EBERHARD KARLS
UNIVERSITÄT
TÜBINGEN

Disentangling Sources of Uncertainty
in Medical Image Analysis

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Prof. Philipp Berens (First Examiner), Prof. Dr. Philipp Hennig (Second Examiner)

Background: Lung nodule segmentation

127070 deaths from lung cancer (67160 in men and 59910 in women) [1]

[1] https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html

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Lung nodule detection and segmentation

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Lung nodule detection and segmentation

Time Cost

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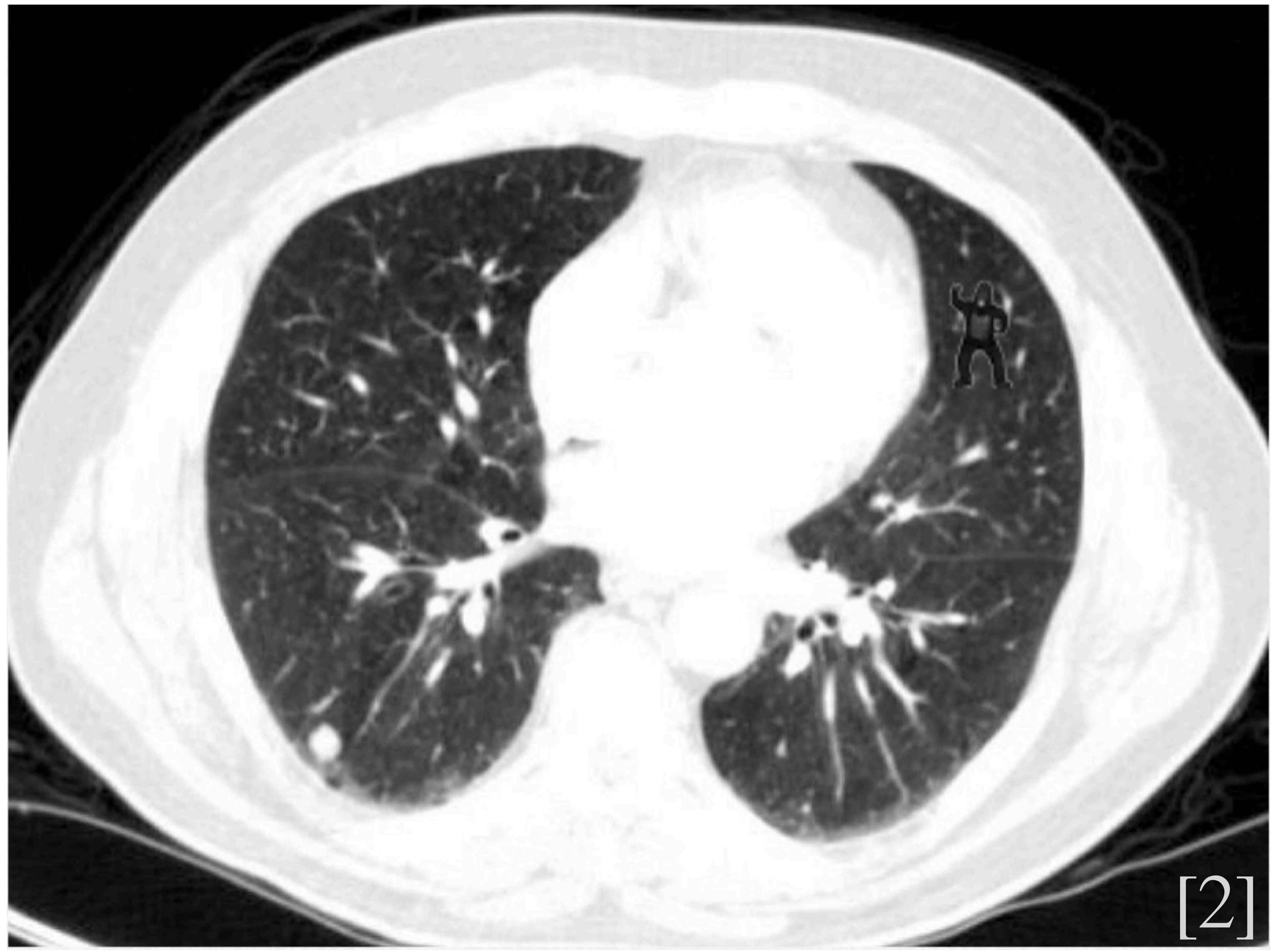
Lung nodule detection and segmentation

Time Cost

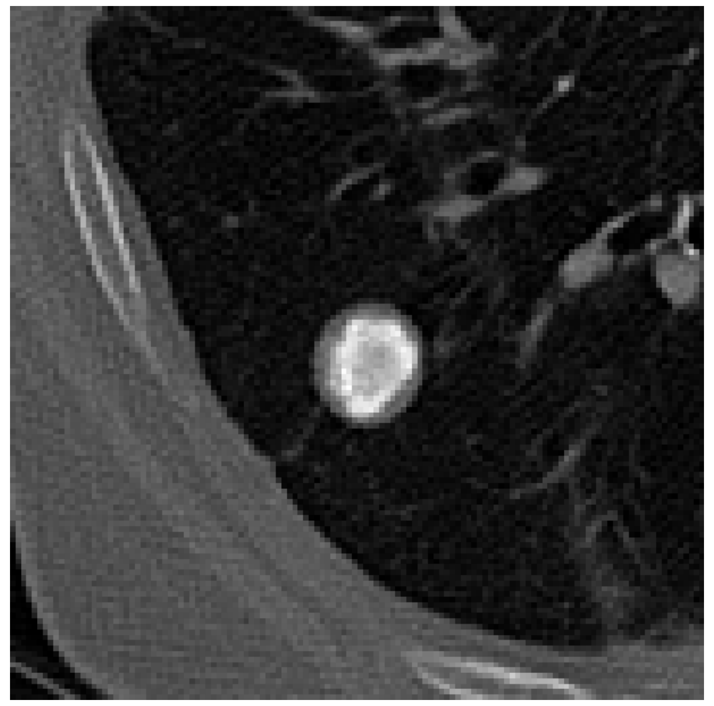
Inattentional Blindeness



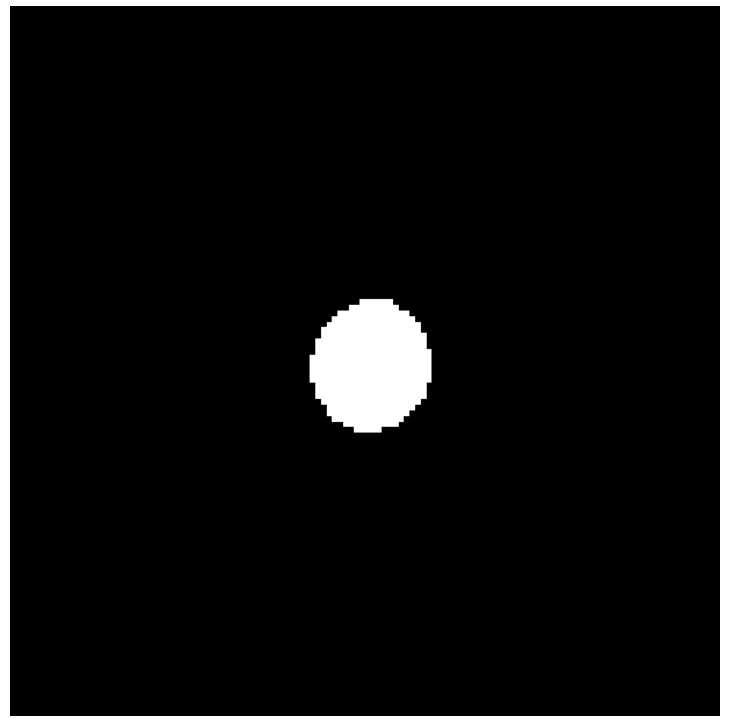
[1] https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html
[2] http://medicalood.dkfz.de/web/

