1 Introduction

In this project, we propose a new algorithm that recovers the rigid motion parameters and the underlying density function from a set of noisy measurements of three dimensional (3D) density functions. We measure the Radon transform of each 3D function which are randomly rotated and translated version of a target function that we try to recover. Radon transform is a set of parallel line integrals of a density function taken at various projection angles as shown in the 2D example in Figure 1. We can recover a 3D density function from the associated Radon transform using filtered back-projection method. (See Figure 1 B and C.) These are called reconstructions or tomograms. In the field of structural biology, aligning 3D tomographic reconstructions is a common practice to improve the resolution of the density function of a molecular structure of bacterial cells and viruses [MS09]. The Radon transform of frozen cells and viruses are measured by transmission electron microscope, and this particular imaging modality is called cryo-Electron tomography.

One major complication of using a transmission electron microscope to acquire Radon transforms is that we cannot cover the entire angular range of the 3D function due to the sample holder geometry as shown in Figure 1 A. These missing angular components are called missing wedge. According to the projection-slice theorem [Bra56], pictorially described in Figure 2, each Radon integral value corresponds to a frequency component of the function,

![Figure 1: Left: Radon transform of a 2D function taken at the projection angle of φ. Right: A: Transmission electron microscope sample holder rotations. B: Projection of a 3D function, C: Back-projection of 2D Radon transform of a 3D function](image)
and therefore, the reconstructions with missing wedge have distorted appearances and they are difficult to align them directly. In Figure 2, the top and bottom edges of the head phantom is not present because of the missing wedge along Y axis. One of the most common approaches to align tomograms with missing wedge is to recover the alignment parameters that maximize the constrained correlation coefficient between the reference function and the reconstructions. This approach is only valid if we have a reliable reference density function. Therefore, we need a different approach if a reference function is not available.

In this project, we formulate the problem of reference-free alignment of 3D tomographic reconstructions with missing wedge as a constrained convex optimization problem. There are various metrics to evaluate how well functions are aligned if we want to obtain a single function. However, since we are also interested in recovering two or more functions in the noisy measurements, we use a metric that can also measure how heterogeneous the observed reconstructions are. One candidate is a matrix rank which is the number of linearly independent columns in a matrix. If we create a matrix whose columns are vectorized reconstructions, it has rank 1 when all the reconstitutions contain the aligned identical functions. If the underlying functions are not exactly aligned, the rank of the matrix increases. It also increases when observations contain multiple functions. The idea of using a matrix norm heuristic and formulating the alignment problem as a convex optimization problem originates from [PGW+12], where they used it to align natural images and remove sparse corruptions.

2 Problem Formulation

Let us start formulating the alignment problem by defining key parameters and functions involved. First, we have a target 3D density function, which is \( s : \mathbb{R}^3 \rightarrow \mathbb{R}_+ \), and we have \( n \) randomly rotated and translated copies of \( s \), \( v_i = T_{p_i}(s) \in \mathbb{R}_+^N, i \in \{1, \ldots, n\} \). \( T_{p_i} : \mathbb{R}_+^N \rightarrow \mathbb{R}_+^N \) is a rigid body transform operator whose parameter \( p_i = (\phi_i^x, \phi_i^y, \phi_i^z, t_i^x, t_i^y, t_i^z) \). The first three elements \( (\phi_i^x, \phi_i^y, \phi_i^z) \) define the rotation in degrees around each axis \( (x, y, \text{and } z) \) and the second three elements, \( (t_i^x, t_i^y, t_i^z) \), define the translation in pixels along each axis. \( N \) is the number of pixels sampled for each 3D function. Second, we do not observe these transformed copies of the target function directly but we take their Radon transforms. A Radon transform contains \( m \) tomographic projections of the 3D function of interest taken at a set of angles, \( \theta = \{\theta_1, \theta_2, \ldots, \theta_m\} \). These angles specify the amount of sample holder rotation around Y axis. (See Figure 1 for the pictorial description.) These images are vectorized and stacked vertically together as a single vector for easiness of defining the operator in our formulation.
Therefore, our Radon operator is defined as $R_\theta : \mathbb{R}^N \rightarrow \mathbb{R}^{mM}$ where $M$ is the number of pixels in each projection.

