



UNIVERSITY OF COPENHAGEN

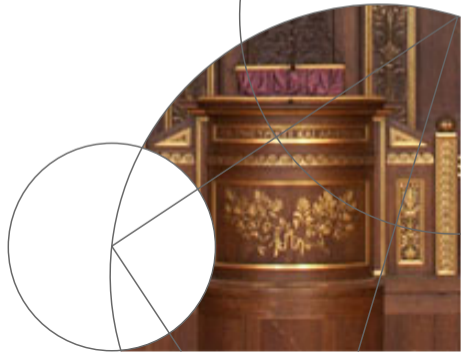
# Graph Refinement based Airway Extraction

## Using Mean-field and Graph Neural Networks

**Raghavendra Selvan**

raghav@di.ku.dk

Department of Computer Science



# Outline

- ① Airway Diseases
- ② Understanding the Data
- ③ Methods
  - Existing Methods
  - Graph Refinement Model
  - Mean-Field Networks
  - Graph Neural Networks
- ④ Experiments



# Outline

## ① Airway Diseases

## ② Understanding the Data

## ③ Methods

Existing Methods

Graph Refinement Model

Mean-Field Networks

Graph Neural Networks

## ④ Experiments



# COPD: Leading Factor of Morbidity & Mortality

- Tobacco Smoking
- Indoor & Outdoor Air pollution



# COPD: Leading Factor of Morbidity & Mortality

- Tobacco Smoking
- Indoor & Outdoor Air pollution
- Third leading cause of death by 2030
- 174.5M affected; 3.2M deaths (2015)



# COPD: Leading Factor of Morbidity & Mortality

- Tobacco Smoking
- Indoor & Outdoor Air pollution
- Third leading cause of death by 2030
- 174.5M affected; 3.2M deaths (2015)
- Destruction of lung tissue (Emphysema)
- Change of airway morphology (Bronchiectasis)



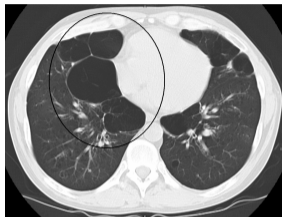
# COPD: Leading Factor of Morbidity & Mortality

- Tobacco Smoking
- Indoor & Outdoor Air pollution
- Third leading cause of death by 2030
- 174.5M affected; 3.2M deaths (2015)
- Destruction of lung tissue (Emphysema)
- Change of airway morphology (Bronchiectasis)



# COPD: Leading Factor of Morbidity & Mortality

- Tobacco Smoking
- Indoor & Outdoor Air pollution
- Third leading cause of death by 2030
- 174.5M affected; 3.2M deaths (2015)
- Destruction of lung tissue (Emphysema)
- Change of airway morphology (Bronchiectasis)





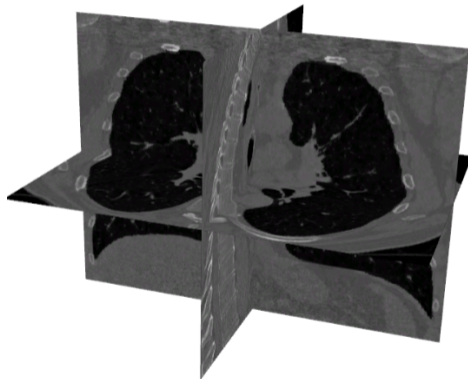
# Existing Diagnostics are Rudimentary & Tedious

- Lung Function Tests
  - + Simple and inexpensive
  - Patient dependent
  - Low reproducibility
  - Mild cases go unnoticed



# Existing Diagnostics are Rudimentary & Tedious

- Lung Function Tests
  - + Simple and inexpensive
  - Patient dependent
  - Low reproducibility
  - Mild cases go unnoticed
- 3D CT Scans
  - + Provide more information
  - Arduous to read the data; even for experts
  - Low inter-observer agreement



# Objective

**Automatic** Airway Segmentation and obtain **useful** COPD biomarkers



# Outline

## ① Airway Diseases

## ② Understanding the Data

## ③ Methods

Existing Methods

Graph Refinement Model

Mean-Field Networks

Graph Neural Networks

## ④ Experiments



# Primary Data from Danish Lung Cancer Study

- Danish Lung Cancer Screening Trial <sup>1</sup>
- Low-dose CT
- > 10,000 scans
- Age 50-70 years.
- Smoker or former smoker (> 20 pack years)
- 32/10,000 have segmentations verified by an expert user!

