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

HIBALL
HELMHOLTZ International BigBrain Analytics & Learning Laboratory

Claude Lepage[1*], Hartmut Mohlberg[2*], Lindsay B. Lewis[1], Paule J. Toussaint[1], Susanne Wenzel[2], Alan C. Evans[1], Katrin Amunts[2,3]

[1] Montreal Neurological Institute, McGill University, Canada; [2] Institute of Neuroscience and Medicine (INM-1), Forschungszentrum Jülich, Germany; [3] C. and O. Vogt Institute for Brain Research, Universitätsklinikum Düsseldorf, Germany [*]equal contribution

Overview

3D reconstruction of BigBrain2 contributes new insight on inter-subject variability at whole-brain cytoarchitectonic level

Compared to BigBrain (65 years old) [1], **BigBrain2** (30 years old) provides

- Better staining quality, favourable to regional segmentation and registration
- Fewer artefacts due to sectioning and staining

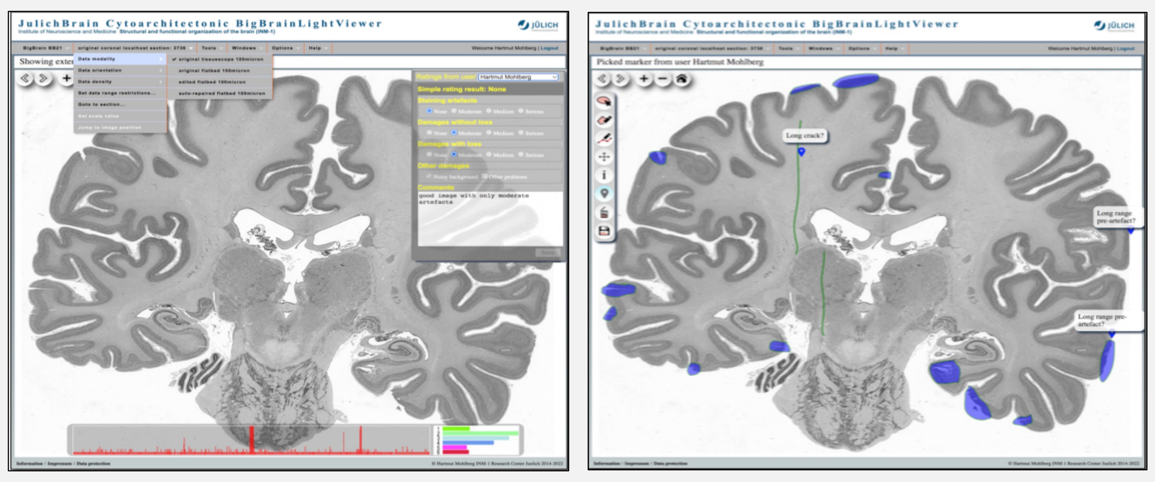
Main components of the 3D reconstruction pipeline

- Data acquisition and quality control
- Full provenance tracking for reproducibility
- **Manual and semi-automatic repairs:** Crucial for the quality of the subsequent processing steps and therefore for the quality of the 3D reconstruction
- 3D alignment and reconstruction at 20µm
- Optical-balancing
- Visualization and data curation

