# A Framework for fast 3-D Histomorphometric Reconstructions

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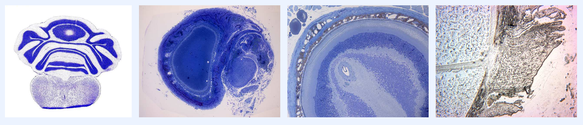
## Motivation

Three-dimensional (3-D) histomorphometric reconstructions have been used in the past to investigate structural changes in the eye due to diseases like glaucoma [1]. Manual interaction during the reconstruction, however, makes the process **time-consuming and error-prone**.
We propose a framework for **fast 3-D reconstruction** of histological data sets, with minimal user interaction, making histomorphometric reconstructions feasible for **everyday use**.

## Data + Setup

Four data sets were available for testing. One was specially prepared for 3-D reconstruction [4], and is mostly free of artifacts. The other data sets are standard serial section sequences, created for visual inspection.



(a) (b) (c) (d)

**Figure 1:** Example images: (a) Mouse brain, (b,c) mouse optici, (d) human optic nerve head.

1. **Mouse Brain** [4]
   - 350 cryo sections, Nissl-stained, of an adult mouse brain.
2. **Mouse optic nerve head (ONH) I + II**
   - 100, resp. 138, images of adult mouse ONH, stained with toluidine blue.
   - Leica DC 500 digital camera, mounted on a Leica DMR microscope.
3. **Human ONH**
   - 82 images of a human optic nerve head, unstained, saggital sections.

## Methods

Since the processing is solely intensity driven, we do not have to rely on the presence of (artificially introduced) landmarks.
For fast automatic reconstruction of histological images, several steps are performed:

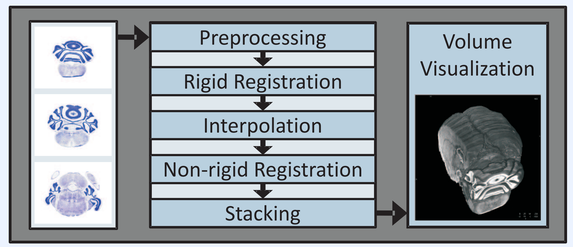
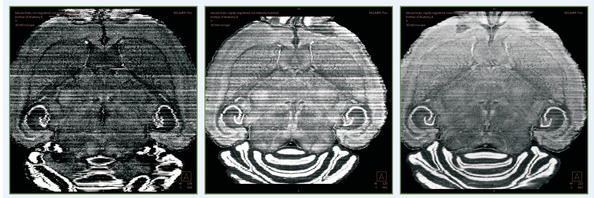



**Figure 2:** General reconstruction pipeline.

1. **Preprocessing**
   Due to histological staining and inhomogeneous lighting, the image intensities have to be normalized. This is done using **histogram equalization** and **bias field elimination**.
2. **Rigid Registration**
   As the displayed tissue is not aligned, **multi-resolution rigid registration** is used to determine a rotation angle and translation vector to realign the image content.
3. **Interpolation**
   In case of gaps in the data set, missing slices can be interpolated. For this, a **non-rigid registration method** calculates a deformation field between neighboring slices. **Partial application of the deformation field** on one neighbor slice then provides an estimate of the missing image.
4. **Non-rigid Registration**
   During slicing, tissue deformations are introduced. Optionally, non-rigid registration is performed to accurately fit the samples to each other.
5. **Stacking**
   For 3-D visualization, the images are stacked to a volume, using the previously calculated spatial transformations.

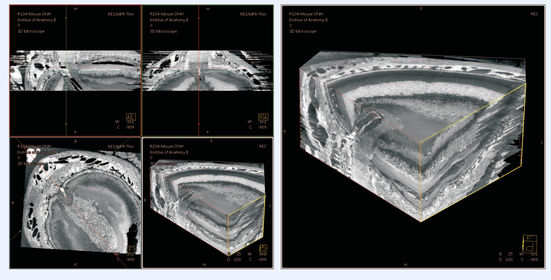
## Results

After improving the image quality using image enhancement methods, the histological data sets were processed and stacked to a 3-D histomorphometric volume (see Fig.3, 4).



(a) (b) (c)

**Figure 3:** Reconstruction pipeline details: Mouse brain: (a) unregistered, unnormalized (b) rigidly registered, unnormalized (c) rigidly registered, normalized.



(a) (b)

**Figure 4:** Reconstructions of a mouse optical nerve head: (a) visualized in InSpace (b) detail: clipped reconstructed volume.

The time needed for reconstruction (see Table 1) is directly related to the
- **image resolution**
- **image quality**
- **initial alignment of the image content**

and also affects the quality of the reconstructed volumes.
Tests were performed on a Core2Duo 2.5 GHz CPU, 4 GB RAM Dell Notebook.

**Table 1:** Time needed for reconstruction.

| | M. brain | Mouse I | Mouse II | Human ONH |
|---|---|---|---|---|
| Recon. time | 5 min. | 2 min | 2 min | 4 min |

## Conclusion

Compared to inspection of a series of 2-D images, reconstructed histological volumes clearly improve the **visibility and understanding** of morphological structures and their **spatial context**.
Depending on the image quality, a first volume reconstruction can be performed within minutes, making **histomorphometric reconstructions feasible for everyday laboratory use** .

**Possible future applications**

With OCT imaging being able to perform in-vivo imaging, the combination of anatomical volume atlases generated using histological data with newly aquired OCT volumes might enrich and broaden the diagnostic possibilites significantly.

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## Commercial Relationship

S. Gaffling, None; M. Scholz, None; M. Eichhorn, None; E. Lütjen-Drecoll, None;

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