Analyzing Regional Organization of the Human Hippocampus in 3D-PLI Using Contrastive Learning and Geometric Unfolding

Alexander Oberstrass[1,2] Jordan DeKraker[3] Nicola Palomero-Gallagher[1,4] Sascha E. A. Muenzing[1]
Alan C. Evans[3] Markus Axer[1,5] Katrin Amunts[1,4] Timo Dickscheid[1,2,6]

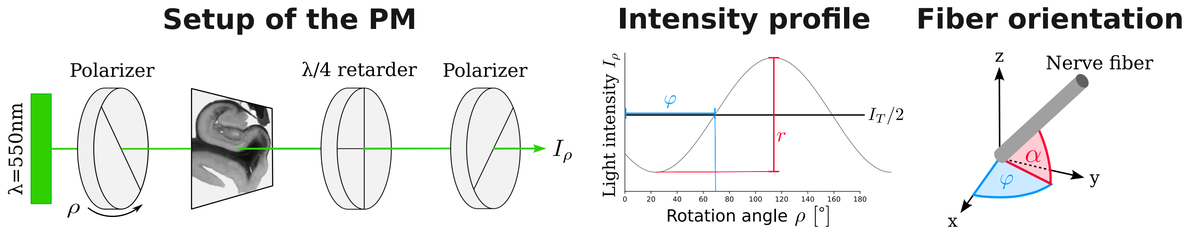
[1] Institute of Neuroscience and Medicine (INM-1), Research Centre Jülich, Jülich, Germany
[2] Helmholtz AI, Research Centre Jülich, Jülich, Germany
[3] Montreal Neurological Institute and Hospital, McGill University, Montreal, Canada
[4] Cécile & Oskar Vogt Institute for Brain Research, University Hospital Düsseldorf, Düsseldorf, Germany
[5] Department of Physics, University of Wuppertal, Wuppertal, Germany
[6] Institute of Computer Science, Heinrich-Heine-University Düsseldorf, Germany

Contact: a.oberstrass@fz-juelich.de

Introduction

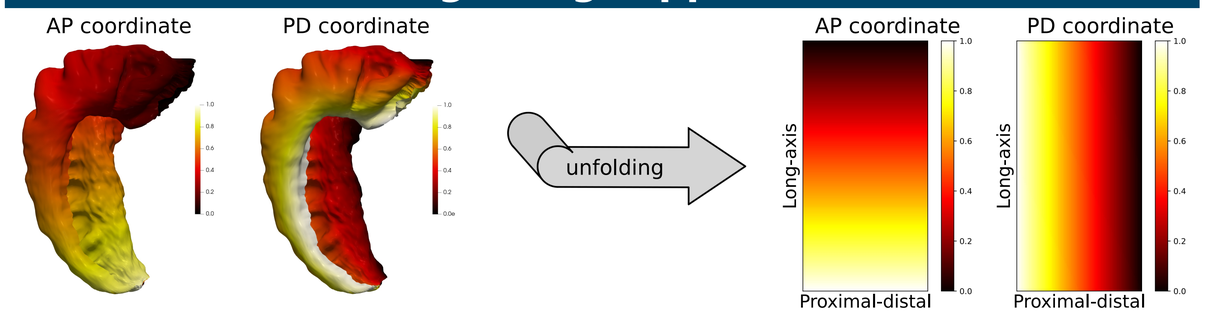
Quantifiable and interpretable descriptors of nerve fiber architecture at microscopic resolution are important for a deeper understanding of human brain architecture [1]. 3D polarized light imaging (3D-PLI) [2] provides insights into the **course and geometry of nerve fibers** in whole postmortem brain sections, represented in large data sets. The complex texture captured in 3D-PLI images therefore makes analysis challenging and limits access to data annotations.
To this end, we demonstrate a novel method to analyze the regional organization of the human hippocampus in 3D-PLI by combining a **geometric unfolding method** [3] with **deep texture features obtained using self-supervised contrastive learning** [4]. We identify clusters in the feature embeddings that correspond well with classical descriptions of hippocampal subfields, lending validity to the developed methodology.

