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3D reconstruction of BigBrain2: Progress report on semi-automated repairs of histological sections

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The BigBrain2 is a second BigBrain data set supplementing and building on our expertise of the first BigBrain [1]. It will provide first insights into inter-subject variability at whole-brain, cytoarchitectonic level. Overall, BigBrain2 offers better quality staining, favourable to regional segmentation and registration, and contains fewer artefacts through sectioning and staining. In order to repair acquisition artefacts due to sectioning and histological preparation (tears, folds, missing tissue, excessive distortion etc.) [2], every fifth section was initially repaired, with comprehensive quality control (QC) [3], enabling an initial reconstruction at 100µm. The large variability with regard to the number, extent, and severity of the damages posed a particular challenge and therefore had to be specially addressed. In this work, we will report on new methods and approaches for repairing the remaining sections in a semi-automatic and cost-effective manner to complete the full reconstruction at 20µm. Based on the manual and semi-automatic repairs carried out so far, we present a new improved 3D reconstruction of BigBrain2.

The paraffin-embedded fixed brain of a 30-year-old male donor was sectioned coronally at 20µm thickness using a large-scale microtome. All 7676 sections were stained for cell bodies (Merker stain), then scanned at 10µm in-plane (flatbed scanner, 8bit grey level encoding) and subsequently at 1µm in-plane (Huron TissueScope scanner). The histological flatbed scanner sections were resampled at 20µm in-plane, to match the section thickness. Every fifth section was initially repaired, with comprehensive quality control (QC) and data provenance tracking of all repair operations [3] providing a means for assessing the extent of the repaired artefacts and for eventual reproducibility at the 1µm in-plane resolution.

A fully automated approach for repairing the remaining sections was deemed unviable given the nature and severity of the artefacts, therefore a semi-automated approach was developed with the objective to minimize human intervention. Sections with major artefacts were first identified and broken pieces were manually moved in place (about 10% of the sections). Subsequently, the section to repair was registered to the closest two previously repaired sections of the 5-series, 100µm apart, and a virtual reference image was interpolated from these two sections at the position of the section under review. Minor artefacts were corrected by interpolating good tissue from the reference section in place of missing tissue in manually identified regions. These masks ensure tracking of the extent of the repaired artefacts, with eventual reproducibility at 1µm.

Ongoing work includes the semi-automatic repairs of the remaining sections to obtain a complete volume at 20µm isotropic resolution onto which sections at the cellular resolution of 1µm can be progressively overlaid.

References:

[1] Amunts K. et al., BigBrain: An Ultrahigh-Resolution 3D Human Brain Model. Science, 2013.
[2] Mohlberg H. et al., 3D reconstruction of BigBrain2: Challenges, methods, and status of histological section repair –A progress report. BigBrain Workshop 2022
[3] Lepage C. et al., 3D reconstruction of BigBrain2: Progress report on updated processing pipeline and application to existing annotations and cortical surfaces. BigBrain Workshop 2023

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