By filtered back-projecting these Radon transforms, we can reconstruct the 3D functions of $n$ randomly rotated and translated copies of the target. However, since $\theta$ typically does not cover the complete range of 3D angular space, these volumes have distorted appearances, and we do not want to align them directly. To avoid aligning corrupted 3D reconstructions, we also try to estimate the missing information compensated reconstructions by introducing a set of optimization variables, $x_i \in \mathbb{R}^N$, $1 \leq i \leq n$. Each $x_i$ is a vectorized missing information compensated reconstruction. Then, we try to align these new copies by minimizing the rank of a matrix $X = [x_1, \ldots, x_n]$, while limiting the discrepancy between the observed Radon transforms and the Radon transforms of the rotated and translated $x_i$'s by the estimated alignment parameter $p_i$'s. We try to limit this discrepancy up to the noise limit $\sigma_i$ which is an estimated standard deviation of additive noise on each measurement. We assume that each reconstruction can have different noise level since each Radon transform could have been taken at different conditions. Finally, the alignment problem is defined as below.

\[
\begin{align*}
\text{minimize} & \quad \text{rank}(X) \\
\text{subject to} & \quad \|R_\theta(T_{p_i}(x_i)) - R_\theta(v_i)\|_2 \leq \sigma_i, \quad 1 \leq i \leq n,
\end{align*}
\]

where $X = [x_1, \ldots, x_n] \in \mathbb{R}^{N \times n}$ and $p_i \in \mathbb{R}^6$ are the optimization variables. $R_\theta(v_i) \in \mathbb{R}^{mM}$ are the observed Radon transforms.

Problem (1) is not a convex optimization problem because the objective function is not convex and $T_{p_i}$ is not a linear operator. To utilize convex optimization algorithms, we relax the objective function to be a nuclear norm ($\| \cdot \|_*$) and we also linearize the rigid 3D rigid body transformation operator $T_{p_i}(x_i)$, using its first order approximation at the initial alignment parameters $p_i$ and the initial reconstruction $x_i$. Since this linear approximation is only valid when the alignment parameters do not deviate much from the initial alignment parameters, we instead calculate an incremental adjustment on the alignment parameters within a small range around the initial alignment parameters. To fully align all functions, we need to solve a sequence of optimization problems and iteratively update the alignment parameters by adding the incremental parameter adjustments to the parameters found in the previous iteration. Then, our algorithm becomes

\[
\begin{align*}
X(0) & \leftarrow X_0, p_i \leftarrow 0, \quad 1 \leq i \leq n \\
\text{for} \quad k = 1, \ldots, n_{\text{iters}} \text{ do} & \\
& \quad \text{Solve the subproblem defined in Eq. (2), which returns } X \text{ and } \Delta p_i. \\
& \quad X^k \leftarrow X, \quad p_i^k \leftarrow p_i^{k-1} + \alpha \Delta p_i, \quad 1 \leq i \leq n \\
\text{end}
\end{align*}
\]

and, the subproblem is

\[
\begin{align*}
\text{minimize} & \quad \|X\|_* \\
\text{subject to} & \quad \|R_{\theta}^{p_i^k}(x_i) + J_{p_i^k}(x_i^k) \Delta p_i - R_\theta(v_i)\|_2 \leq \sigma_i, \quad 1 \leq i \leq n,
\end{align*}
\]

where $X \in \mathbb{R}^{N \times n}$ and $\Delta p_i \in \mathbb{R}^6$ are the optimization variables. $\alpha$ is a step size, and $\Delta p_i$'s are the parameter updates. $J_{p_i^k}(x_i^k) \in \mathbb{R}^{mM \times 6}$ is a matrix whose columns are the Jacobian matrices of $T_{p_i^k}(x_i^k)$ with respect to each parameter in $p_i^k$. Notice that $R_\theta(T_{p_i^k})$ can be combined as a single linear operator $R_{\theta}^{p_i^k}$ since $p_i^k$ is not an optimization variable any more. Finally we can use convex optimization methods to solve Problem (2).
3 Optimization Method

One way to solve the problem is to utilize the convex cone problem solver, TFOCS, developed by Becker and E. J. Candès and M. C. Grant in [BCG11]. To utilize TFOCS, we need to re-formulate the subproblem into a conic form as below:

\[
\begin{aligned}
\text{minimize} & \quad \|X\|_* \\
\text{subject to} & \quad \begin{bmatrix} R_g^p & J_p(x^k_i) \\ 0 & 0 \end{bmatrix} \begin{bmatrix} x_i \\ \Delta p_i \end{bmatrix} + \begin{bmatrix} b_i \\ \sigma_i \end{bmatrix} \in \mathcal{K},
\end{aligned}
\]

where \( \mathcal{K} = \{(x, \tau) | \|x\|_2 \leq \tau \} \) and \( b_i = -R_\theta(v_i) \). TFOCS requires three functions defined: the proximal operator of the objective function, the proximal operator of the quadratic cone, and the linear measurement operator and its adjoint. In our case, the proximal operator of the objective function is the singular value thresholding operator of a matrix \( X = U\Sigma V^* \), which is defined as \( \text{svt}_\gamma(X) = UD_\gamma(\Sigma)V^* \), where \( D_\gamma(\Sigma) = \text{diag}((\sigma_i - \gamma)^+) \). To calculate the singular values, we calculate the eigenvalues of \( X^TX \) to obtain the singular values of \( X \) to speed up. The linear measurement operator is the Radon transform constraint defined in Eq. 2, and it has a block diagonal structure.

