Registration of Histology and MRI using Blockface as Intermediate Space

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1. Introduction

Registering histological images with MR data is challenging due to:

- 3D deformations between MR scanning and histological block,
- 2D deformations during sectioning and mounting histology on slides (even tears, missing tissue),
- differences in tissue appearance between the stained histology and MR images.
- We use **blockface images** (i.e., images of the top surface of the tissue block as it is being sectioned [1]) as the target space for all registrations, instead of a histological volume [2].
- We register the blockface volume with the MR volume using a 3D variational optical flow method [3].
- We then register histological images with MR slices via a 2D variational optical flow and boundary information.

2. Methods

1. Blockface Segmentation

i. Initial segmentation based on thresholding the red channel.

ii. Refined segmentation based on 3D foreground/background histograms (RGB channels).

2. Normalize Images

i. Compute local entropy images [4] for histology, blockface and MR images.

ii. Blend exterior boundaries to accommodate different foreground/background contrasts.

3. Register Blockface with MRI (3D)

i. Initial 3D affine registration MRI to blockface (mean absolute difference of entropy images).

ii. Non-linear 3D registration using a variational optical flow [3].

4. Register Histology with MRI

i. Resample 2D MR slices for each blockface slice (non-linear, see 3.ii).

ii. Register each entropy histological image with corresponding entropy MR slice (2D affine).

iii. Construct 2D non-linear correspondence via variational flow [3].

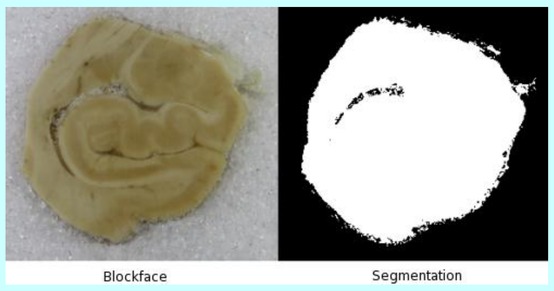
3. Results

Blockface Volume - Cross Section

Stack of 2D blockface photos to create a 3D volume.

Employing the blockface volume as an intermediate space is essential because histological staining often occurs only in selected slices (e.g. every 5th slice) and is accompanied by shrinkage in the histological stained section. Registering single histological slices into the MRI volume is an extremely **ill posed** problem, as they will be **curved surfaces** due to the non-linear deformations.

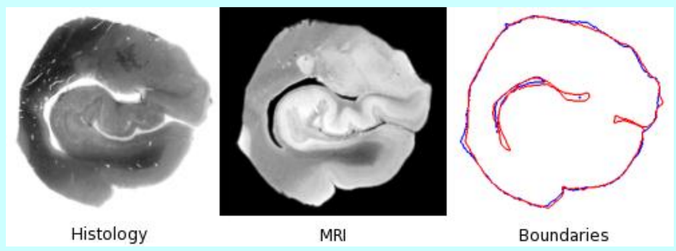
Blockface Segmentation



Left: a single blockface photo, showing the top surface of the tissue block embedded in ice.

Right: The corresponding foreground/background segmentation.

Registration and Boundary Overlay



A registered pair of slices together with the boundary overlay, indicating accurate correspondence.

After the affine and non-linear 3D registration of the MRI volume into the blockface volume, histology slices are individually registered (affine and non-linear 2D) to the resampled MRI in blockface space.

4. Conclusion

- Histological analysis remains the gold standard of neuroanatomy, and is a critical component of validating the anatomical features detected in ultra-high resolution *ex vivo* MRI.
- Our method produces accurate registrations by using the blockface volume as an intermediate space.
- The method will be validated by quantifying overlap in manual labels created on the histology slices and in the MRI volume.
- The ability to transfer information from stained sections to MRI will enable the direct calculation of the MR correlates of histologically derived properties such as cell density or degree of myelination, potentially facilitating automated architectonic and laminar segmentation directly on 3D, undistorted MRI volumes.

5. References

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[4] *Wachinger, C. (2010), 'Structural image representation for image registration', in Proceedings of IEEE Computer Vision and Pettern Recognition Workshops, pp. 23-30.*

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