Graph Denoising for Molecular Imaging

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Outline

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Cryo-Electron Microscopy (Cryo-EM)

- Major motivation
- Enables observation of molecules in near atomic resolution

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- Enables observation of molecules in near atomic resolution
- Observation through an electron microscope
- Frozen state of molecules required for observation
  - Frozen molecules are fragile $\mapsto$ electron microscope low power
  - During freezing, molecules rotate randomly
- Observations can be reconstructed to a 3D model
- Single particle Cryo-EM

Cryo-Electron Microscopy (Cryo-EM) - Illustration

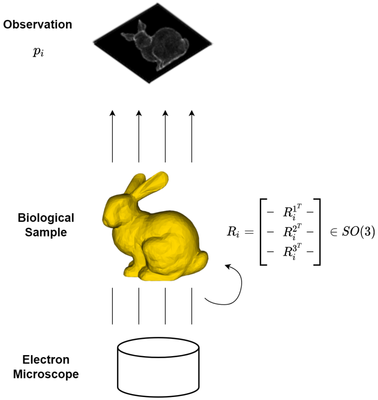
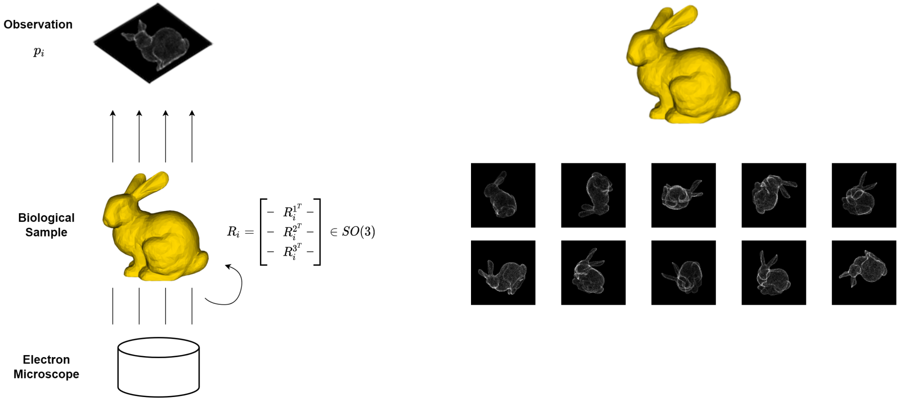


Figure: Cryo-EM overview

Cryo-Electron Microscopy (Cryo-EM) - Illustration



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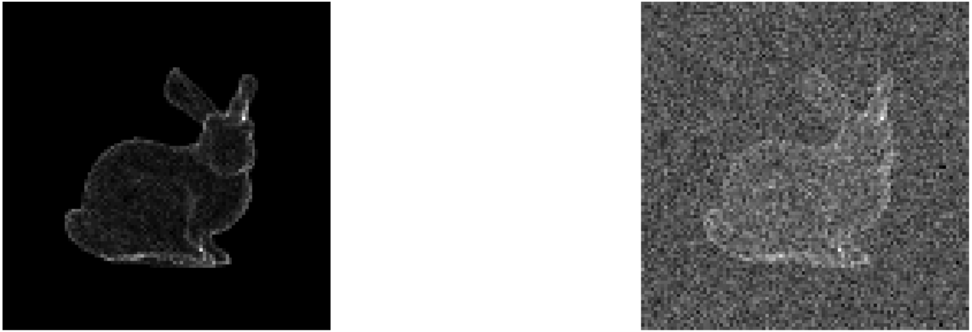

(a) Clean micrograph (b) Noisy micrograph

Computed Tomography (CT)

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- Similar to Cryo-EM
- Can be seen as a simpler version in 2D with known observation angles
- Good to start with towards a Cryo-EM algorithm

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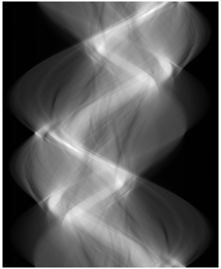
(a) Biological sample



