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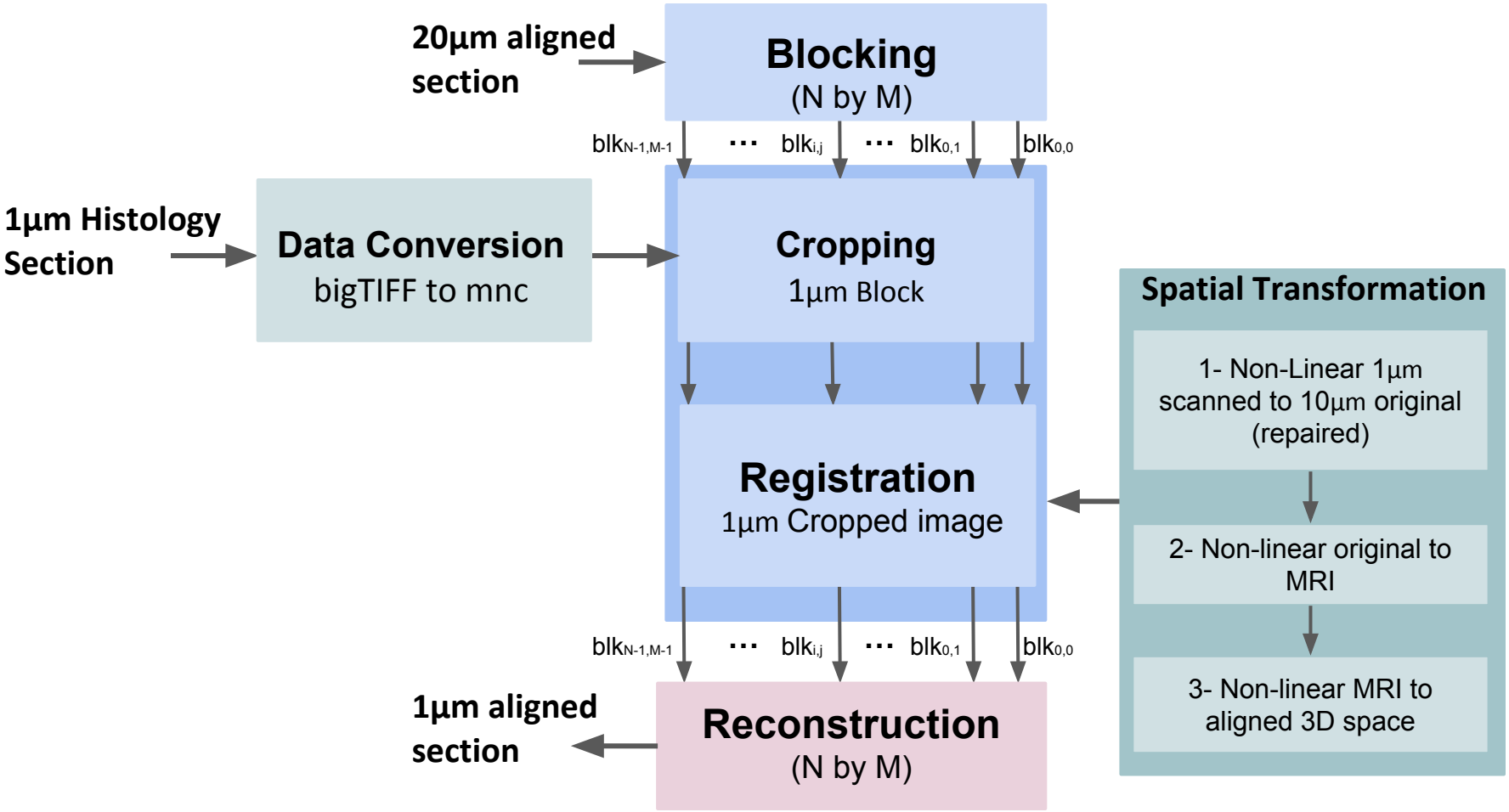
Non-linear registration of 1µm Histology Sections into 3D 20µm BigBrain Space