---

<sup>1</sup>Pedersen, J. H., et.al : The Danish randomized lung cancer CT screening trial overall design and results of the prevalence round. Journal of Thoracic Oncology, (2009)



# CT Images are noisy, low contrast & low-res.



- Volume resolution  $\sim 300 \times 250 \times 275$
- Voxels  $\sim 0.75\text{mm} \times 0.75\text{mm} \times 1\text{mm}$
- Challenges
  - Acquisition noise
  - Inter-patient variability
  - Several “interfering” structures
  - Labels/Annotations



# Outline

## ① Airway Diseases

## ② Understanding the Data

## ③ Methods

Existing Methods

Graph Refinement Model

Mean-Field Networks

Graph Neural Networks

## ④ Experiments



# Most Existing Methods handle occlusions poorly

- State-of-the-art: Region-growing (!) based methods
- EXACT Study<sup>2</sup> compares 15 methods; No clear winner
- Small airways are challenging
- Challenging to overcome occlusions

---

<sup>2</sup>Lo, P., et.al : Extraction of airways from CT (EXACT'09). IEEE Transactions on Medical Imaging, (2012)





# Graph Refinement Model for Airway Extraction



# Graph Refinement Model for Airway Extraction

## Desired Properties

- Exploratory (to overcome occlusions)
- Detect small airways
- Uncertainty estimates



# Preprocess Image to Graph Model

One possibility ....



# Preprocess Image to Graph Model

One possibility ....



**Figure 1:** Visualisation of the pre-processing carried out to transform the input image (left) into a probability image (center) and then into graph format (right). Nodes in the graph are shown in scale to capture the variations in their local radius.



# Graph Refinement Model

- Input graph:  $\mathcal{G}_i : \{\mathcal{N}, \mathcal{E}_i\}$
- Node features:  $\mathbf{X} \in \mathbb{R}^{F \times N}$
- Input adjacency:  $\mathbf{A}_i \in \{0, 1\}^{N \times N}$



# Graph Refinement Model

- Input graph:  $\mathcal{G}_i : \{\mathcal{N}, \mathcal{E}_i\}$
- Node features:  $\mathbf{X} \in \mathbb{R}^{F \times N}$
- Input adjacency:  $\mathbf{A}_i \in \{0, 1\}^{N \times N}$

