Contrastive Learning from Probabilistic Maps for Cytoarchitectonic Classification of the Cortex

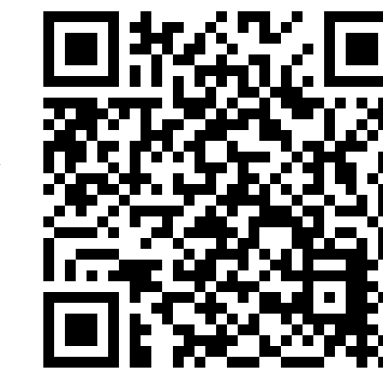Christian Schiffer[1,2], Katrin Amunts[1,3], Timo Dickscheid[1,2,4]

[1]Institute of Neuroscience and Medicine (INM-1), Research Centre Jülich, Germany
[2]Helmholtz AI, Research Centre Jülich, Germany
[3]Cécile & Oscar Vogt Institute for Brain Research, University Hospital Düsseldorf, Germany
[4]Institute of Computer Science, Heinrich-Heine-University Düsseldorf, Germany
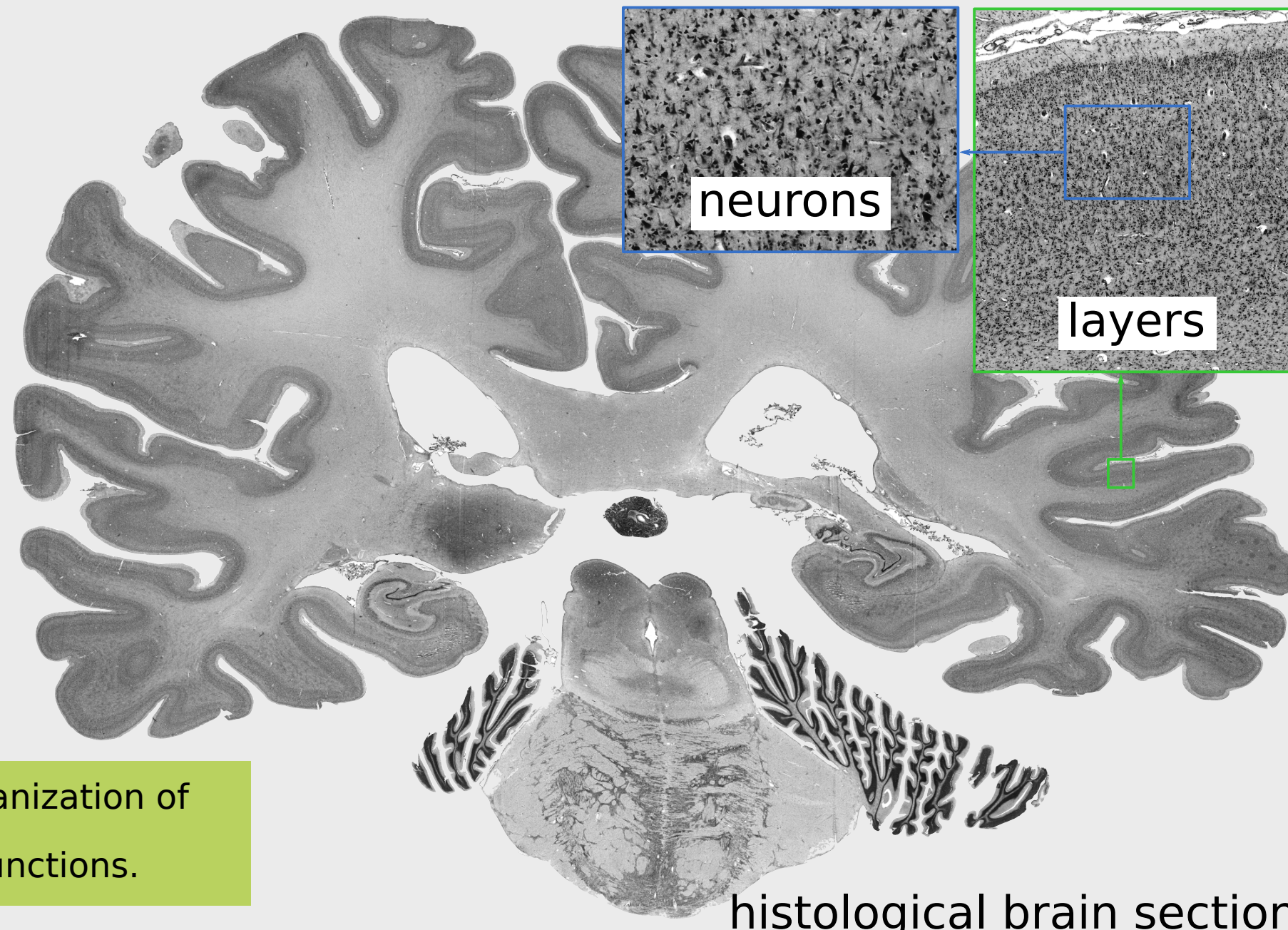
Visit us!