3D Polarized Light Imaging



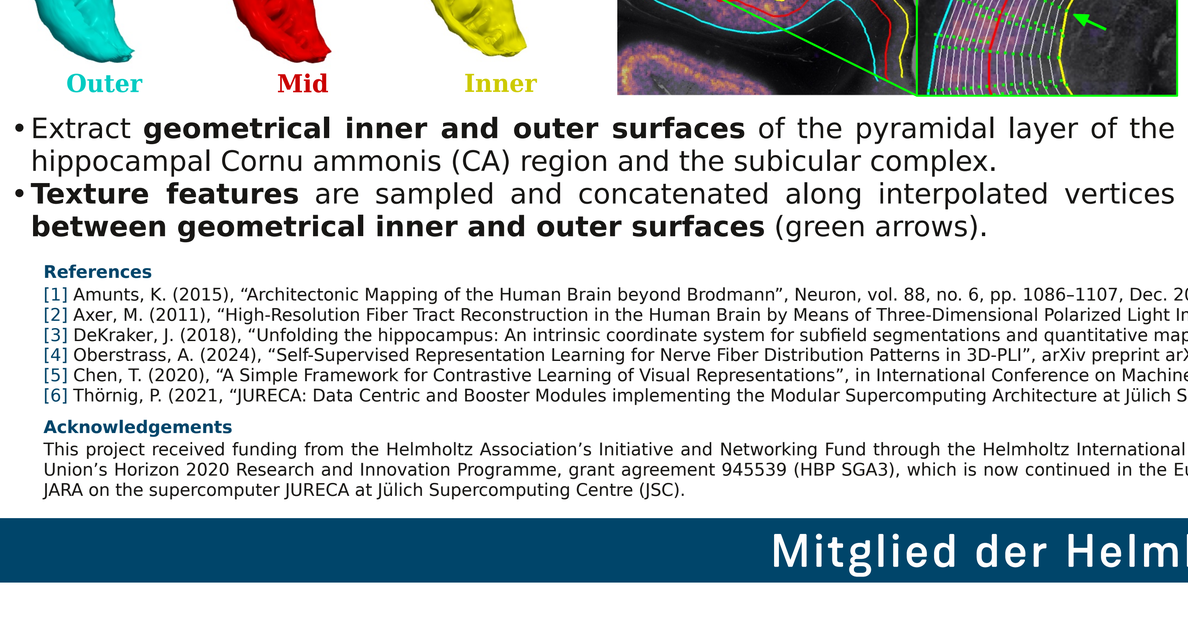
- Individual brain sections are scanned using a **polarizing microscope (PM).**
- 3D-PLI parameter maps **transmittance I_T, direction φ** and **retardation r** are derived from recorded light intensity profiles at each pixel.
- **3D fiber orientations** are computed from direction and retardation.

Human Hippocampus Dataset



- Use PM measurements of a **human hippocampus of an 87-year-old male**.
- 1.33 µm in-plane resolution, 60 µm section thickness.
- The regional organization can be divided into labels **CA1, CA2, CA3, CA4 and the subicular complex.**
- Sections are **reconstructed to a volume** of 26757 × 547 × 22734 voxels.
- **Surfaces of the pyramidal layer** are extracted, manually extrapolated to missing data regions.

