Spatial Contrastive Learning for Anchoring Histological Human Brain Sections Within a Reference 3D Model

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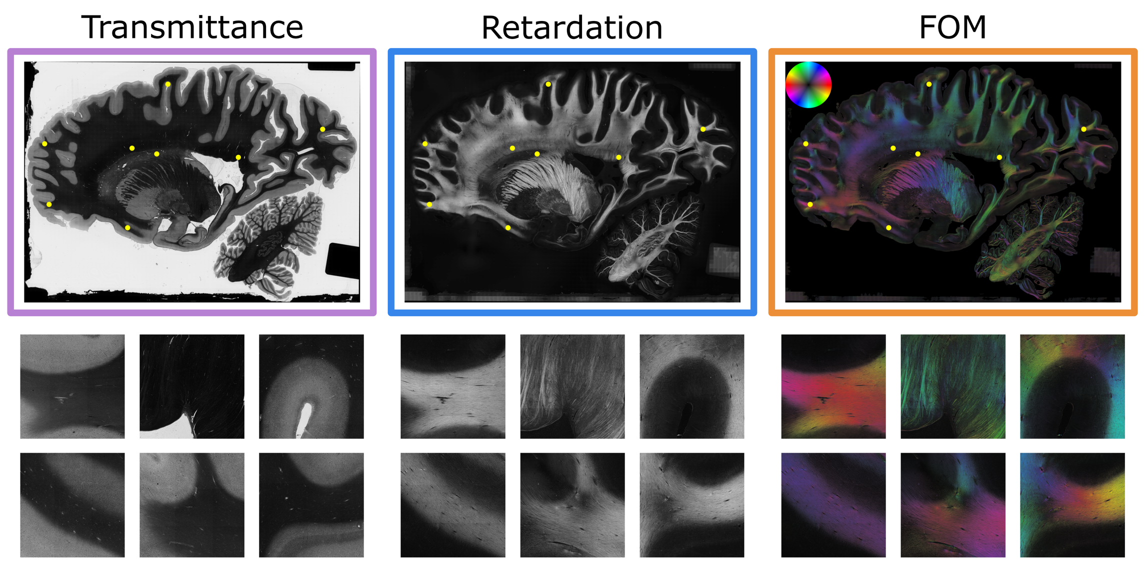
Introduction

Brain atlases serve as a spatial framework for **comparing brain structures** across individuals and imaging modalities. Histological techniques like **Nissl staining** and **3D-PLI** offer complementary insights into cytoarchitecture and fiber architecture, respectively. To enable integrative analysis, these sections must be aligned to a standard 3D reference space. Traditional image registration methods rely on estimating transformations from image features or landmarks, but they often require manual handling, are sensitive to modality differences, and scale poorly to large datasets.

We propose an alternative, **learning-based approach** that anchors image patches from histological sections into a 3D reference brain using spatial contrastive learning. By training on high-resolution image patches, we learn embeddings that capture local microstructural patterns. We hypothesize that these representations support coarse **spatial anchoring** via cosine similarity in latent space, yielding patch correspondences that define point pairs for estimating 3D transformations.

