Robust Registration to a template brain for the Drosophila larva

Interim presentation

- Harsha Yogeshappa

Supervisor: Dr.rer.nat. Martin Strauch

Lehrstuhl für Bildverarbeitung

RWTH AACHEN UNIVERSITY

Contents

Model organism – Drosophila larva

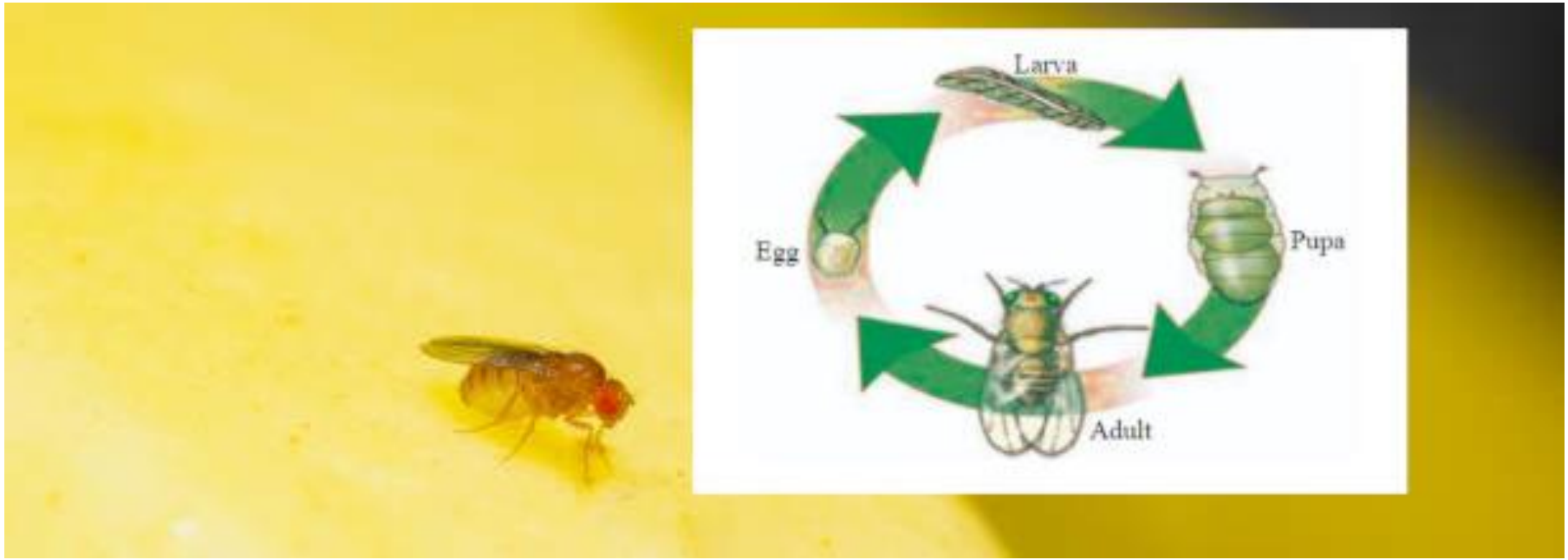
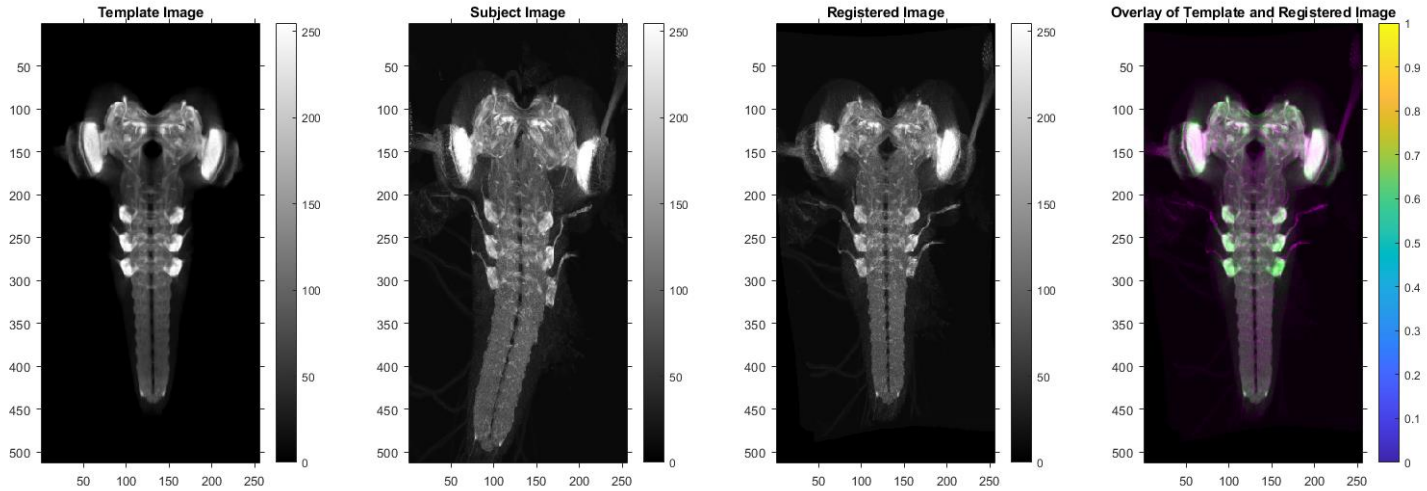