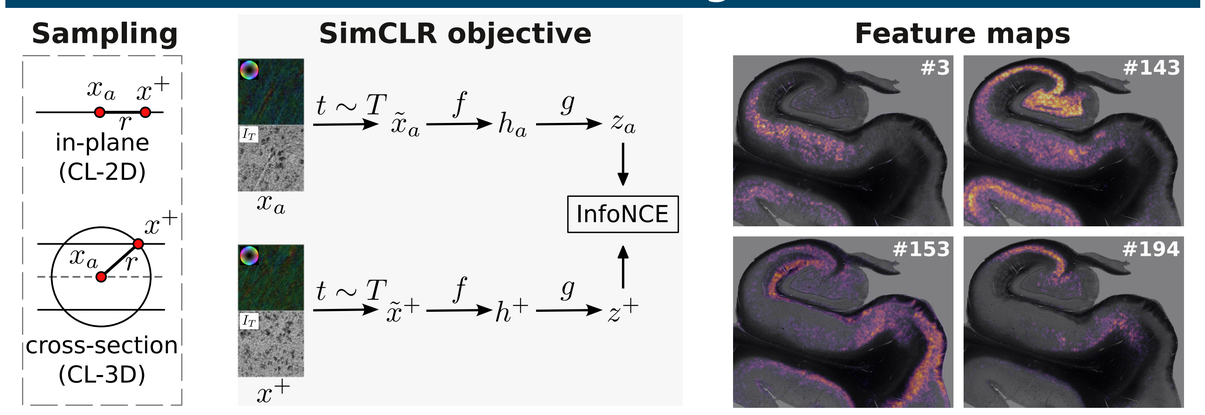
Geometric Unfolding using HippUnfold



- Calculate Laplacian potential fields between **anterior-posterior (AP)** and **proximal-distal (PD)** ends of the hippocampus.
- The fields form 2D coordinates along the **long-axis** and **proximal-distal axis**.
- AP and PD coordinates provide a mapping between folded and unfolded space.
- Surfaces have **30004 nodes, isotropic in unfolded space** [3].

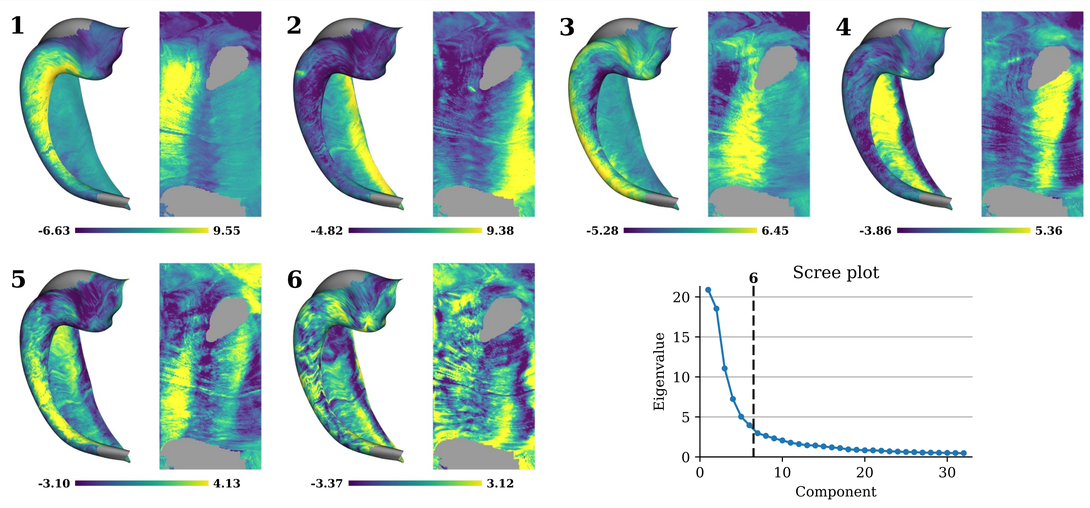
- Extract **geometrical inner and outer surfaces** of the pyramidal layer of the hippocampal Cornu ammonis (CA) region and the subicular complex.
- **Texture features** are sampled and concatenated along interpolated vertices **between geometrical inner and outer surfaces** (green arrows).

3D Context Contrastive Learning



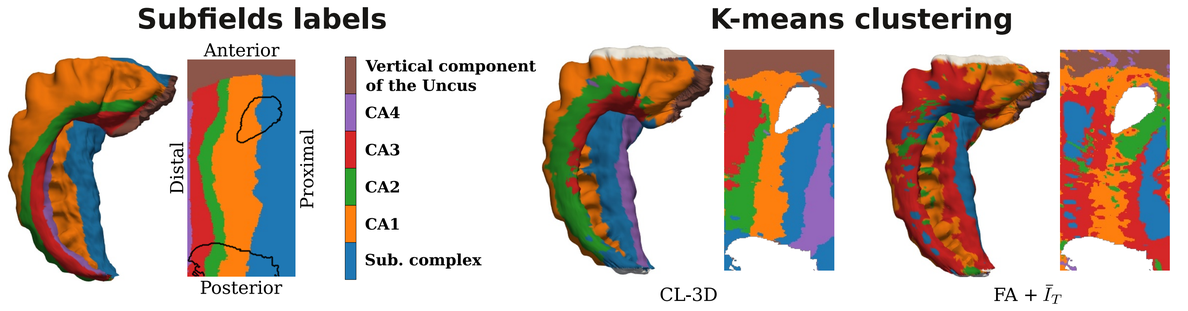
- **Sample positive pairs in a 2D or 3D context** of individual brain sections [4].
- Extract square image patches with **128 pixels (166 µm) size** from transmittance, direction and retardation maps showing 3D-PLI texture.
- Use set of **3D-PLI-specific data augmentations** T [4].
- Train **encoder** f and **projection head** g in the **SimCLR** [5] **framework**.
- Reduced ResNet-50 encoder f extracts **256 features per patch**.
- Training took **17 hours** on **4 Nvidia A100 GPUs** on JURECA-DC [6].