Background: Three sources of Uncertainty

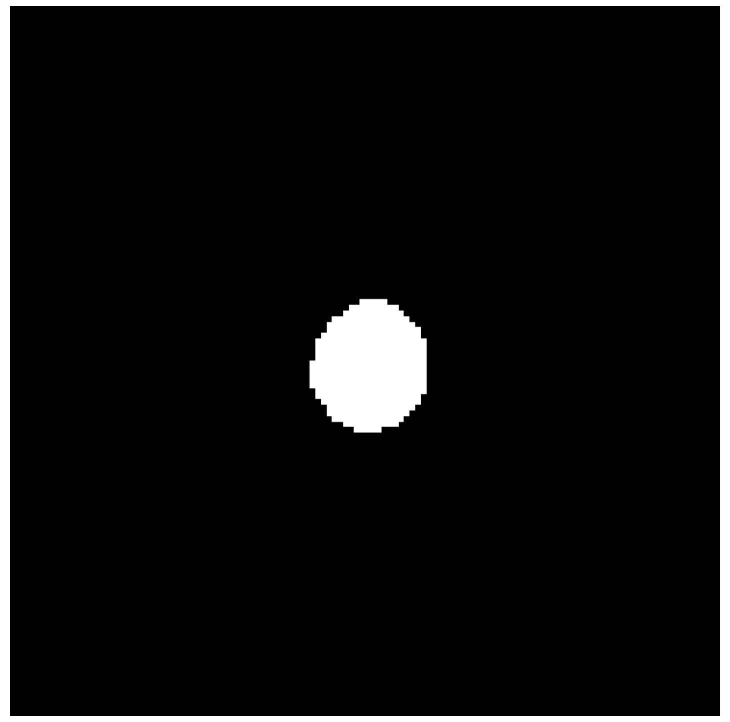
Model Uncertainty



Input



Segmentation 1



Segmentation 2

Background: Three sources of Uncertainty

Model Uncertainty

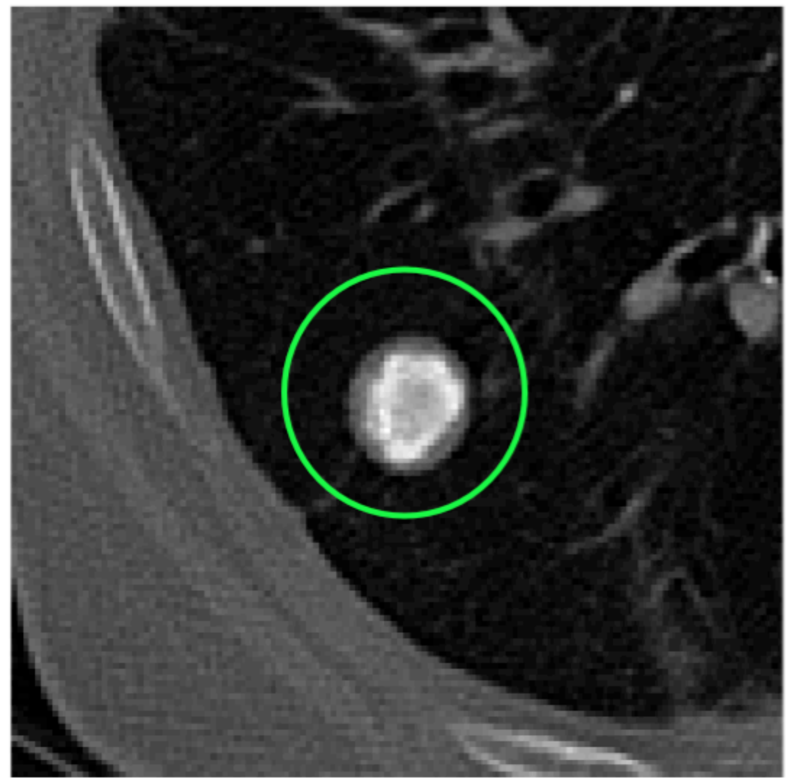
Input

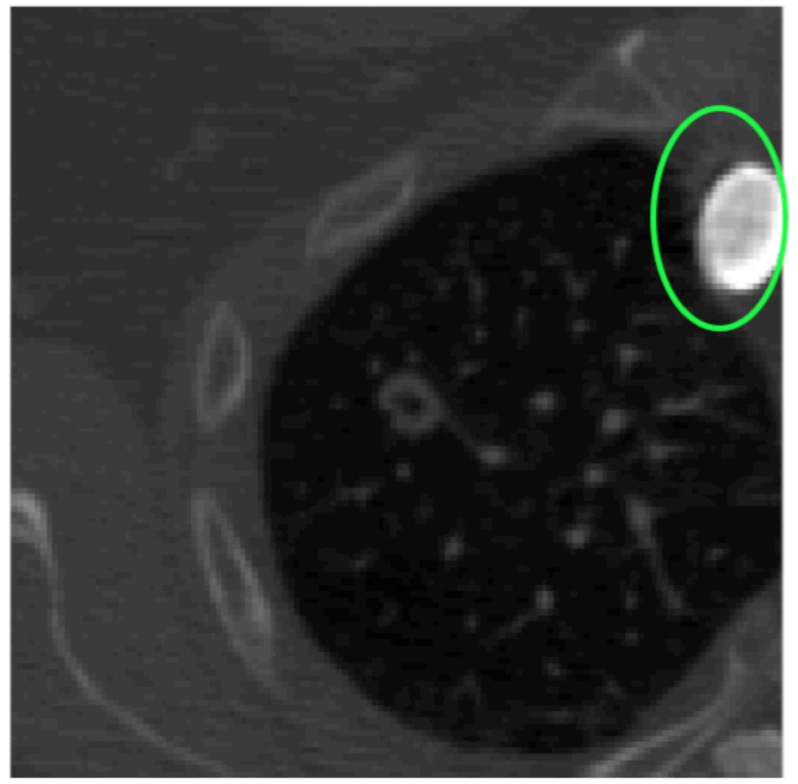
Segmentation 1

Segmentation 2

Distributional Uncertainty

Nodule

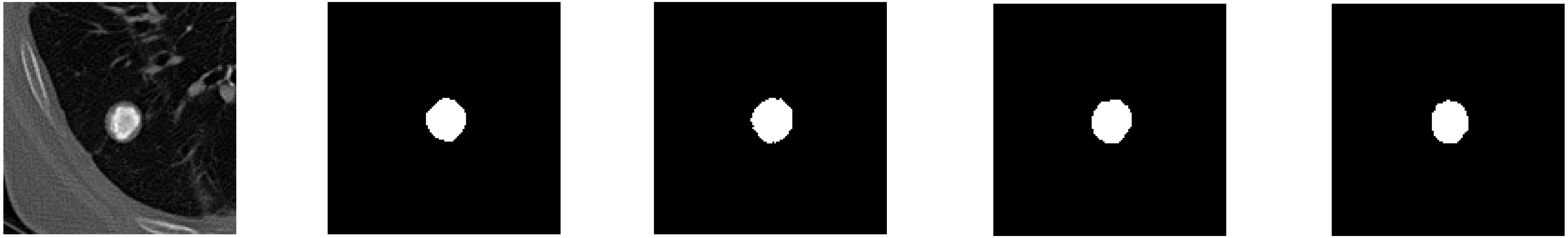




Out-of-distribution data

Data Uncertainty

Boundary ?



Expert 1 Expert 2 Expert 3 Expert 4

Data Uncertainty

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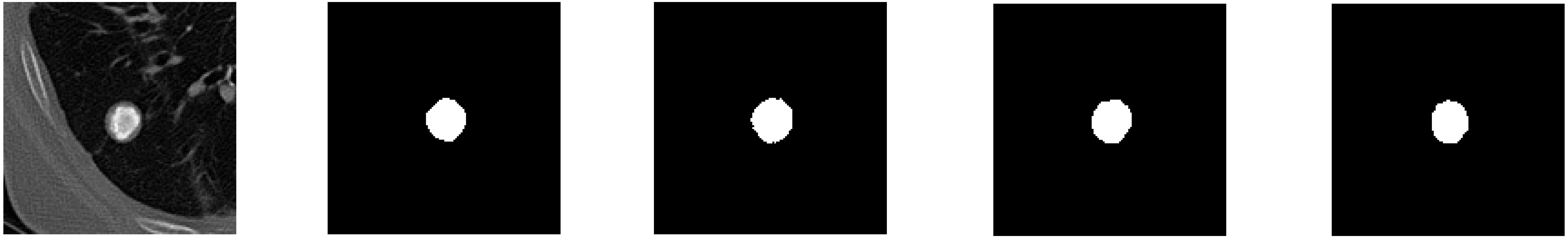


Expert 1 Expert 2 Expert 3 Expert 4

Existence ?

Expert 1 Expert 2 Expert 3 Expert 4

Background: Related works

Model Uncertainty:

- MCMC: Welling(2011), Ma(2015)
- Dropout: Gal(2016), Tanno(2017), Jungo(2018), Hu(2019)

Data Uncertainty:

- Pixel-wise: Kendall(2017), Wang(2019)
- Spatial correlation: Kohl(2018), Hu(2019), Baumgartner(2019), Monteiro(2020)

Distributional Uncertainty:

Limitations ?

- Classification: Malinin(2018,2019)

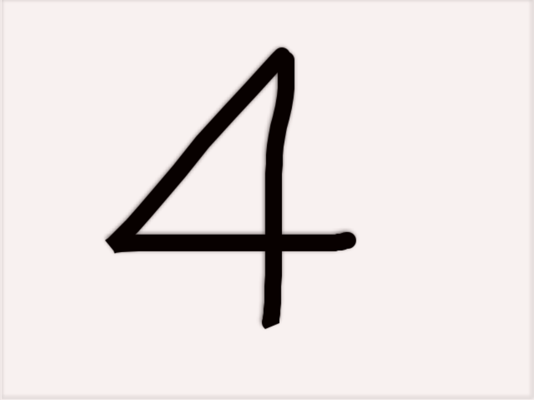
  → The Dirichlet Prior Network on MNIST

Contribution

- The Dirichlet Prior Network for nodule segmentation
- The limitations of two state-of-the-art methods
- Disentangling different sources of uncertainty on lung CT images with synthetic and authentic out-of-distribution data

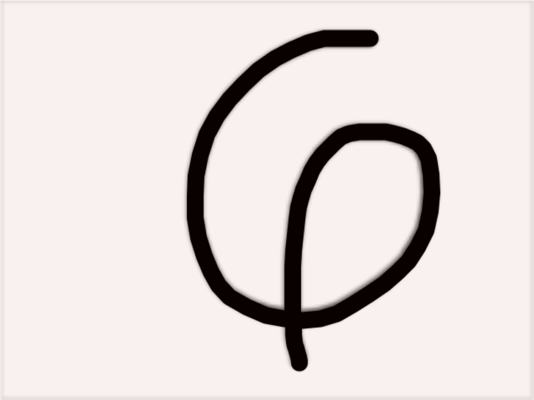
Recap: The Dirichlet Prior Network (DPN) for classification

