Graph Denoising for Molecular Imaging

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Outline

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Cryo-Electron Microscopy (Cryo-EM)

- Major motivation for Thesis
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Only single particle cryo-EM is considered.

Cryo-Electron Microscopy (Cryo-EM) - Illustration

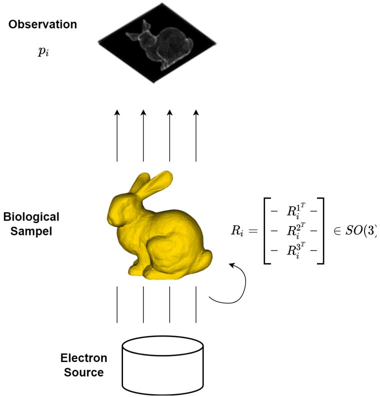

Figure: Cryo-EM overview

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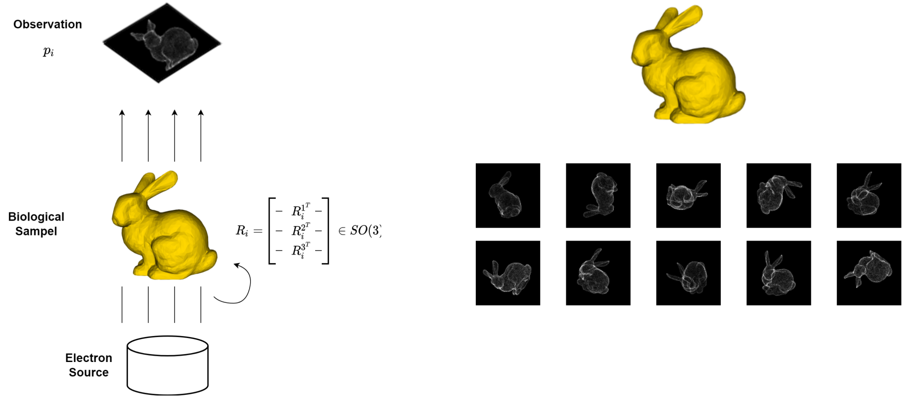

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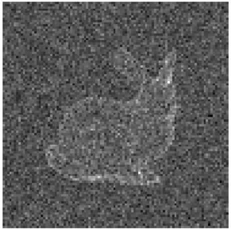
Cryo-Electron Microscopy (Cryo-EM) - Challenges

- High-noise level
- Unknown rotation during freezing
- (Structural variety of observations)

(a) Clean micrograph



(b) Noisy micrograph

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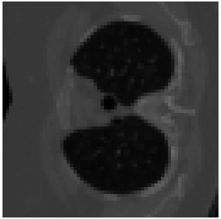
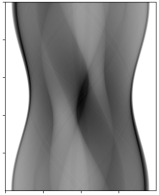


(a) Biological sample



(b) Clean observation (sinogram)

Shared Observation Model

Shared Observation Model

Observation

$$y = p + \eta \tag{1}$$

- y: noisy observation
- p: noiseless observation
- η: noise, assumed $\eta_i \sim \mathcal{N}(0, \sigma^2)$

Shared Observation Model

Observation

$$
\begin{aligned}
y &= p + \eta \\
y_i[j] &= p_i[j] + \eta_i[j] \quad \text{with } 1 \leq i \leq N, 1 \leq j \leq M
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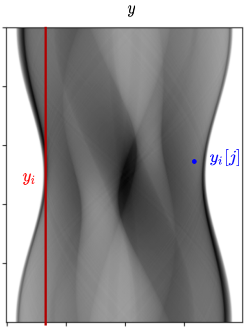
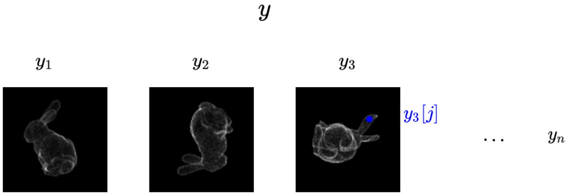
$$\begin{aligned} y &= p + \eta \\ y_i[j] &= p_i[j] + \eta_i[j] \qquad \text{with } 1 \leq i \leq N, 1 \leq j \leq M \\ y_i &= A(x, \theta_i) + \eta_i \end{aligned} \tag{1}$$

- y: noisy observation
- p: noiseless observation
- η: noise, assumed $\eta_i \sim \mathcal{N}(0, \sigma^2)$
- x: biological sample
- N: number of observations
- M: observation dimension
- $A : x \mapsto A(x; \theta_i) \in \mathbb{R}^M$: a non-linear operator
- θ_i: observation angle

Observation - Illustration



(a) CT Observation - sinogram



(b) Cryo-EM Observation - micrographs

Reconstruction

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$$Recon : \mathbb{R}^{M \times N} \to \mathbb{R}^{M \times M} \quad y \mapsto Recon(y; \theta) \tag{2}$$

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SNR is used as a metric for the quality of reconstructions.

