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CytoNet: A Deep Neural Network for Whole-brain Characterization of Human Cytoarchitecture

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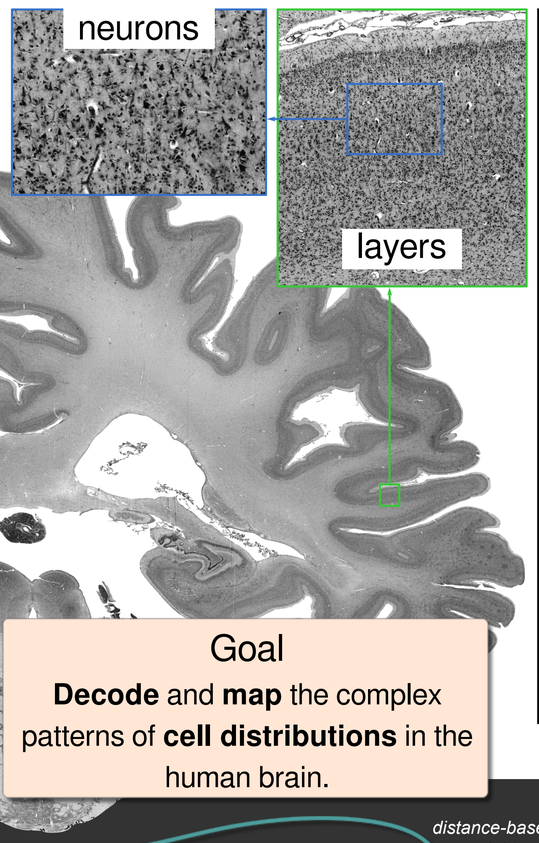
Cytoarchitectonic Analysis in Histological Brain Sections

The characterization of **cytoarchitecture** in the **human brain** provides an essential building block for the creation of a high-resolution multi-modal **brain atlas** [1,2]. **Cytoarchitecture** is defined by the spatial organization of neuronal cells, including their shape, density, size, cell type, as well as their columnar and laminar arrangement, which differ between brain regions. High-throughput **light-microscopic scanning** of large, cell-body stained histological sections obtained by sectioning **postmortem human** brains enables detailed examination of cytoarchitectonic organizational principles across multiple brain samples, which is mandatory to capture the highly variable cytoarchitectonic organization.

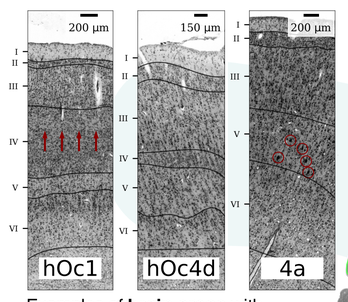
Histological processing & Imaging [1,2]
- **Sectioning**
  - 6000-8000 sections per brain
  - Thickness: 20µm
- **Staining** for cell bodies
- **Light-microscopic** scanning (1µm/px)

Sectioning of a **postmortem human brain** that was embedded in **paraffine**



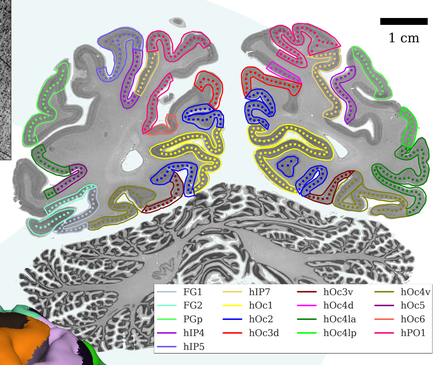
Goal

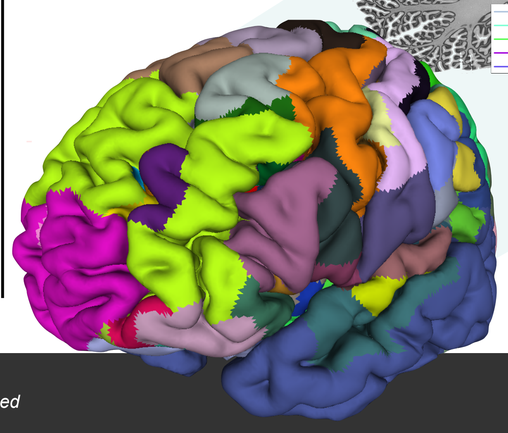
Decode and **map** the complex patterns of **cell distributions** in the human brain.



