University of Basel

Graph Denoising for Molecular Imaging

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29.06.2022

Outline

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Cryo-Electron Microscopy (Cryo-EM)

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Only single particle cryo-EM is considered.

Cryo-Electron Microscopy (Cryo-EM) - Illustration

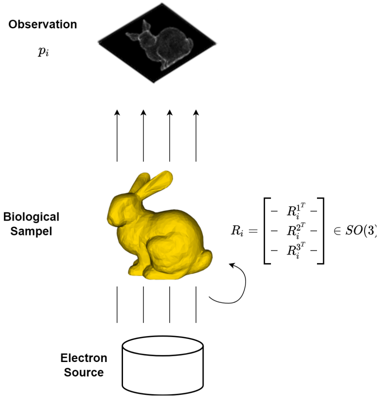
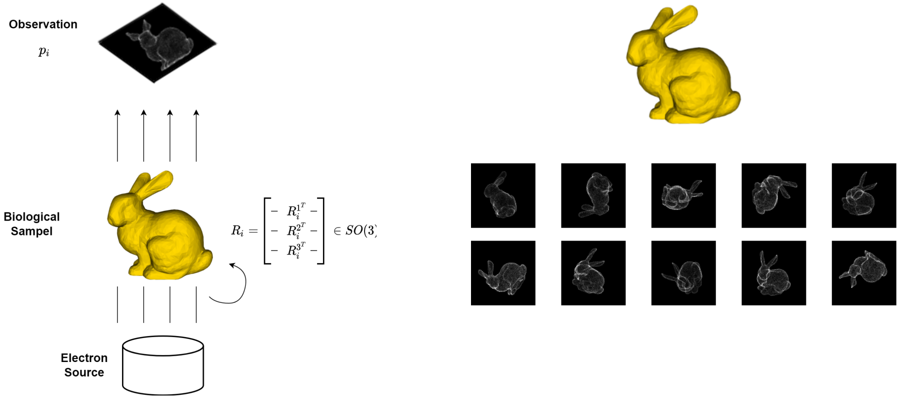


Figure: Cryo-EM overview

Cryo-Electron Microscopy (Cryo-EM) - Illustration



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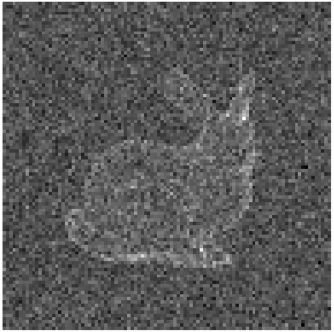
Cryo-Electron Microscopy (Cryo-EM) - Illustration

(a) Clean micrograph



(b) Noisy micrograph

Computed Tomography (CT)

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- Similar to Cryo-EM
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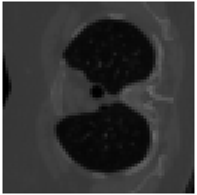
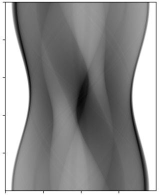


(a) Biological sample



(b) Clean observation (sinogram)

Shared Observation Model

Shared Observation Model

Observation

$$y_i = p_i + \eta_i \quad \text{with } 1 \leq i \leq N \tag{1}$$

- y: noisy observation
- p: noiseless observation
- η: noise, assumed $\eta_i \sim \mathcal{N}(0, \sigma^2)$
- $y_i \in \mathbb{R}^M$, M: observation dimension
- N: number of observations

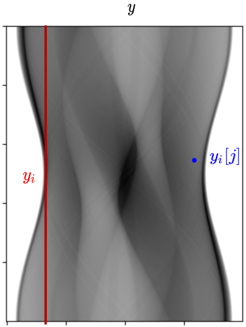
Shared Observation Model

Observation

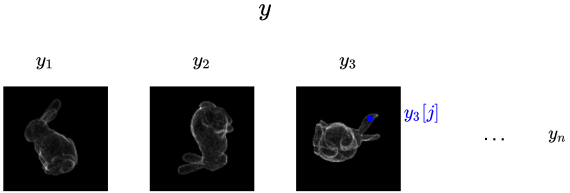
$$\begin{aligned} y_i &= p_i + \eta_i && \text{with } 1 \le i \le N \\ y_i &= A(x, \theta_i) + \eta_i && \text{with } 1 \le i \le N \end{aligned} \tag{1}$$

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

Observation - Illustration



(a) CT Observation - sinogram



(b) Cryo-EM Observation - micrographs

Reconstruction

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.