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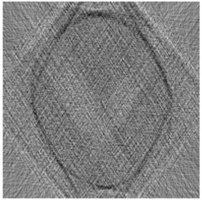

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Reconstruction - Computed Tomography

- Filter Backprojection (FBP)
  - Can be considered historical approach
  - Enables reconstruction for moderate noise
- Neural Network Approaches
  - Today state-of-the art
  - Using result of FBP and further denoise
  - U-Net **unet-tomography**

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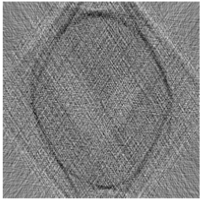

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Goal

$$denoiser : y_i = (p_i + \eta) \mapsto p_i^* \approx p_i$$

$$Recon\,(denoiser(y; \theta)) \approx x$$

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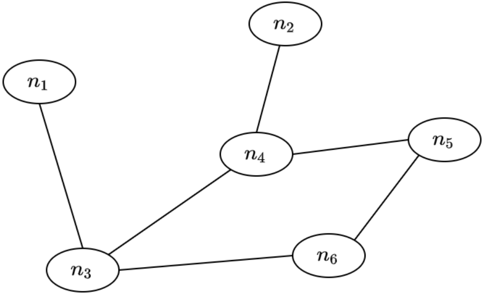

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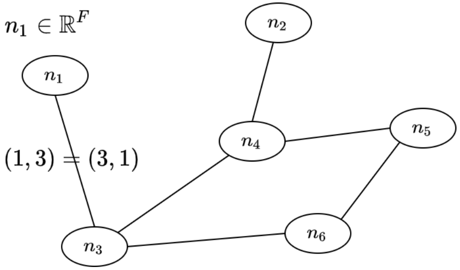
Nodes

$(n_1, n_2, \ldots) \in \mathbb{R}^F$, with F as node feature dimensions.

Edges

Edges are defined as a set of tuples (i, j), where i and j determine the index of the nodes.



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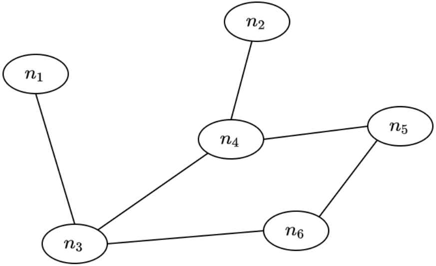

$$A = \begin{bmatrix} 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 & 1 \\ 0 & 1 & 1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 0 & 1 & 0 \end{bmatrix}$$

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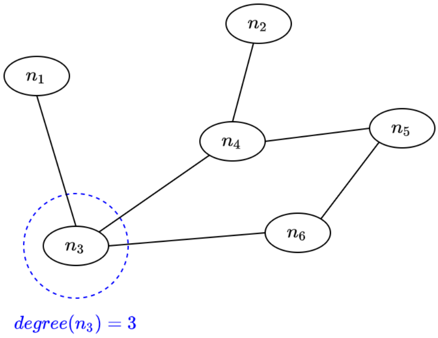

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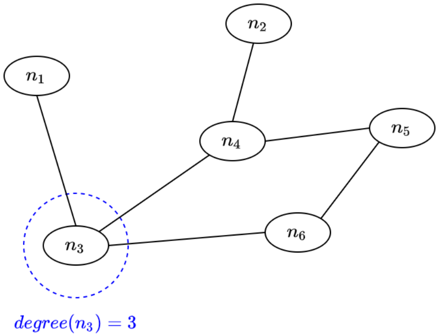
Degree Matrix of Graph G

Is a diagonal matrix with degree of nodes as entries.

