4: The paper has several grammatical issues and could use a more thorough editing

A4: Thanks for bringing to our notice about the language.

We have taken help of professional editing services and we believe this revised manuscript is of better quality.

C5: In my opinion the applicability to MRI is overstated since most pulse sequences do not use radially acquired lines of k-space. At least some indication of how this might be adapted to other pulse sequences would be needed to justify such optimism.

A5: Thanks for your comment.

After a thorough investigation, we have removed the claim of the applicability of our method to MRI imaging in the revised manuscript. We have moved it to the future work. In short, our method can be adapted to MRI data with some modification.
However, as our proposed method belongs to a category of data re-organization with special manifold constraints, it has the potential to apply to other related research areas with modifications in the constraint conditions.

**C7C6:** Including the source to the dijkstra.dll would make it easier for people to replicate the work on platforms other than Microsoft Windows.

**A7A6:** Thank you for the suggestion.

We have changed our implementation to MATLAB and the corresponding function in MATLAB for ‘dijkstra’ is ‘graphAllShortest’ which is already built in. The new program is now working well independent of the type of OS as long as the Matlab is installed properly. We have tested the program on Matlab 2009 and we believe it works well on other version of Matlab.

**C8C7:** The short "introductory" parts of each section could be removed without affecting readability.

**A8A7:** Thanks for your comment.

We followed up the suggestions and have removed the short introductory of each section in the revised manuscript.
Answers to Reviewer 2's Comments
(Notations: Ci: the ith comment; Ai: answer to the ith comment.)

**C1:** The paper proposes the sMDS method to sort the projection data that are measured at unknown view angles. The method involves 1) computing the pair-wise distance matrix \( M \) on Fourier transformed projection data, 2) finding the first two eigenvectors of \( \text{Tao}(M) \), 3) Computing the initial angles using the two eigenvectors, 4) uniformly rearranging the view angles along the circle. Image reconstruction from projection data after viewing angles are recovered is less concerned in this study. A few experiments are conducted to study the effects by the number of projection angles and by levels of detector noises. A 2D MR brain image is used in the study, with all projection data and noise levels are simulated.

**A1:** Thanks for the comments.

This comment reflects a correct understanding of the motivations and the principles of our proposed method and its applications.

**C2:** Are there particular reasons to compute distances between projections after Fourier transformation, instead of distance on the original projection data themselves? I cannot find any discussion about the benefits, and comparing to results using the original projection data without Fourier transformation. In fact, if it is working fine to compute the distance on the original projection data, the whole thing about Fourier transformation, and central slice theorem can be removed, and the method can be greatly simplified.

**A2:** Thanks for this good question.

In our method, the similarity between two lines is measured in the Fourier domain, instead of computing directly on the space domain, i.e., original projection data. Performing the computations on the Fourier domain helps us to handle noise by allowing us to choose a proper subset range of frequency instead of the complete range. The figure below shows the plot (Figure 1) between ‘magnitude of noise’ and ‘magnitude of signal’ along different frequencies. As it can be seen, when the noise is kept constant across different frequencies, the signal decays rapidly. The optimal range of the frequency is in the low frequency region to minimize the noise effect.

Another advantage of Fourier domain over the space domain is its invariance to center-shift. It should be noted that we use only the magnitude information of the Fourier transform and not its phase information. The figure (Figure 2) below shows
that the computed similarity in Fourier domain is robust to center shift of the acquired data.

![Figure 1: The logarithmic value of the magnitude of signal and noise as a function of frequency, X-axis denotes the frequency range from 0 to 0.5 (0.5 denotes Nyquist frequency), Y-axis denotes logarithmic value of the magnitude of the Fourier transform of signal and noise. (SNR=1 in the Figure)](image)

Please note that we have added the reasons why we compute the pairwise distance in the Fourier domain.
Figure 2: The first row shows the image and its center shifted image. The second row shows that the magnitudes of their Fourier transforms.

