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

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Quantifiable and interpretable descriptors of nerve fiber architecture at microscopic resolution are an important basis for a deeper understanding of human brain architecture. 3D polarized light imaging (3D-PLI) provides detailed insights into the course and geometry of nerve fibers in whole postmortem brain sections, represented in large datasets. The large amounts of data, combined with complex textures in 3D-PLI images, however, make analysis challenging and limit access to data annotations. To this end, we propose using self-supervised contrastive learning to extract deep texture features for fiber architecture in 3D-PLI. We use the texture features to analyze the regional organization of the human hippocampus in combination with geometric unfolding to reduce the effects of its folded topology and project the features to a canonical reference space.

We analyze the fiber architecture of a human hippocampus of an 87-year-old male, measured with a polarizing microscope (PM) at 1.3 µm in-plane resolution on 60 µm thick brain sections. The volume comprises 545 brain sections, each 26757 × 22734 pixels in size. We apply contrastive learning to learn robust and descriptive representations by contrasting similar (positive) and dissimilar (negative) pairs of texture examples. Here, we leverage the volume reconstruction of individual brain sections in the learning objective to identify positive pairs based on a fixed distance between example image patches either in-plane (CL-2D) or across brain sections in 3D (CL-3D) (Fig. 1A). The objective is used to train a width-reduced ResNet-50 architecture on the full hippocampus, extracting 256 texture features for square patches of 128 pixels size (166 µm). After training, inference is performed using a sliding window approach to generate feature maps for whole brain sections (Fig. 1B). To analyze the folded architecture of the hippocampus, we apply HippUnfold and sample features from the feature maps at multiple depths of the pyramidal layer of the hippocampal Cornu ammonis (CA) region and the subicular complex (Fig. 1C). Subsequently, PCA is performed to reduce feature dimensionality for visualization and improve computational stability in further analysis (Fig. 1E).

To assess how well the deep texture features reflect the regional organization of the hippocampus, we perform k-means clustering for 6 clusters and compare the results with subfield labels. Clusters in CL-3D features show good visual agreement with hippocampal CA1 - CA4 regions and the subicular complex. In terms of mutual information (0.72), they align more clearly compared to clustering of baseline characterizations based on fractional anisotropy and mean transmittance (0.40), as well as CL-2D (0.61).

Without any supervisory signal, CL-3D features form a well-structured embedding space, following the general regional organization pattern of the hippocampus and additionally highlight an expected functional rostro-caudal heterogeneity. Projecting deep texture features to unfolded space using HippUnfold enables subsequent comparison with diverse modalities. This work thus lays the foundation for incorporating 3D-PLI texture information into a comprehensive multimodal mapping of the human hippocampus.

Primary author: OBERSTRASS, Alexander

Co-authors: DEKRAKER, Jordan (McGill University); PALOMERO-GALLAGHER, Nicola (Juelich Forschungszentrum); Dr MUENZING, Sascha E. A (Forschungszentrum Juelich); EVANS, Alan C. (McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, Canada.); Prof. AXER, Markus

(Forschungszentrum Juelich); AMUNTS, Katrin (Forschungszentrum Jülich (INM-1) and Cécile and Oskar Vogt Institute for Brain Research, University Hospital Düsseldorf, Medical Faculty, Heinrich-Heine-University Düsseldorf); DICKSCHEID, Timo (Forschungszentrum Jülich)

Presenter: OBERSTRASS, Alexander

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