PCA



- **CL-3D features** concatenated between geometrical inner and outer surfaces are projected onto **PCA components** with largest explained variance.
- **PCA projections** are visualized on the **smoothed mid-surface (left)** and in **unfolded space (right)**, where gray marks missing data.
- First 6 components with largest eigenvalues follow the general hippocampal regional organization pattern.

Clustering



- **K-means clusters** are compared with anatomically identified **subfield labels**.
- Clusters of CL-3D texture features more closely resemble the subfield labels than clusters of mean transmittance I_T and fractional anisotropy FA.
- Black contours and white spots mark missing data.

Method	Input	Purity ↑	ARI ↑	MI ↑
CL-3D	I_T, φ, r	**0.67**	**0.33**	**0.72**
	I_T	0.65	0.30	0.66
	φ, r	0.52	0.16	0.49
CL-2D	I_T, φ, r	0.63	0.26	0.61
	I_T	0.58	0.21	0.50
	φ, r	0.51	0.13	0.40
$\bar{I}_T$ + FA	I_T, φ, r	0.53	0.15	0.40
$\bar{I}_T$	I_T	0.51	0.13	0.36
FA	I_T, φ, r	0.50	0.11	0.27

- Compare evaluation metrics for k-means clusterings for 6 clusters of features by different feature extraction methods.
- Deep texture features achieve higher scores than baseline features.
- CL-3D outperforms CL-2D.
- Including fiber orientation information as input for feature extraction improves scores over transmittance alone.

Conclusions

- **CL-3D features follow the general regional organization pattern** without providing explicit prior information on anatomy in training.
- Cross-section sampling of positive pairs in contrastive learning (CL-3D) improves clustering of 3D-PLI texture by subfields over in-plane sampling (CL-2D).
- Unfolding 3D-PLI texture features facilitates their **integration into a comprehensive multimodal mapping** of the human hippocampus.
- Future work will apply the approach to **other brains, specimens, and microscopic modalities** with available 3D reconstructions.

References
[1] Amunts, K. (2015), "Architectonic Mapping of the Human Brain beyond Brodmann", Neuron, vol. 88, no. 6, pp. 1086–1107, Dec. 2015.
[2] Axer, M. (2011), "High-Resolution Fiber Tract Reconstruction in the Human Brain by Means of Three-Dimensional Polarized Light Imaging", Frontiers in Neuroinformatics, vol. 5, 2011, doi: 10.3389/fninf.2011.00034.
[3] DeKraker, J. (2018), "Unfolding the hippocampus: An intrinsic coordinate system for subfield segmentations and quantitative mapping", NeuroImage, vol. 167, pp. 408–418, Feb. 2018.
[4] Oberstrass, A. (2024), "Self-Supervised Representation Learning for Nerve Fiber Distribution Patterns in 3D-PLI", arXiv preprint arXiv:2401.17207, 2024.
[5] Chen, T. (2020), "A Simple Framework for Contrastive Learning of Visual Representations", in International Conference on Machine Learning, Nov. 2020, vol. 119, pp. 1597–1607.
[6] Thörnig, P. (2021, "JURECA: Data Centric and Booster Modules implementing the Modular Supercomputing Architecture at Jülich Supercomputing Centre", Journal of large-scale research facilities JLSRF, 7:A182–A182. 9

Acknowledgements
This project received funding from the Helmholtz Association's Initiative and Networking Fund through the Helmholtz International BigBrain Analytics and Learning Laboratory (HIBALL), Helmholtz International Lab grant agreement InterLabs-0015, and the European Union's Horizon 2020 Research and Innovation Programme, grant agreement 945539 (HBP SGA3), which is now continued in the European Union's Horizon Europe Programme, grant agreement 101147319 (EBRAINS 2.0 Project). Computing time was granted through JARA on the supercomputer JURECA at Jülich Supercomputing Centre (JSC).