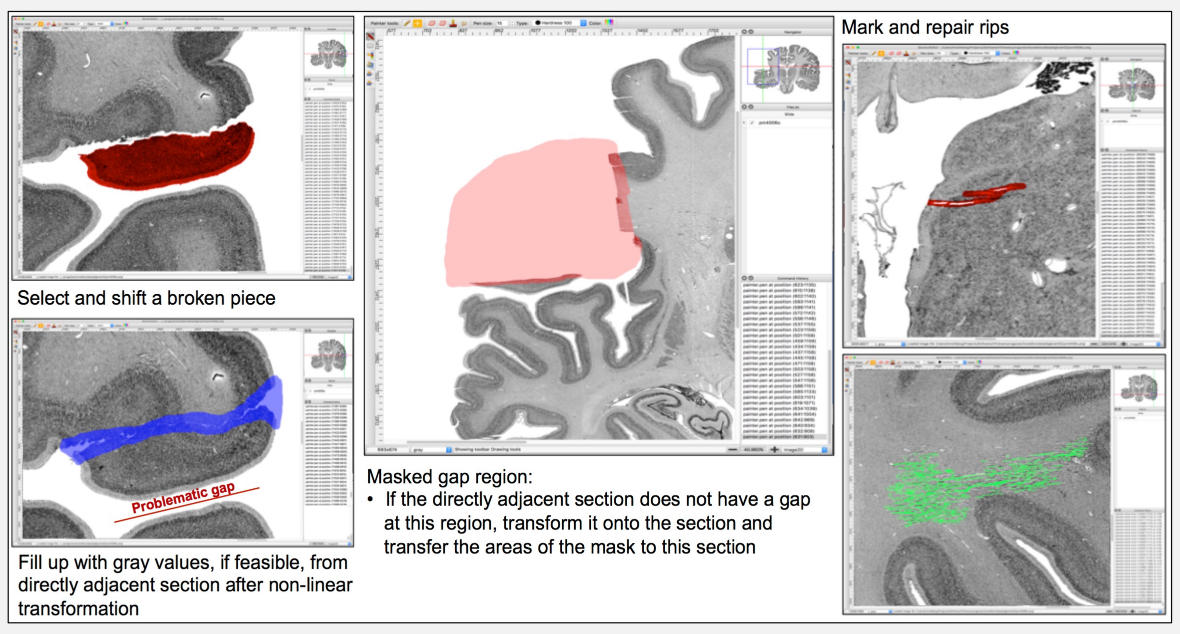
Repairs are essential and we will report new methods and approaches for repairing sections in a semi-automatic and cost-effective manner

Manual repair of every 5th image

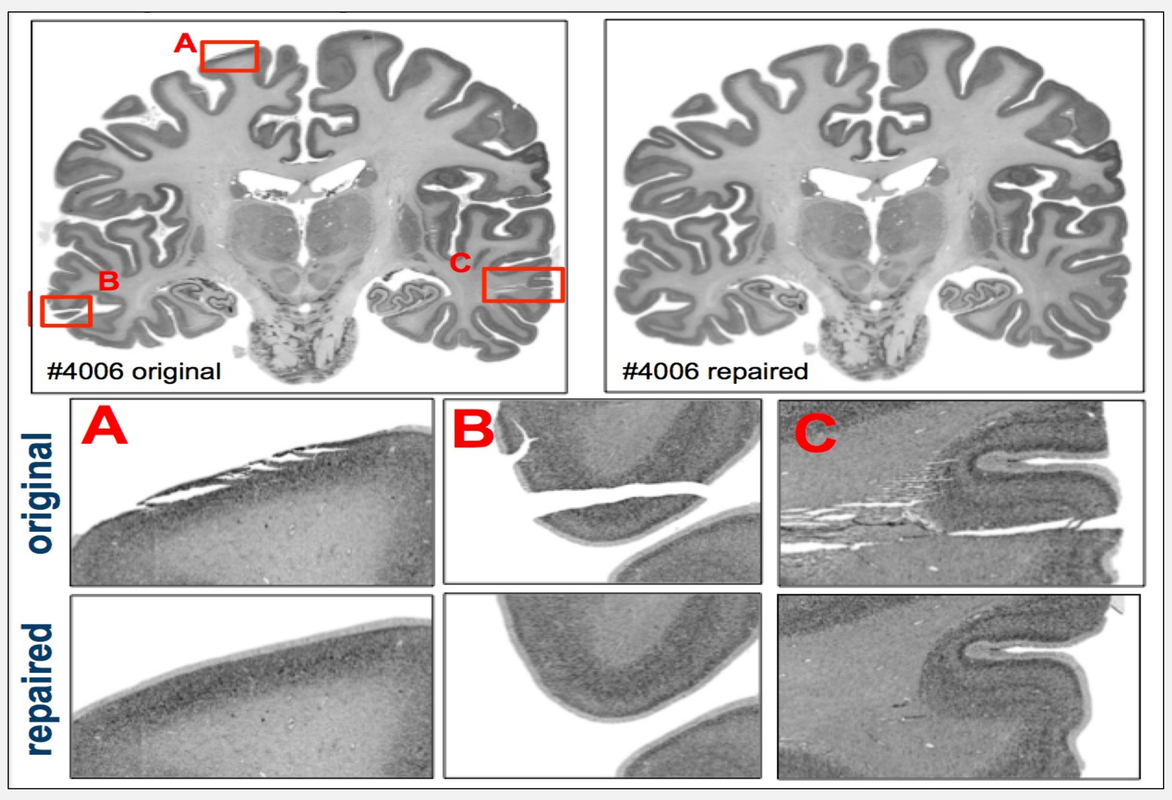
Identify and mark regions that need manual repairs (In-house online tool)