✉ c.schiffer@fz-juelich.de

JÜLICH Forschungszentrum

HELMHOLTZ AI

HIBALL Helmholtz International BigBrain Analytics & Learning Laboratory

hhu Heinrich Heine Universität Düsseldorf

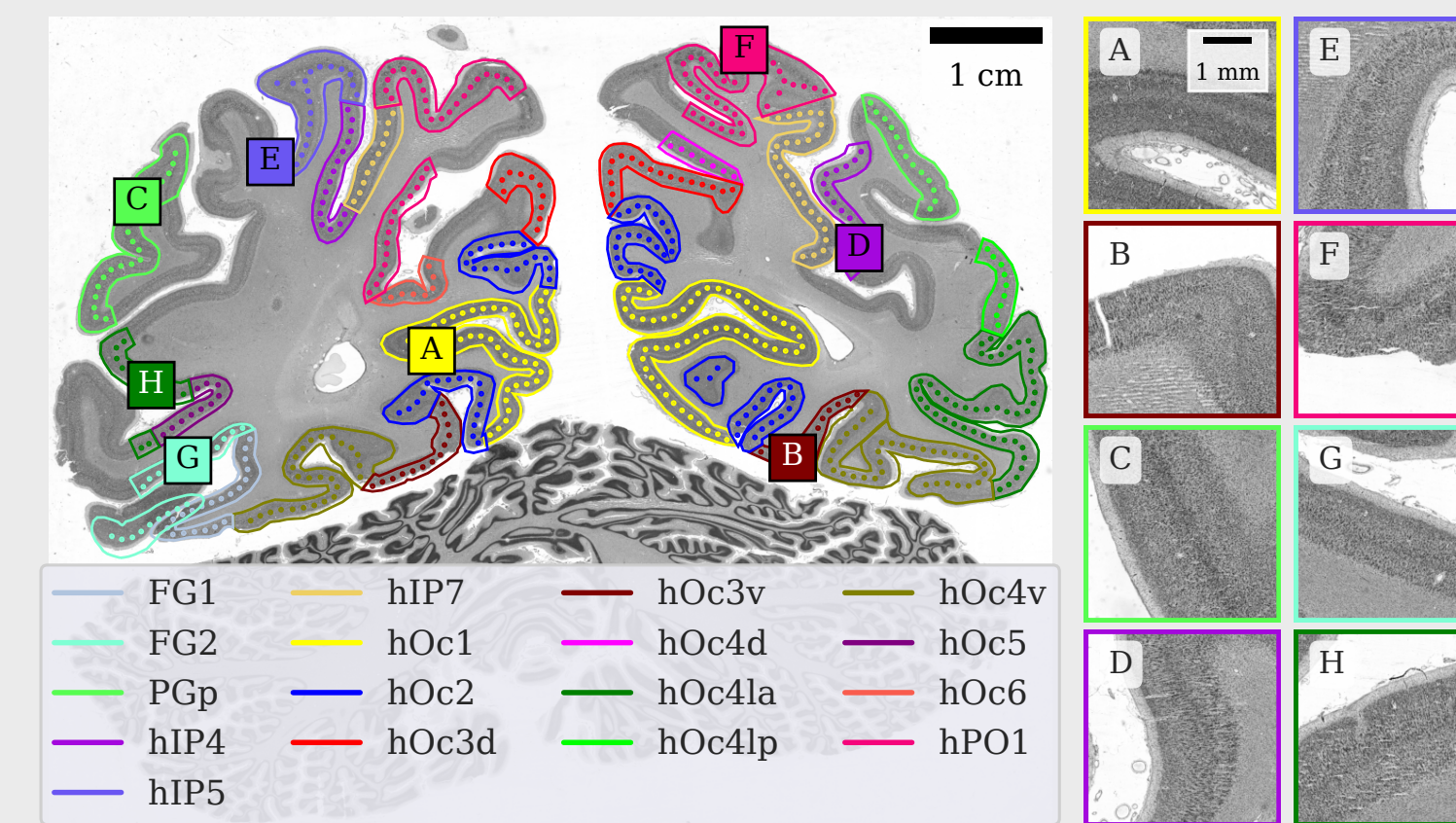## Histological Human Brain Sections

- **Postmortem** human brains
- Fixation in paraffine
- **Cut** into histological sections
  - 6000-8000 sections per brain
  - Thickness: 20µm
- Staining for **cell bodies**
- **Light-microscopic** imaging
  - Resolution: 1µm/pixel
  - up to 100'000 x 136'000 pixels
  - up to 15 GB per image