(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

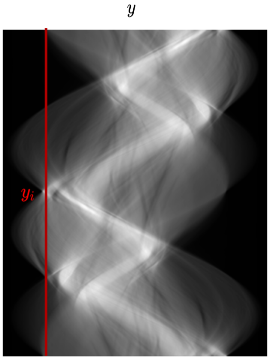
Shared Observation Model

Observation

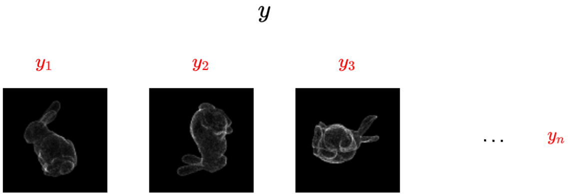
$$\begin{aligned} y_i &= p_i + \eta_i && \text{with } 1 \leq i \leq N \\ y_i &= A(x, \theta_i) + \eta_i && \text{with } 1 \leq i \leq N \end{aligned} \tag{1}$$

- 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

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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

- Filter Backprojection (FBP)
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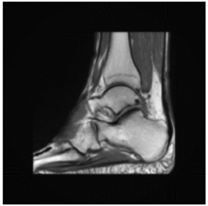
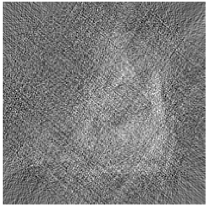


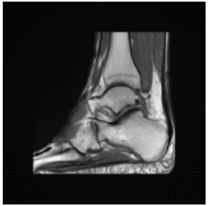
(a) Reconstruction clean: $Recon(p, \theta) \approx x$



(b) Reconstruction noisy with SNR_y 5 dB: $Recon(y, \theta) \not\approx x$

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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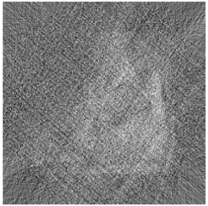

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Problem and Goal

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p not observable directly only access to y.

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Goal

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

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

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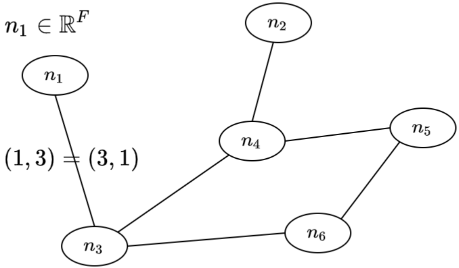

Figure: Sample graph

Graph - Definitions - Adjacency Matrix

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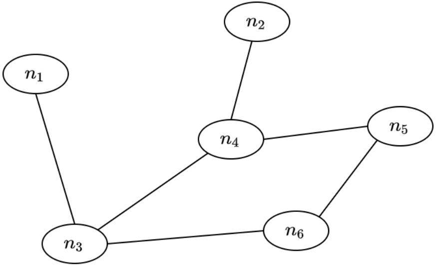
Adjacency Matrix

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

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



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

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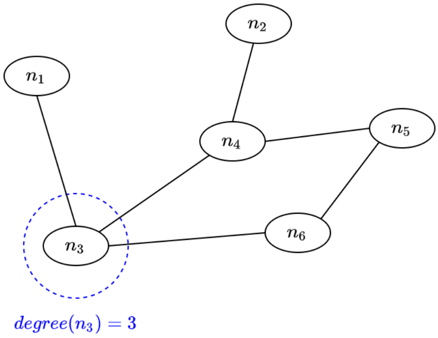
Degree of a node

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



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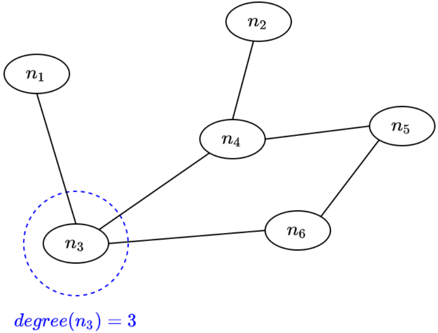
Degree Matrix of Graph G

Is a diagonal matrix with degree of nodes as entries.

