DENOISING DIFFUSION PROBABILISTIC MODELS FOR IMAGE INPAINTING OF CELL DISTRIBUTIONS IN THE HUMAN BRAIN

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Introduction

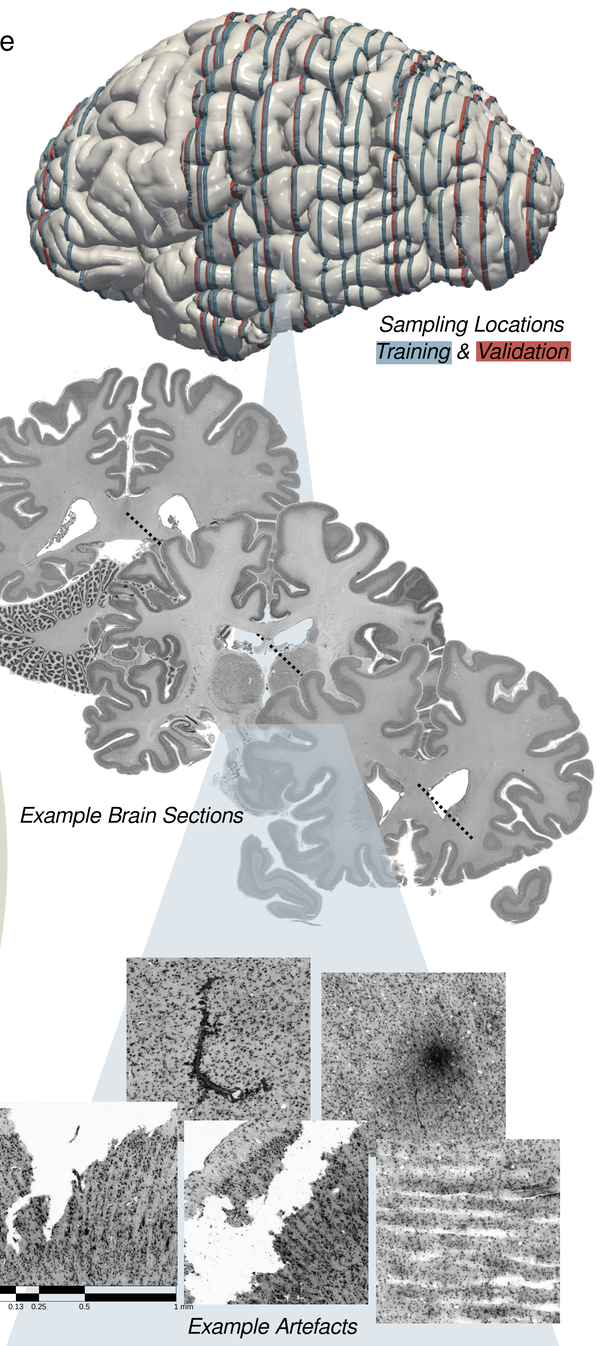
Recent advances in imaging and machine learning enable the imaging of whole human brains at **cellular-level**, where novel methods automate the **cytoarchitectonic mapping** [1] and **detection of cell bodies** [2].
However, the presence of processing induced **artefacts** in the image data caused by missing sections, tears in the tissue or staining errors, need to be addressed to facilitate the analysis.

We propose a method to **fill in missing information** in the high-resolution microscopic scans of histological brain sections by using **denoising diffusion probabilistic models**.

Data and Artefacts

The training and validation data were derived from the **BigBrain** dataset [3] at 1micron resolution. All the data was **screened for artefacts** to ensure **that only intact** data was used to train and validate the model.

64 sections of the BigBrain dataset were used for **training** and **10** sections were used for **validation**.