Goal: Study the microstructural organization of the human brain to understand its functions.

neurons

layers

histological brain section

Cytoarchitectonic Brain Areas

FG1, FG2, PGp, hIP4, hIP5, hIP7, hOc1, hOc2, hOc3d, hOc3v, hOc4d, hOc4la, hOc4lp, hOc4v, hOc5, hOc6, hPO1

hOc1   hOc4d   4a

- Areas defined by the spatial organization of neurons into **layers** and **columns**
- Indicators for **connectivity** and **function**
- Microstructural reference for **brain atlases** [1, 2]

Goal: Automatically identify cytoarchitectonic areas using **deep learning** to enable large-scale analysis

Challenges: limited annotations; complex and ambiguous structures; multi-scale patterns; artifacts


Probability-guided Contrastive Feature Learning

Idea: Train a neural network to map image patches from **similar brain areas** to **similar feature vectors**
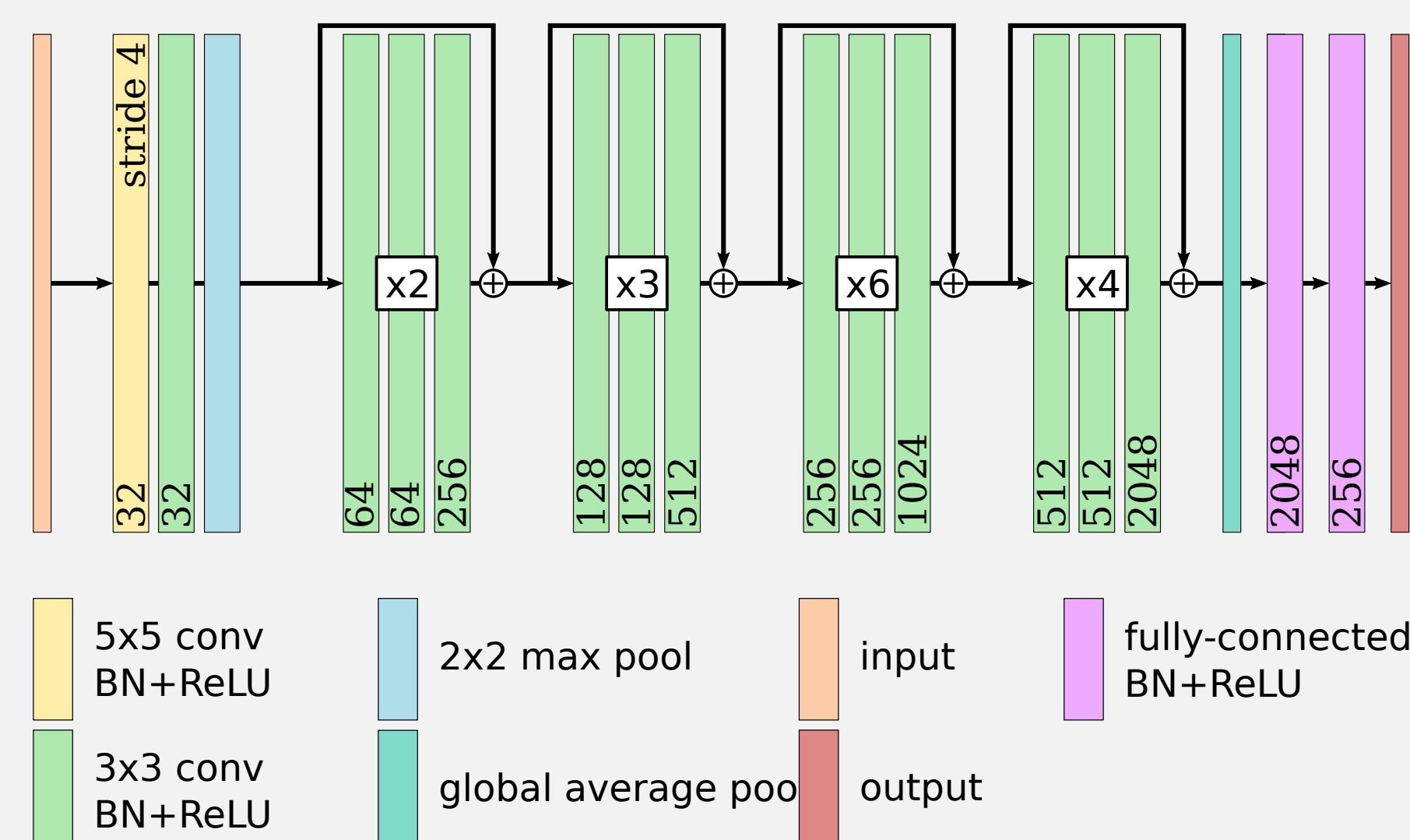
Cytoarchitecture Learning