Reconstruction - Computed Tomography

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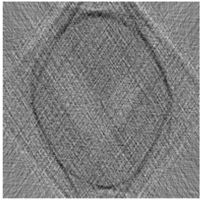

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Reconstruction - Computed Tomography

- 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 Ronneberger, Fischer, and Brox 2015

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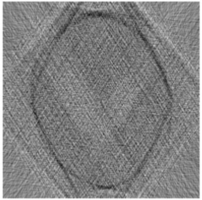

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Problem and Goal

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p not observable directly only access to y.

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Goal

$$denoiser : y_i \mapsto y_i^* \approx p_i$$

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

Outline

Graph - Definitions

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Graph Definition

A graph is defined as $G = \langle V, E \rangle$, where V is a set of nodes and E is a set of edges.

Nodes

$(n_1, n_2, \dots) \in \mathbb{R}^F$, 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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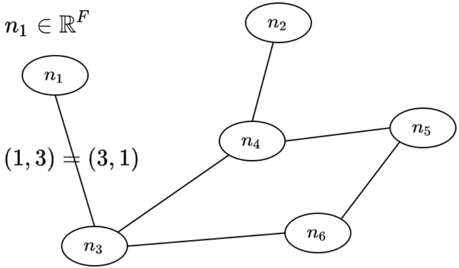

Figure: Sample graph

Graph - Definitions - Adjacency Matrix

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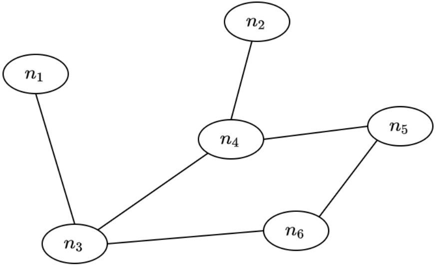
Adjacency Matrix

The binary adjacency matrix of graph $G = \langle V, E \rangle$ is defined as:

$$A_{ij} = \begin{cases} 1 & \text{if } (i,j) \in E \\ 0, & \text{otherwise} \end{cases} \tag{3}$$



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

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Graph - Definitions - Degree

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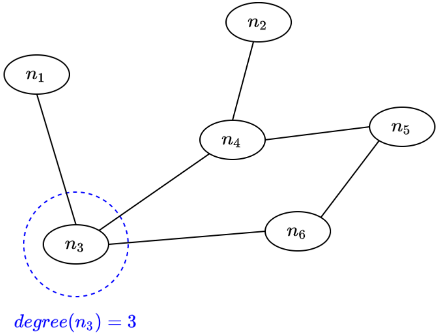
Degree of a node

The *degree* of a node is defined as the number of (incoming) edges.



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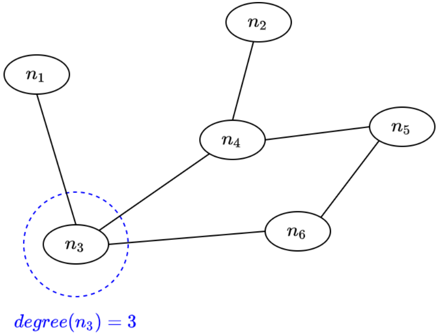
Degree Matrix of Graph G

Is a diagonal matrix with degree of nodes as entries.

