# Robust Registration of Mouse Brain Slices with Severe Histological Artifacts

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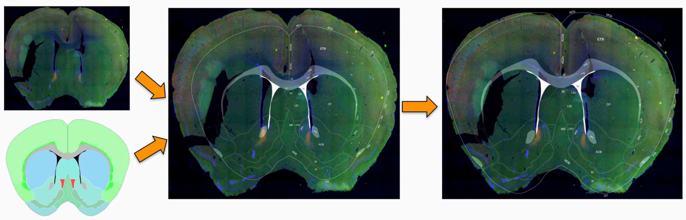
## MOTIVATION & CONTRIBUTION

Modern neuroscience is increasingly exploiting three-dimensional digital brain models for understanding complex brain anatomy, localizing experimental data, and planning experiments. Building high-resolutions three-dimensional digital brain models starts by first aligning digital images of mouse brain slices to standardized atlas framework. However, conventional processing of these brain slices introduces many histological artifacts such as tears and missing regions in the tissue, which make the alignment process extremely challenging.

**We present an end-to-end fully automatic registration pipeline for alignment of digital images of mouse brain slices that may have histological artifacts, to a standardized atlas space.**

## OUR MODULAR PIPELINE

### 1. Course Alignment

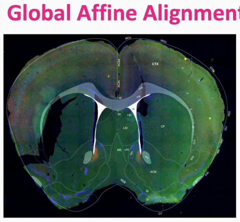


- A **novel edge-detection algorithm** to automatically computes dominant edges.
- Align two OBBs computed using unbiased PCA on resampled convex hull.

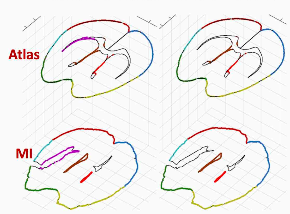
### 2. Detecting Damaged Regions

- Compute all exterior medial axis using Constrained Delaunay Triangulation (CDT)[1].
- Damage regions are detected as those with long and vertically asymmetric exterior medial axis.

### 3. Global Affine Alignment

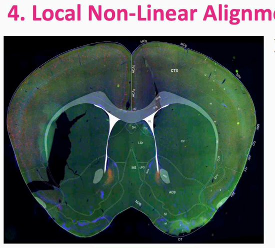


ACCURATE CORRESPONDENCES




- Damage region points are removed from correspondence finding.
- Correspondences are iteratively found by comparing normal vectors in nearby regions.
- Global affine alignment is performed using a variant of ICP.

### 4. Local Non-Linear Alignment



- Once accurate point correspondences are computed, non-linear warping is performed by solving **Laplace's equation with Dirichlet boundary conditions**.