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



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Graph for Molecular Imaging Observation

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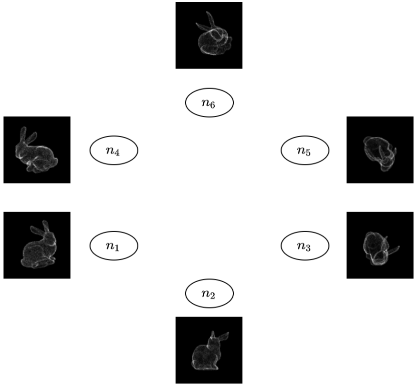

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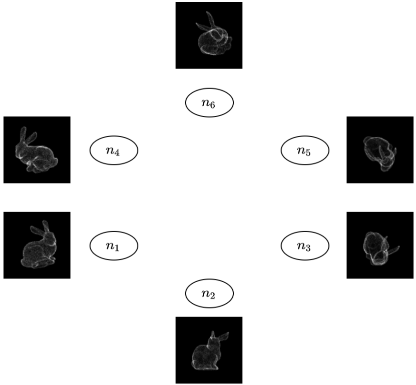

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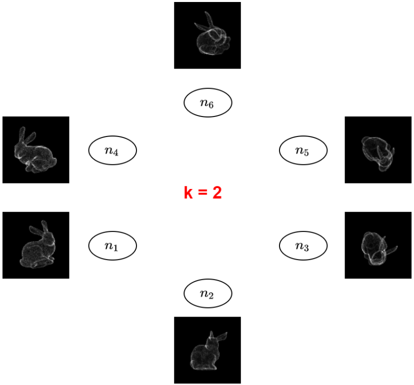

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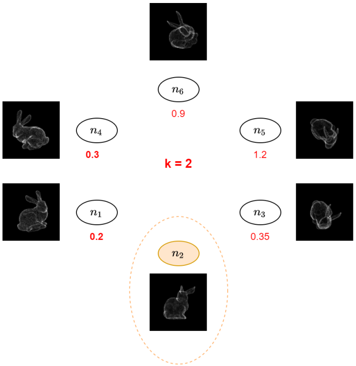

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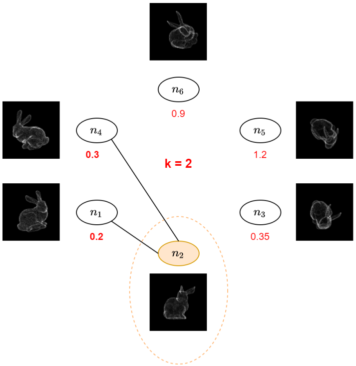

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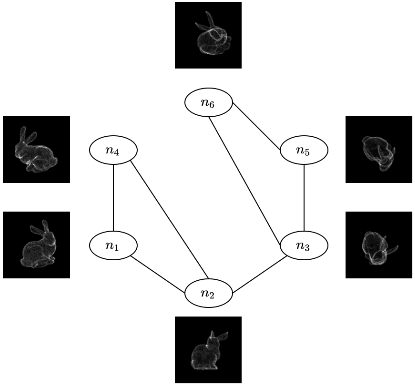

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Graph for Molecular Imaging Observation - Noise

What happens with our noisy observations?

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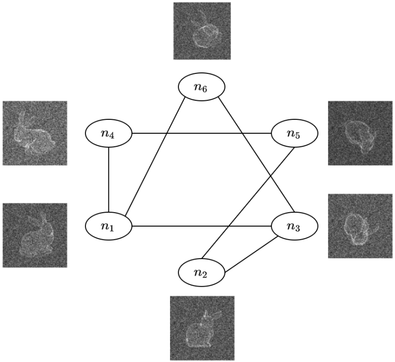
What happens with our noisy observations?

- With noise, graph will capture neighborhood inaccurately.