Manual repairs (SectionEditor using standard image editing methods)



Example of a manual repair of a complete section [2]



Strategy for repairs of BigBrain2 sections

Two-stage repair process

Manual repair

- Every 5th section (*1 and *6) manually with highest accuracy (20µm)

Semi-automated repair

- Intermediate sections based on *1 and *6 using registration
- Region determined by painted masks and interpolating good tissue from *1 and *6 repaired section

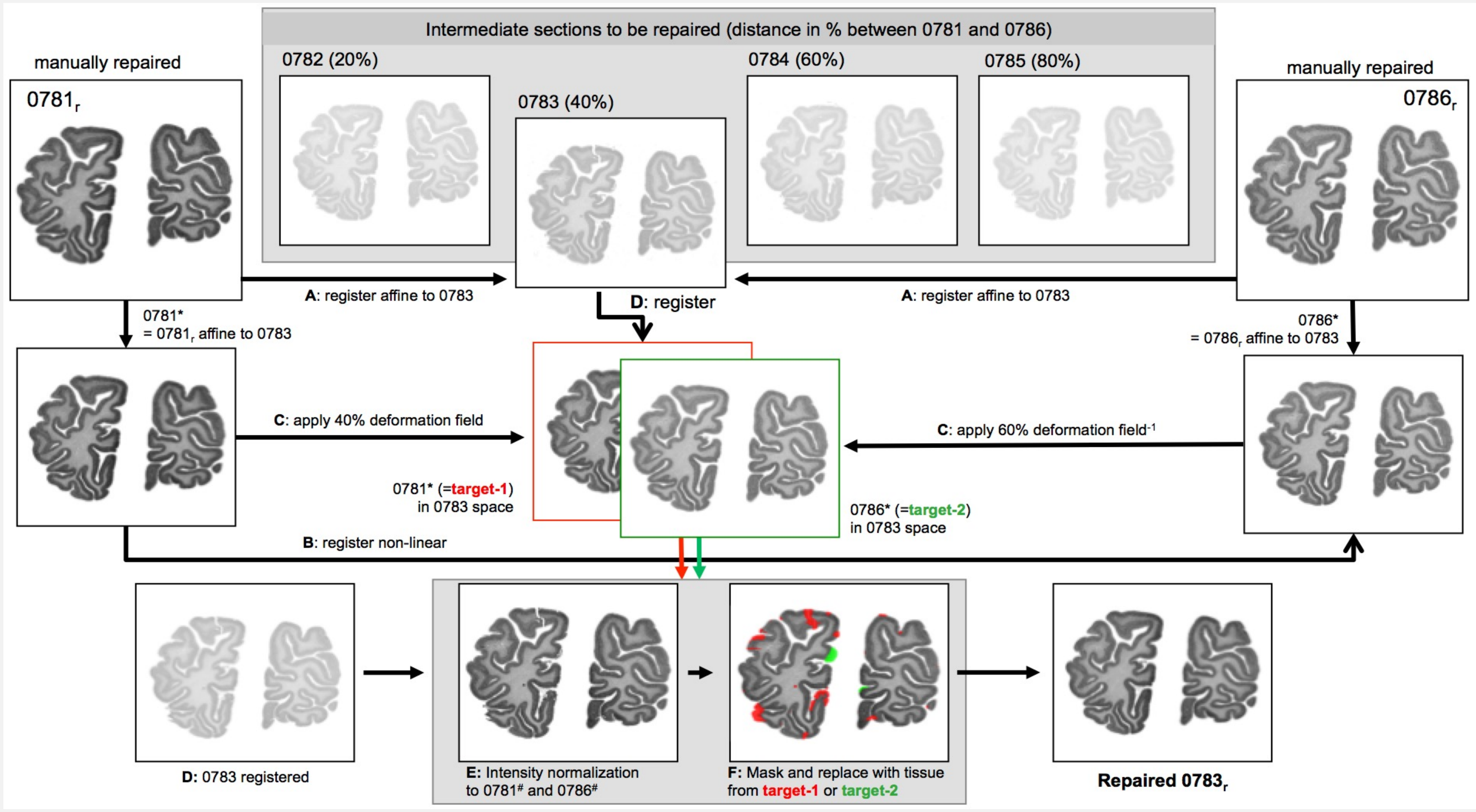
Advantages over BigBrain strategy [3]:

- Minimize manual interventions
- Track operations for reproducibility
- Simplified, more cost efficient-solution

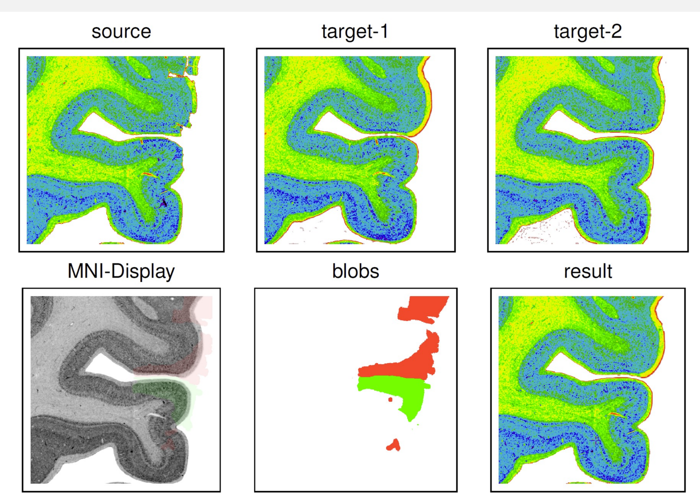
Challenges:

- Various types of artefacts through histological data acquisition (e.g., tears, folds, missing tissue, excessive distortion)
- Consecutive sections tend to have similar artefacts for missing tissue
- Preserve as much good original tissue as possible

Semi-automated repair



Repair process



- Interactive tissue update during painting using MNI Display
- Replace label=1 by target-1 and label=2 by target-2, with intensity normalization

Intensity normalization

Subtract difference in mean intensities:

$$source^* = source + (mean(target) - mean(source))$$

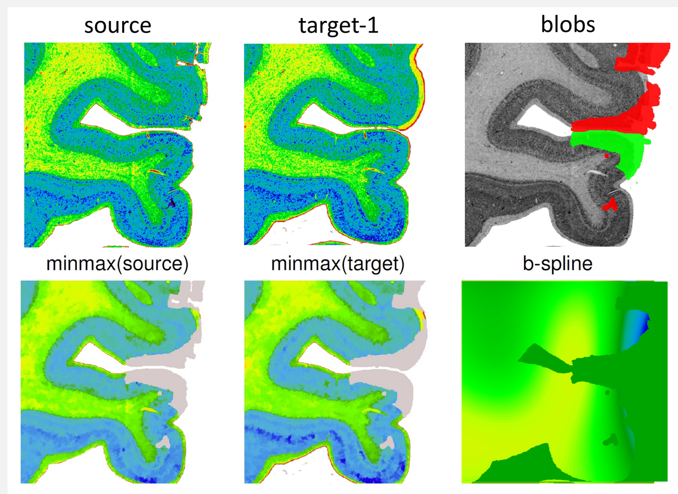
Mean intensity is ill-defined across artefacts

- Mask off labelled regions from source & target
- Extrapolate difference in mean intensities across masked region using b-spline:

$$source^*_{mskd} = source_{mskd} + bspline\,(mean(target_{mskd}) - mean\,(source_{mskd}))$$