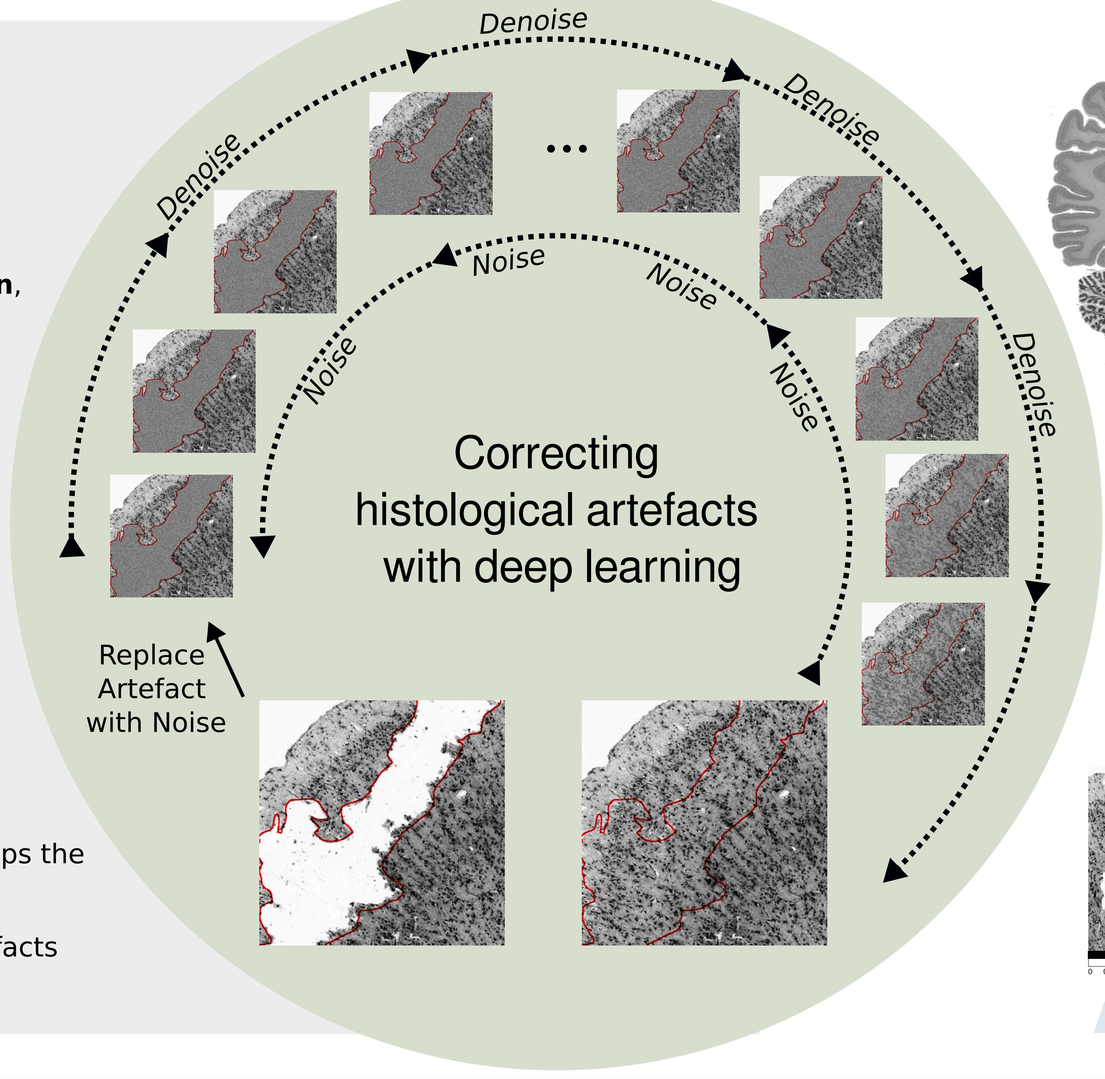


Denoising Diffusion Probabilistic Models

- **DDPM**s [4] map between noise and data distributions by gradually removing noise
- The model architecture closely follows [4] a deep **residual** U-Net with **Self-Attention**, **SiLU** activation functions**, 256** diffusion steps and **a cosine noise schedule**
- Our DDPM was trained on 1.25 million histological image patches of size 1 mm^2 @ 1 micron resolution
- The model was trained for 12 hours on 64 GPUs on JURECA-DC [5].

RePaint

- **RePaint** [6] extends our model to fix artefacts and fill in missing data
- The DDPM gets conditioned on the known part in every diffusion step
- To increase the correlation the methods loops the diffusion steps multiple times
- This method needs annotations of the artefacts (here done by hand)