C4C3: The whole discussion about dimensional reduction (Figure 7, from F to Q) is not very useful. The only useful information about the vector Qs are their direction, or the angles, that are equal to (in one way or another) the viewing angles of the original projection data. The thing about dimensional reduction is basically about “ok, each projection is done on an angle, and angles are the dimensional reduction of the projection data”. Am I right? If I am correct, the proposed procedure could be simplified, and related discussion can be removed.

A4A3: Thank you for keen observation.

C5C4: I suggest authors to remove anything referring to 4DCT and motion artifacts reduction. The proposed method won’t be very useful on such problems in that the tissue motions are mostly in/out the 2D slice instead of within a 2D slice. The 3D implementation of the proposed method won’t work either for 4DCT problems since CT projections can only be in axial directions.
A5A4: Thank you for your suggestion and we agree with your comment.

After a thorough investigation, we have removed the claim of the applicability of our method to 4DCT in the revised manuscript. If the CT projection is along the axial direction, then the manifold will be along a line instead of a circle, in which case our proposed spherical MDS method becomes inapplicable. However, I would like to bring to your attention that manifold learning methods are powerful for reorganizing high dimensional data in general and can also be used for addressing 4DCT problems [1]. Our method can address only those situations where the manifold is a circle. We agree with the reviewer that our proposed method will not be applicable for in/out motions, as our method is only proposed for spherical constraint motion, for example, in cryo EM applications.


C6C5: Without discussion about how tissue motion affects the projection, I fail to see the usefulness of the proposed method (and other previously published similar methods) in real-world applications, e.g. MRI scanning with patient motion. Problems with such applications are really not about unknown viewing angles, or at least the problems cannot be solved by uniformly rearranging the recovered viewing angles. BTW, MRI imaging is not, like CT imaging, by line integral projections. This may bring up the question that the example applications discussion in the paper maybe not the good candidates for this proposed method, even though other published papers also refer to the same applications.

A6A5: Thank you for the critical comment about the usefulness of our method in real world applications and we agree with the reviewer on this aspect.

We regret to have over claimed the applications of our proposed method. We totally understand the reviewers concerns regarding applicability of our method – in 4DCT and MRI scanning. After a thorough investigation, we have removed the claim of the applicability of our method to these applications. At this moment, we have addressed the problem of recovering view angles from projection data, for example, in the application of cryoEM macromolecular reconstruction. The orientation determination for cryoEM images can equivalently be modeled as the view angles estimation problem and our method is a prototype in 2D case and we are working on the extension for 3D reconstruction now. If such a recovery is not sufficient for the final application, then it is beyond the scope of our current paper.

As mentioned in A5, our method is applicable only to those situations with spherical motion constraints which can be solved just by recovering the unknown view angles like the structuring of viruses using electron microscopy.
Authors may consider to somehow rearrange the flow of this paper, to make the flow more linear. There are multiple examples that one thing is briefly introduced, and then explained in details in a far later section. For another example, is Figure 4 really useful since it is pretty much the same as Figure 1B and C? Writing is good in general, but need to tighten up.

Thank you for valuable suggestions to improve the quality of our manuscript. We have re-arranged the flow of the paper in the revised manuscript and we believe it is of better quality now. Figure 1 in the revised manuscript shows the pipeline / flowchart of our paper and it is just a representation of our overall method, where as Figure 4 in the revised manuscript shows the actual experiment conducted and the values present in the figure are needed for discussion.

Since the most important contributions of the manuscript is a new method to recovery projection angles (or order or angles), shall authors consider to present some results of the recovered angles versus the known ground truth (known angles before projections are randomized), and cases when the method fails? Such results may be useful to directly/indirectly compare to other published methods.

Thank you for this good question.

As per your suggestion, we registered the original and final images and compared the two to evaluate the performance of our method. The results are included in the revised manuscript. We designed the experiment in the following way. We registered the two images by a global rotation which can be referred from the correspondence between the original projections and re-ordered projections. As we know the ground truth of original projections, we can easily refer the global rotation angle by finding the position difference between the corresponding projections. We provide the measure of quality of reconstruction by using peak signal-to-noise ratio (PSNR) and mean squared error (MSE). They are computed by the following equations:

\[ MSE = \frac{1}{mn} \sum_{i=0}^{m-1} \sum_{j=0}^{n-1} [I(i,j) - K(i,j)]^2 \]

\[ PSNR = 20 \cdot \log_{10} \left( \frac{MAX}{\sqrt{MSE}} \right) \]

Where I is the original image and K is the reconstructed image and m, n are the size of the images respectively.