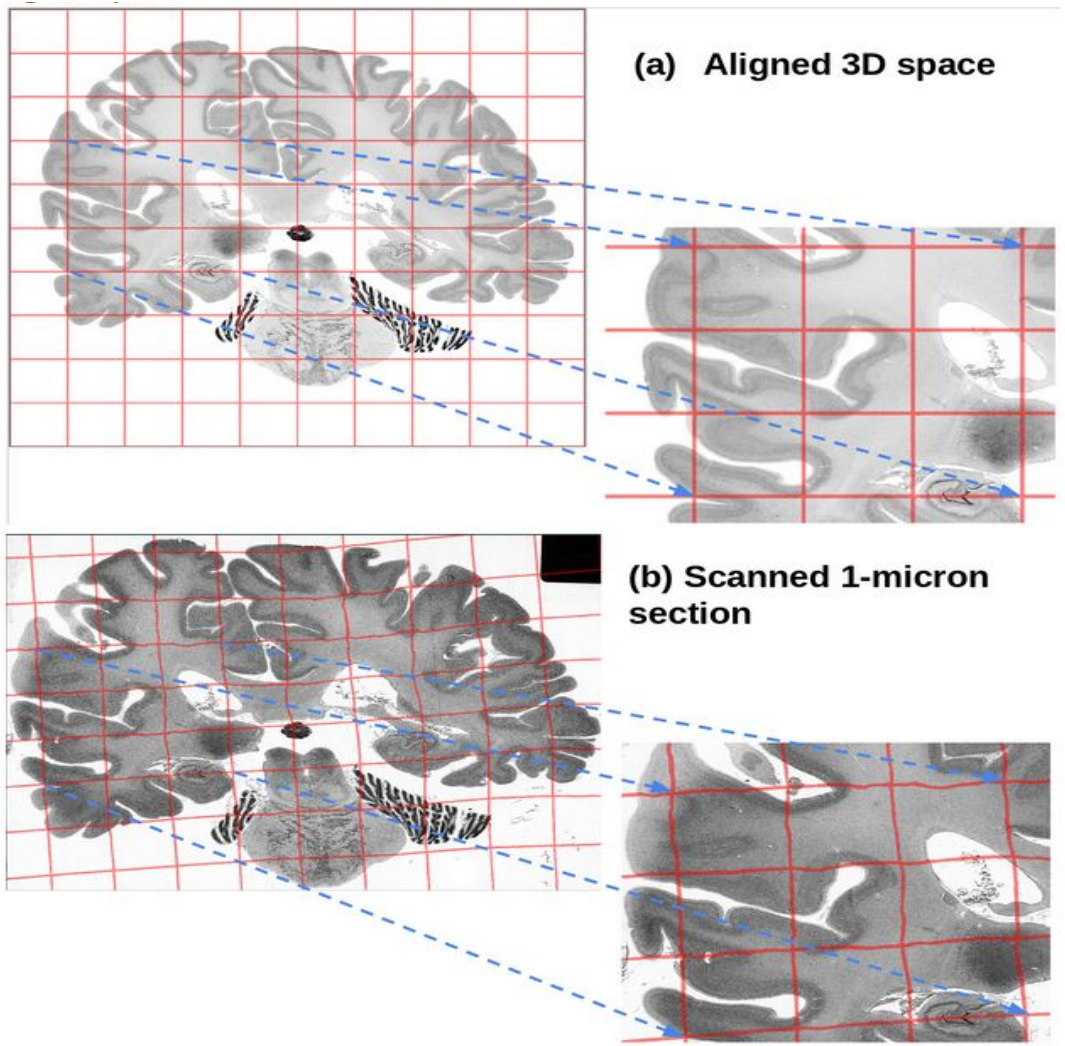
Mona Omidyeganeh, Claude Lepage, Konrad Wagstyl, Hannah Spitzer, Timo Dickscheid, Katrin Amunts, Alan Evans