$$D_{ii} = degree(n_i)$$



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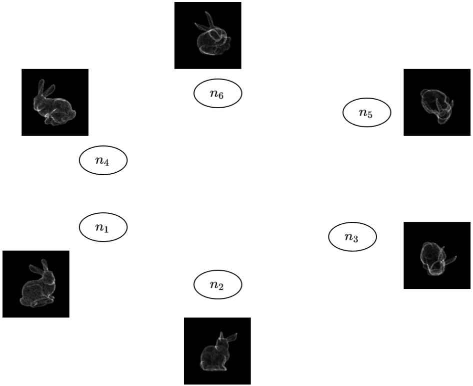

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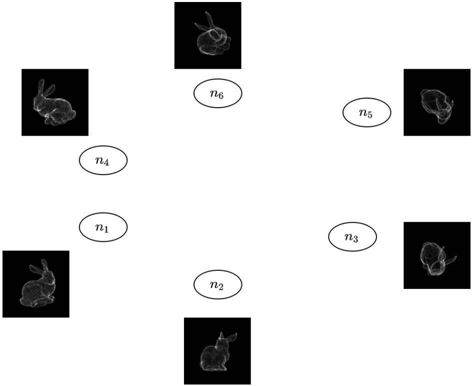

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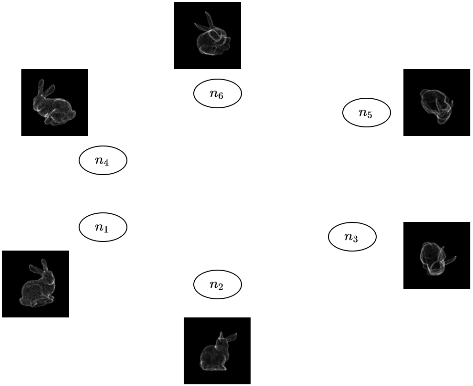

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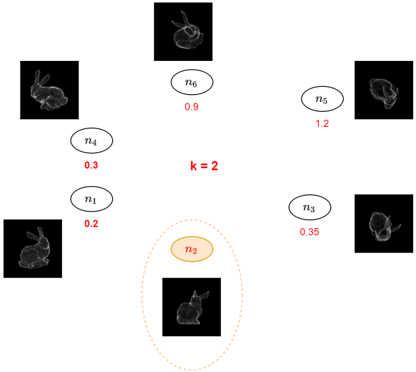

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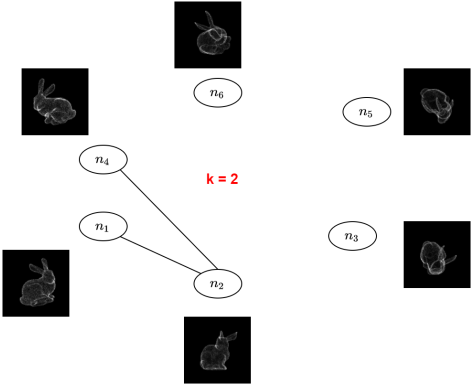

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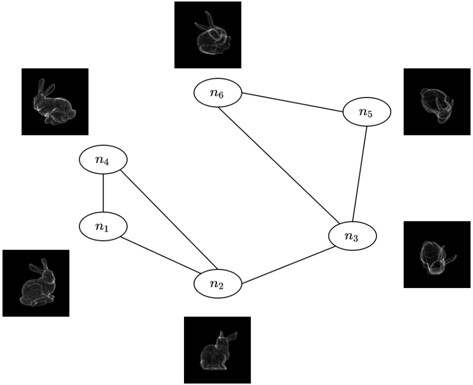

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Graph for Molecular Imaging Observation - Noise

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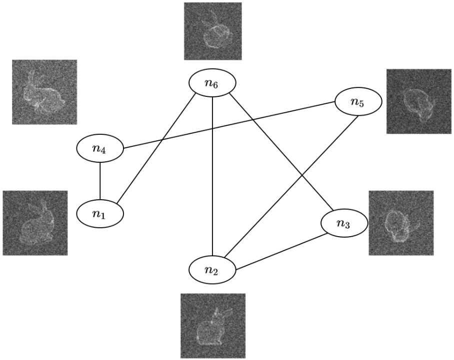
- With noise, graph will capture neighborhood inaccurately.



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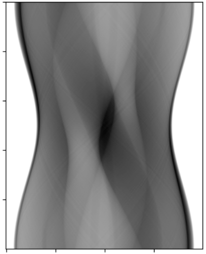
Low-dimensional Embedding

1. Construct a k-NN graph from observations.
2. Calculate $L = D - A$
3. Get 2nd and 3rd smallest eigenvalue with corresponding eigenvectors.