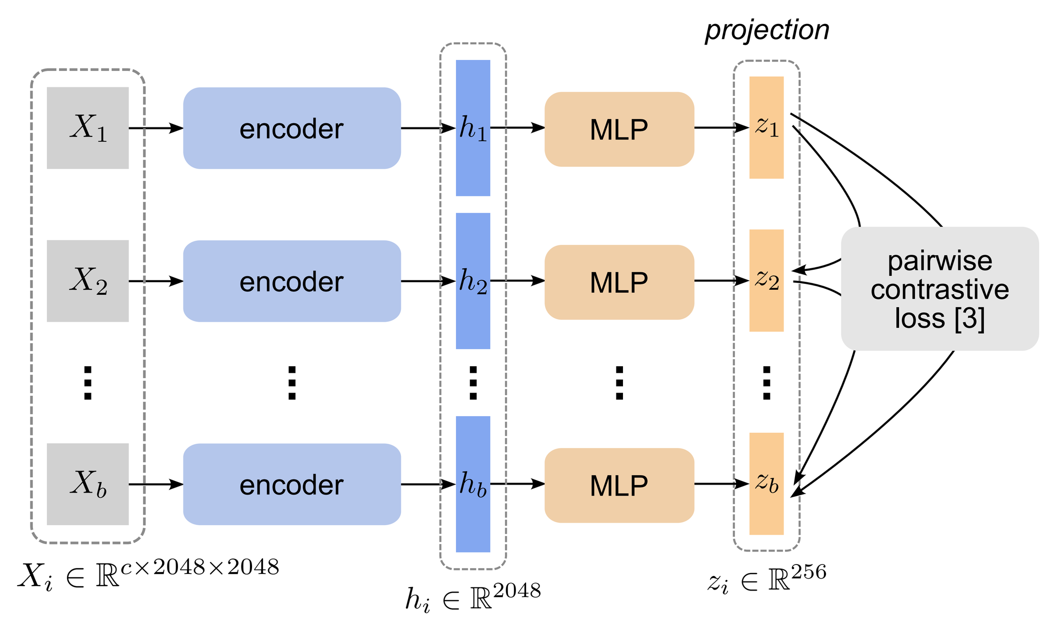
3D-PLI Human Brain Sections



3D-PLI: Enables the visualization of single nerve fibers and fiber bundles with a resolution of 1.33μm/px.

Available brain tissue:
- Left hemisphere of a single brain
- Cutting results in 1260 brain slices
- Section thickness: 50 μm
- Registration into MNI-Colin27 space
- Number of PLI sections is lower
- After filtering: 26 sections were used
- PLI sections were distributed irregularly across the right-left axes