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



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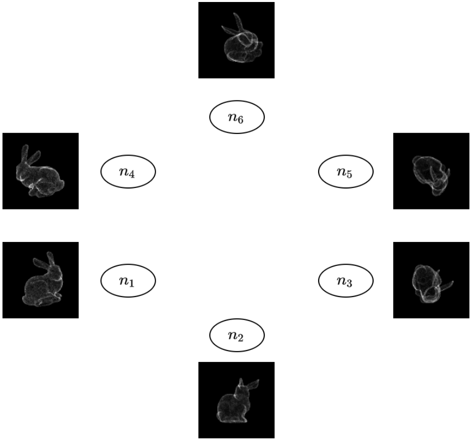

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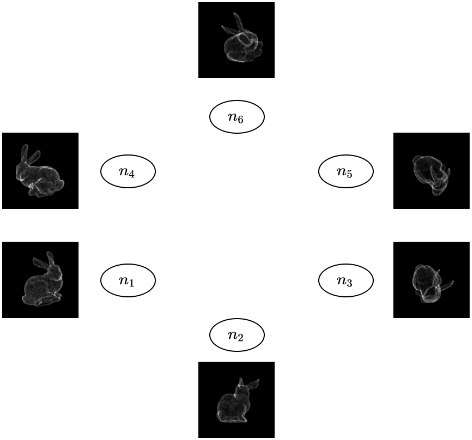

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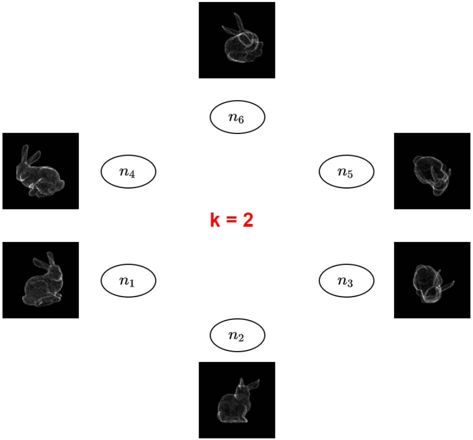

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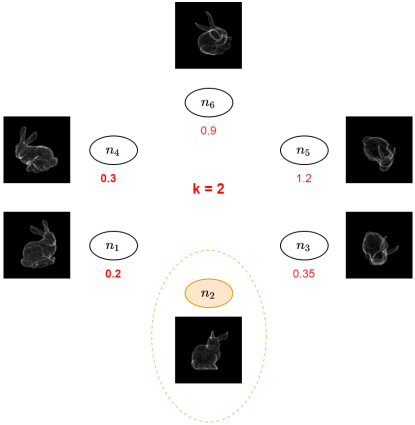

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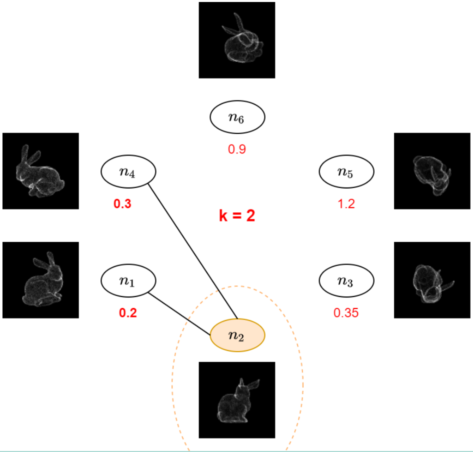

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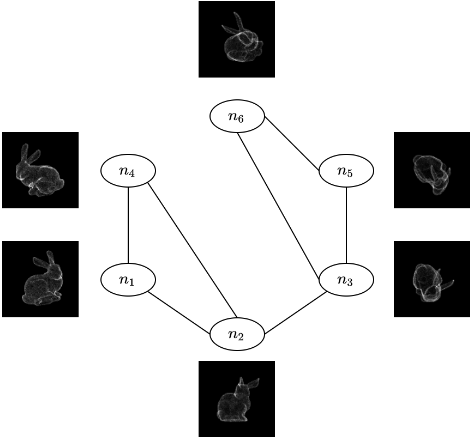

Graph for Molecular Imaging Observation - Noise

What happens with our noisy observations?