Low-dimensional Embedding for Computed Tomography



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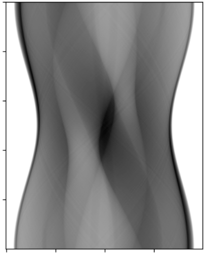

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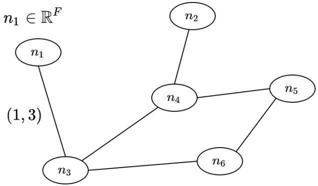

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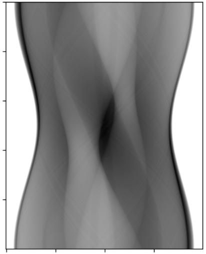

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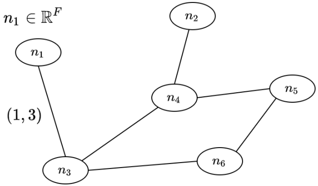

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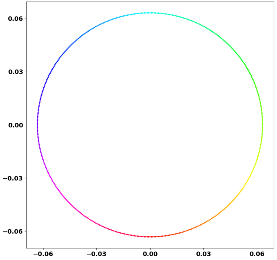

(c) 2_{nd} and 3_{rd} smallest eigenvectors of $L = D - A$

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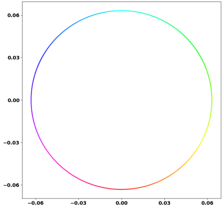

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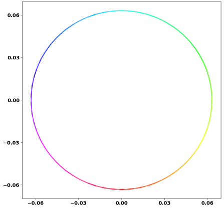

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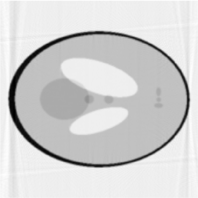

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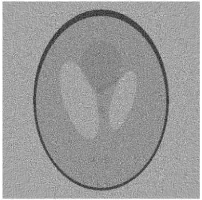

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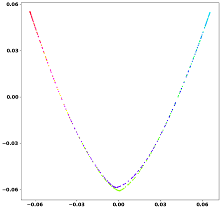
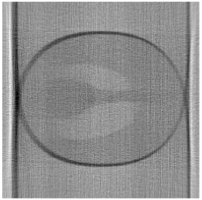


(b) GL-Embedding from $k = 6$ and SNR_y : 10 dB



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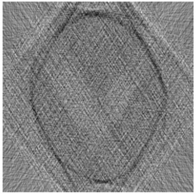

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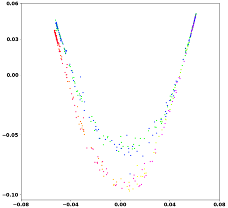

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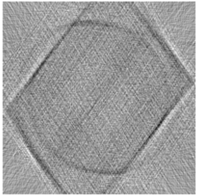

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Exploit graph as a data structure and the GL-embedding.

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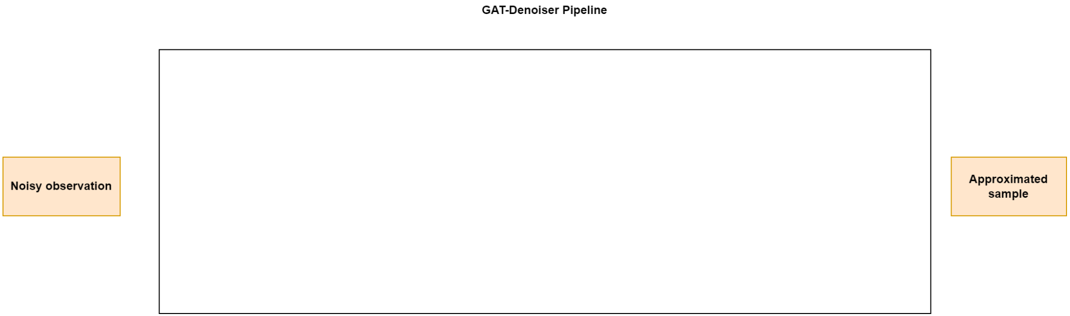