hOc1   4a
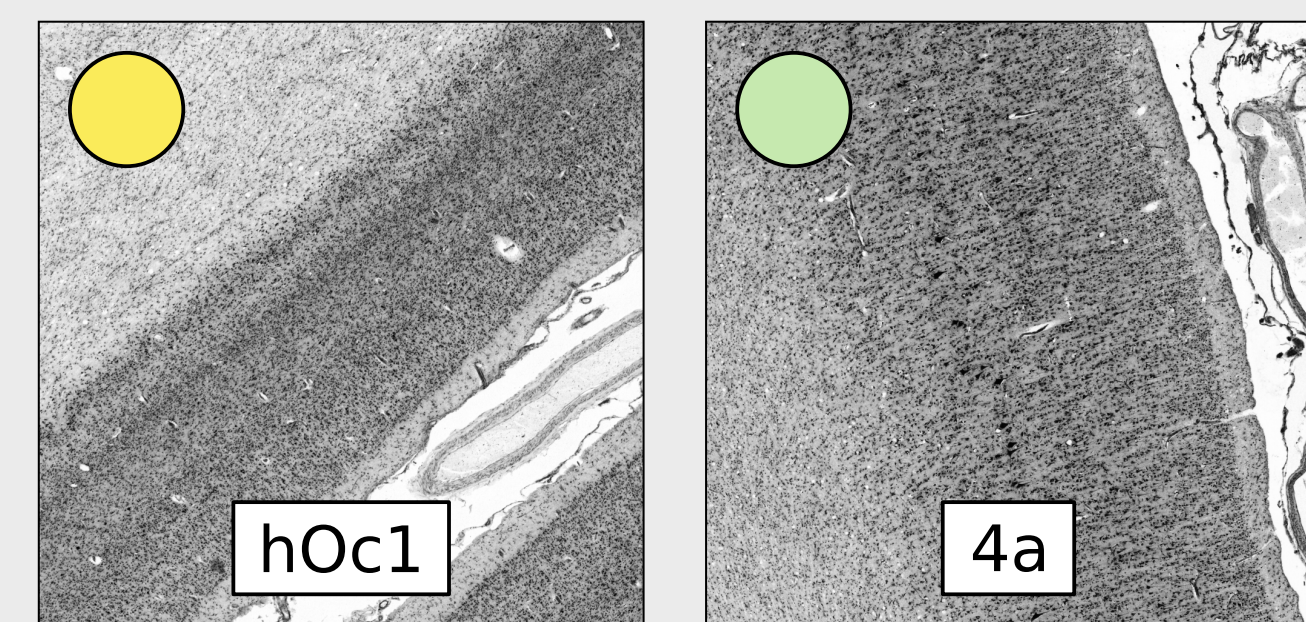
- Extract **image patches** from microscopic images
- Each image patch is associated with a discrete **probability vector** over cytoarchitectonic areas
- Probability vector indicates **how likely** a specific area occurs at a **specific location** in the brain
- Pairwise **similarity weight** is defined as cross-correlation between probability vectors
  - High correlation → similar area → **similar features**
  - Low correlation → different area → **diferent features**
- **Contrastive learning:** Learn by comparing image patches in a training batch [3]
- Learned features enable cytoarchitecture classification