Class 0



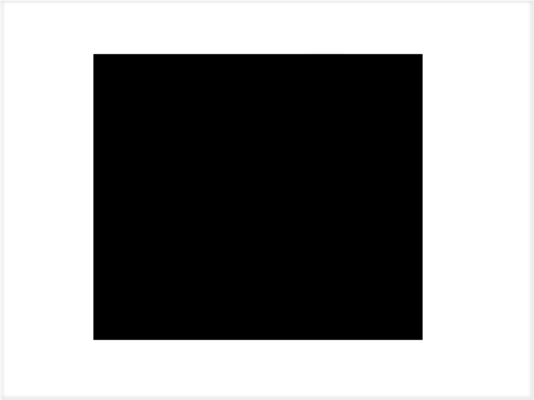
Class 1

Class 2



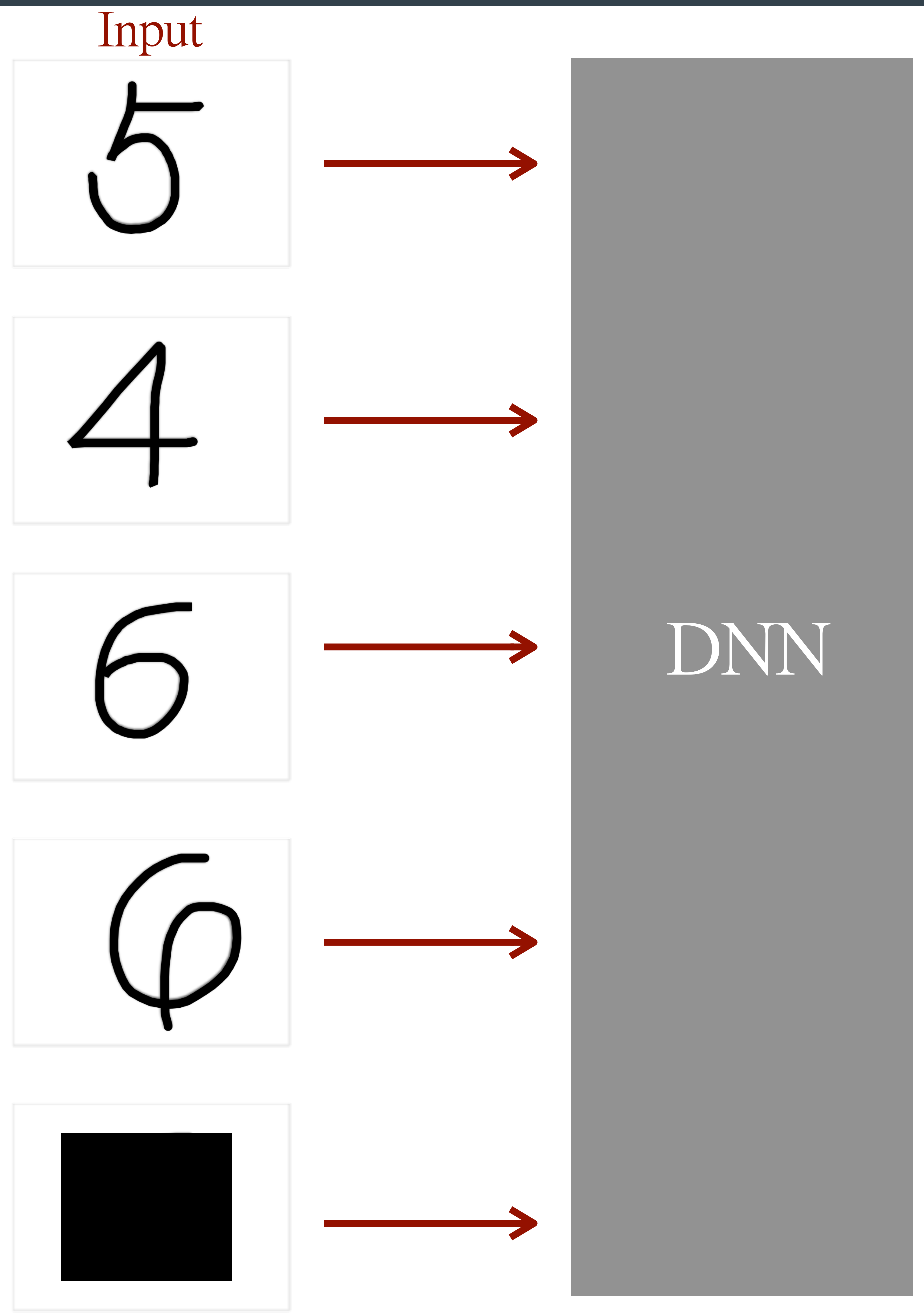
Overlap of
class 1 and class 2

→ In-domain data



→ Out-of-distribution data

Recap: The Dirichlet Prior Network (DPN) for classification



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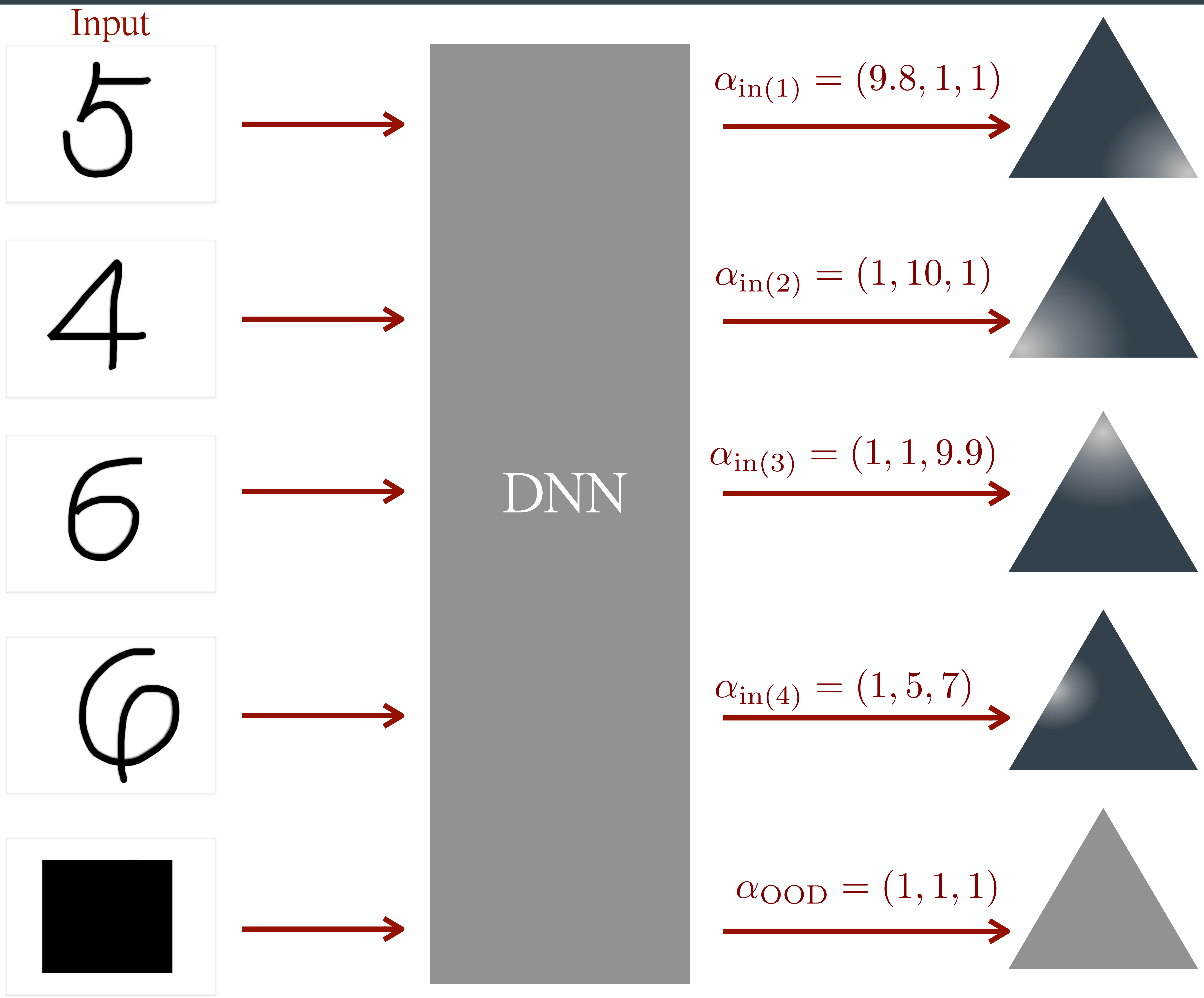

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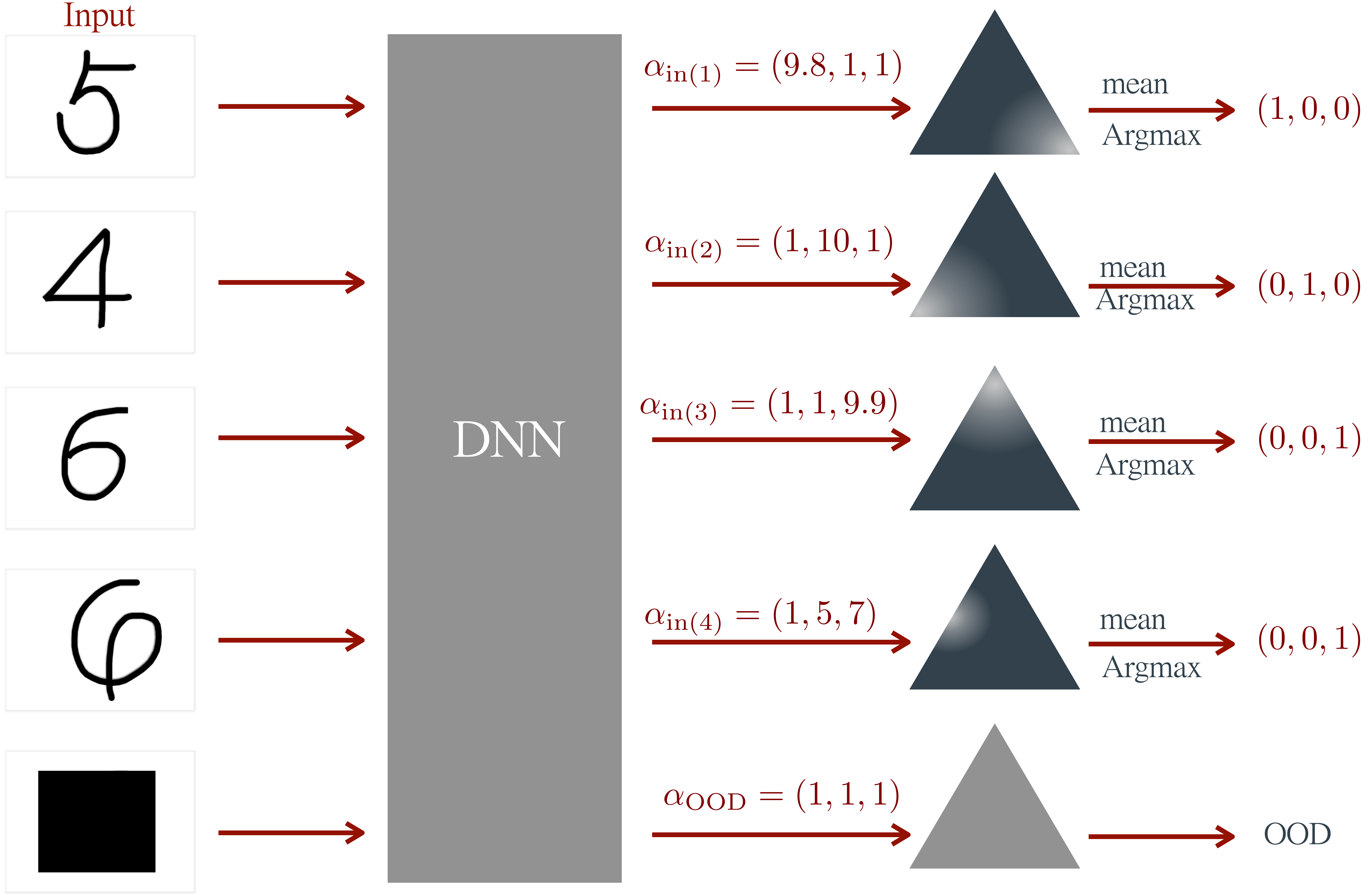