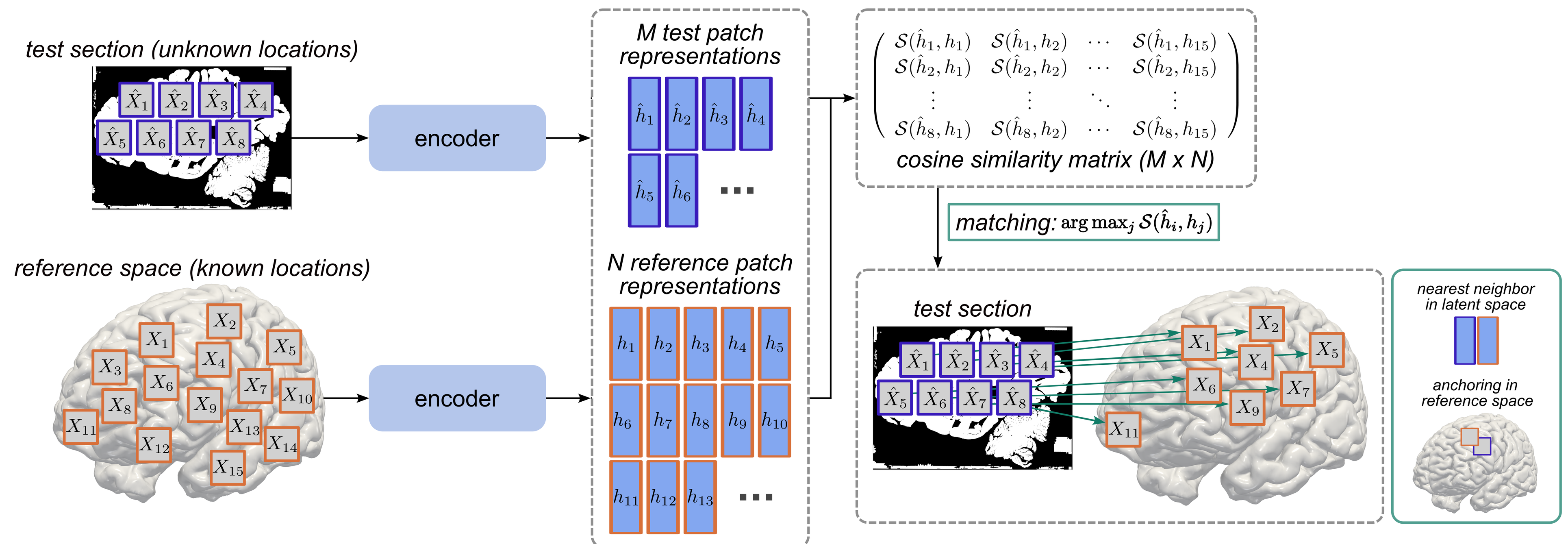
Spatial Contrastive Learning



$$\ell_{dist}(i) = -\frac{1}{\sum_{j=1}^{b}\mathbb{I}_{i\neq j}\,\omega_{ij}}\sum_{j=1}^{b}\mathbb{I}_{i\neq j}\,\omega_{ij}\log\frac{\exp(\langle z_i, z_j\rangle/\tau)}{\sum_{k=1}^{b}\mathbb{I}_{k\neq i}\exp(\langle z_i, z_k\rangle/\tau)}$$

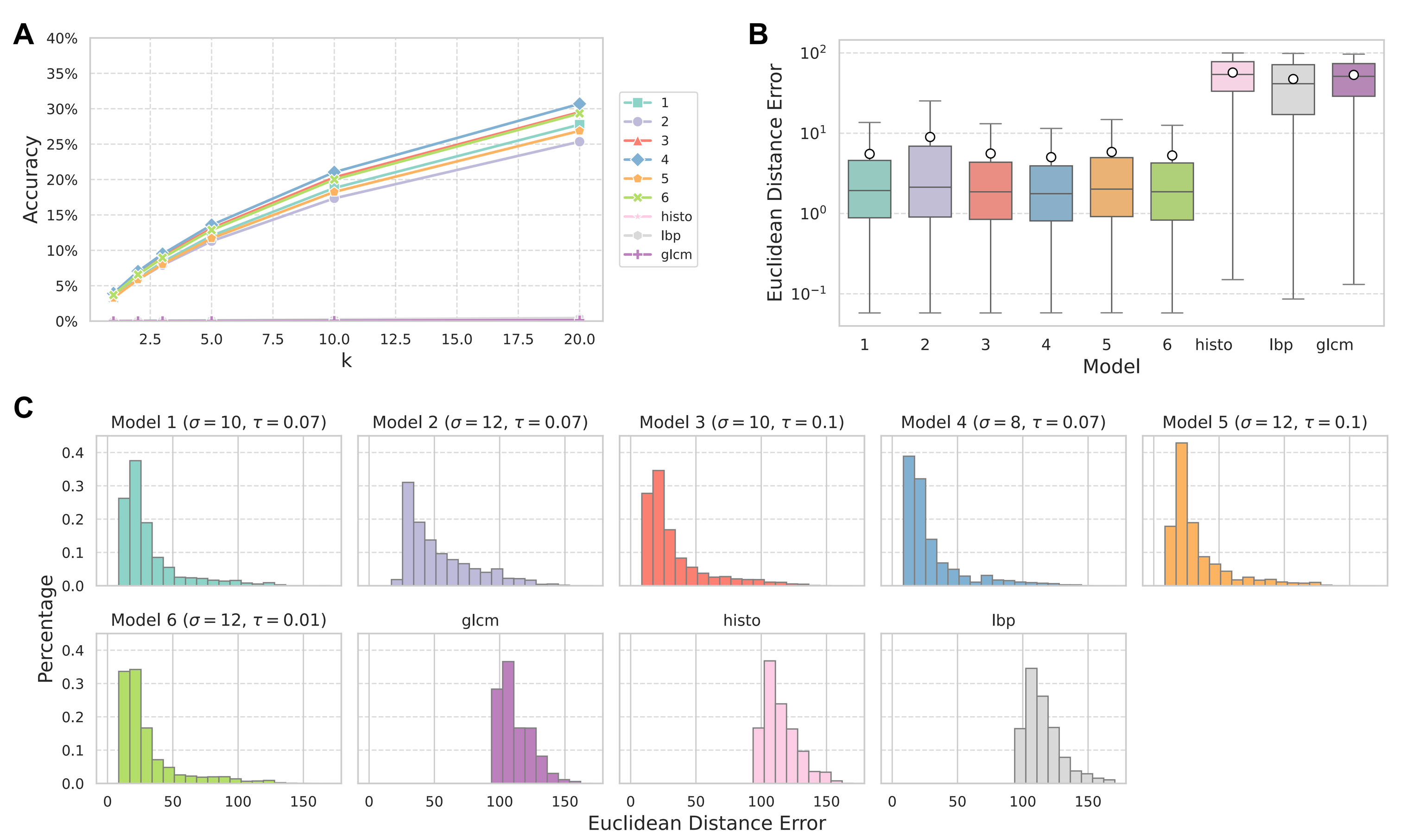
Number of samples in a batch; Scalar product; Temperature; Sample in the batch at index i; Weighting of pairs using RBF kernel; L2 normalized feature vector computed by the neural network

