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Closing the Gaps: A Multi-Branch Diffusion Model for a Gapless 1-µm BigBrain

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Advances in microscopic imaging and high-performance computing allow analyzing the complex cellular structure of the human brain in great detail. This progress has greatly aided in brain mapping and cell segmentation, and the development of automated analysis methods. 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 presented a convolutional neural network model that reconstructs corrupted data from surrounding tissue, while preserving precise cellular distributions. Our approach uses a denoising diffusion probabilistic model trained on light-microscopy scans of cell-body stained histological sections. We extended this model with the RePaint method to impute corrupted image data. We evaluate its performance with established deep learning models trained on the same type of histological data.
A key challenge of our initial model was its difficulty in accurately reconstructing tissue boundaries and larger anatomical structures such as blood vessels. We address these challenges by an enhanced diffusion-based model that incorporates contextual information from adjacent sections of the brain. This model integrates three tissue patches from neighboring sections using a siamese network architecture with cross-attention mechanisms. Leveraging spatially aligned information across consecutive sections, our approach achieves a more anatomically coherent reconstruction.
We demonstrate that our model significantly improves realism and anatomical plausibility of reconstructed cellular distributions, as measured by both cell density prediction and brain area classification tasks. The error in predicted cell density was reduced to below 5% across large inpainting regions, marking a notable improvement over previous approaches. In addition the model was evaluated on its ability to handle multiple missing sections at once, which resulted in no performance loss over the single missing section case. The model reliably preserves tissue borders and reconstructs larger structures like blood vessels, which are crucial for accurate cytoarchitectonic mapping.
These findings underscore the potential of generative deep learning models for cytoarchitectonic research, opening new avenues for the automated reconstruction of histological data. Beyond inpainting small regions, our approach paves the way for the reconstruction of entirely missing brain slices, offering a powerful tool for bridging data gaps in high-resolution brain mapping efforts.

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