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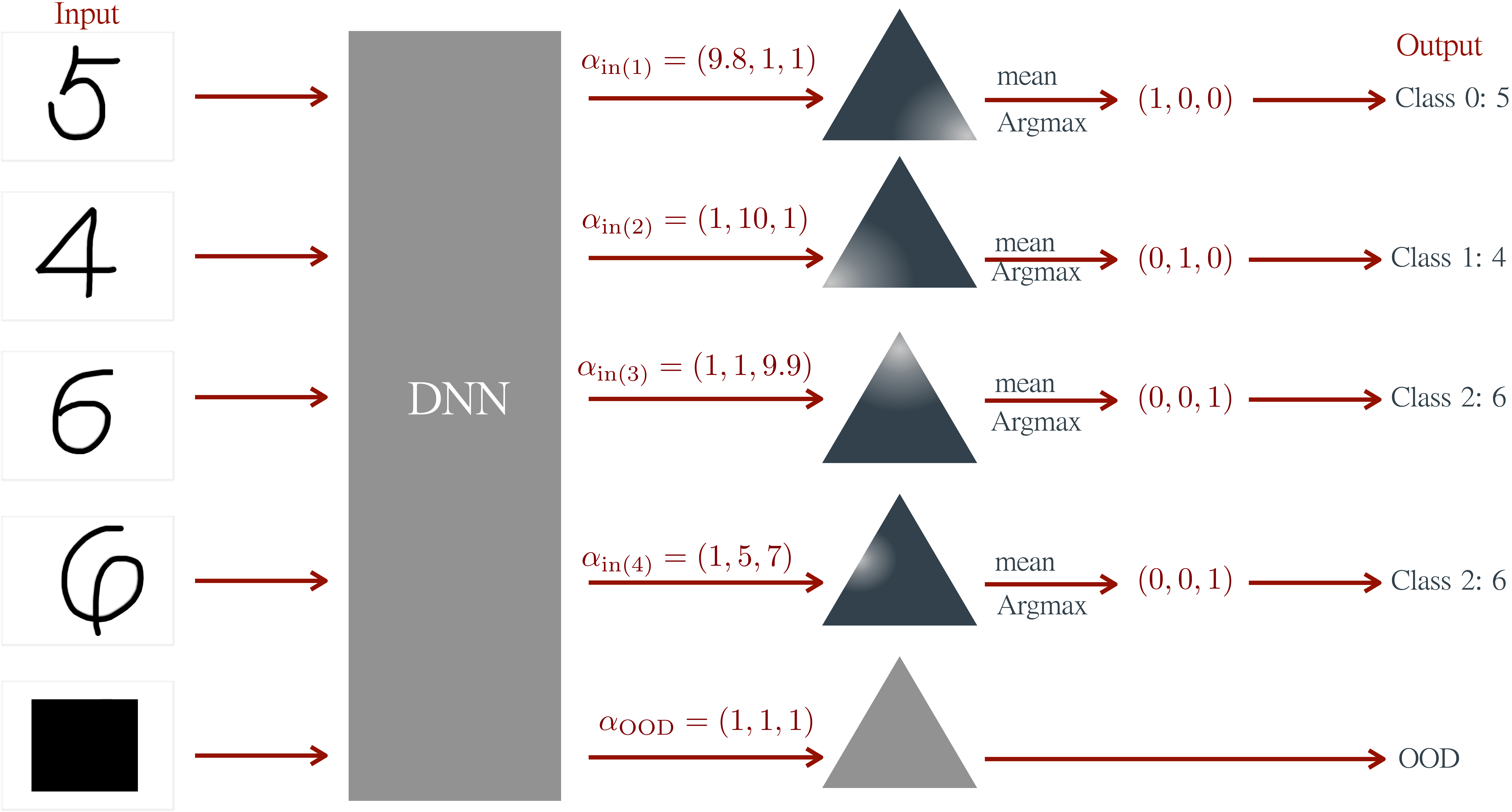
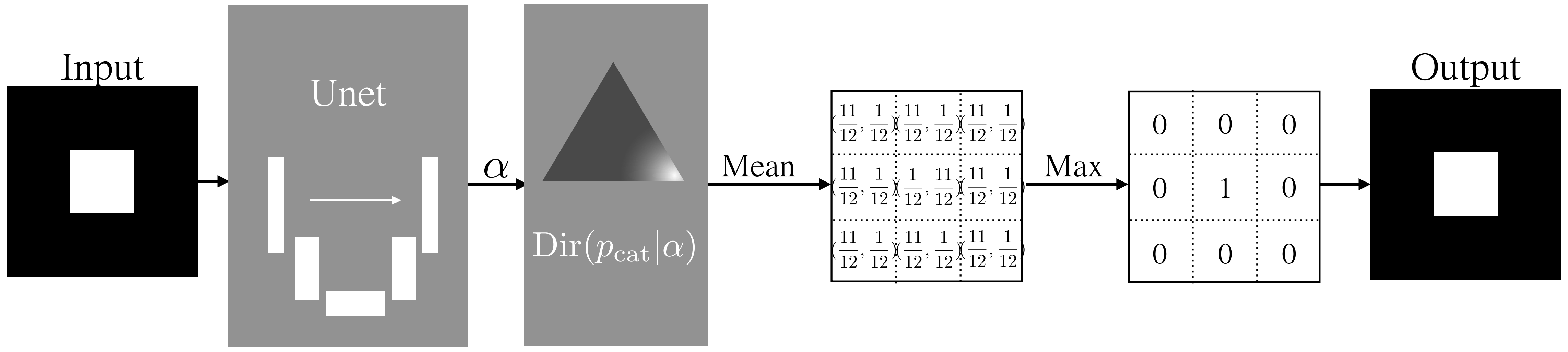


Dirichlet Prior Network (DPN)

Reverse KL-divergence Loss

Ground truth label for each pixel:

- Background: $\alpha = (11, 1)$
- Nodule: $\alpha = (1, 11)$
- Out-of-distribution data: $\alpha = (1, 1)$



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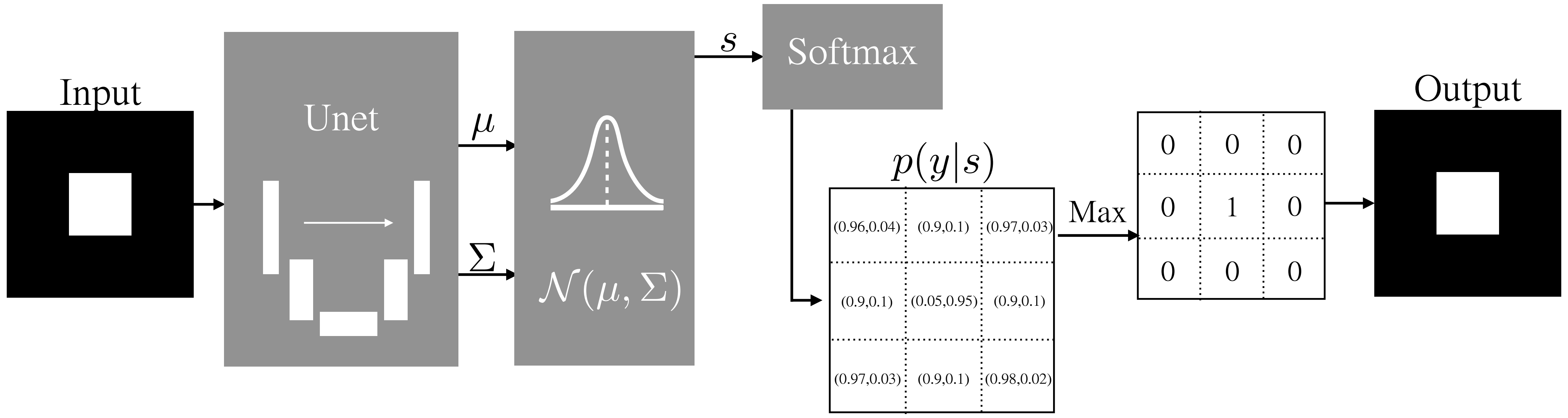
Stochastic Segmentation Network (SSN)

Negative Log-likelihood Loss

Ground truth label for each pixel:

- Background: 0
- Nodule: 1



Method: Network Structures

Dirichlet Prior Network (DPN)

Reverse KL-divergence Loss

Ground truth label for each pixel:

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Stochastic Segmentation Network (SSN)

Negative Log-likelihood Loss

Ground truth label for each pixel:

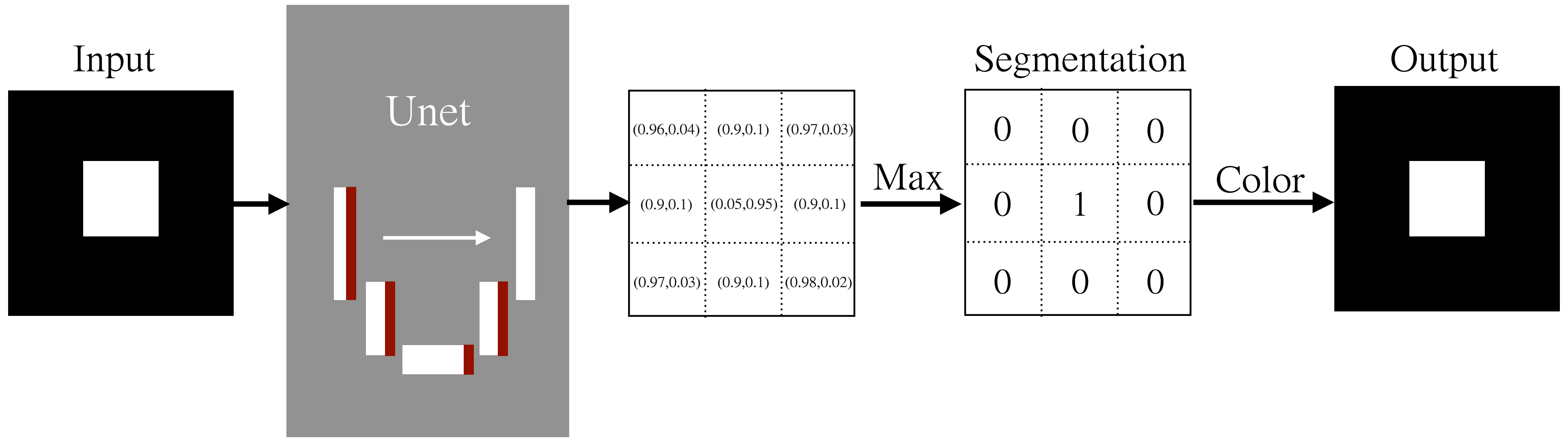
- Background: 0
- Nodule: 1

Monte Carlo Dropout Unet (MCD)

Cross-entropy Loss

Ground truth label for each pixel:

- Background: 0
- Nodule: 1



Measures: Uncertainty Estimation

For each x_{input} and the training dataset $\mathcal{D}_{\text{train}}$

The predictive posterior over class labels

$$p(y = y_0 | x_{\text{input}}; \mathcal{D}_{\text{train}}) \qquad p(y = y_1 | x_{\text{input}}; \mathcal{D}_{\text{train}})$$

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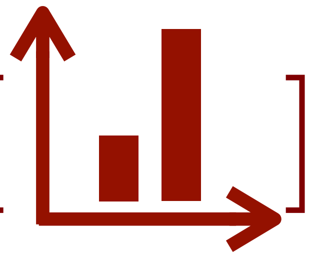
Total Entropy (TE):

$$\mathcal{H}[p(y|x_{\text{input}}; \mathcal{D}_{\text{train}})] \longrightarrow \mathcal{H}[\quad]$$



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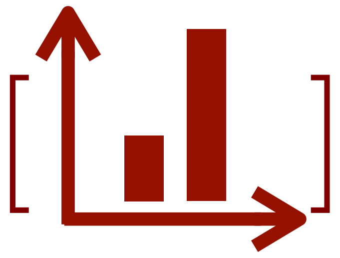
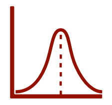
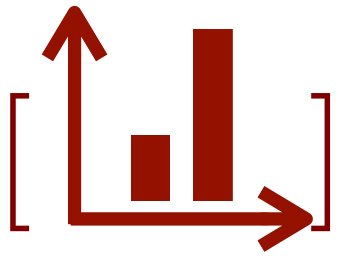
$\mathcal{H}[p(y|x_{\text{input}}; \mathcal{D}_{\text{train}})] \longrightarrow \mathcal{H}[$  $]$

Expected data uncertainty (EDU):

$\mathbb{E}_{p(\pi|x_{\text{input}}; \mathcal{D}_{\text{train}})} \mathcal{H}[p(y|\pi)] \longrightarrow \mathbb{E}_{\pi \sim}$  $\mathcal{H}[$  $]$