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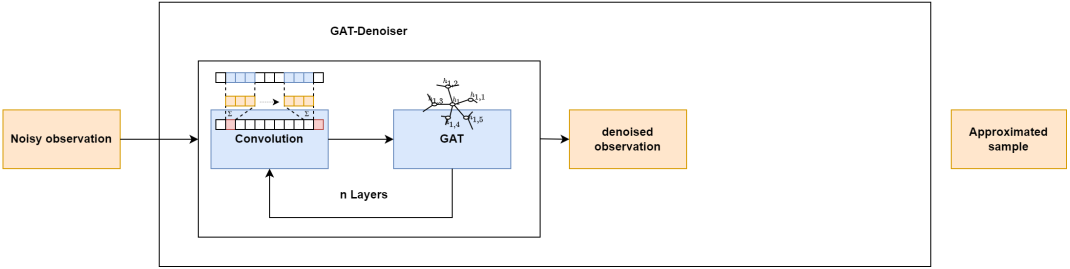

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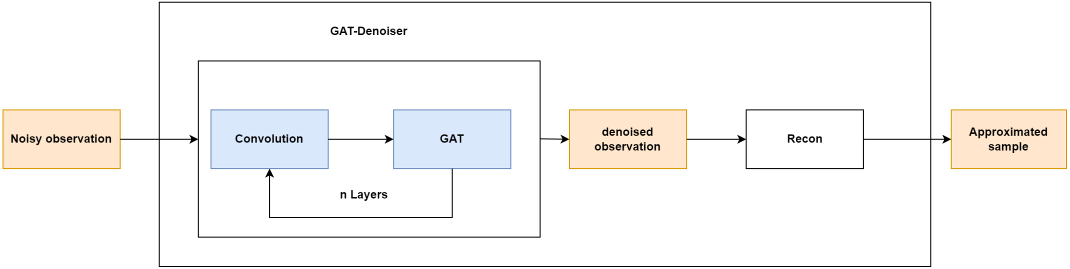

GAT-Denoiser Components

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- Convolution
  - Denoise single observation

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  - Denoise neighboring observation

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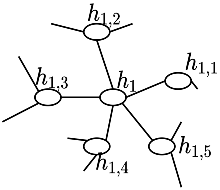
- Convolution
  - Denoise single observation
- Graph Attention Network (GAT) GAT
  - Denoise neighboring observation
- End-to-End Learning
  - Optimize for reconstruction quality
  - $\mathcal{L} = \| x - Recon(GAT\text{-}Denoiser(A(x,\theta) + \eta)) \|_2^2$
  - $\mathcal{L}_{sino} = \| p - GAT\text{-}Denoiser(A(x,\theta) + \eta) \|_2^2$

Graph Attention Network - GAT

- Extends Graph Convolution Network with attention (weights)
- Compute new node features
- Averages graph over neighborhood
- Multi-head available, motivated by transformer



Graph Attention Network - GAT

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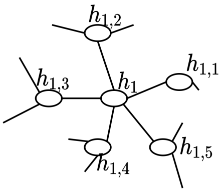
- Compute new node features
- Averages graph over neighborhood
- Multi-head available, motivated by transformer
- σ: activation function (Exponential Linear Unit)
- W: learnable weight matrix
- α: normalized attention coefficients



$$h'_1 = \sigma\left(\sum_{i=1}^{5} \alpha_i W h_{1,i}\right)$$

Input Graph

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- Exploit information from GL
- Low-dimensional embedding estimates angles
- Dominant information in data can be considered observation angles.

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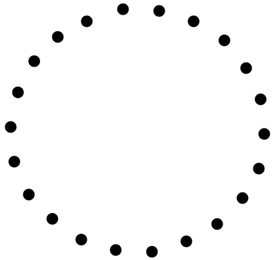

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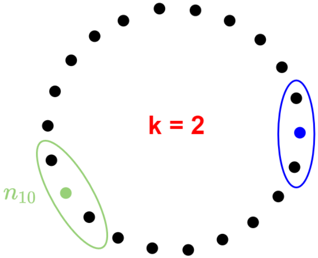

> Observation angles θ are assumed to be equally spaced.

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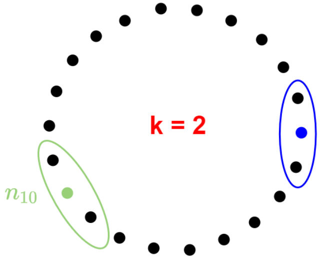


Observation angles θ are assumed to be equally spaced.