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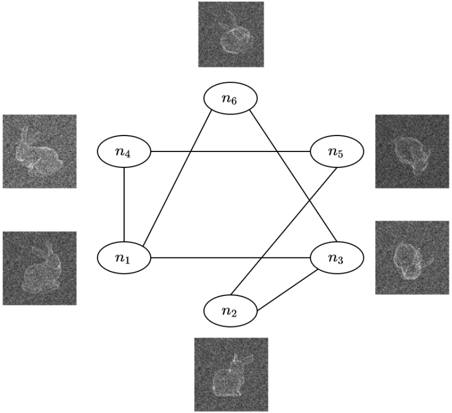
- With noise, graph will capture neighborhood inaccurately.



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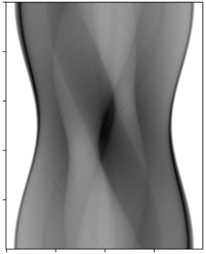
Low-dimensional Embedding

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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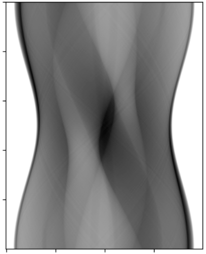

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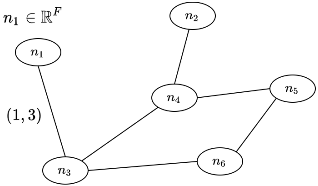

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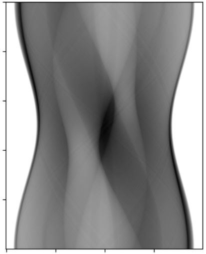

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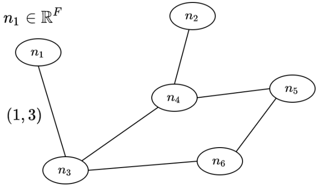

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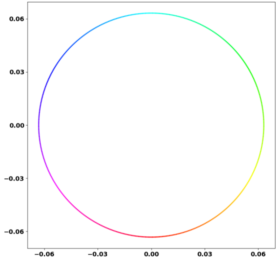

(c) 2_{nd} and 3_{rd} smallest eigenvectors of $L = D - A$

Computed Tomography with unknown angles

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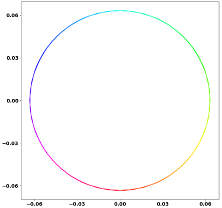

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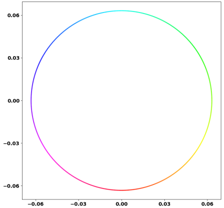

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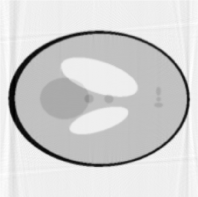

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What happens in the noisy case?

Computed Tomography with unknown angles

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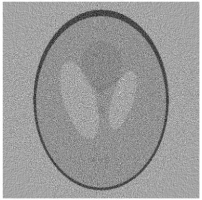
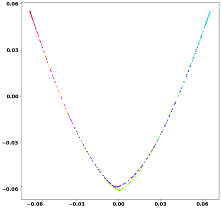
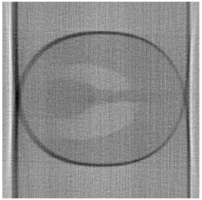


(a) Reconstruction known angles SNR_y : 10 dB



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



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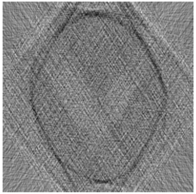

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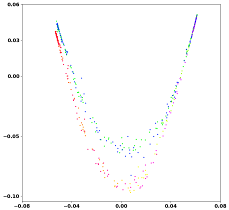

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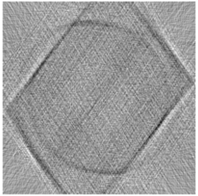

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  - No graph as data structure
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Exploit graph as a data structure and the GL-Embedding

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GAT-Denoiser

- GAT-Denoiser is a graph neural network (GNN) to denoise observations.
- Consists of three components:
  - Convolution
  - Graph Attention Network (GAT) Veličković et al. 2017
  - End-to-End Learning