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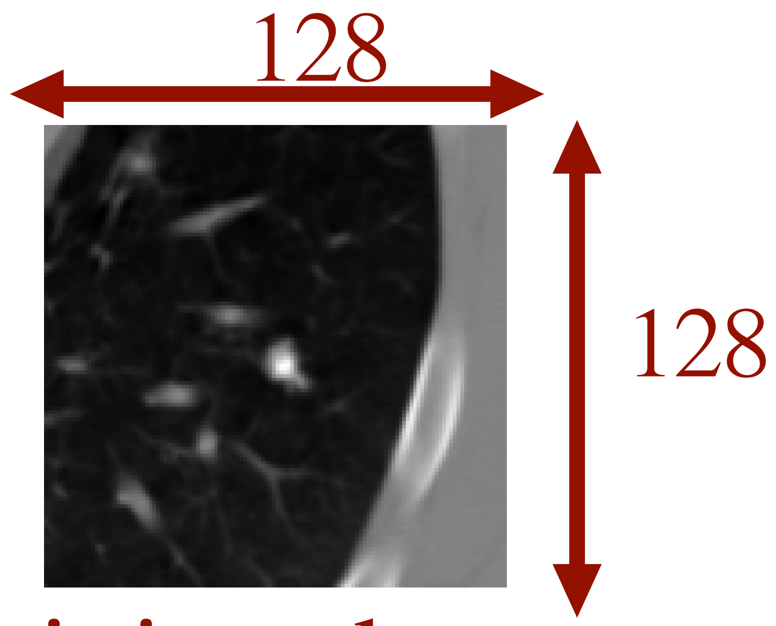
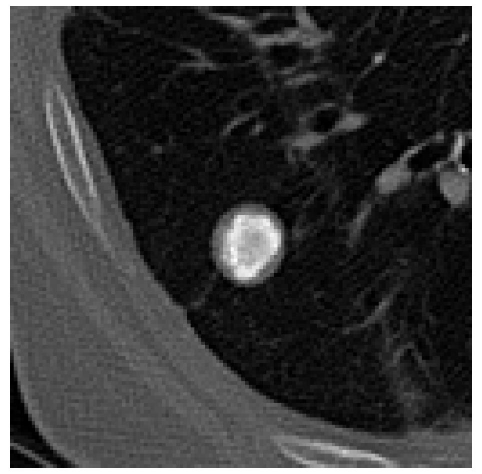
Mutual Information (MI): TE - EDU

Setup:

- LIDC-IDRI database, preprocessing by Stefan Knegt
- Each image has 4 annotations (ground truth mask) by 4 experts



Training dataset



Test dataset

Experiment 1: Lung nodule segmentation

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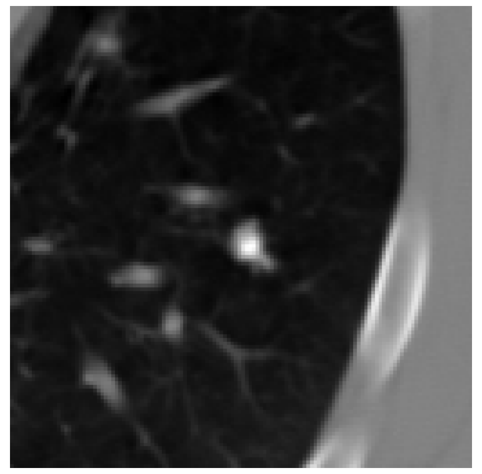
128



128

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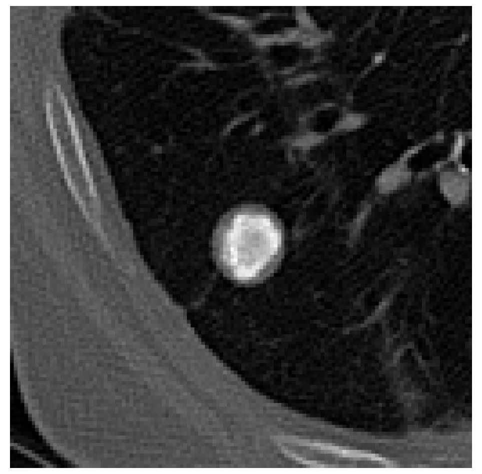
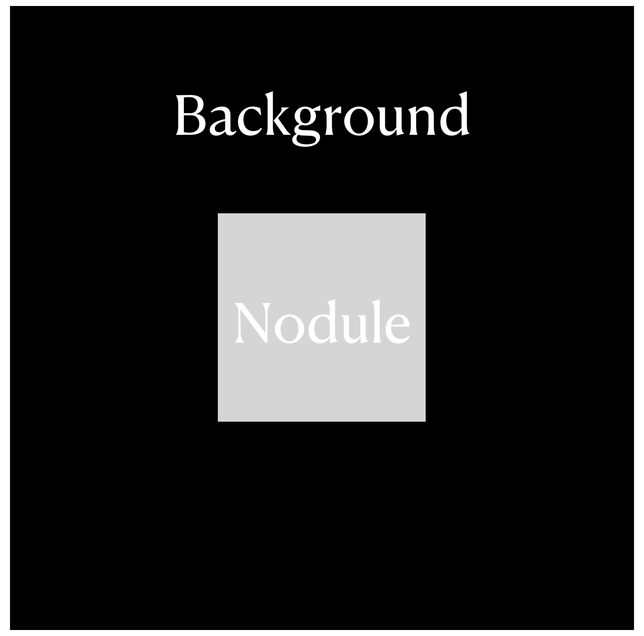


Test dataset

Simplified



Input image

0	0	0
0	1	0
0	0	0

Ground truth (MCD, SSN)

(11,1)	(11,1)	(11,1)
(11,1)	(1,11)	(11,1)
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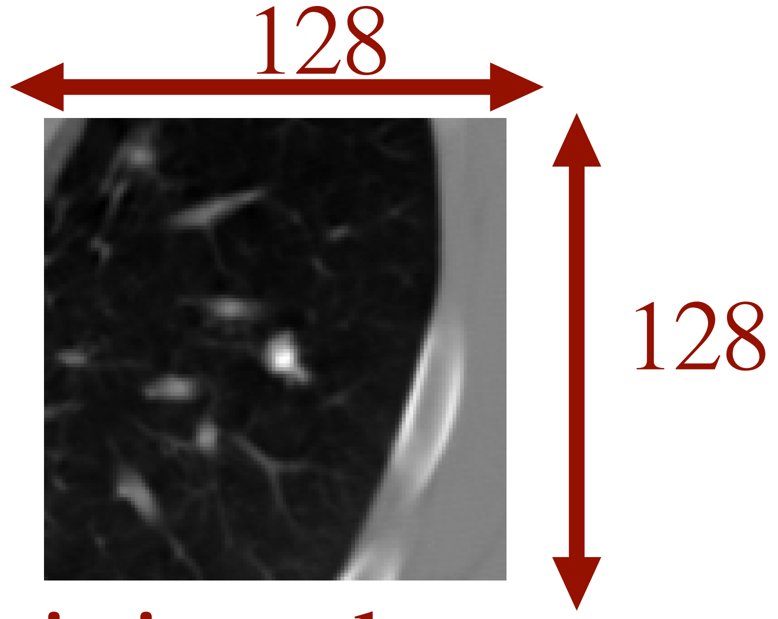

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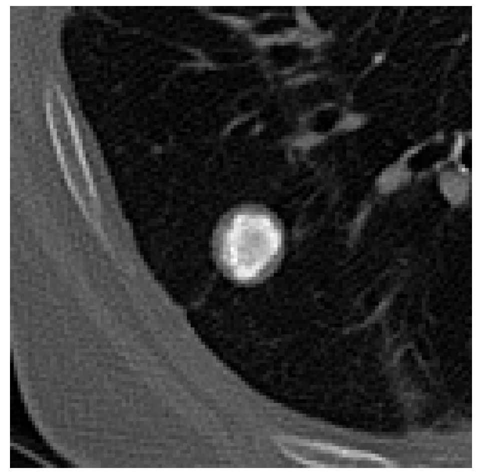

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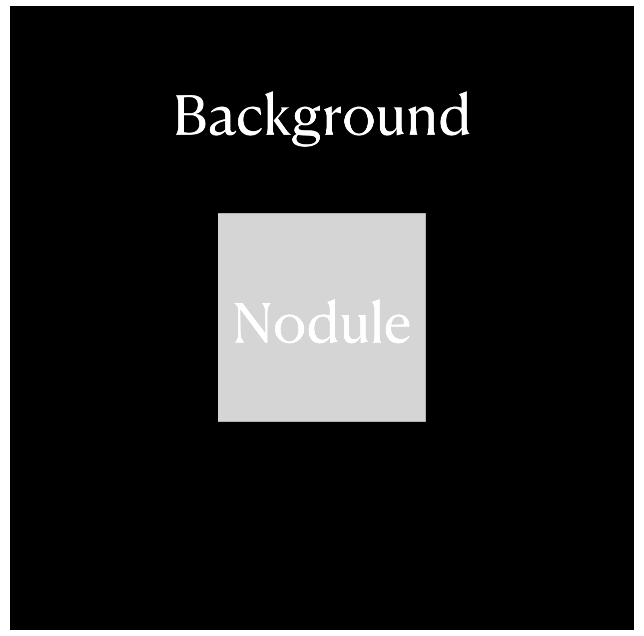

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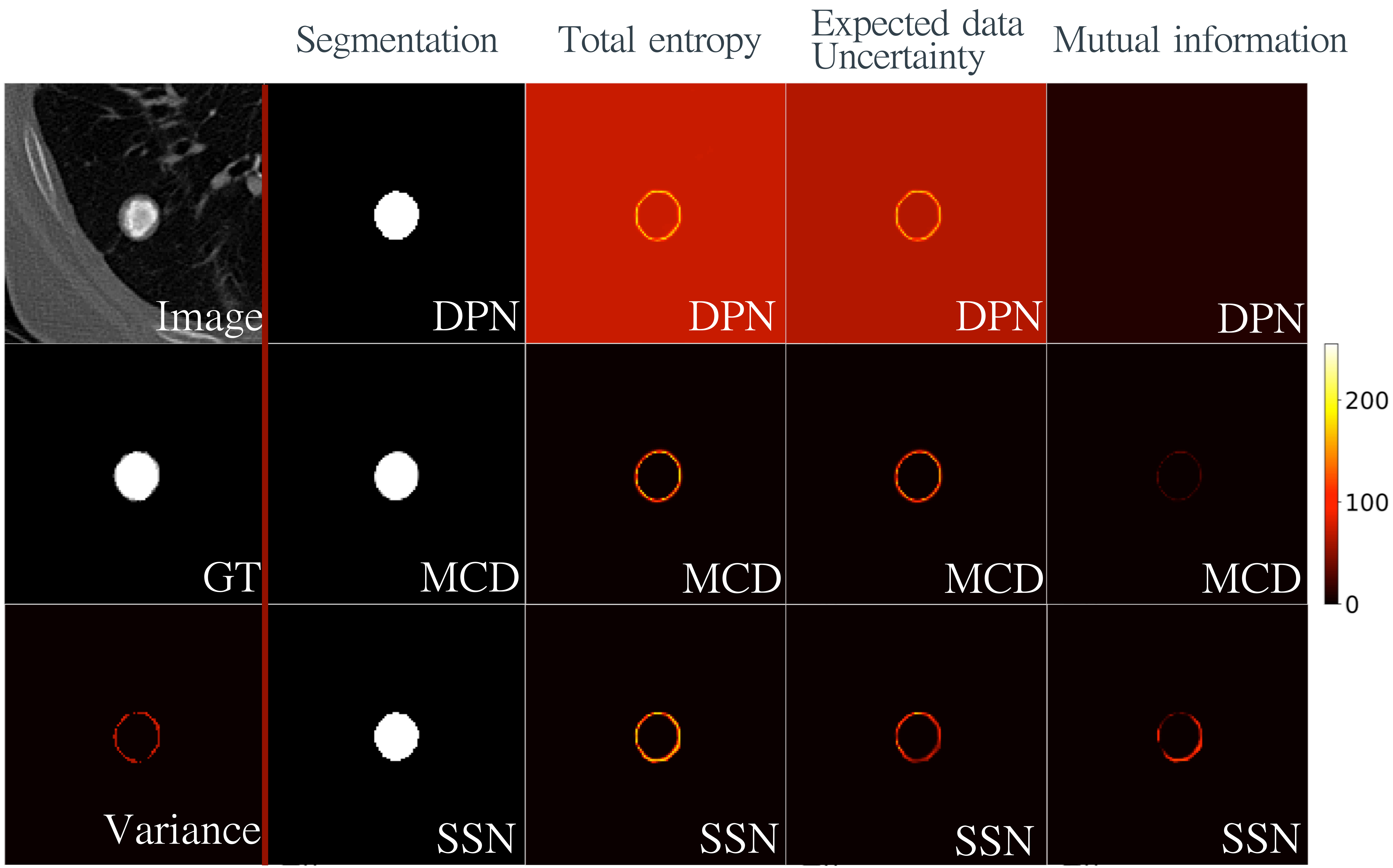
Ground truth (DPN)