Examples of **brain areas** with different **cytoarchitecture**

Mapping of cytoarchitectonic areas in a histological brain section

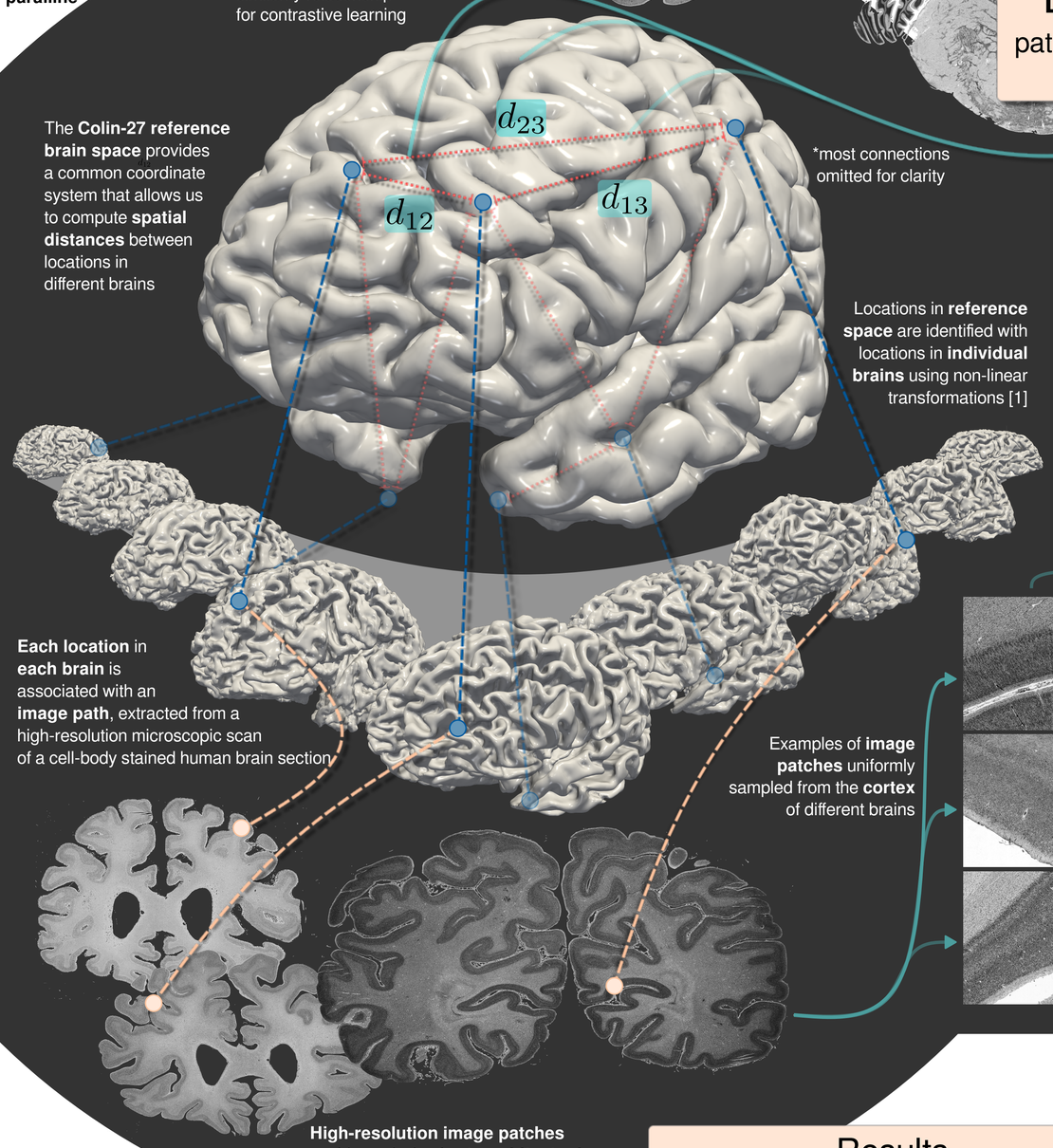




Julich-Brain [1] cytoarchitectonic human brain atlas

Pairwise **euclidean distances** in the reference **coordinate space** define the similarity relationship for contrastive learning

The **Colin-27 reference brain space** provides a common coordinate system that allows us to compute **spatial distances** between locations in different brains



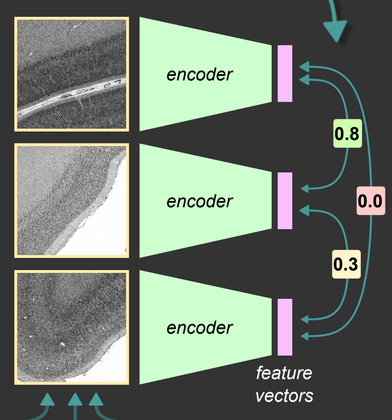
*most connections omitted for clarity

Locations in **reference space** are identified with locations in **individual brains** using non-linear transformations [1]