The Figure 3 below displays the three images – the original, reconstructed and the registered from left to right. The middle image is reconstructed from 512 projections. The image on the right is the registered image by a global rotation for the image in the
middle. As per the experiment we conducted, the MSE and PSNR between the image on the right and left are 0.0037 and 24.2804 respectively. Please note that this new experiment is added in the Section 3.2 in the revised MS, starting with “We further verify … “.

![Figure 3: Original Image, Reconstructed Image and Registered Image](image)

Furthermore, we provide another measure for the accuracy of the recovered angles. We calculated the difference between the estimated view angles and original angles after a global registration.

\[ \text{AngDif} = \sum_{i=1}^{L} [\text{EAng}_i - \text{OAng}_i]^2 \]

Where \( L \) is the number of the projections, \( \text{EAng} \) denotes the estimated angle for the projection and \( \text{OAng} \) denotes the original angle. In the above test, AngDif is 0 when there is no noise added to the images.

**C10C8:** I don't feel Figure 5, which analyzes the method on different number of projection angles, is important, unless the authors want to show this method is superior than other published methods for these situations.

**A10A8:** Thank you for your comments.

We totally understand that the reviewer has the concern about the testing of different number of the projections angle. The reason for us to carry out this experiment is that the number of samples is important for manifold reconstruction. In this experiment, we want to see that how many samples are sufficient enough to reconstruct the manifold and we wanted to see whether the number of samples will affect the estimation of view angles.
**C11C9:** Shall the results section in the abstract be divided into two sections “method” and “results”? It is usually not enough to tell only the results in the abstract without mentioning the methods.

**A11A9:** Thank you for your observation.

We understand the concerns of the reviewer. However, the format that we have is as per the requirement of this journal. We have put the content of method and result together in the “result” subsection. We have made the changes in the revised manuscript.

**C12C10:** In fact, I cannot tell how view parameters are estimated from the abstract, which means the abstract is not adequate.

**A12A10:** Thank you for your comment.

We have revised our abstract for clarity and we believe it addresses your concern.

**C13C11:** I see some confusion among the terms of “object orientations”, “view angle”, and “acquisition positions”. In the 3 examples you give in page 2, I agree that the “object orientations” are changing during the measurements (collection of the line-integral projections), but the “view angles” and “acquisition positions” are apparently well defined (respecting to the detectors, or the CT scanners) without uncertainties. They are certainly uncertain respecting to the objects, but the object orientations are not. Besides, you may really mean the internal objects in the patient body, but not the whole patient as an object. Please try to make it clearer in the introduction section (or/and in the abstract).

**A13A11:** Thank you for pointing out the confusion in the use of different terms.

We believe that this has been addressed in the revised manuscript. The motivation of this work is driven by the cryoEM macromolecular structure determination. In that application, the uncertain parameter is the orientation of the virus which can be equivalently modeled as estimation of view angles. The view angle in our work is generalized to be treated as the object orientation or other acquisition parameters. In order to make the term clear, we revised the manuscript and deleted the term of acquisition position. Please check Line 6 of Section 1.1 on the page 2 starting from “For example…”. 
C14C12: References please at section 1.3, line 3; please add line numbers for the entire manuscript; In Fig 7, the vector $Q_1$ does not seem to be perpendicular to $F_1$. $Q_2$ is ok, though.

A14A12: Thank you for your comments.

We have addressed the changes in the revised manuscript. We are sorry that the manuscript does not include the line number in the entire manuscript. This is because we are using the latex template provided by BMC medical center and the manuscript does not include the line number in the manuscript. Please refer to Figure 8 in the revised MS.