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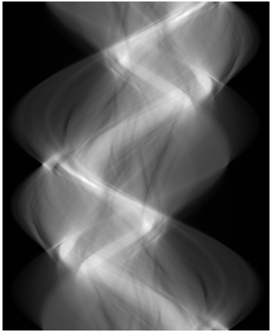
Low-dimensional Embedding

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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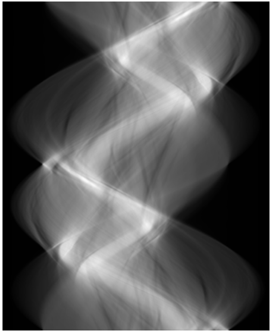

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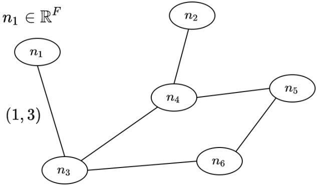

(b) Building k-NN graph with $k = 2$

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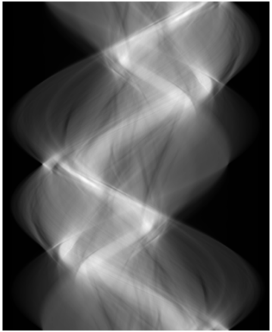

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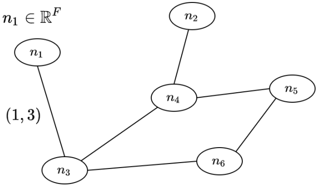

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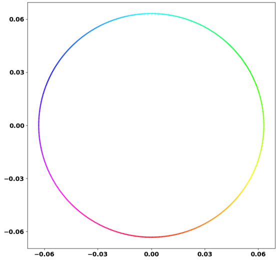

(c) 2_{nd} and 3_{rd} smallest eigenvectors of $L = D - A$

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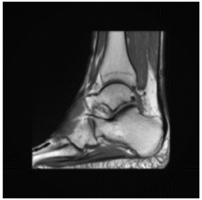

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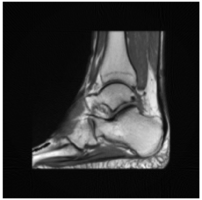

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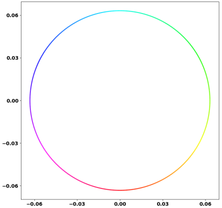

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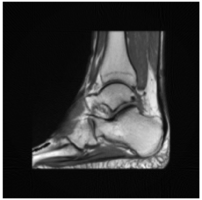

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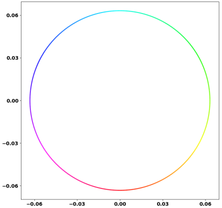

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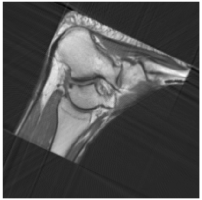

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What happens in the noisy case?

Computed Tomography with unknown angles

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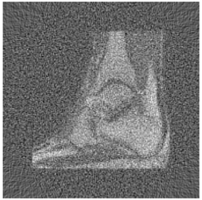

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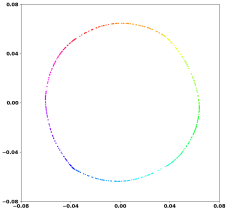
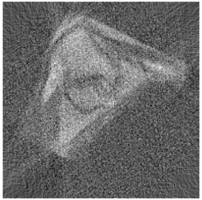


(b) GL-Embedding from $k = 8$ and SNR_y : 10 dB



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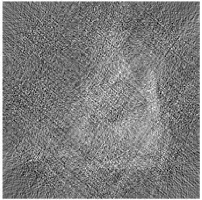

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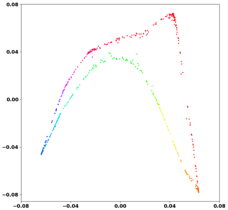

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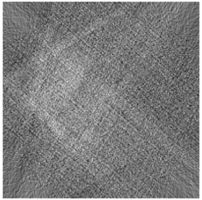

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  - No graph as data structure
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Exploit graph as a data structure and the GL-Embedding