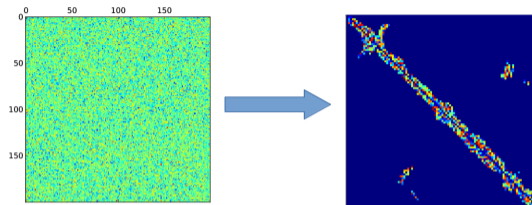
## Graph Refinement Task

$$f(\mathcal{G}_i) \rightarrow \mathcal{G}$$

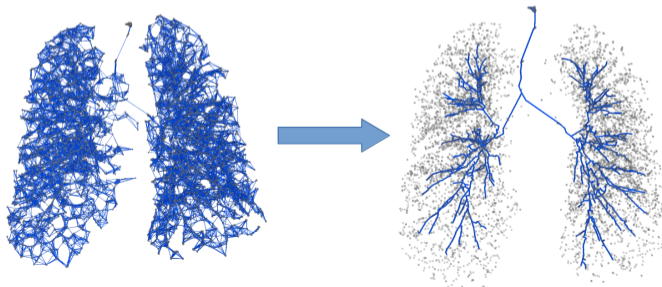
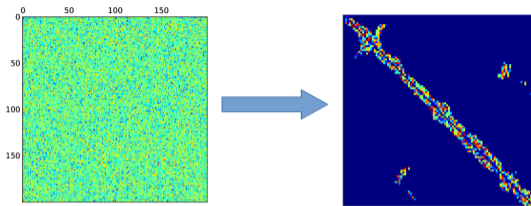
Output subgraph  $\mathcal{G}$  with  $\mathcal{E} \subset \mathcal{E}_i$ ;  $\mathbf{A} \in \{0, 1\}^{N \times N}$



# Visualise Graph Refinement Task



# Visualise Graph Refinement Task





# Updating Probabilistic Graphical Model

- Binary random variable to capture existence of edge between nodes
- $s_{ij} \in \{0, 1\}$  with prob.  $\alpha_{ij} \in [0, 1]$



## Updating Probabilistic Graphical Model

- Binary random variable to capture existence of edge between nodes
- $s_{ij} \in \{0, 1\}$  with prob.  $\alpha_{ij} \in [0, 1]$
- For each node:  $\mathbf{s}_i = \{s_{ij}\} : j = 1 \dots N$
- Global connectivity variable:  $\mathbf{S} = [\mathbf{s}_1 \dots \mathbf{s}_N]$
- Each instance of  $\mathbf{S}$  an  $N \times N$  adjacency matrix



## Updating Probabilistic Graphical Model

- Binary random variable to capture existence of edge between nodes
- $s_{ij} \in \{0, 1\}$  with prob.  $\alpha_{ij} \in [0, 1]$
- For each node:  $\mathbf{s}_i = \{s_{ij}\} : j = 1 \dots N$
- Global connectivity variable:  $\mathbf{S} = [\mathbf{s}_1 \dots \mathbf{s}_N]$
- Each instance of  $\mathbf{S}$  an  $N \times N$  adjacency matrix

Input Graph  $\mathcal{G}_i$  is completely described by  $\mathbf{X}, \mathbf{A}_i,$



## Updating Probabilistic Graphical Model

- Binary random variable to capture existence of edge between nodes
- $s_{ij} \in \{0, 1\}$  with prob.  $\alpha_{ij} \in [0, 1]$
- For each node:  $\mathbf{s}_i = \{s_{ij}\} : j = 1 \dots N$
- Global connectivity variable:  $\mathbf{S} = [\mathbf{s}_1 \dots \mathbf{s}_N]$
- Each instance of  $\mathbf{S}$  an  $N \times N$  adjacency matrix

Input Graph  $\mathcal{G}_i$  is completely described by  $\mathbf{X}, \mathbf{A}_i$ ,

Posterior density of interest:  $p(\mathbf{S} | \mathbf{X}, \mathbf{A}_i)$



# Updating Probabilistic Graphical Model

- Binary random variable to capture existence of edge between nodes
- $s_{ij} \in \{0, 1\}$  with prob.  $\alpha_{ij} \in [0, 1]$
- For each node:  $\mathbf{s}_i = \{s_{ij} : j = 1 \dots N\}$
- Global connectivity variable:  $\mathbf{S} = [\mathbf{s}_1 \dots \mathbf{s}_N]$
- Each instance of  $\mathbf{S}$  an  $N \times N$  adjacency matrix

Input Graph  $\mathcal{G}_i$  is completely described by  $\mathbf{X}, \mathbf{A}_i$ ,

Posterior density of interest:  $p(\mathbf{S}|\mathbf{X}, \mathbf{A}_i)$

$$\begin{aligned} \ln p(\mathbf{S}|\mathbf{X}) &\propto \ln p(\mathbf{S}, \mathbf{X}) \\ &= -\ln Z + \sum_{i \in \mathcal{N}} \phi_i(\mathbf{s}_i) + \sum_{(i,j) \in \mathcal{E}} \phi_{ij}(\mathbf{s}_i, \mathbf{s}_j), \end{aligned}$$



# Variational Approximate Inference



# Variational Approximate Inference

$p(\mathbf{S}|\mathbf{X}, \mathbf{A}_i)$  is intractable except for in trivial cases.



