

# Negative-Unlabeled Learning for Diffusion MRI



Technische Universität München

Phillip Swazinna<sup>1</sup> Vladimir Golkov<sup>1</sup> Ilona Lipp<sup>2</sup> Eleonora Sgarlata<sup>2,3</sup> Valentina Tomassini<sup>2,4</sup> Derek K. Jones<sup>2</sup> Daniel Cremers<sup>1</sup>

<sup>1</sup>Computer Vision & Artificial Intelligence, Department of Informatics, Technical University of Munich, Germany <sup>2</sup>CUBRIC, Cardiff University, United Kingdom

<sup>3</sup>Department of Neurology and Psychiatry, Sapienza University of Rome, Italy <sup>4</sup>Division of Psychological Medicine and Clinical Neurosciences, Cardiff University, United Kingdom

golkov@cs.tum.edu

Overview of Methods for Diffusion MRI		Fitting of handcrafted representation (DTI, DKI, NODDI, ...)	Analytic computation of handcrafted metrics [1]	Machine learning							
				Voxel-wise supervised learning (of handcrafted metrics) [2]	Voxel-wise supervised learning (of tissue properties) [2]	Voxel-wise semi-supervised learning [hypothetical method]	Scan-wise supervised learning [3]	Weakly-supervised learning [3]	Multiple-instance learning [hypothetical method]	Novelty detection [4,5,6]	Negative-unlabeled learning [proposed]
Works with few q-space measurements		No	✓	✓	✓	✓	✓	✓	✓	✓	✓
Object of direct study		Handcrafted metrics	Handcrafted metrics	Handcrafted metrics	Tissue properties (for example abnormality)	Tissue properties (for example abnormality)	Tissue properties (for example abnormality)	Tissue properties (for example abnormality)	Tissue properties (for example abnormality)	Abnormality	Abnormality
Location of labels		None	None	Voxel-wise from fitting (which requires none)	Voxel-wise	Voxel-wise	Scan-wise	Scan-wise	Scan-wise	Any (only normal)	Any (only normal)
Location of prediction		Voxel-wise	Voxel-wise	Voxel-wise	Voxel-wise	Voxel-wise	Scan-wise	Voxel-wise clues for global prediction	Voxel-wise	Voxel-wise	Voxel-wise
Usage of unlabeled data during training		No	No	No	No	✓	No	No	No	Usually no	✓
Used knowledge	(a) Voxels from one scan belong together	N/A	N/A	N/A	N/A	N/A	✓	✓	✓		
	(b) All voxels from healthy-control scan are healthy	N/A	N/A	N/A	✓	N/A	✓		✓	✓	✓
	(c) Disease clues may depend on context (other voxels)	N/A	N/A	N/A	N/A	N/A	✓	✓			

## Setting & Approach

- q-Space deep learning [2,3,4,5,6]: Prediction of tissue properties directly from q-space measurements
- Every voxel is a sample
  - Features are q-space measurements
- Only negative (healthy) and unlabeled samples are given
  - i.e. **negative-unlabeled learning** [8]
- No positive (multiple sclerosis) labels are given
  - i.e. **no knowledge about disease is required**
- Goal: distinguish negative and positive samples
- Treating unlabeled samples as positive (which introduces "label noise") is (for certain cost functions) a good method for negative-unlabeled learning [Zhung&Lee]
  - We use a simpler cost function that yields similar results

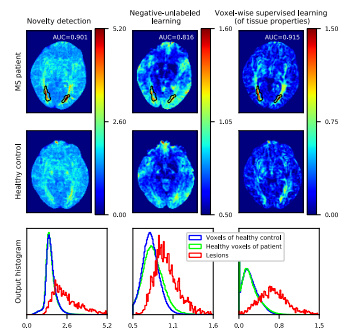
## Data

- 94 multiple sclerosis patients, 26 healthy controls
- Six b=0 images, 40 diffusion directions ( $b_{max}=1200s/mm^2$ )
- SE-EPI, TR=16s, TE=94.5ms, voxel size 1.8mm×1.8mm×2.4mm, matrix 128×128, 57 axial slices, motion/distortion-corrected [9]

## Neural Network

- Feature scaling: divide each channel by its mean taken over all scans
- To prevent overfitting of intensity values: divide each scan by its mean and multiply with random scalar between 0.8 and 1.2 in every epoch
- 3D ConvNet**: ReLU, 128,256,512,1 filters 1×1×1, Adam

## Results



## Discussion & Conclusions

- Deep learning for diffusion MRI:**
  - data-driven:** diagnosis directly from raw q-space data
  - many advantages:** ultra-short scans, optimal usage of information, ...
  - applicable in **various situations:** coarse or missing labels, unknown disease effects, ...
- As expected, supervised q-Space Deep Learning yields best AUC
- Negative-unlabeled learning yields good AUC (0.77) but is surprisingly outperformed by novelty detection (0.89)
- More research is necessary

## References

- Hansen et al.: "Fast imaging of mean, axial and radial diffusion kurtosis", NeuroImage 2016
- Golkov et al.: "q-Space Deep Learning: Twelve-Fold Shorter and Model-Free Diffusion MRI Scans", IEEE TMI 2016
- Golkov et al.: "q-Space Deep Learning for Alzheimer's Disease Diagnosis: Global Prediction and Weakly Supervised Localization", ISMRM 2018
- Golkov et al.: "Model-Free Novelty-Based Diffusion MRI", ISBI 2016
- Golkov et al.: "q-Space Novelty Detection in Short Diffusion MRI Scans of Multiple Sclerosis", ISMRM 2018
- Vasilev et al.: "q-Space Novelty Detection with Variational Autoencoders", arXiv 2018
- Zhang & Lee: "Learning Classifiers without Negative Examples: A Reduction Approach", ICDM 2008
- Niu: "Recent Advances on Positive Unlabeled (PU) Learning", IBISML 2017
- Klein et al.: "elastix: A toolbox for intensity-based medical image registration", IEEE TMI 2010