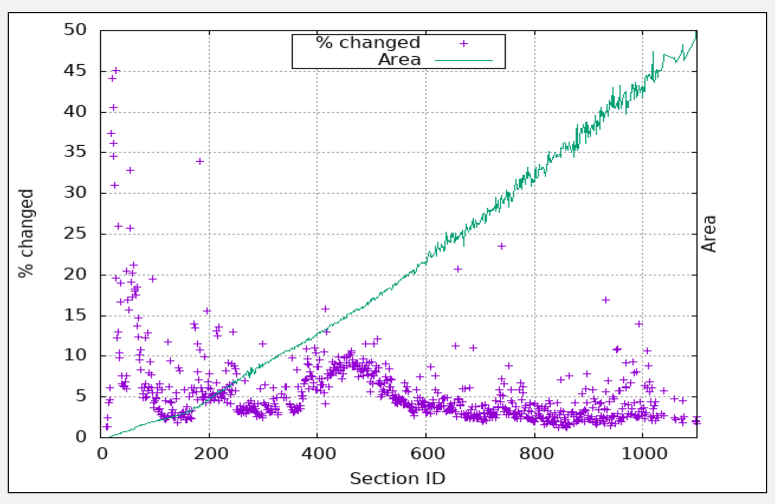
- Source corrected by b-spline in common tissue only
- Replace good tissue from target to source: $source^* = source^*_{mskd} + target - target_{mskd}$

Mean of image



- Replace local min/max by mean of surrounding voxels
- No blurring across tissue classes (WM, GM, Layer-1, BG)
- No interference from artefacts

Cross-sectional area of repaired section



- Cross-sectional area increasing smoothly over range 1-1100
- Less than 5% of tissue replaced in 60% of sections
- Provide map of replaced tissue in 3D volume

Inter-rater reliability

ID	% changed (% common)		Dice coeff
	Claude	Lindsay	
0438	8.78% (81.31%)	8.39% (85.07%)	83.15%
0439	11.02% (78.99%)	10.18% (85.53%)	82.13%
0497	6.65% (78.08%)	5.45% (95.19%)	85.79%
0498	7.65% (70.82%)	6.01% (90.15%)	79.32%
0638	3.03% (87.71%)	3.29% (80.90%)	84.17%
1048	4.23% (84.35%)	4.12% (86.44%)	85.38%

Dice coefficient over 80% shows good inter-rater agreement

Summary and Outlook

Full automation not feasible: Manual intervention required to enable high quality 3D registration of all sections, e.g., to cope for large-scale artefacts and to manually identify loose pieces to move

Work in progress: Continuing semi-automatic repair pipeline, under continuous quality control targeting a full 3D reconstruction at 20µm

References

[1] K. Amunts et al. 2013. BigBrain: an ultrahigh-resolution 3D human brain model. Science 340 (6139): 1472-1475
[2] Mohlberg H. et al. 2022. 3D reconstruction of BigBrain2: Challenges, methods, and status of histological section repair – A progress report. BigBrain Workshop 2022
[3] Lepage C. et al. 2023. 3D reconstruction of BigBrain2: Progress report on updated processing pipeline and application to existing annotations and cortical surfaces. BigBrain Workshop 2023

Acknowledgements

This work was funded in part by the Helmholtz Association's Initiative and Networking Fund under the Helmholtz International Lab grant agreement InterLabs-0015, and the Canada First Research Excellence Fund (CFREF Competition 2, 2015-2016) awarded to the Healthy Brains, Healthy Lives initiative at McGill University, through the Helmholtz International BigBrain Analytics and Learning Laboratory (HIBALL).
It was further supported by the Helmholtz Portfolio Supercomputing and Modeling the Human Brain (SMHB), and the European Union's Horizon Europe Programme under the Specific Grant Agreements No. 101147319 (EBRAINS 2.0 Project) and No. 945539 (Human Brain Project SGA3).

HELMHOLTZ RESEARCH FOR GRAND CHALLENGES
HEALTHY BRAINS HEALTHY LIVES
www.bigbrainproject.org
@BigBrain Project
McGill
JÜLICH Forschungszentrum