**SECOND ORDER PDE's**

$$\phi_x = \frac{d^2\phi_x}{dx^2} + \frac{d^2\phi_x}{dy^2} = 0$$

$$\phi_y = \frac{d^2\phi_y}{dx^2} + \frac{d^2\phi_y}{dy^2} = 0$$

**Warping function** $\phi(s,t) = (\phi_x(x,y), \phi_y(x,y))$

**Boundary Conditions**

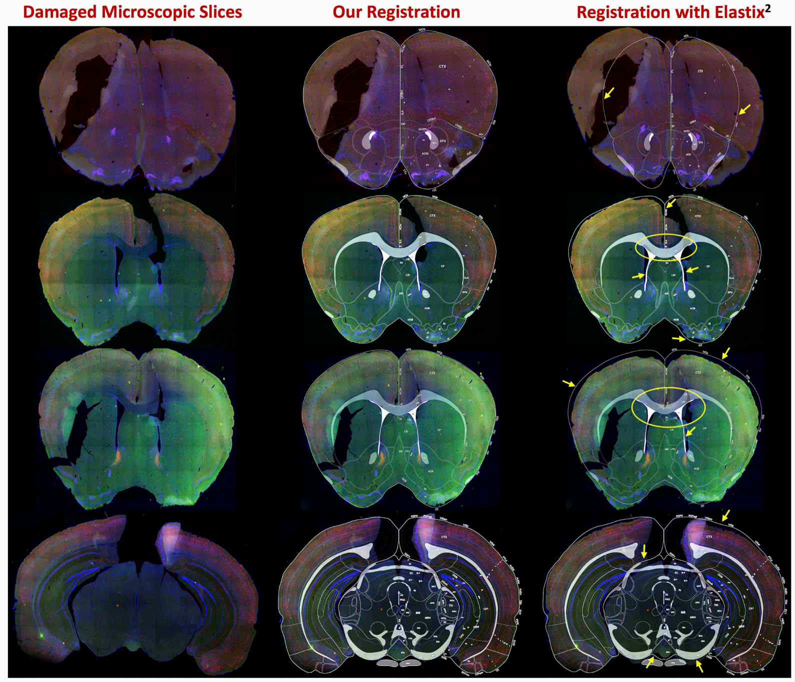
$$\phi(s,t) = (B_x(s,t), B_y(s,t)), (s,t) \in P_M^*$$

$$\phi(s,t) = 0, \forall (s,t) \notin P_M$$

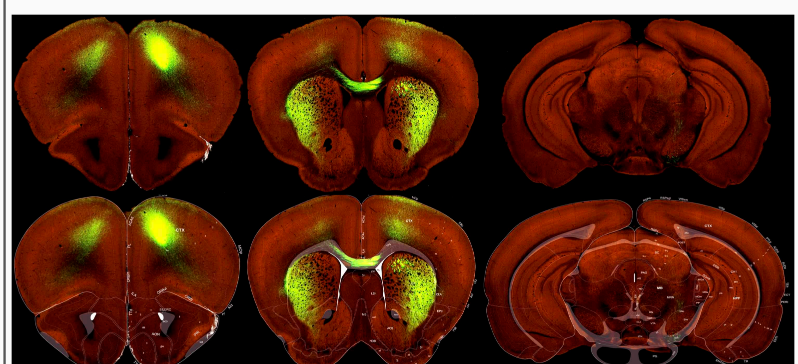
*$P_M$ = Points in Microscopic Edge Image

## COMPARISON OF REGISTRATION RESULTS ON DAMAGED SLICES

Damaged Microscopic Slices | Our Registration | Registration with Elastix[2]



## OUR REGISTRATION RESULTS ON CLEAN SLICES



| Registration Errors (in pixels) | | Clean Slices (88 slices) | | | Damaged Slices (52 slices) | | |
|---|---|---|---|---|---|---|---|
| | | Average RMSE** | Average MEE | Average MAE | Average RMSE** | Average MEE | Average MAE |
| After Affine Transformation | Intensity-Based | 11.79 | 9.33 | 24.71 | 18.96 | 11.55 | 40.57 |
| | Proposed | 12.91 | 10.58 | 23.92 | 13.37 | 10.66 | 25.27 |
| After Non-Linear Transformation | Intensity-Based | 4.68 | 3.20 | 8.03 | 8.88 | 6.55 | 24.69 |
| | Proposed | 3.61 | 2.51 | 5.7 | 3.91 | 2.53 | 6.01 |

**RMSE – root mean square error; MEE – median error; MAE – maximum error

## CONCLUSION

- We present the **first complete automatic registration pipeline** for alignment of high-resolution mouse brain slice images with histological artifacts to a standardized atlas framework.
- Since we do not use intensity information, we can register slices produced from a **variety of imaging modalities.**
- Our robust damaged region detection with contour registration technique condones histological artifacts thereby **facilitating extremely thin tissue sectioning**, which is important for accurate 3D reconstruction.
- We show the **robustness of our algorithm** through accurate alignment of over 200 mouse brain slices.

## REFERENCES

1. Automatic detection of histological artifacts in mouse brain slice images. MICCAI'16 in Athens, Greece.
2. Elastix: a toolbox for intensity-based medical image registration. Trans. on Medical Imaging' 10.

## FUTURE WORK

- Automatically selecting slice correspondences among the two stacks using a good error metric.
- Accurate 3D surface reconstruction.

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