- Training / Test (90% / 10%)
- 800 epochs, Adam learning rate of 0.0001

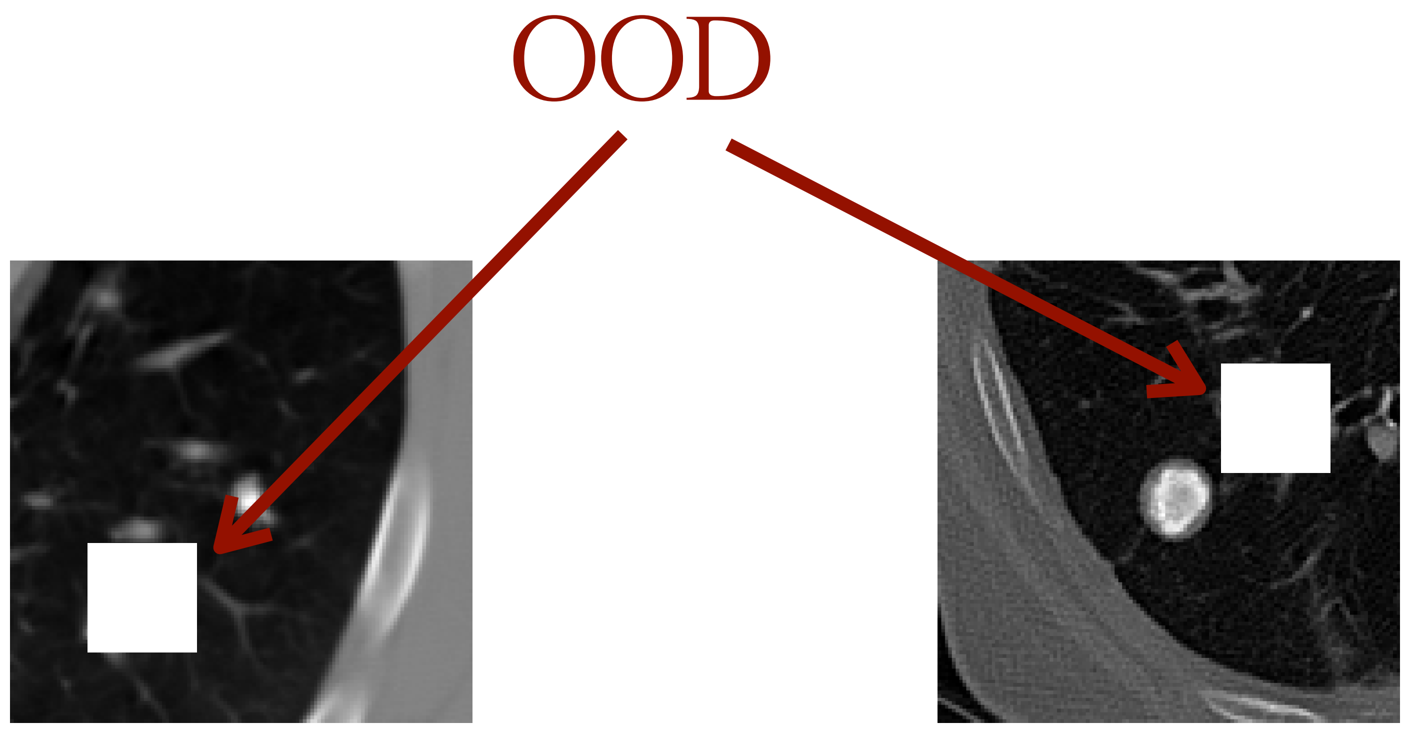
Experiment 1: Lung nodule segmentation



Approach	DSC
MCD	0.5964
SSN	0.5267
DPN	0.6156

Experiment 2: Limitations of baseline approaches

Setup:



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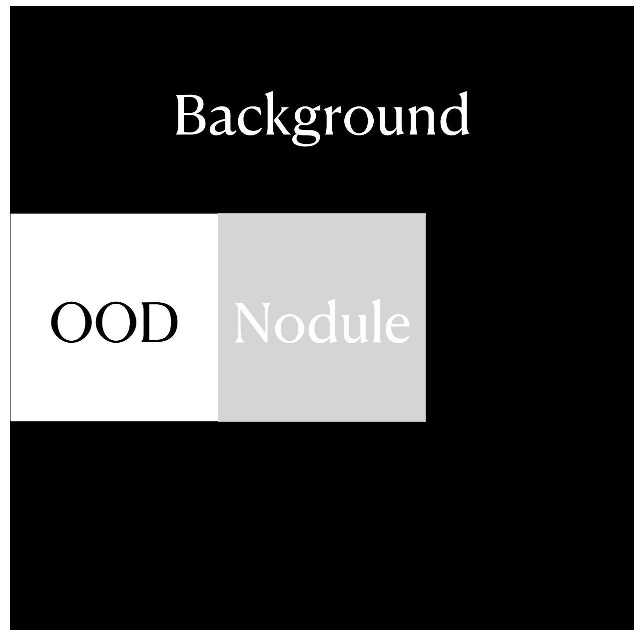

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Ground truth (DPN)

- Training / Test (90% / 10%)
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- 800 epochs for MCD and DPN
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Experiment 2: Limitations of baseline approaches

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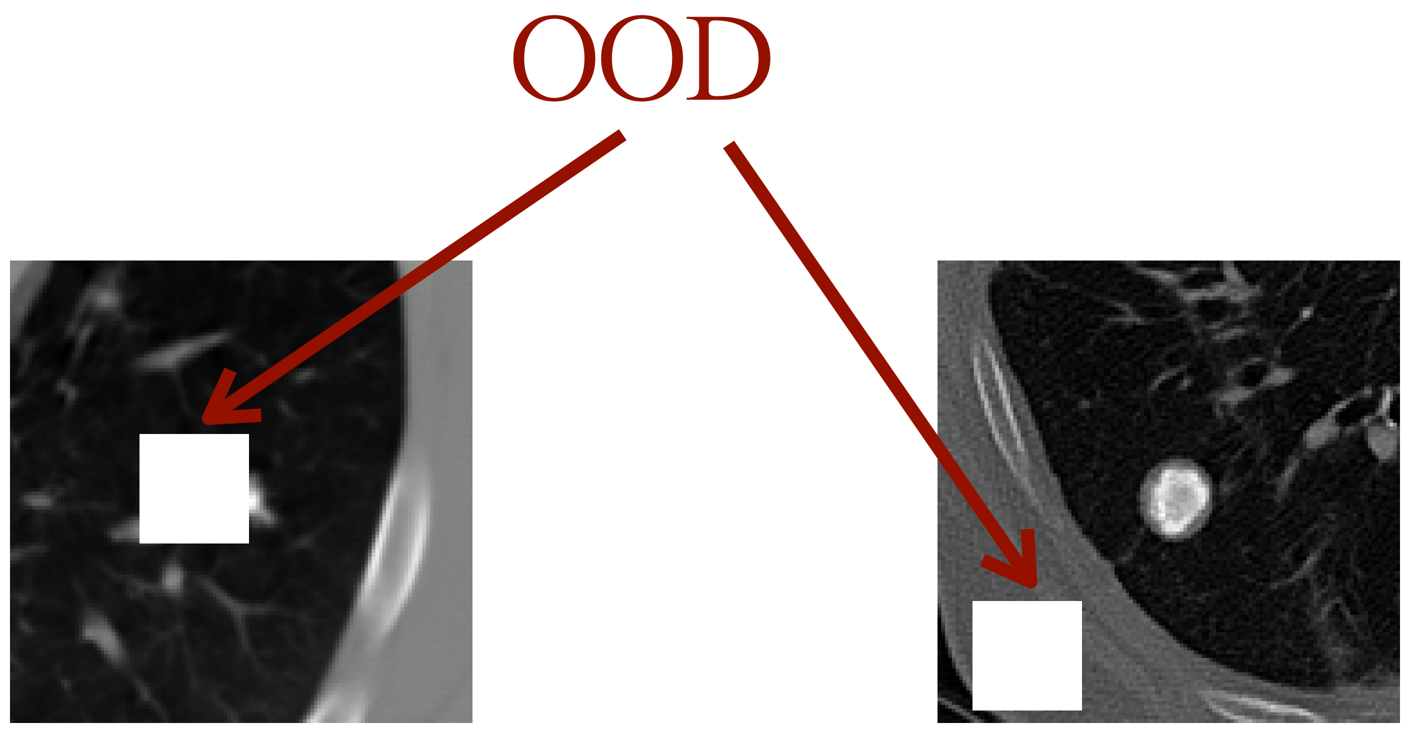
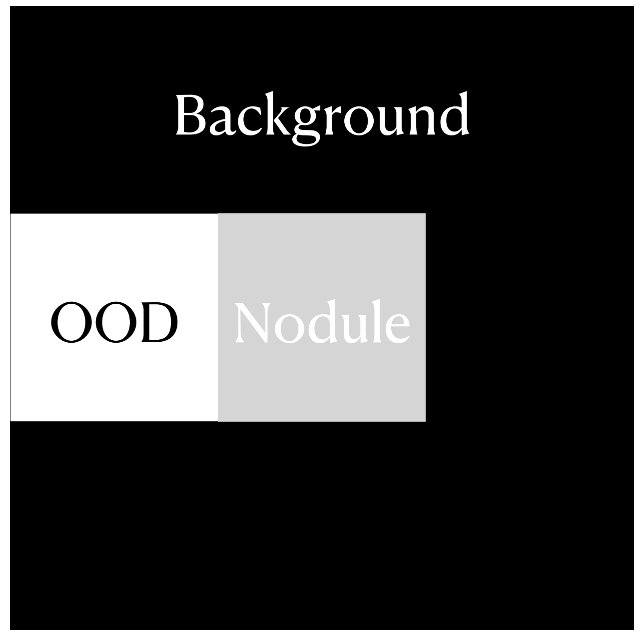