GAT-Denoiser Implementation for Computed Tomography

- Use U-Net for reconstruction
- During Trainig, U-Net might be trained jointly

Outline

LoDoPaB-CT dataset

- Dataset for low-dose Computed tomography
- 35’820 train samples
- 3’553 test samples
- BM3D as baseline algorithm
- Resolution 64 x 64

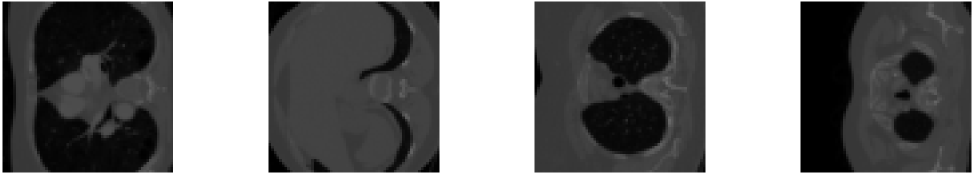


Figure: Some samples from the LoDoPaB-CT dataset.

Evaluation

- Small Scale Experiments
  - 1024 train samples
  - 100 test samples
  - 200 epochs
- Large Scale Experiments
  - Complete LoDoPaB-CT dataset
  - 20 - 40 epochs

Evaluation

- Small Scale Experiments
  - 1024 train samples
  - 100 test samples
  - 200 epochs
  - Goal: Find most promising architecture
- Large Scale Experiments
  - Complete LoDoPaB-CT dataset
  - 20 - 40 epochs
  - Goal: Find best model

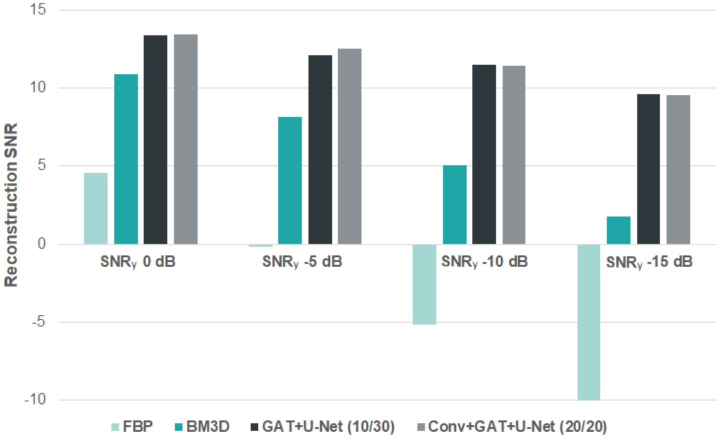
Training

- U-Net used for reconstruction
  - Pre-trained with complete dataset and SNR_y in [-10, 0] for 200 epochs
- Mini-batch gradient descent with batch size 64
- Adam optimizer
- Joint U-Net training possible

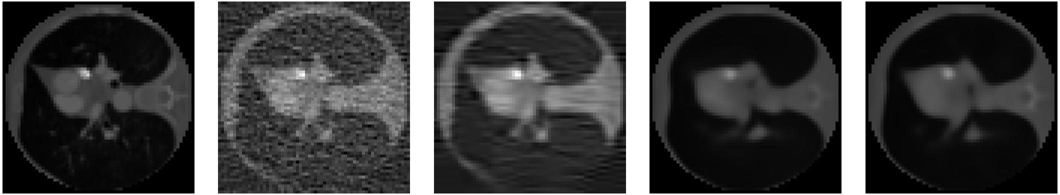
Small Scale Results

- Learning fails with random graph
- Learning succeeds with defined input graph
- Components contribute to success of GAT-Denoiser
- Best model with joint U-Net training

Large Scale Results



Large Scale Results - Visual - SNR_y 0 dB



(a) Clean sample (b) FBP (c) BM3D (d) *GAT+U-Net(10/30)* (e) *Conv+GAT+U-Net(20/20)*

Figure: Large Scale Experiment: Visual results for SNR_y 0 dB.