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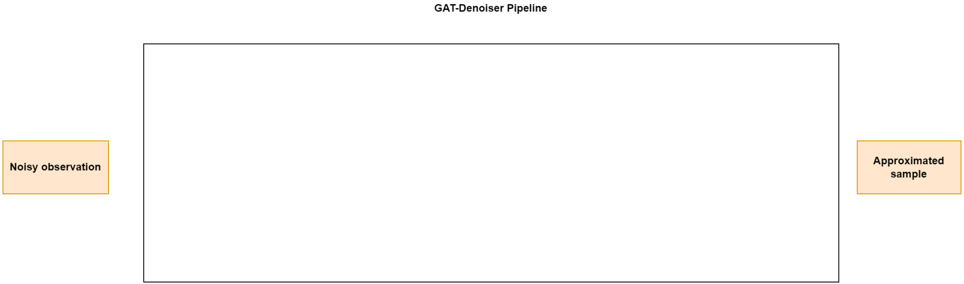

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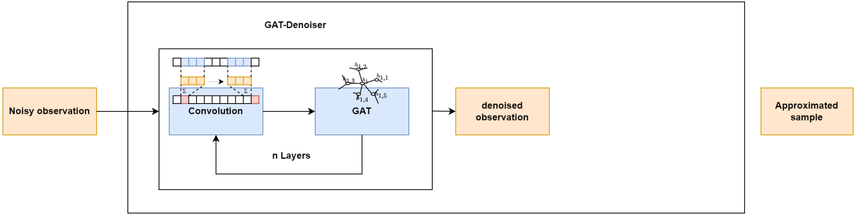

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  - Graph Attention Network (GAT) Veličković et al. 2017
    - Denoise neighboring observation
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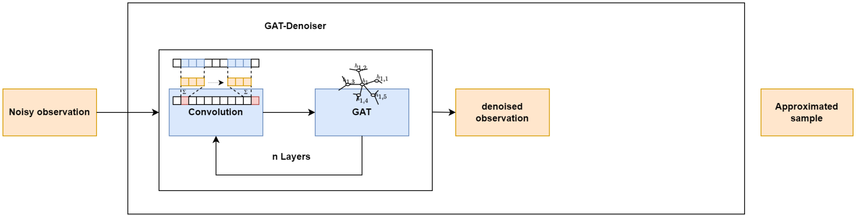

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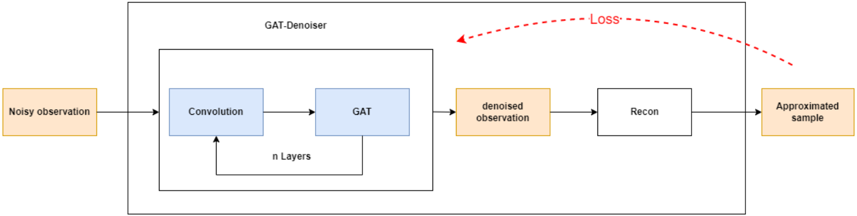

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  - End-to-End Learning
    - Optimize for reconstruction quality
    - Loss: $\mathcal{L}_{reconstruction} = \| x - Recon(GAT\text{-}Denoiser(y)) \|_2^2$

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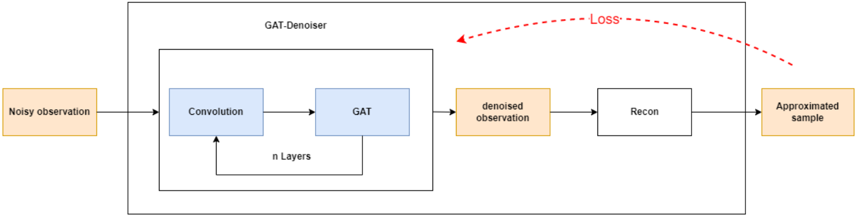