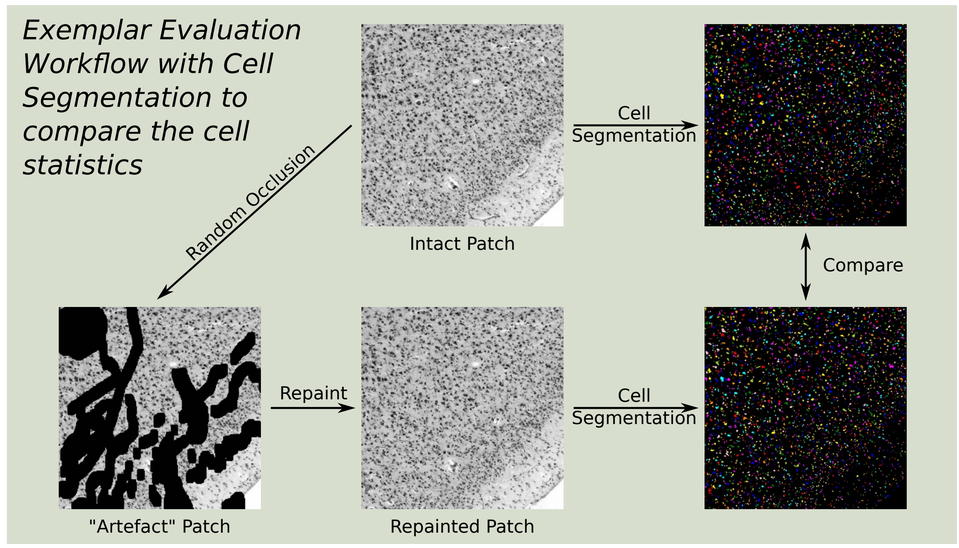
How do we know that the generated data matches the cell distribution?

Evaluating the Cell Distribution with Downstream Models

- Estimating the cell distribution is **intractable**
- Compare characteristics
  - **Density**
  - **Size**
  - **Position**
  - **Arrangement**

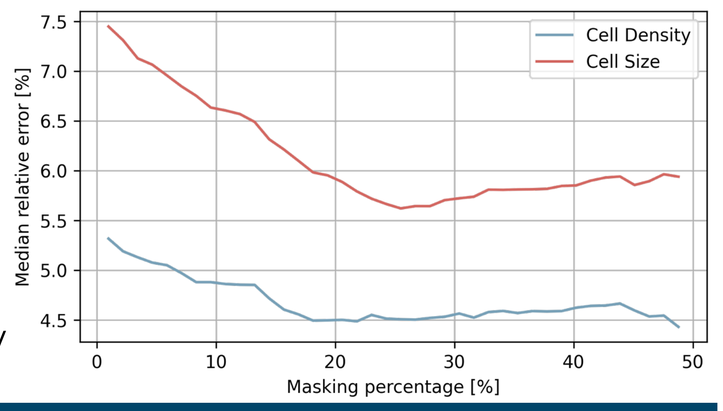
  } **Cytoarchitecture**

- Repaint **known areas** with our diffusion model in **intact patches**
- We evaluated the model on **10,000 patches**
- The repaint areas were randomised ranging from **5 to 50%** of a given patch
- **Established models** are used to extract charactersitics



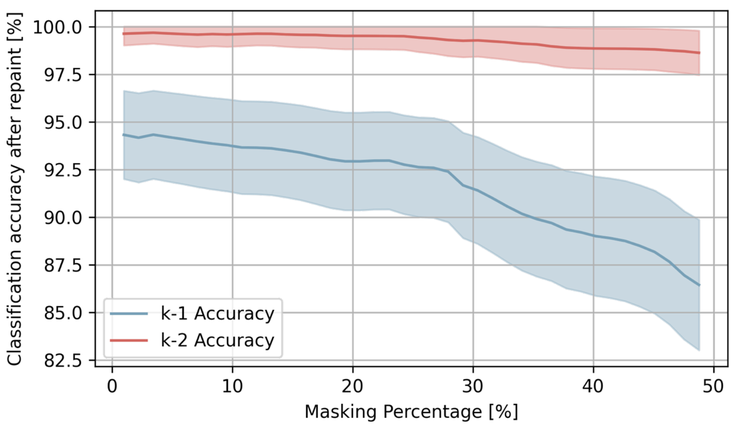
Cell Statistics - Density and Size

- Segment the cells with the CPN [2] and measure **cell density and size**
- Compare the average error in **cell density** and **size** before and after the repaint
- Our model closely follows the distribution with median relative **errors below 8%**
- Relative errors are slightly larger for small regions, as slight inaccuracies are relatively larger



Classification Flips - Cytoarchitecture

- Classify the images using [1] to compare the **cytoarchitecture**
- **Classification flips** occur, when the predicted class changes for the repaint
- Very few classification flips occur with small inpainted regions, increasing for larger areas to ~15%
- When accounting for the second likeliest guess, the accuracy increases to above 98%



Conclusion & Future Work

- We propose an evaluation method for generated **light-microscopy images of human brain sections**
- Our DDPM is able to accurately fill in missing data, within an error margin of **less than 8% for cell statistics**
- We aim to incoporate information from **neighbouring sections** using **crossattention** to improve the classification consistency
- Our models enables an **automatic correction** of processing artefacts at **full 1 mircon resolution**

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