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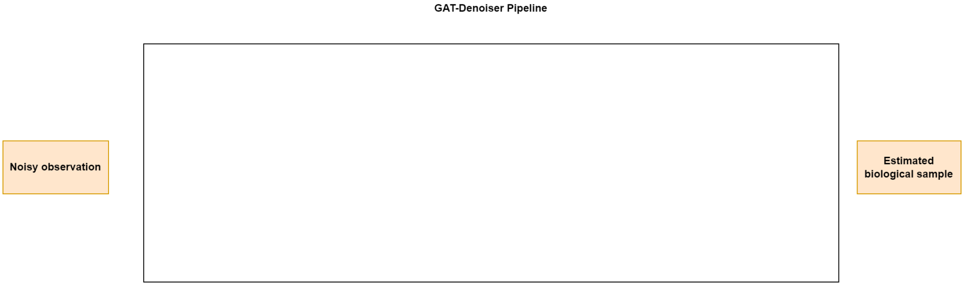

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    - Denoise neighboring observation
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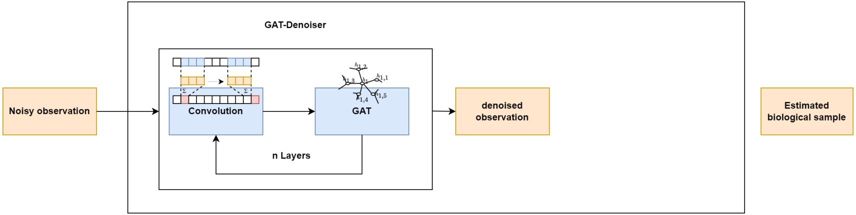
GAT-Denoiser Pipeline



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

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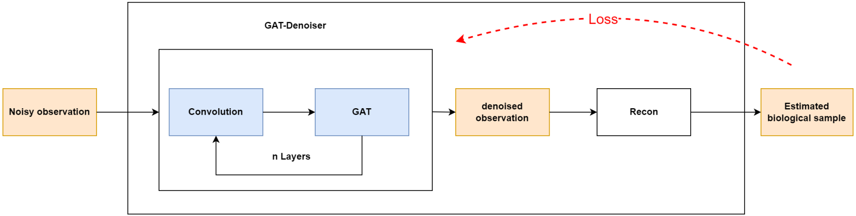

Graph Attention Network - GAT

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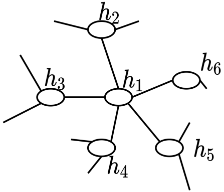
- Averages graph over neighborhood
- Multi-head available, motivated by Vaswani et al. 2017
- α: normalized attention coefficients
- W: learnable weight matrix
- σ: activation function (Exponential Linear Unit)



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

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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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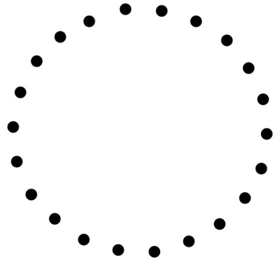
  - Map angles to unit-circle / unit-sphere



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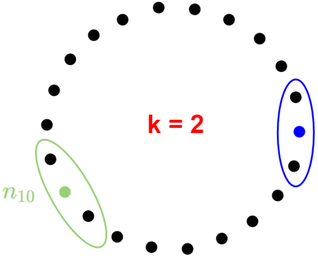
  - Apply k-NN with great-circle distance



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  - Low-dimensional embedding estimates angles
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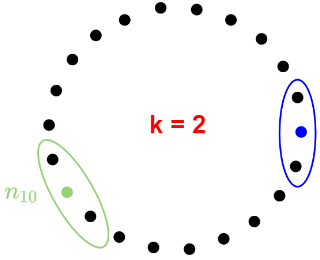


Observation angles θ are assumed to be equally spaced on the unit-circle / unit-sphere.

Outline

LoDoPaB-CT dataset

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

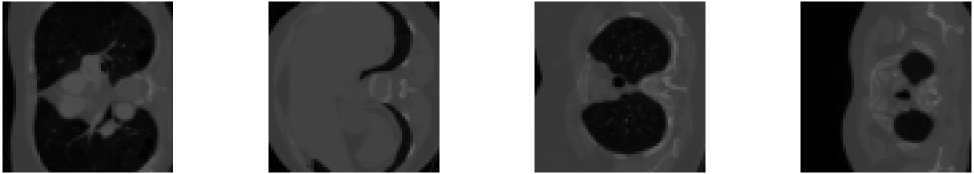


Figure: Some samples from the LoDoPaB-CT dataset.