visual area hOc1

motor area 4a
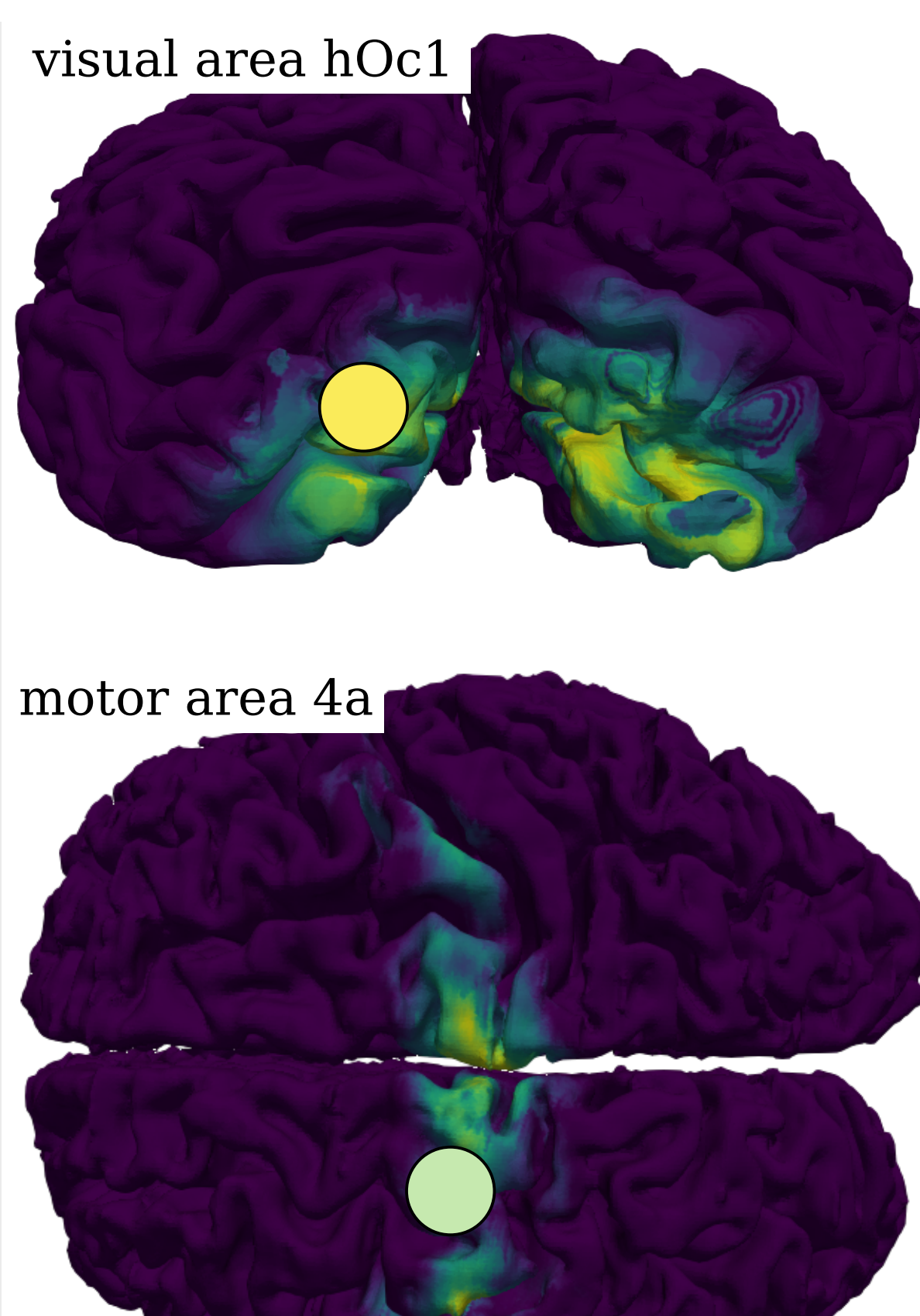
Probabilistic maps from Julich-Brain [1] indicate the occurence probability of areas at different locations

Training & Neural Network Architecture

stride 4

x2   x3   x6   x4

32 32   64 64 256   128 128 512   256 256 1024   512 512 2048   2048 256

- 5x5 conv BN+ReLU
- 3x3 conv BN+ReLU
- 2x2 max pool
- global average pool
- input
- output
- fully-connected BN+ReLU

- Based on **ResNet50**
- **Custom head** to account for large input image size
- **Input size:** 2048px@2µm/px
- **Batch size:** 2048 images
- **Projection head** [3]
- 3679 brain sections (8 brains)
- **Hardware configuration**
  - JURECA-DC [4] (16 nodes)
  - **GPUs:** 64 NVidia A100
  - **Training time:** 18 hours

Probabiliy-guided Contrastive Loss

Idea: Compute a continuous similarity indicator for the contrastive loss based on corrleation of probabilistic maps

feature vectors encoded by a neural network

$$z_i = f(X_i)$$

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

similarity weight between two probability vectors

$$\omega_{ij} = \langle p_i, p_j \rangle$$

probability vector associated with an image patch $p_i \in \mathbb{R}^P$

image patch extracted from a microscopic brain scan X_i

number of image patches in a training batch N

**temperature** scaling parameter τ

Graph Neural Networks for Cytoarchitecture Classification

Idea: Model cytoarchitecture classification as **graph node classification task** on approximate brain reconstructions