Training dataset

Test dataset

Simplified



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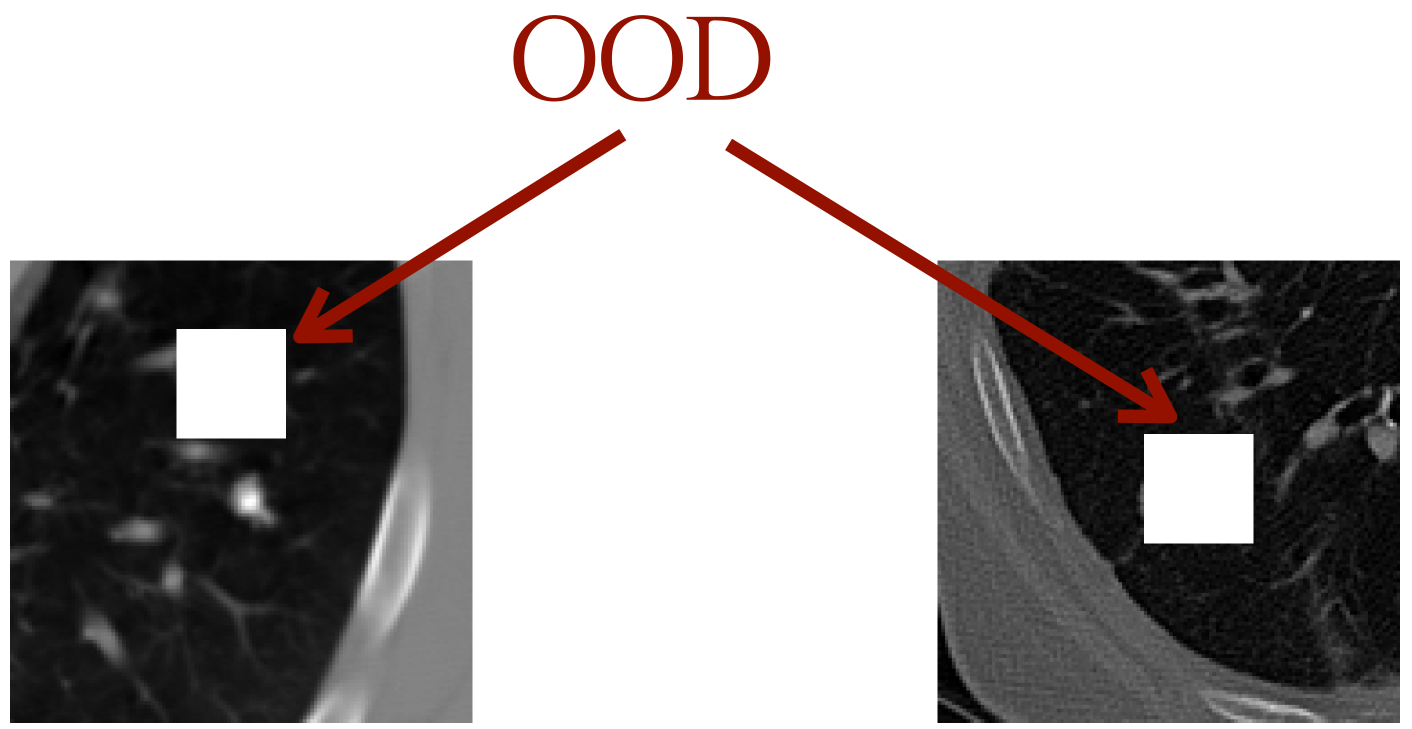

Training dataset   Test dataset

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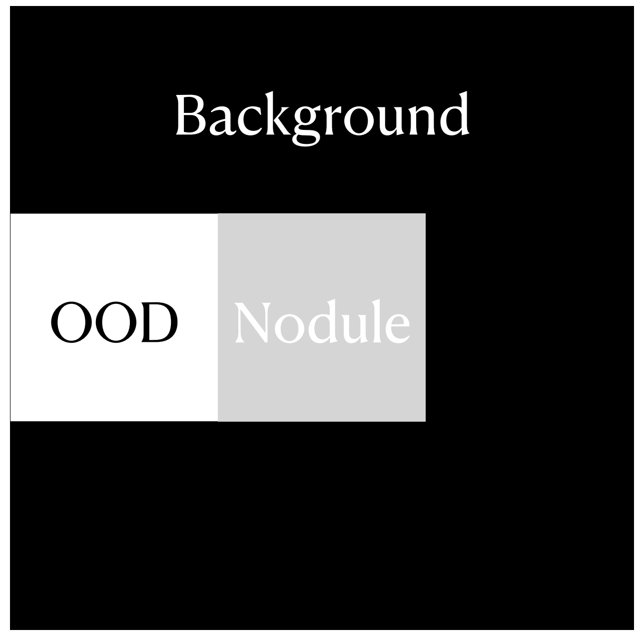

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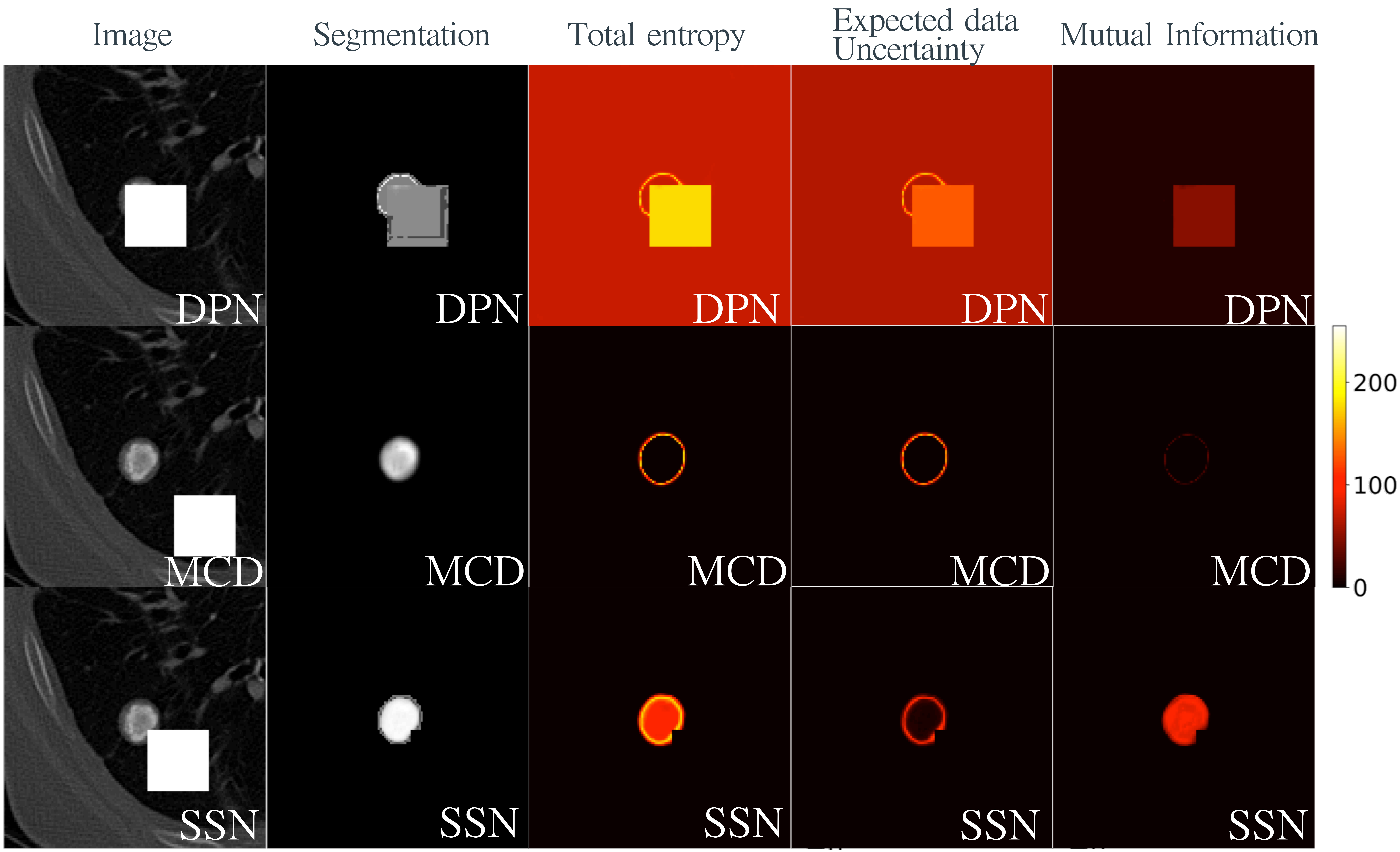


Experiment 2: Limitations of baseline approaches

Misclassification Detection:
Incorrect prediction as positive class, correct prediction as negative class

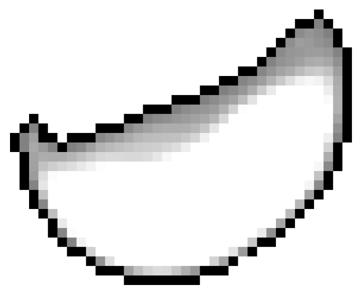
Out-of-distribution Detection:
Out-of-distribution input as positive class, in-domain input as negative class

Differentiation Detection:
Out-of-distribution input as positive class, in-domain incorrect prediction as negative class

Detection	Approach	AUROC TE	AUROC EDU	AUROC MI	AUPR TE	AUPR EDU	AUPR MI	AUPR Baseline
Misclassification	MCD	0.98970	0.98952	0.98831	0.06296	0.06559	0.04360	0.00074
	SSN	0.99388	0.99270	0.98530	0.40909	0.32836	0.40032	0.00396
	DPN	0.98946	0.98648	0.99055	0.64509	0.56044	0.67487	0.03855
Out-of-distribution	MCD	0.41887	0.41504	0.43050	0.04479	0.04444	0.04578	0.05493
	SSN	0.38976	0.38998	0.46258	0.05184	0.05191	0.05656	0.05493
	DPN	0.99999	0.99378	1.00000	0.99956	0.74996	1.00000	0.05493
Differentiation	MCD	0.00455	0.00473	0.00431	0.94192	0.94192	0.94200	0.98660
	SSN	0.00016	0.00016	0.00999	0.89070	0.89132	0.90773	0.93277
	DPN	0.99038	0.19879	1.00000	0.99944	0.89742	1.00000	0.96547