Each location in **each brain** is associated with an **image path**, extracted from a high-resolution microscopic scan of a cell-body stained human brain section

High-resolution image patches enable analysis of **cytoarchitectonic organization** and are used as input for our **deep neural networks**

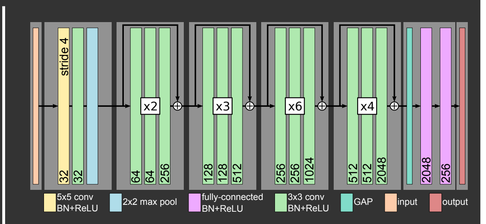
distance-based weights



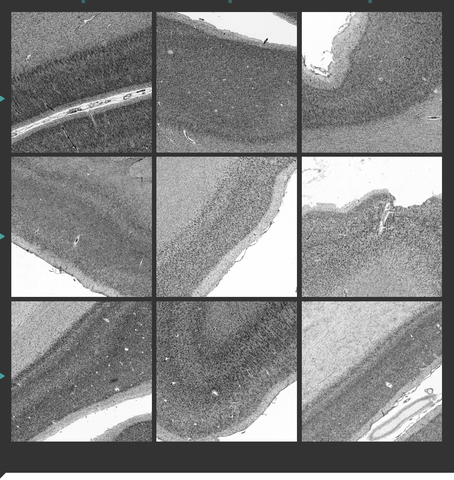
Idea

Spatially **close locations** in the brain are likely to **share** cytoarchitectonic structures.

The contrastive training objective **attracts** feature representations of **spatially close** samples, while **repelling** representations of **distant** samples.



The model uses a modified **ResNet50/101 architecture** [3,4] with an additional downsampling head that accounts for the **large input image patch size**. Fully-connected projection layers are replaced by a **linear classifier** when **finetuning** for brain area classification.



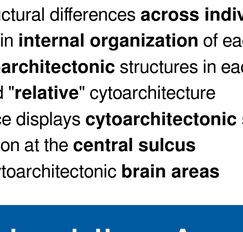
Examples of **image patches** uniformly sampled from the **cortex** of different brains

Dataset, training, evaluation
- 9 brains, 4128 sections
- Patch size: 2048px@2µm/px
- Batch size: 2048
- **Hardware configuration**
  - JURECA-DC [5] (16 nodes)
  - 64 A100 GPUs
- **Linear finetuning**
  - 135600 samples
  - 113 annotated brain areas
  - 80/20 train/test section split
  - 8/1 test/validation brain split
  - Comparison to training from **Scratch** and **SupCon** [4]
- **Feature embedding analysis**
  - UMAP [6] (subsample 50)
  - Color coding by Julich Brain [1]

Distance-Weighted Contrastive Loss

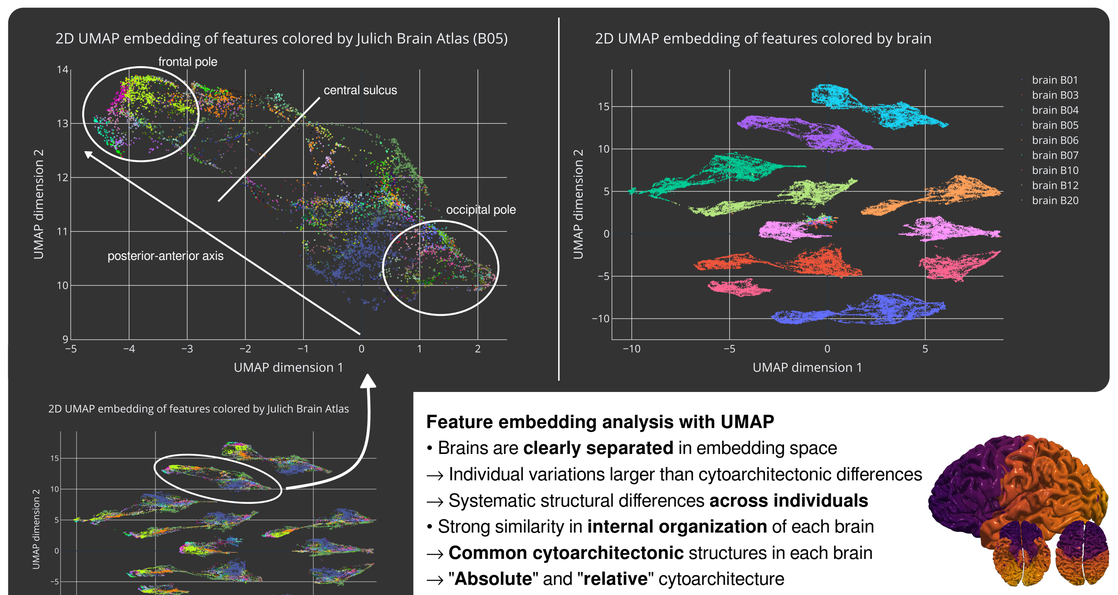
$$\mathcal{L} = \frac{1}{B}\sum_{i=1}^{B} \frac{1}{\sum_{j=1}^{B} g(d_{ij})} \sum_{j=1}^{B} \mathbb{1}_{i\neq j}\, g(d_{ij}) \log \frac{\exp(\langle z_i, z_j/\tau\rangle)}{\sum_{k=1}^{B} \mathbb{1}_{i\neq k} \exp(\langle z_i, z_k/\tau\rangle)}$$