# Variational Approximate Inference

$p(\mathbf{S}|\mathbf{X}, \mathbf{A}_i)$  is intractable except for in trivial cases.

$$p(\mathbf{S}|\mathbf{X}, \mathbf{A}_i) \approx q(\mathbf{S})$$





# Variational Approximate Inference

$p(\mathbf{S}|\mathbf{X}, \mathbf{A}_i)$  is intractable except for in trivial cases.

$$p(\mathbf{S}|\mathbf{X}, \mathbf{A}_i) \approx q(\mathbf{S})$$

## Variational Approximate Inference

Minimize ELBO to obtain  $q(\mathbf{S}) \in \mathcal{Q}$

$$\mathcal{F}(q_{\mathbf{S}}) = \ln Z + \mathbb{E}_{q_{\mathbf{S}}} \left[ \ln p(\mathbf{S}|\mathbf{X}) - \ln q(\mathbf{S}) \right]$$



# Simpler approximation using MFA



# Simpler approximation using MFA

## Factorisable $q(\mathbf{S})$

$$q(\mathbf{S}) = \prod_{i=1}^N \prod_{j=1}^N q_{ij}(s_{ij}),$$

$$\text{where, } q_{ij}(s_{ij}) = \begin{cases} \alpha_{ij} & \text{if } s_{ij} = 1 \\ (1 - \alpha_{ij}) & \text{if } s_{ij} = 0 \end{cases},$$



# Simpler approximation using MFA

## Factorisable $q(\mathbf{S})$

$$q(\mathbf{S}) = \prod_{i=1}^N \prod_{j=1}^N q_{ij}(s_{ij}),$$

$$\text{where, } q_{ij}(s_{ij}) = \begin{cases} \alpha_{ij} & \text{if } s_{ij} = 1 \\ (1 - \alpha_{ij}) & \text{if } s_{ij} = 0 \end{cases},$$

Assumes edges to be independent.



# Node and Pairwise Potentials for MFA



# Node and Pairwise Potentials for MFA

## Node Potential

For each node  $i \in \mathcal{N}$ ,

$$\phi_i(\mathbf{s}_i) = \sum_{v=0}^D \beta_v \mathbb{I} \left[ \sum_j s_{ij} = v \right] + \mathbf{a}^T \mathbf{x}_i \sum_j s_{ij},$$



# Node and Pairwise Potentials for MFA

## Node Potential

For each node  $i \in \mathcal{N}$ ,

$$\phi_i(\mathbf{s}_i) = \sum_{v=0}^D \beta_v \mathbb{I} \left[ \sum_j s_{ij} = v \right] + \mathbf{a}^T \mathbf{x}_i \sum_j s_{ij},$$

## Pairwise Potential

For each edge,  $(i, j) \in \mathcal{E}_i$

$$\phi_{ij}(\mathbf{s}_i, \mathbf{s}_j) = \lambda(1 - 2|s_{ij} - s_{ji}|) + (2s_{ij}s_{ji} - 1) \left[ \boldsymbol{\eta}^T |\mathbf{x}_i - \mathbf{x}_j| + \boldsymbol{\nu}^T (\mathbf{x}_i \mathbf{x}_j) \right].$$

Parameters =  $[\boldsymbol{\beta}, \mathbf{a}, \lambda, \boldsymbol{\eta}, \boldsymbol{\nu}]$