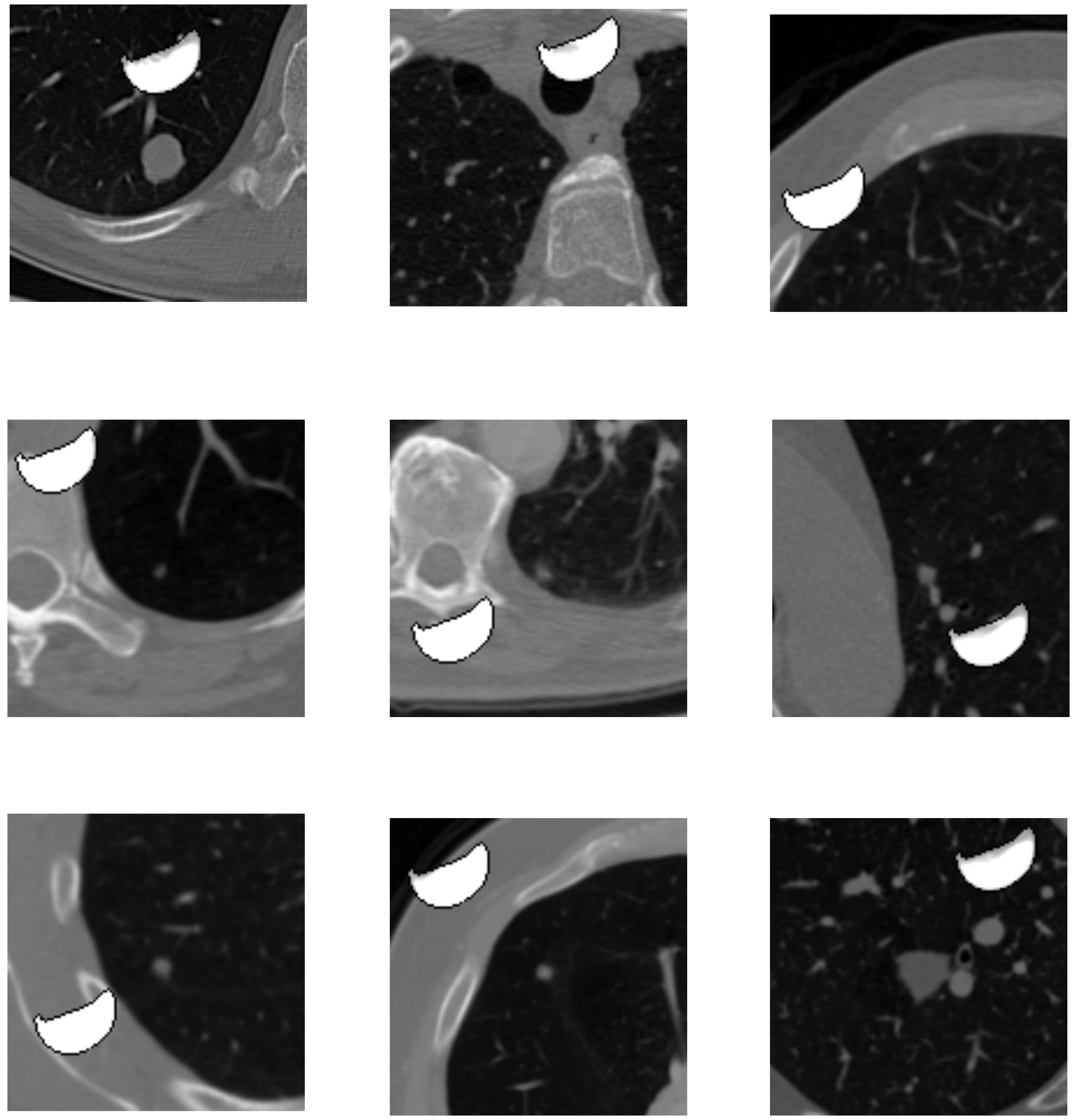
Experiment 3: Authentic out-of-distribution data

Setup:



Synthetic
Out-of-distribution data

Training dataset



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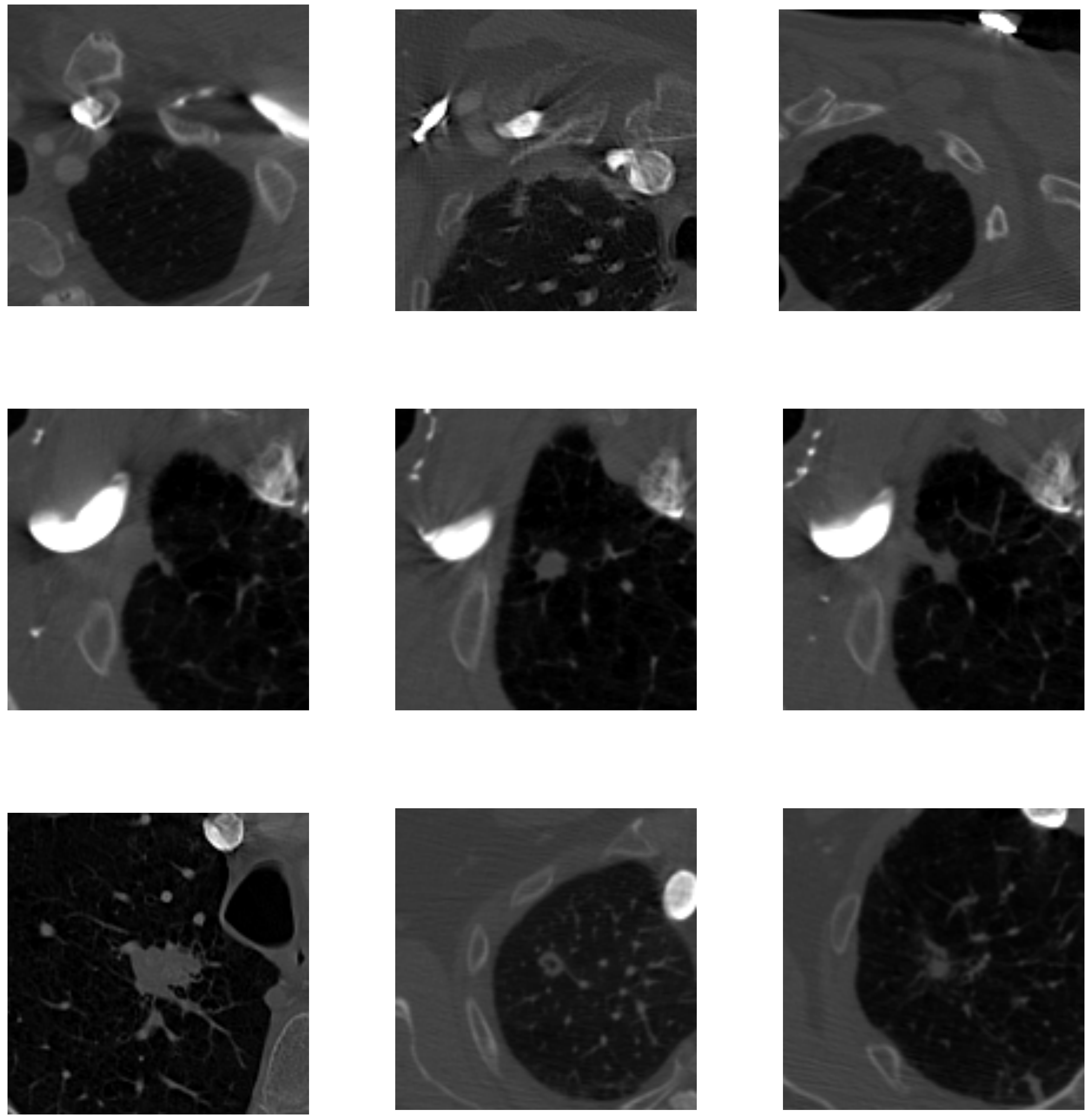
Test dataset



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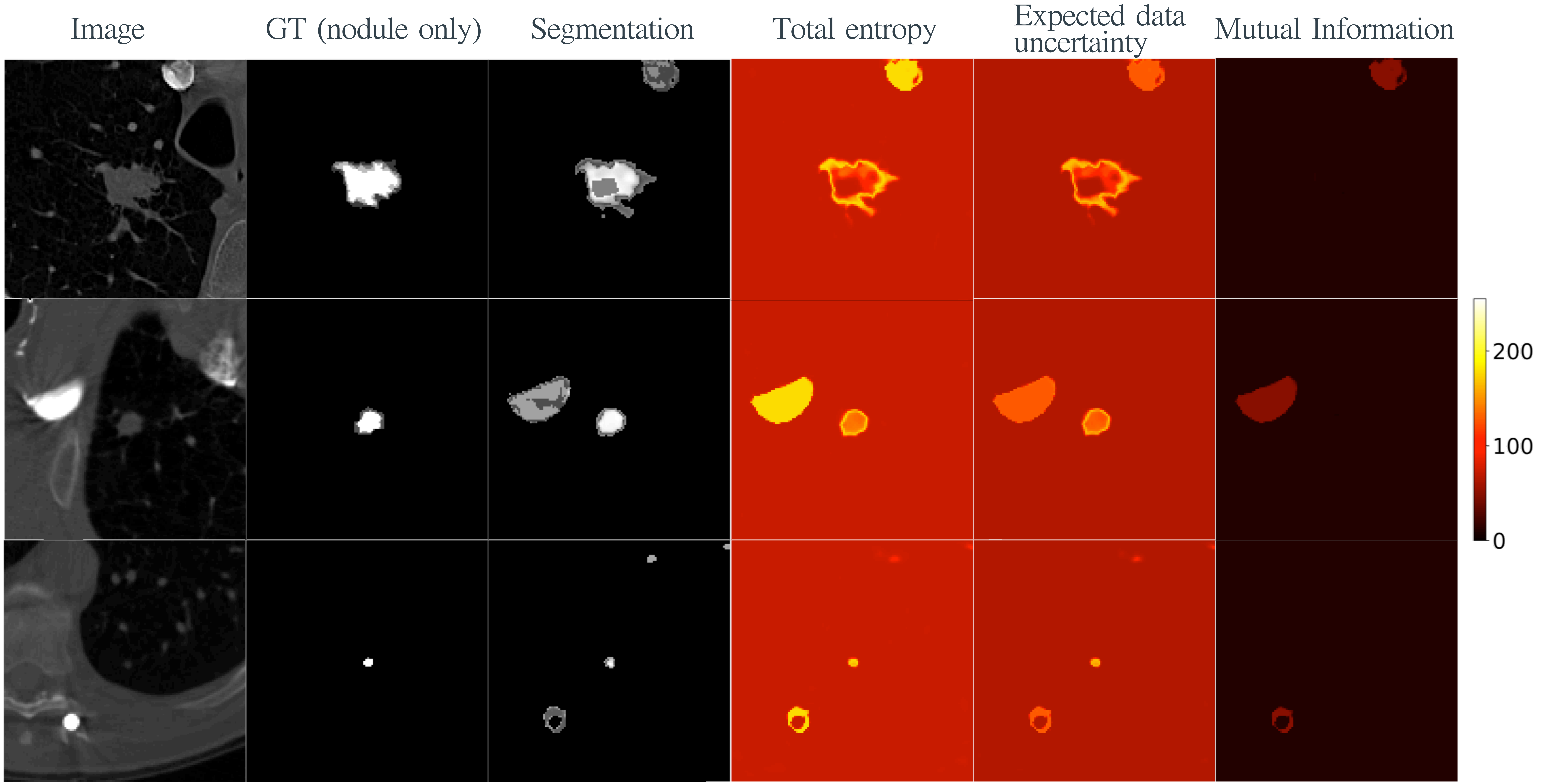
Authentic Out-of-distribution data

(Potential CT artifacts, flowing of blood …)

Experiment 3: Authentic out-of-distribution data



Conclusion:

The Dirichlet Prior Network can differentiate different uncertainties in the CT image with varied types of authentic out-of-distribution data by only training with one type of synthetic out-of-distribution data.

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Open questions:

- The non-invertible problem of the covariance in SSN
- Dark Bands Segmentation

Conclusion:

The Dirichlet Prior Network can differentiate different uncertainties in the CT image with varied types of authentic out-of-distribution data by only training with one type of synthetic out-of-distribution data.

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Thank you!