4 Result

4.1 Experiment Set-up Details

To test the algorithm, \( n = 100 \) copies of a target 3D function of size \( 32 \times 32 \times 32 \) pixels \( (N = 32768) \), shown in Figure 3, are generated by first rotating the target function by \( (\phi_x^i, \phi_y^i, \phi_z^i) \in [-180, 180] \times [-180, 180] \times [-180, 180] \), and then translating the rotated ones by \( (t_x^i, t_y^i, t_z^i) \in [-5, 5] \times [-5, 5] \times [-5, 5] \). The Radon transform of each rigid-body transformed function is taken at \( \theta = \{-60, -55, \ldots, 60\} \). Each Radon projection has \( 46 \times 46 \) pixels and each Radon transform has 25 projections, and they are noiseless. Each column of the optimization variable matrix \( X \) is initialized to be the filtered back-projected reconstruction of each Radon transform. The initial translation parameters are calculated by finding the center of gravity of each tomographic reconstruction, and the initial rotation is randomly selected within a range of \([-15, 15]\) degrees from the correct value. The noise level estimate \( \sigma_i \) is set to be 0.1 to avoid numerical issues when it is set to the true value 0. The sequential loop terminates when all of the measurement residuals \( \|R_g^p(x_i) + J_p(x^k_i)\Delta p_i - R_\theta(v_i)\|_* \), the objective value \( \|X\|_* \) and the nuclear norm of manually aligned tomograms using the recovered alignment parameter do not decrease any more.

To evaluate the quality of alignment, we mainly use two metrics. One is the discrepancy between the recovered alignment parameters and the true alignment parameters. For rotation, we calculate the rotation matrix using the recovered alignment angles and calculate the discrepancy between them by calculating the Frobenius norm. For translation, we calculate the \( l_2 \) norm between the recovered translation parameters and the true ones. The other metric for evaluation is how correlated the recovered density function is with the true target density function in terms of Fourier shell correlation (FSC) [HvH86]. FSC can tell how much the recovered function is correlated to the true one at each spatial
frequency up to the Nyquist rate. Typically, a good reconstruction has high FSC at the high spatial frequency range as well as the row one.

4.2 Recovering All Six Parameters

The rotation matrix discrepancy converges toward to zero as the outer iteration increases on although it tends to diverge a little at the end. However, the translation parameter discrepancies do not converge much, and the spread of misalignment remains about one pixel while the center of all tomograms tends to migrate all together. Shown in the center right column of Figure 3. The appearances of the recovered function and the improved FSC also tells that the recovered function is reasonably close to the true function. However, the objective value does not converge smoothly since it is difficult meet the measurement constraints, and the measurement residuals do not really converge to the specified level probably because we have reached a local minimum. It took about 6 hours to solve this particular problem.

4.3 Recovering Only Angular Alignment Parameters

Since the initial translation alignment parameter estimates given by the mass centering does not improve much and it is reasonably accurate, centering all the functions within a pixel distance range, only the rotation parameters are estimated by fixing the translation parameter at the initial value. This reduces the computation time (about 5 hours) and also stabilizes the angular alignment parameter convergence. (See the right column in Figure 4.) The alignment accuracy is not necessarily improved. The alignment result with different initial $X$, which is simply a random matrix, and the different initial rotation parameters are displayed in Figure 5. This result also shows similar parameter convergence and the reconstruction quality improvement in terms of FSC.
5 Conclusion and Future Work

In this project, the sequential convex programming algorithm for aligning 3D functions has been implemented utilizing the convex cone solver. The result shows that the nuclear norm heuristic and the linear approximation of the rigid-body transform can be useful tools to solve this non-convex problem. However, it is very slow and the tool has to be tested on real data sets which are much more noisy and whose features have very low contrast.

6 Acknowledgement

Prof. Boyd, EE364b TA’s, Nicholas Dwork and all my peer reviewers of EE364b class for their feedback and Ewout van den Berg for his initial contribution for the project.
References