batch size | euclidean distance | model output | temperature



The **distance transfer function** converts euclidean distances computed in the reference space into weights that define sample similarity for the contrastive loss.

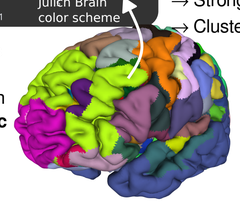
Contrastive Learning from 3D Spatial Relationships



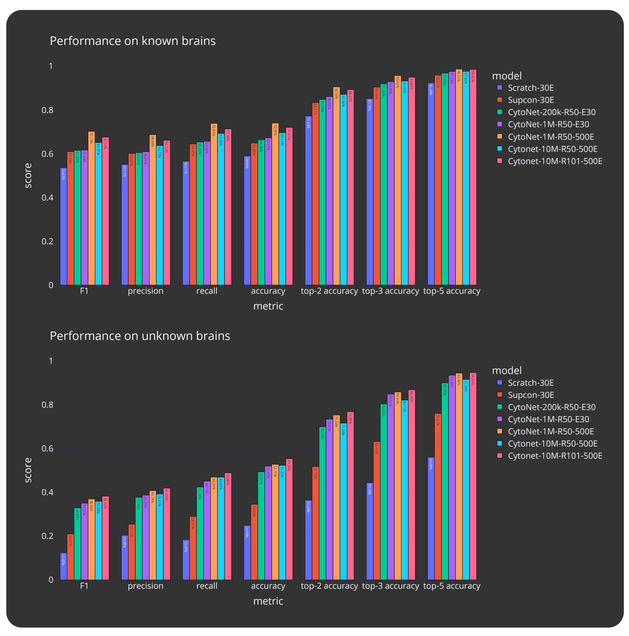
Feature embedding analysis with UMAP
- Brains are **clearly separated** in embedding space
  → Individual variations larger than cytoarchitectonic differences
  → Systematic structural differences **across individuals**
- Strong similarity in **internal organization** of each brain
  → **Common cytoarchitectonic** structures in each brain
  → "**Absolute**" and "**relative**" cytoarchitecture
- Embedding space displays **cytoarchitectonic structures**
  → Strong separation at the **central sulcus**
  → Clustering of cytoarchitectonic **brain areas**

First UMAP dimension on the surface of brain B20, showing a clear separation at the **central sulcus**.

The **latent space** of CytoNet is anatomically **highly plausible**, demonstrating it's ability to learn **meaningful cytoarchitectonic** representations from **spatial relationships**.



Embedding Analysis of Learned Feature Representations



Results

CytoNet outperforms **existing methods** for **brain area classification**, particularly on unknown brains. Learned features are **anatomically highly plausible** and reflect important principles of **cytoarchitectonic organization**. **CytoNet** is the first step towards a foundation model for **microstructural brain organization**.

Classification Metrics for Automatic Brain Mapping
E30/E500 - Epochs for finetuning
R50/R101 - ResNet50/101-based encoder
200k/1M/10M - CytoNet pre-training sample count

Performance for Large-scale Automatic Brain Mapping

[1] Amunts et al., 2020. Julich-Brain: A 3D probabilistic atlas of the human brain's cytoarchitecture. Science 369, 988.
[2] Amunts et al., 2013. BigBrain: An Ultrahigh-Resolution 3D Human Brain Model. Science 340.
[3] Schiffer et al., 2021. Contrastive Representation Learning For Whole Brain Cytoarchitectonic Mapping In Histological Human Brain Sections, in: ISBI 2021. pp. 603–606.
[4] He et al., 2016. Deep residual learning for image recognition, in: 2016 IEEE Conference on Computer Vision and Pattern Recognition (CVPR). pp. 770–778.
[5] Thörnig, 2021. JURECA: Data Centric and Booster Modules implementing the Modular Supercomputing Architecture at Jülich Supercomputing Centre. JLSRF 7.
[6] McInnes et al., 2018. UMAP: Uniform Manifold Approximation and Projection. Journal of Open Source Software 3, 861.

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