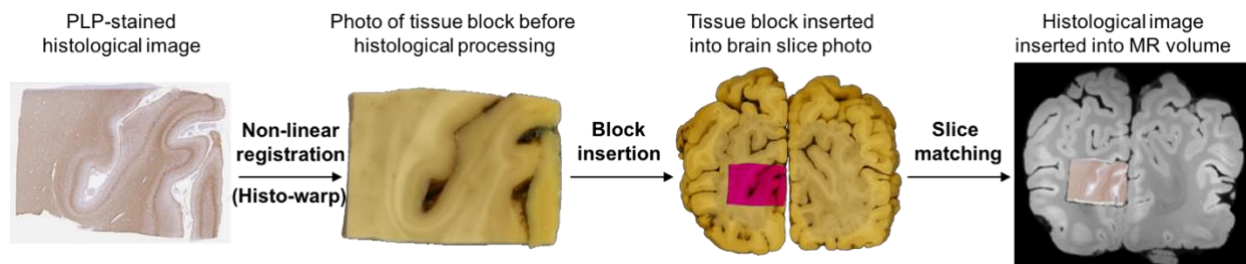


Registration of Histological Images to Post-Mortem MRI

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Introduction: Establishing a clinically useful quantitative mapping between microstructural features and MRI signals requires accurate spatial alignment between MRI and histology. This is hindered by the ill-conditioned problem of slice-to-volume registration, the three-orders-of-magnitude resolution mismatch, inherent differences in image contrast, and artefacts related to tissue processing. Here, we present a semi-automated prototype of a fully automated registration pipeline that can accurately align digital histological images with 3-dimensional whole-brain MRI.



Methods: Multi-modal MRI [1] was acquired from post-mortem brains, photographs were taken during dissection of the brains [1], histological sections were digitised using an Aperio® slide scanner, and a novel registration pipeline was implemented using Python 3.6. Deformable registration [2] was used to align histological images with block-face photographs of the corresponding tissue blocks, and to insert the blocks into the brain slice photographs. Slice-to-volume registration was achieved by fitting a polynomial surface to 20 hand-annotated anatomical landmarks in MRI space, then resampling the MR at surface points and performing deformable registration [2] to the slice photo.

Results & Discussion: Five different PLP-stained histological images were registered to a structural MR image from the same subject. A representative result is shown in the rightmost panel of the figure. Registration accuracy was found to be almost exclusively dependent on slice-to-volume registration. The average distance between manual and final alignments of the segmented slices was measured to be 0.84 mm at 100 anatomically identifiable points (20 points per slice).

Conclusion: The proposed method provides a reliable and efficient alternative to existing methods that require full-slice whole-brain histology. Work is in progress to make the pipeline fully automated.

References

1. Pallegage-Gamarallage, M., et al. *BMC Neuroscience*, 2018; 19(1), 11.
2. Heinrich, M.P., et al. *Med Image Anal.* 2012; 16:1423-1435.

Acknowledgments

Tissue was provided by the Oxford Brain Bank. Funding was provided by EPSRC, MRC [EP/L016052/1] and Wellcome Trust.