ITERATIVE METHODS IN LARGE FIELD ELECTRON MICROSCOPE TOMOGRAPHY

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Outline

- Background
- Problem
- Our work
- Future work
Microscopy and Scale

1m → 1mm → 1μm → 1nm

tissue → cell → organelle

amino acid/nucleotide → protein and nucleic acid → protein complexes

Computed Tomography (CT) → Optical Microscopy → Confocal Microscopy → STED Microscopy → Electron Microscopy → X-ray crystallography
Microscopy and Scale

Background

CT, Optical Microscopy

Computed Tomography (CT)
Optical Microscopy
Confocal Microscopy
Electron Microscopy
X-ray Crystallography

Cryo-electron microscopy

NMR
X-Ray
Methods for protein structures

Protein Structures

- NMR
- X-ray crystallography
- Structure Prediction
- Electron Microscopy

20kD
virus
20kD
200kD
3D-EM Structures

http://www.ebi.ac.uk/pdbe/emdb/index.html
Electron Microscopy

Single Particle Electron Tomography

Electron Source

Complexes embedded in vitrified buffer

Magnetic lens

Image Analysis

2D projection

Determination of orientation/center

3D model

3D data merging

3D Fourier transformation

Tilt Series

Serial Slices

3D model

Electron Tomography

CNCP 2014
Electron Tomography (ET) Background

Source:
2D Projection images

Goal:
3D reconstruction
Electron Tomography (ET)
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Technical Problems in ET Problem

Noise (SNR < 0.1)

Caveolae of PAE cell

-60 °  -50 °
Technical Problems in ET

- Noise
- Incomplete Data
Technical Problems in ET

- Noise
- Incomplete Data
- Distortions in large-scale reconstruction
Technical Problems in ET Problem

- Noise
- Incomplete Data
- Distortions in large-scale reconstruction
- Large computational resources and processing time
  - 8K*8K, TB
  - several months
  - an exascale computing problem
Outline

- Background
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3D-ET reconstruction for large data

Quality
- Curvilinear model
- Iterative method

Speed
- Cluster
- GPU

ATOM
Our methods

- Straight-line projection model

Straight-line electron path

Biological sample
Our methods

- Curvilinear projection model
Our methods

- Curvilinear projection model

\[ \Gamma = \{ \gamma_{x,\omega}(t) | t_0 \leq t \leq t_1 \} \]

\[ I = I_0 e^{-\int_{t_0}^{t_1} u[\gamma_{x,\omega}(t)] dt} \]
Our methods

- Generalized radon transform

\[ R_{\Gamma}u(x, \omega) \equiv v(x, \omega) = \int_{t_0}^{t_1} u[\gamma_{x,\omega}(t)] dt \]

- Determination of the curves \( \gamma_{x,\omega}(t) \)

Projection map:

\[ P_{\omega}(\gamma_{x,\omega}^1(t), \gamma_{x,\omega}^2(t), \gamma_{x,\omega}^3(t)) = (x_1, x_2) \]
Our methods

Reconstruction

Two reconstruction methods:
- Filter Backprojection (FBP) (easy)
- Iterative methods (noisy+incomplete data)
Our methods

- ASART based on a curvilinear projection map
  - Initial value (BPT and FBP)
  - Modified multilevel scheme for data access
  - Adaptive adjustment for relaxation parameters
  - Curvilinear projection map

\[
\begin{align*}
    u_j^{(0)} &= \frac{\sum_{i=1}^{M} w_{ij} v_i(P_b(j))}{\sum_{i=1}^{M} w_{ij}} \\
    u_j^{(k+1)} &= u_j^{k} + \sum_{s=1}^{S} \frac{\lambda w_{ij} u_j^{(k)}}{\sum_{s=1}^{S} w_{ij} \sum_{h=1}^{N} w_{ih} u_h^{(k)}} \left( v_i(P_b(j)) - \sum_{h=1}^{N} w_{ih} u_h^{(k)} \right)
\end{align*}
\]

Results

There is a distortion because of the straight-line projection model.

There is no distortion because of the curvilinear projection model.
Results

Results

- Straight-line projection model + FBP
Results

- Curvilinear projection model + ASART
Our methods

- Parallel strategy for iterative reconstructions
  - Decomposition of reconstruction into independent slabs along Z-axis
  - Computing the polynomials of each X-line in parallel
  - Blob-ELLR
Results

- Blob-ELLR

![Graph showing memory requirements for different datasets and methods.]

### Results

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<tr>
<th>node num</th>
<th>1</th>
<th>4</th>
<th>8</th>
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<th>64</th>
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<td>5.5</td>
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</tbody>
</table>

Results - ATOM
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Future work

- Large-scale Electron Tomography
- How to combine light microscopy and electron microscopy
  - New techniques in fluorescence microscopy allow us to label specific biological molecules for light microscopy and then stain for electron microscopy.

Fluorescence Microscopy  ➤  Electron Microscopy
Future work

- Large-scale Electron Tomography

Thin section of neuropil
(How we look at the brain)
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