Graph Attention Network - GAT

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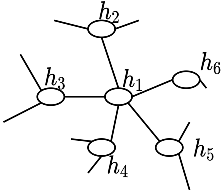
- Extends Graph Convolution Network with attention (weights)
- Computes new node features
- Averages graph over neighborhood
- Multi-head available, motivated by Vaswani et al. 2017

Graph Attention Network - GAT

- Extends Graph Convolution Network with attention (weights)
- Computes new node features
- Averages graph over neighborhood
- Multi-head available, motivated by Vaswani et al. 2017
- σ: activation function (Exponential Linear Unit)
- W: learnable weight matrix
- α: normalized attention coefficients



$$h'_1 = \sigma\left(\sum_{i=1}^{6} \alpha_i W h_i\right)$$

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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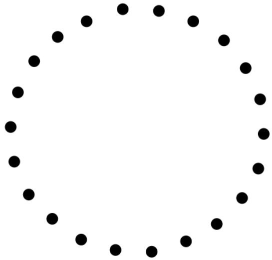
- Construct graph from observation angles
  - Map angles to unit-circle / unit-sphere



Input Graph

- Exploit information from GL
  - Low-dimensional embedding estimates angles
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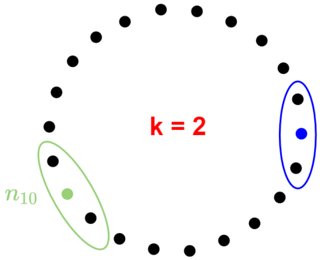

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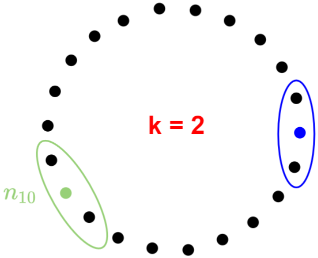


Observation angles θ are assumed to be equally spaced on the unit-circle.

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

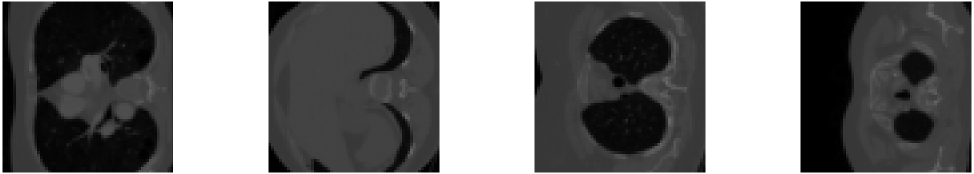


Figure: Some samples from the LoDoPaB-CT dataset.

GAT-Denoiser - Implementation for Computed Tomography

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

Evaluation

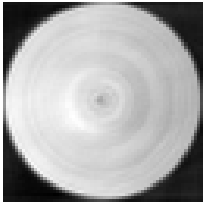
- Small Scale Experiments
  - 1024 train samples
  - 100 test samples
  - 200 epochs
- Large Scale Experiments
  - Complete LoDoPaB-CT dataset
  - 20 - 40 epochs

Evaluation

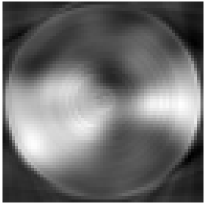
- Small Scale Experiments
  - 1024 train samples
  - 100 test samples
  - 200 epochs
  - Goal: Find most promising architecture
- Large Scale Experiments
  - Complete LoDoPaB-CT dataset
  - 20 - 40 epochs
  - Goal: Find best model

Small Scale Experiments - Overall Results

- Learning fails with random graph (Erdős–Rényi)
- Learning succeeds with defined input graph



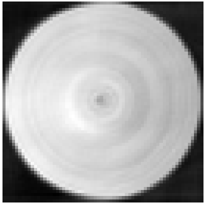
(a) Reconstruction with random Erdős–Rényi graph with $p = 0.01$



(b) Reconstruction with k-NN input graph $k = 10$

Small Scale Experiments - Overall Results

- Learning fails with random graph (Erdős–Rényi)
- Learning succeeds with defined input graph
- Single components contribute to success of GAT-Denoiser:
  - GAT: 2 layers and 4 heads
  - Convolution: kernel size 3 and padding 1
  - k-NN with k=2
  - Joint U-Net training