Graph-based Framework

- Approximately reconstruct **brain surface meshes**
- Associate mesh nodes with **image locations**
- Compute **deep cytoarchitectonic features**
- Add **additional features** (location, probabilistic maps, annotations) to graph nodes
- Train **graph neural networks (GNNs)** to classify corresponding **cytoarchitectonic areas** for each node in the graph [5]
- GNNs combine local local **high-resolution image features** with **neighborhood information**

reconstructed brain surface

corresponding image locations
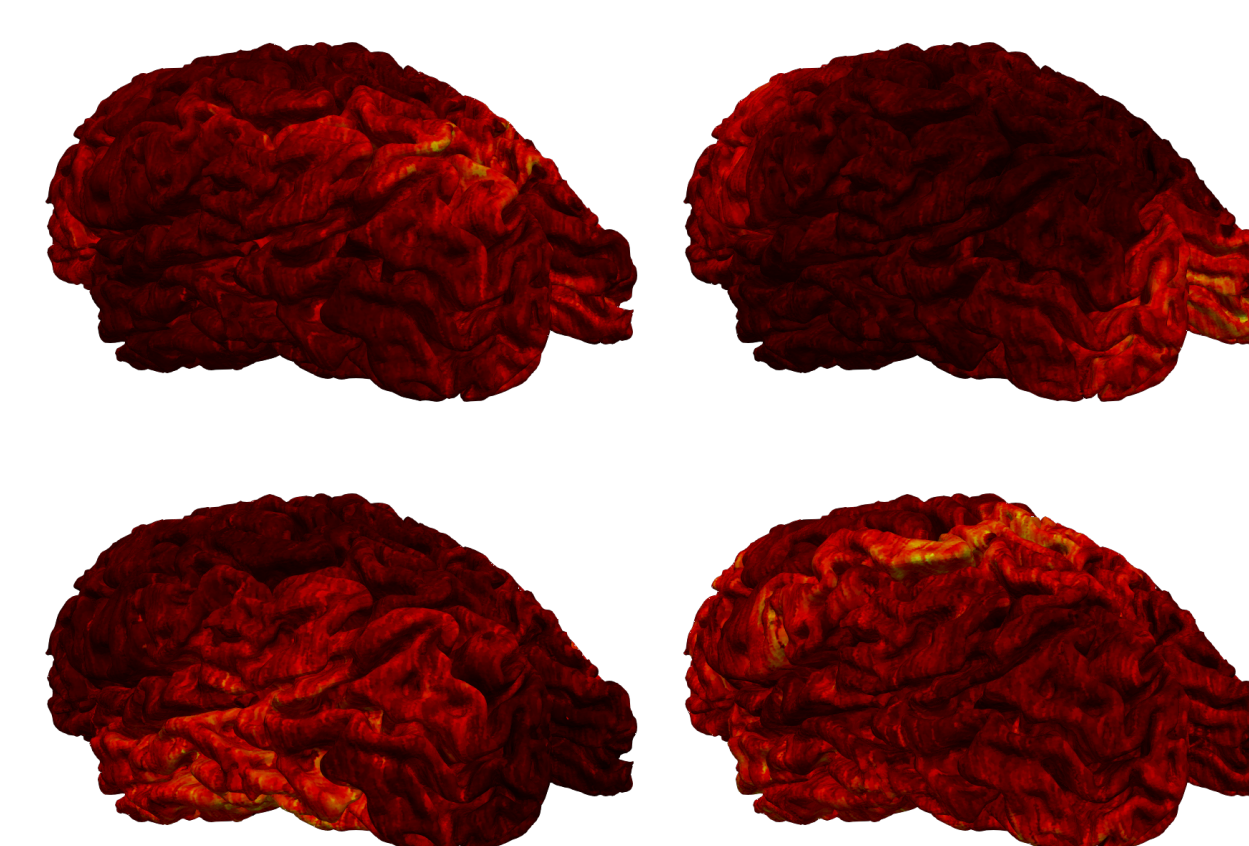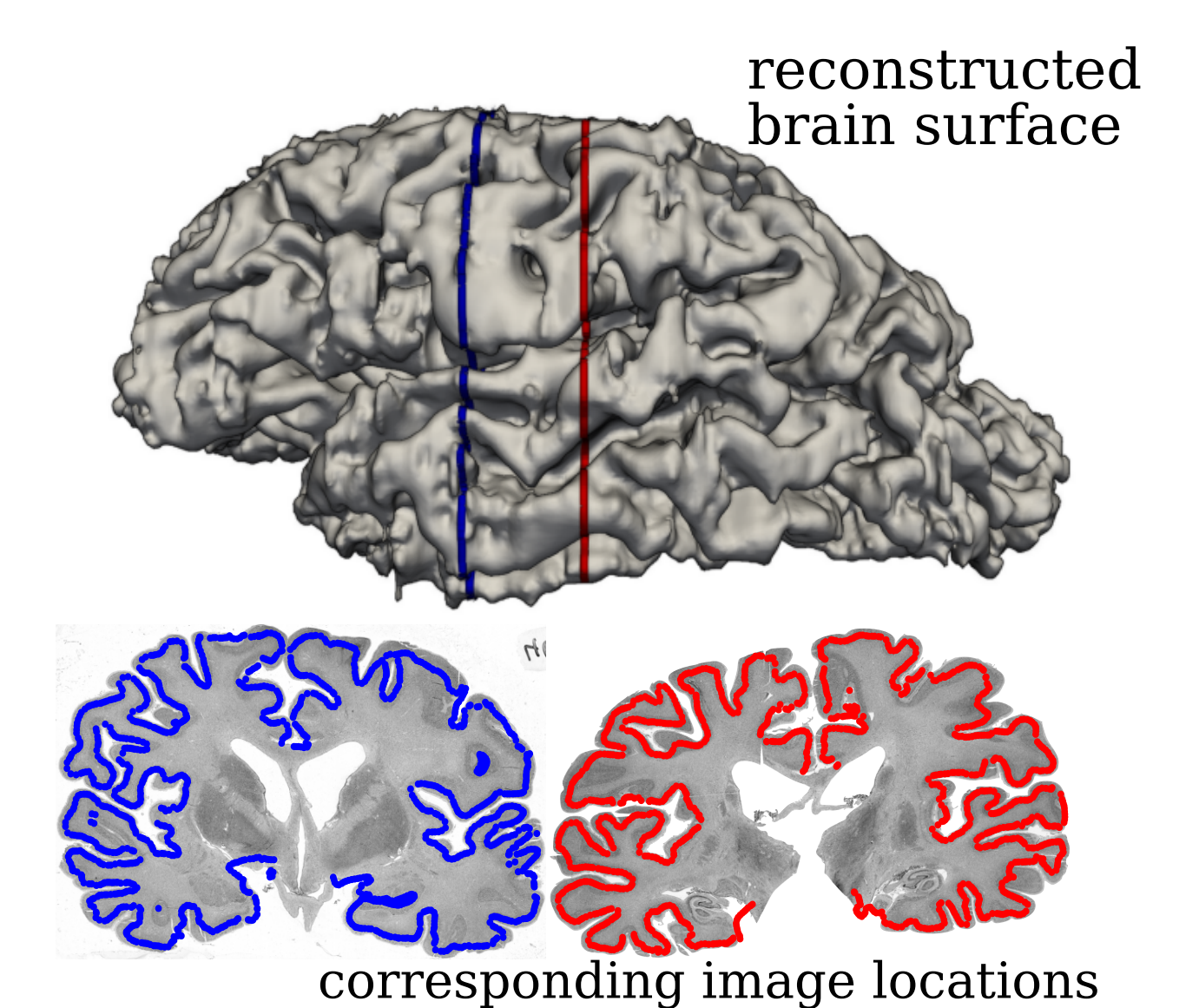
cytoarchitectonic features