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
- Modular architecture which allows disabling of Convolution and U-Net
- Mini-batch gradient descent

Evaluation

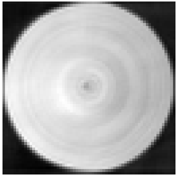
- Small Scale Experiments
  - 1024 train samples
  - 100 test samples
  - 200 epochs
- Large Scale Experiments
  - Complete LoDoPaB-CT dataset
  - 20 - 40 epochs

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

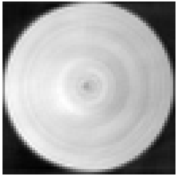
- Learning fails with random graph (Erdős–Rényi)
- Learning succeeds with defined input graph



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

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:
  - N=1024
  - M=64
  - GAT: 2 layers and 4 heads
  - Convolution: kernel size 3 and padding 1
  - k-NN with k=2
  - Joint U-Net training

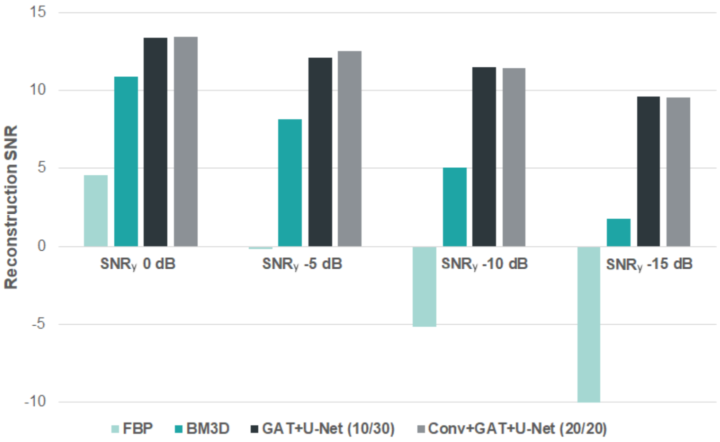


(a) Reconstruction with random Erdős–Rényi graph with $p = 0.01$

Large Scale Experiment - SNR Results

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

Large Scale Experiment - SNR Results



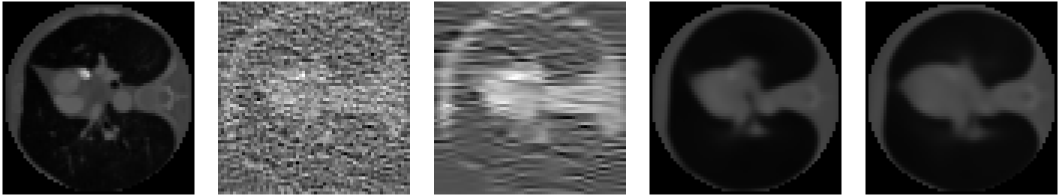
Large Scale Experiment - Visual Results - SNR_y 0 dB

(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.

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

Large Scale Experiment - Visual Results - SNR_y -10 dB

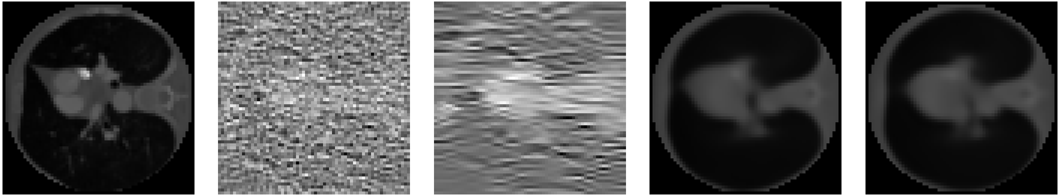


(a) Clean sample (b) FBP (c) BM3D (d) *GAT+U-Net(10/30)* (e) *Conv+GAT+U-Net(20/20)*

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

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.

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

Summary

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

Future Work

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

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- Computed Tomography
  - 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

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