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Step by Step: Towards a gapless 1 micron BigBrain with Diffusion Models

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Advances in microscopic imaging and high-performance computation have made it possible to analyze the complex cellular structure of the human brain in great detail. This progress has greatly aided in brain mapping and cell segmentation, leading to the development methods for automated analysis of tissue architecture and cell distribution in histological brain sections. However, histological image data can contain data gaps due to inevitable processing artifacts, which, despite careful precautions, may arise during histological lab work, such as missing sections, tissue tears, or inconsistent staining.

To address this issue, we present a convolutional neural network model that reconstructs missing or corrupted data from surrounding tissue, while preserving precise cellular distributions. Our approach is based on recent advancements in image generation and involves utilizing a denoising diffusion probabilistic model (DDPM) that is trained on light-microscopy scans of cell-body stained histological sections. We extend this model with the RePaint method to impute missing or replace corrupted image data.

To validate the model, we propose two new validation metrics based on two established deep learning models that were trained on the same type of data. In validation, we want to confirm a) the correct reproduction of cell statistics like cell size and count, and b) the generation of plausible cytoarchitectonic patterns, including brain area-specific laminar and columnar organization . We compare cell statistics using CPN, a cell segmentation model that provides precise cell statistics. Additionally, a model trained for cytoarchitecture classification is used to validate the structure of the inpainted regions by comparing how the inpainting process affects classification performance.

We find that images generated by the proposed DDPM exhibit realistic and anatomically highly plausible cell distributions, effectively filling in data gaps resulting from histological artifacts. The model achieves low errors in cell statistics of less than 10% and high accuracies in cytoarchitecture classification of above 85%, even with inpainted regions as large as 50% of the input patch. Our results demonstrate the potential of the proposed generative model to improve the accuracy and completeness of analysis workflows for histological brain imaging data and to provide the basis for the development of future whole-brain human brain atlases.

Primary author: KROPP, Jan-Oliver (Institute of Neuroscience and Medicine (INM-1), Forschungszentrum Jülich, Germany & Helmholtz AI, Forschungszentrum Jülich, Jülich, Germany)

Co-authors: SCHIFFER, Christian (Institute of Neuroscience and Medicine (INM-1), Forschungszentrum Jülich, Germany & Helmholtz AI, Forschungszentrum Jülich, Jülich, Germany); AMUNTS, Katrin (Institute of Neuroscience and Medicine (INM-1), Forschungszentrum Jülich, Germany & & Cécile and Oskar Vogt Institute for Brain Research, University Hospital Düsseldorf, Medical Faculty, Heinrich-Heine-University Düsseldorf); DICKSCHEID, Timo (Institute of Neuroscience and Medicine (INM-1), Forschungszentrum Jülich, Germany & Helmholtz AI, Forschungszentrum Jülich, Jülich, Germany & Institute for Computer Science, Faculty of Mathematics and Natural Sciences, Heinrich Heine University Düsseldorf, Germany)

Presenter: KROPP, Jan-Oliver (Institute of Neuroscience and Medicine (INM-1), Forschungszentrum Jülich, Germany & Helmholtz AI, Forschungszentrum Jülich, Jülich, Germany)

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