Training & Evaluation

- Training with **categorical cross-entropy** using available expert annotations
- 1860 sections from 7 brains (80% train, 20% test)
- 325 sections from 8th brain (transferability check)
- **Architecture:** Graph Attention (GAT) [6] (3 layers)
- **Input:** cytoarchitecture features, probability vectors, canonical spatial coordinates [5]
- Performance measurement using **macro-F1 score**

Conclusion & Future Work

- **Probability-guided contrastive learning** enables learning of useful cytoarchitectonic features without annotated training data
- **Graph Neural Networks** efficiently integrate local features from high-resolution images with neighborhood information encoded in graphs
- **Future work**
  - **End-to-end** learning of image and graph features
  - **Cluster analysis** as basis for **data-driven brain parcellation** and knowledge discovery
  - Investigation of **limited transferability** to unseen brains
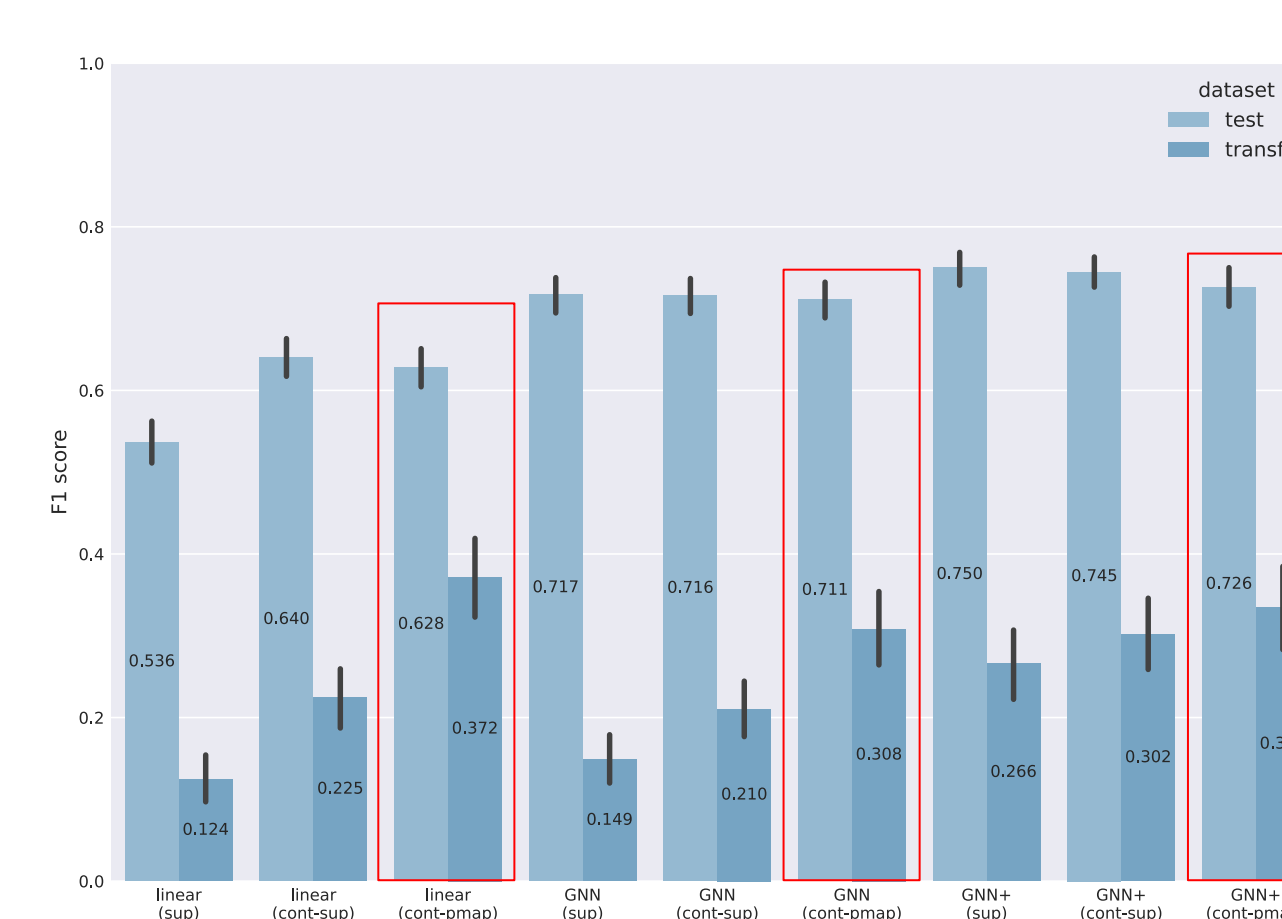
Macro F1-scores for known (test) and unknown (transfer) brains. **sup:** supervised; **cont-sup:** contrastive supervised [5]; **cont-pmap:** contrastive pmap; **linear:** linear classification; **GNN:** GNN w. cytoarchitecture features; **GNN+:** GNN w. cytoarchitecture features, pmaps, and coordinates.

1. Amunts, K. et al. Julich-Brain: A 3D probabilistic atlas of the human brain's cytoarchitecture. Science 369 (2020).
2. Amunts, K. & Zilles, K. Architectonic Mapping of the Human Brain beyond Brodmann. Neuron 88 (2015).
3. Chen, S. et al., A simple framework for contrastive learning of visual representations. ICML, (2020)
4. Thörnig, P., JURECA: Data Centric and Booster Modules implementing the Modular Supercomputing Architecture at Jülich Supercomputing Centre. JLSRF 7 (2021)
5. Schiffer, C. et al. 2D Histology Meets 3D Topology: Cytoarchitectonic Brain Mapping with Graph Neural Networks. MICCAI (2021)
6. Veličković, P. Graph Attention Networks, arXiv:1710.10903 (2018)