Spatial Anchoring Within 3D Reference Model



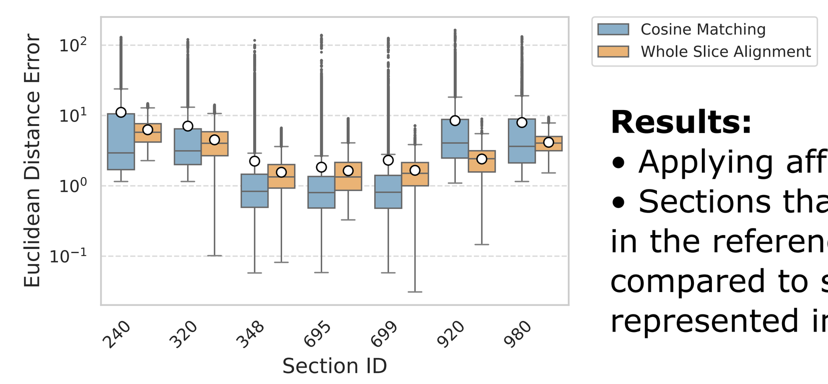
- Sample image patches from the test section and the reference sections, and then encode them.
- Determine the most similar reference patch in latent space for each test patch.
- Similarity is defined by the cosine similarity between the representations of any two patches.
- Matched patches then give rise to corresponding point pairs between the image coordinate system and the 3D model.

Zero-Shot Spatial Anchoring of Image Patches



A: The top-k accuracy demonstrates how well the most similar patches in the latent space correspond to the geometrically closest points in MNI space.
B: Boxplot of euclidean distance errors between the test points and matched reference points. Whiskers are shown up to the 90th percentile.
C: Histogram of outlier euclidean distance errors.

Improving Whole Slice Alignment



Results:
- Applying affine alignment significantly reduces outliers.
- Sections that correspond to regions with denser samples in the reference frame exhibit lower alignment errors compared to sections from regions that are more sparsely represented in the reference frame.

Conclusion

- Our work demonstrates that meaningful features can be learned from 3D-PLI histological sections, enabling effective spatial anchoring of both individual image patches and whole brain slices within a reference frame.
- Our analysis shows that the density of the reference frame affects the precision of the anchoring process.
- The affine transformation for aligning the whole brain slice is estimated purely from correspondences derived from matching single image patches. We show that this leads to a subsequent improvement in anchoring accuracy.
- This method generalizes across histological imaging modalities, including 3D-PLI and Nissl staining, as well as across subjects.

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ACKNOWLEDGEMENTS
This project received funding from the European Union’s Horizon 2020 Research and Innovation Programme, grant agreement 101147319 (EBRAINS 2.0 Project), and the Helmholtz Association port-folio theme "Supercomputing and Modeling for the Human Brain", and the Helmholtz Association’s Initiative and Networking Fund through the Helmholtz International BigBrain Analytics and Learning Laboratory (HIBALL) under the Helmholtz International Lab grant agreement InterLabs-0015, and by HELMHOLTZ IMAGING, a platform of the Helmholtz Information & Data Science Incubator [X-BRAIN, grant number: ZT-I-PF-4-061]. Computing time was granted through JARA on the supercomputer JURECA-DC at Jülich Supercomputing Centre (JSC).