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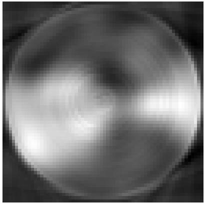
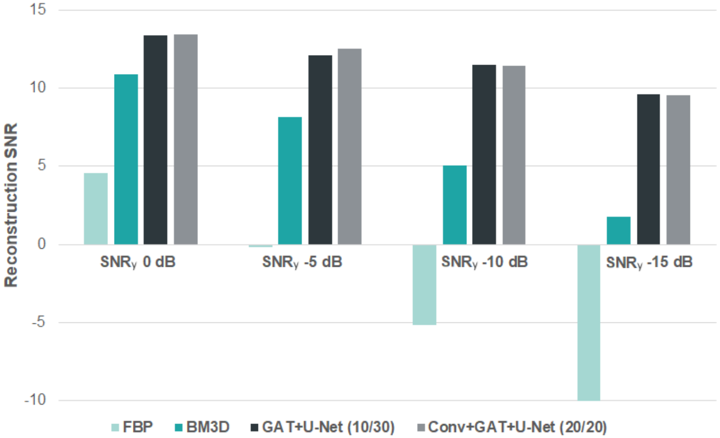


(b) Reconstruction with k-NN input graph $k = 10$

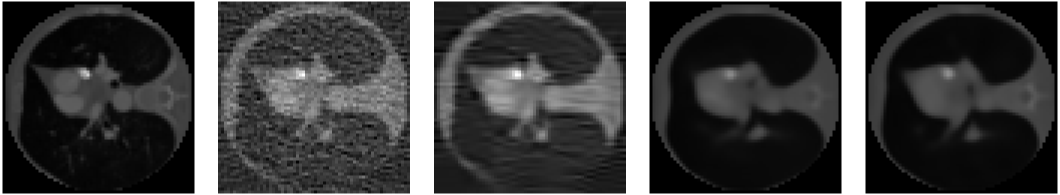
Large Scale Experiment - SNR Results

- 3'553 test samples
- Different algortihms / GAT-Denoiser models:
  - FBP
  - BM3D
  - GAT + U-Net (10/30)
  - Conv + GAT + U-Net (20/20)
- Reconstruction SNR averages over all test samples

Large Scale Experiment - SNR Results



Large Scale Experiment - Visual Results - 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.

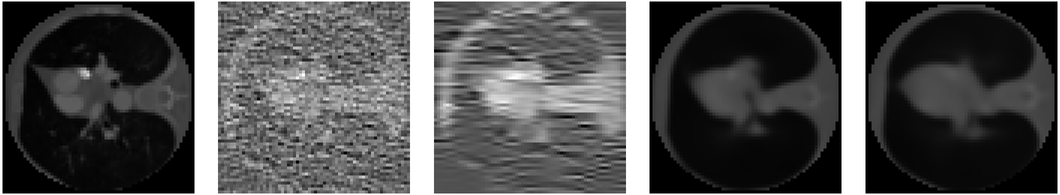
Large Scale Experiment - Visual Results - SNR_y 0 dB

(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.

GAT-Denoiser improves BM3D for SNR_y 0 dB by 27.6%.