# Minimize ELBO to get MFA Iterations

## MFA Iterations

$$\alpha_{kl}^{(t+1)} = \sigma(\gamma_{kl}) = \frac{1}{1 + \exp^{-\gamma_{kl}}} \quad \forall k = \{1 \dots N\}, l \in \mathcal{N}_k,$$

where  $\sigma(\cdot)$  is sigmoid activation,  $\mathcal{N}_k$  are neighbours of node  $k$ , and





# Minimize ELBO to get MFA Iterations

## MFA Iterations

$$\alpha_{kl}^{(t+1)} = \sigma(\gamma_{kl}) = \frac{1}{1 + \exp^{-\gamma_{kl}}} \quad \forall k = \{1 \dots N\}, l \in \mathcal{N}_k,$$

where  $\sigma(\cdot)$  is sigmoid activation,  $\mathcal{N}_k$  are neighbours of node  $k$ , and

$$\begin{aligned} \gamma_{kl} = & \prod_{j \in \mathcal{N}_k \setminus l} (1 - \alpha_{kj}^{(t)}) \left\{ \sum_{m \in \mathcal{N}_k \setminus l} \frac{\alpha_{km}^{(t)}}{(1 - \alpha_{km}^{(t)})} [(\beta_2 - \beta_1) \right. \\ & \left. - \beta_2 \sum_{n \in \mathcal{N}_k \setminus l, m} \frac{\alpha_{kn}^{(t)}}{(1 - \alpha_{kn}^{(t)})}] + (\beta_1 - \beta_0) \right\} + \mathbf{a}^T \mathbf{x}_k \\ & + (4\alpha_{lk}^{(t)} - 2)\lambda + 2\alpha_{lk}^{(t)} (\boldsymbol{\eta}^T |\mathbf{x}_k - \mathbf{x}_l| + \boldsymbol{\nu}^T (\mathbf{x}_k \mathbf{x}_l)). \end{aligned} \quad (1)$$



# MFA to Mean-Field Networks



# MFA to Mean-Field Networks

- MFA Iterations resemble feed-forward operations in neural network

$$\alpha_{kl}^{(t+1)} = \sigma(\gamma_{kl}) = \frac{1}{1 + \exp^{-\gamma_{kl}}} \quad \forall k = \{1 \dots N\}, l \in \mathcal{N}_k,$$

$\alpha$  is soft prediction of global connectivity variable



# MFA to Mean-Field Networks

- MFA Iterations resemble feed-forward operations in neural network

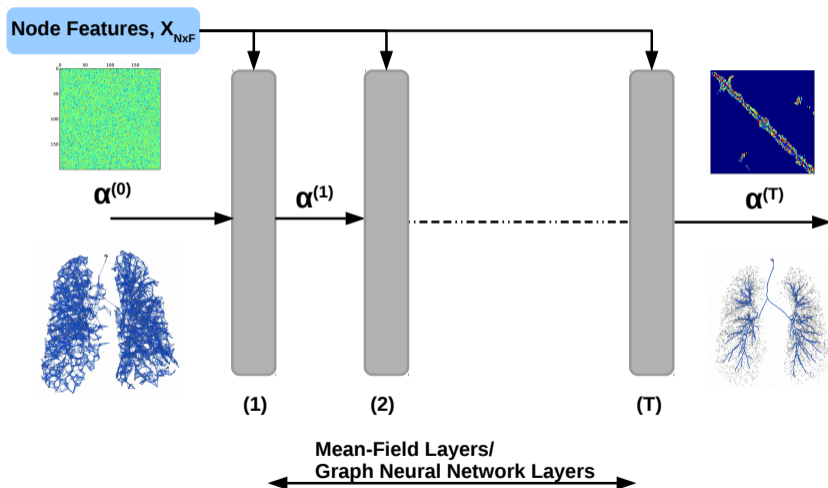
$$\alpha_{kl}^{(t+1)} = \sigma(\gamma_{kl}) = \frac{1}{1 + \exp^{-\gamma_{kl}}} \quad \forall k = \{1 \dots N\}, l \in \mathcal{N}_k,$$

$\alpha$  is soft prediction of global connectivity variable

- $T$ -iterations as a  $T$ -layered network
- Automatic differentiation to learn parameters:  $\mathcal{L}(\alpha, \mathbf{A}_r)$ , where  $\mathbf{A}_r$  is reference adjacency.