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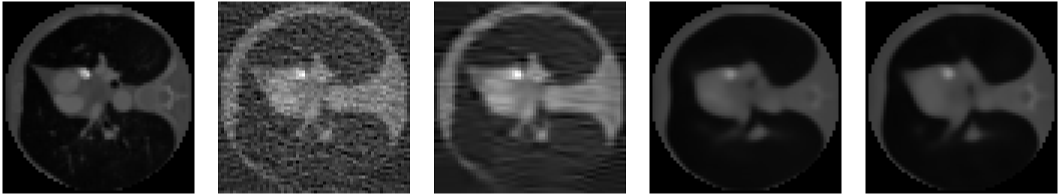

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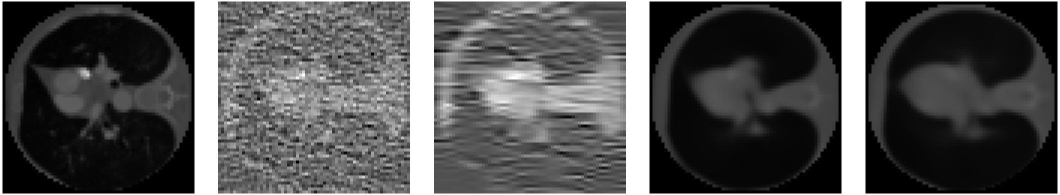
Figure: Large Scale Experiment: Visual results for SNR_y 0 dB.

GAT-Denoiser improves BM3D by 27.6%.

Large Scale Results - Visual - SNR_y -10 dB



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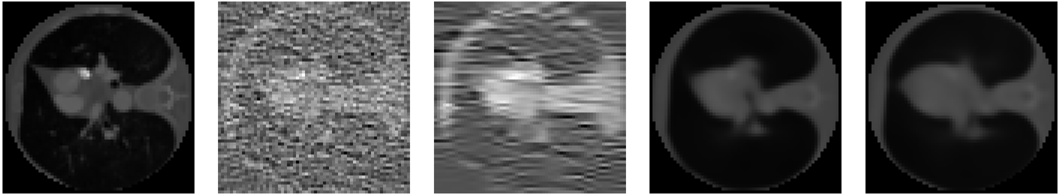

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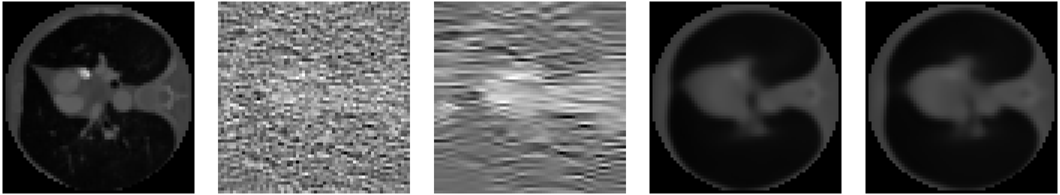
Figure: Large Scale Experiment: Visual results for SNR_y -10 dB.

GAT-Denoiser improves BM3D by 126.0%.

Large Scale Results - Visual - SNR_y -15 dB



(a) Clean sample (b) FBP (c) BM3D (d) *GAT+U-Net(10/30)* (e) *Conv+GAT+U-Net(20/20)*

Figure: Large Scale Experiment: Visual results for SNR_y -15 dB.

Large Scale Results - Visual - SNR_y -15 dB

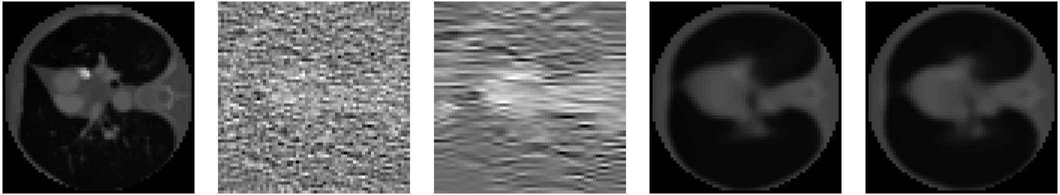


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Figure: Large Scale Experiment: Visual results for SNR_y -15 dB.

GAT-Denoiser improves BM3D by 379.9%.

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Summary

- GAT-Denoiser enables denoising of observations
  - Convolution
  - GAT
  - End-To-End Learning
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- GAT-Denoiser enables denoising of observations
  - Convolution
  - GAT
  - End-To-End Learning
  - Joint U-Net training boost performance
- Evaluated on LoDoPaB-CT dataset
  - Outperformed baseline BM3D by up to 379.9 %

Future Work

- Improve current GAT-Denoiser
- Derive GAT-Denoiser for 3D
- Make it work for unknown angles

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- Improve current GAT-Denoiser
- Derive GAT-Denoiser for 3D
- Make it work for unknown angles
- Cryo-EM
  - Known angles
  - Unknown angles
  - Work with structural variety in observations

Outline

Questions

References