Large Scale Experiment - Visual Results - SNR_y -10 dB



(a) Clean sample

(b) FBP

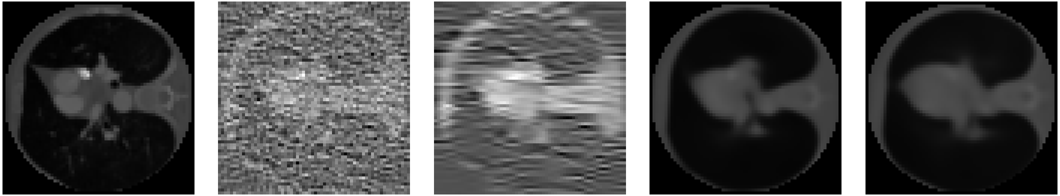
(c) BM3D

(d) *GAT+U-Net(10/30)*

(e) *Conv+GAT+U-Net(20/20)*

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

Large Scale Experiment - Visual Results - SNR_y -10 dB

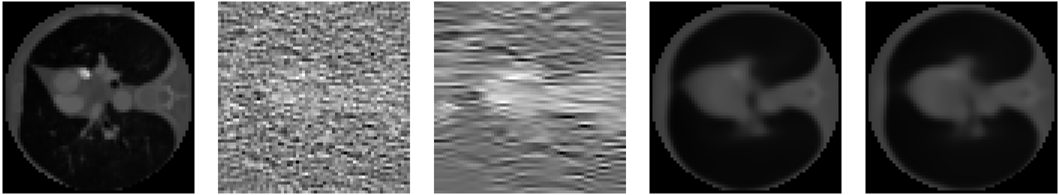


(a) Clean sample (b) FBP (c) BM3D (d) *GAT+U-Net(10/30)* (e) *Conv+GAT+U-Net(20/20)*

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

GAT-Denoiser improves BM3D for SNR_y -10 dB by 126.0%.

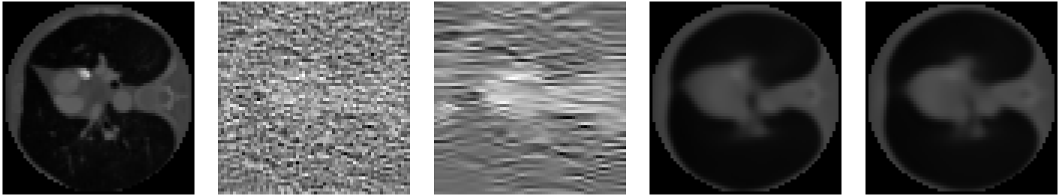
Large Scale Experiment - Visual Results - SNR_y -15 dB



(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 Experiment - Visual Results - 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.

GAT-Denoiser improves BM3D for SNR_y -15 dB by 379.9%.

Outline

Summary

- GAT-Denoiser enables denoising of observations
  - Convolution
  - GAT
  - End-To-End Learning
  - Joint U-Net training boost performance

Summary

- 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

Future Work

- 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 (1)

- Buades, Antoni, Bartomeu Coll, and J-M Morel (2005). "A non-local algorithm for image denoising". In: **2005 IEEE Computer Society Conference on Computer Vision and Pattern Recognition (CVPR'05)**. Vol. 2. IEEE, pp. 60–65. DOI: 10.1109/CVPR.2005.38.
- Coifman, Ronald R et al. (2008). "Graph Laplacian tomography from unknown random projections". In: **IEEE Transactions on Image Processing** 17.10, pp. 1891–1899. DOI: 10.1109/TIP.2008.2002305.
- Dabov, Kostadin et al. (2007). "Image denoising by sparse 3-D transform-domain collaborative filtering". In: **IEEE Transactions on Image Processing** 16.8, pp. 2080–2095. DOI: 10.1109/TIP.2007.901238.
- Leuschner, Johannes et al. (2019). "The lodopab-ct dataset: A benchmark dataset for low-dose ct reconstruction methods". In: **arXiv preprint arXiv:1910.01113**. DOI: 10.1038/s41597-021-00893-z.

References (2)

- Ronneberger, Olaf, Philipp Fischer, and Thomas Brox (2015). "U-net: Convolutional networks for biomedical image segmentation". In: **International Conference on Medical image computing and computer-assisted intervention**. Springer, pp. 234–241. DOI: 10.1007/978-3-319-24574-4_28.
- Vaswani, Ashish et al. (2017). "Attention is all you need". In: **Advances in neural information processing systems** 30. DOI: 10.48550/arXiv.1706.03762.
- Veličković, Petar et al. (2017). "Graph attention networks". In: **arXiv preprint arXiv:1710.10903**. DOI: 10.48550/arXiv.1710.10903.