# Summarising MFN



# Summarising MFN

- Yields approximation to underlying posterior
- Simple factors
- Handful of parameters
- Easy to optimise
- Hand-crafting potentials is cumbersome
- Might not generalise across applications



# Graph Neural Networks



# Graph Neural Networks

- Neural networks operating directly on graph structured data





# Graph Neural Networks

- Neural networks operating directly on graph structured data
- Generalisation of message passing algorithms



# Graph Neural Networks

- Neural networks operating directly on graph structured data
- Generalisation of message passing algorithms
- Arbitrarily complex messages



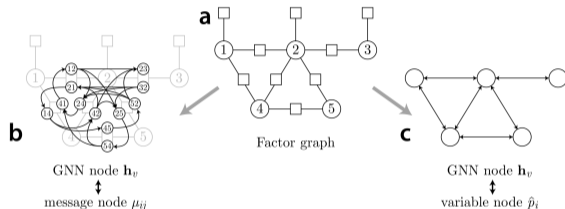
# Graph Neural Networks

- Neural networks operating directly on graph structured data
- Generalisation of message passing algorithms
- Arbitrarily complex messages
- End-to-end trainable inference systems



# Graph Neural Networks

- Neural networks operating directly on graph structured data
- Generalisation of message passing algorithms
- Arbitrarily complex messages
- End-to-end trainable inference systems



**Figure:** Two mappings of Factor Graphs into GNNs

Figure from Yoon et al. "Inference in probabilistic graphical models by Graph Neural Networks" (2018)



# Graph Auto Encoder (GAE) for Graph Refinement



# Graph Auto Encoder (GAE) for Graph Refinement

- Encoder comprises of GNNs; Message passing between nodes



# Graph Auto Encoder (GAE) for Graph Refinement

- Encoder comprises of GNNs; Message passing between nodes
- Jointly train to learn useful embeddings



# Graph Auto Encoder (GAE) for Graph Refinement

- Encoder comprises of GNNs; Message passing between nodes
- Jointly train to learn useful embeddings
- Suitable for graph refinement:  $f(\mathcal{G}_i) \rightarrow \mathcal{G}$





# Graph Auto Encoder (GAE) for Graph Refinement

- Encoder comprises of GNNs; Message passing between nodes
- Jointly train to learn useful embeddings
- Suitable for graph refinement:  $f(\mathcal{G}_i) \rightarrow \mathcal{G}$



# GAE Model for Graph Refinement: Encoder



# GAE Model for Graph Refinement: Encoder

## Encoder:

Node Embedding:  $\mathbf{h}_j^1 = g_n(\mathbf{x}_j)$

Node-to-Edge mapping:  $\mathbf{h}_{(i,j)}^1 = g_{n2e}([\mathbf{h}_i^1, \mathbf{h}_j^1])$

Edge-to-Node mapping:  $\mathbf{h}_j^2 = g_{e2n}\left(\sum_i^{N_j} \mathbf{h}_{(i,j)}^1\right)$

Node-to-Edge mapping:  $\mathbf{h}_{(i,j)}^2 = g_{n2e}([\mathbf{h}_i^2, \mathbf{h}_j^2])$



# GAE Model for Graph Refinement: Encoder

## Encoder:

$$\text{Node Embedding: } \mathbf{h}_j^1 = g_n(\mathbf{x}_j)$$

$$\text{Node-to-Edge mapping: } \mathbf{h}_{(i,j)}^1 = g_{n2e}([\mathbf{h}_i^1, \mathbf{h}_j^1])$$

$$\text{Edge-to-Node mapping: } \mathbf{h}_j^2 = g_{e2n}\left(\sum_i^{N_j} \mathbf{h}_{(i,j)}^1\right)$$

$$\text{Node-to-Edge mapping: } \mathbf{h}_{(i,j)}^2 = g_{n2e}([\mathbf{h}_i^2, \mathbf{h}_j^2])$$