Introduction

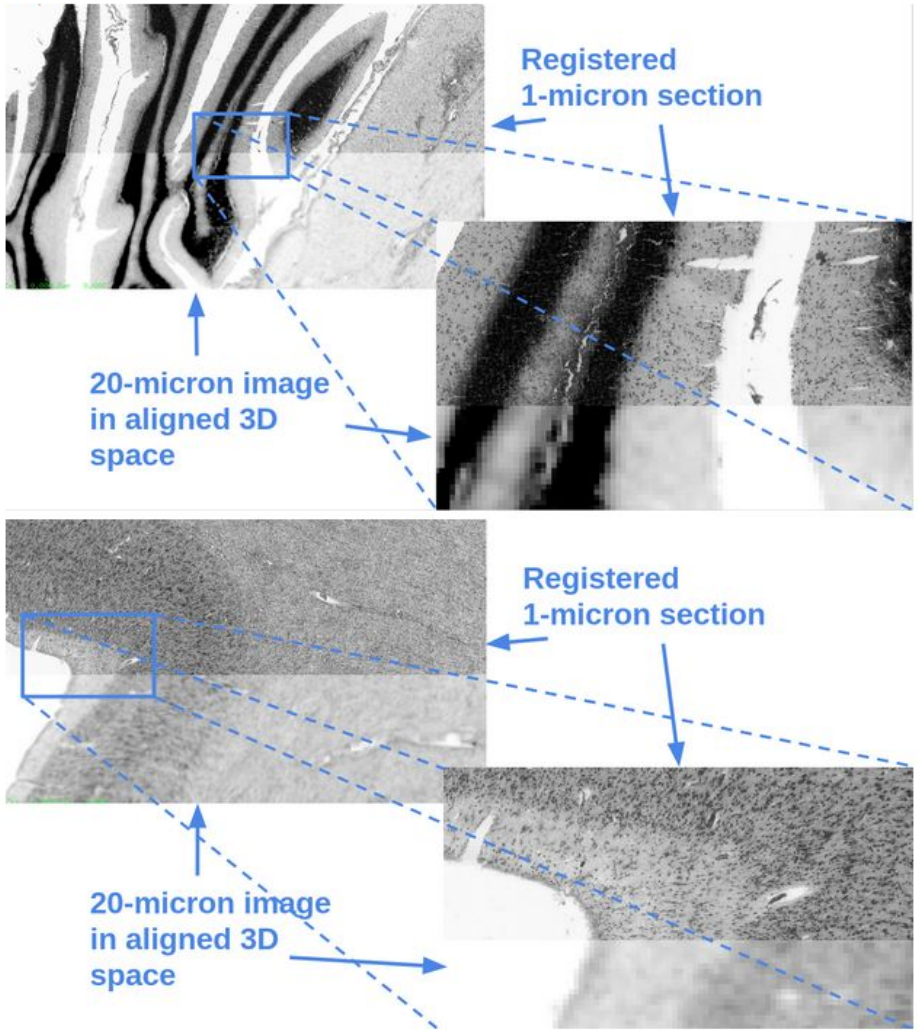
- Processing/visualization of digitized histological sections from human brain is challenging, due to large image size.
- BigBrain was originally scanned at 10μm in-plane resolution but downsampled to yield 20μm isotropic resolution in 3D.
- These sections have now been rescanned at 1μm resolution, which allows the identification of microscopical features at the cellular level obscured at 20μm. This allows to visualize single neurons, while maintaining their topography in 3D space.
- We have registered 2D 1μm histological brain sections to BigBrain.


20µm aligned section
Blocking
(N by M)
blkN-1,M-1 ··· blki,j ··· blk0,1 blk0,0
1µm Histology Section
Data Conversion
bigTIFF to mnc
Cropping
1µm Block
Registration
1µm Cropped image
Spatial Transformation
1- Non-Linear 1µm scanned to 10µm original (repaired)
2- Non-linear original to MRI
3- Non-linear MRI to aligned 3D space
blkN-1,M-1 ··· blki,j ··· blk0,1 blk0,0
1µm aligned section
Reconstruction
(N by M)

Blocking of a 20µm section in aligned 3D space (a) and corresponding blocks on the 1µm input section (b).
The global transformation is applied on the blocks of the 1µm section to produce the output section at 1µm in 3D aligned BigBrain space.



Two examples of blocks at 1µm overlaid on corresponding 20µm section in BigBrain aligned space.
Top: Cerebellum,
Bottom: Cortex.



Conclusion

- **Cutting an image into blocks**, allows resampling of full histological sections at 1μm. Previous tools could not operate on full sections due to prohibitive **memory demands**.
- Each aligned, resampled section had 130,541 x 89,140 pixels for a file size of ~12GB (compressed). A typical block of size 13,100 x 9,000 pixels (10x10 blocks) took 8.4±2.0 mins to transform, using >1.65GB memory. Block concatenation took ~1 hr.
- Total processing time per section was ~15 hours on a single core, without memory bottleneck, allowing **simultaneous processing of multiple sections on multi-core compute nodes**.
- Mapping 1μm 2D histological sections to the 3D BigBrain will offer new opportunities to locate and characterize individual neurons as well as map their distribution across cortical layers, areas and subcortical nuclei.

References

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2. Collins D.L., et al. (1994). ‘Automatic 3D inter-subject registration of MR volumetric data in standardized Talairach space,’ Journal of Comuter Assisted Tomography, 18(2), 192-205.
3. Wagstyl, K., et al. (2020). ‘BigBrain 3D atlas of cortical layers: Cortical and laminar thickness gradients diverge in sensory and motor cortices,’ PLoS Biol 18(4): e3000678.