$g_{\dots}(\cdot)$  are 2-layered MLPs, with ReLU, dropout and layer normalisation



# GAE Model for Graph Refinement: Decoder

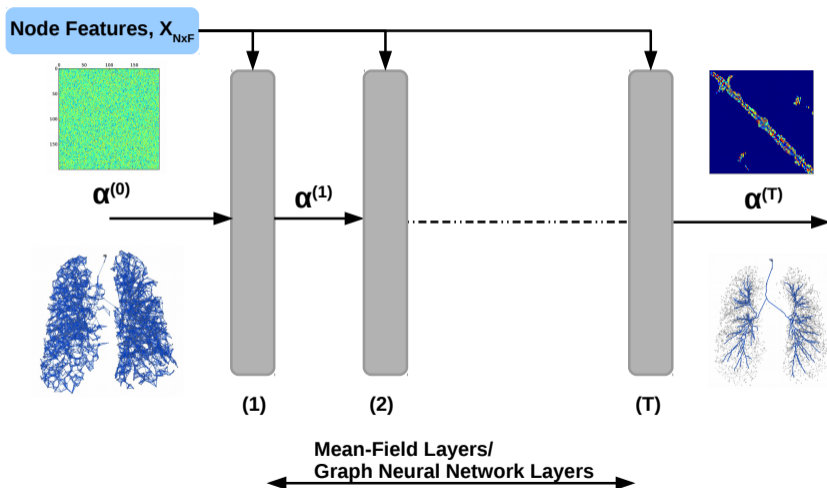
**Decoder:**

$$\alpha_{ij} = \sigma(g_{dec}(\mathbf{h}_{(i,j)}^2)) \quad (2)$$

$g_{dec}$  is a 1D convolutional layer with one output channel  
Model can be trained by computing the loss  $\mathcal{L}\alpha, \mathbf{A}_r$



# Summarising GNNs



# Outline

- ① Airway Diseases
- ② Understanding the Data
- ③ Methods
  - Existing Methods
  - Graph Refinement Model
  - Mean-Field Networks
  - Graph Neural Networks
- ④ Experiments



# Training both models: Dice Loss

To tackle Class Imbalance:





# Training both models: Dice Loss

To tackle Class Imbalance:

$$\mathcal{L}(\boldsymbol{\alpha}, \mathbf{A}_r) = 1 - \frac{2 \sum_{i,j=1}^N \alpha_{ij} A_{ij}}{\sum_{i,j=1}^N \alpha_{ij}^2 + \sum_{i,j=1}^N A_{ij}^2},$$

$A_{ij}$  are individual binary entries  $\mathbf{A}_r$



# Data

- Danish Lung Cancer Screening Trial
- Low-dose Chest CT scans
- 32 scans with “Reference” annotations
- 100 scans with automatic segmentation



# Results

- Error Measure based on centerline distances
- Average of two distances,  $d_{err} = (d_{FP} + d_{FN})/2$
- Compared with Top Performer on Airway Extraction Challenge

**Table I:** Performance comparison

| Method           | $d_{FP}$ (mm) | $d_{FN}$ (mm) | $d_{err}$ (mm)                      |
|------------------|---------------|---------------|-------------------------------------|
| Voxel Classifier | 3.871         | 5.108         | $4.489 \pm 0.754$                   |
| MFN              | 3.716         | 3.992         | $3.845 \pm 0.415$                   |
| <b>GNN</b>       | <b>3.513</b>  | <b>2.890</b>  | <b><math>3.202 \pm 0.386</math></b> |