Image: https://www.istockphoto.com/de/fotos/drosophila-melanogaster
Image: Learn About Metamorphosis In Drosophila | Chegg.com

Motivation

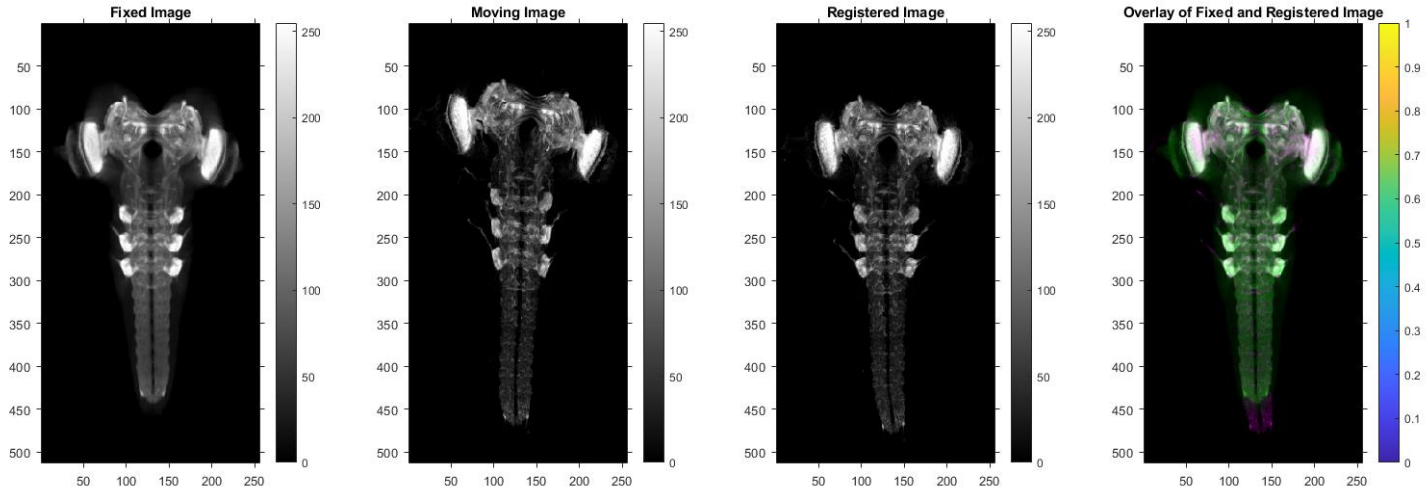
– Thesis work is an extension of the work done in *larvalign: Aligning Gene Expression Patterns from the Larval Brain of Drosophila melanogaster*.



Muenzing, Sascha E A et al. *Neuroinformatics* vol. 16,1 (2018): 65-80.

Motivation

– Thesis work is an extension of the work done in *larvalign: Aligning Gene Expression Patterns from the Larval Brain of Drosophila melanogaster*.



Muenzing, Sascha E A et al. *Neuroinformatics* vol. 16,1 (2018): 65-80.

Motivation

Goal of the thesis

- Analyze if the following is achievable with a learning-based approach.
  - Robust registration.
  - Overcome the failed registrations in larvalign.
  - Improve the registration time.
  - Investigate how landmark points can be inserted into the training as auxiliary information.

- At the end of the thesis, we hope to have a faster and more robust larvalign called larvalign 2.0

Datasets

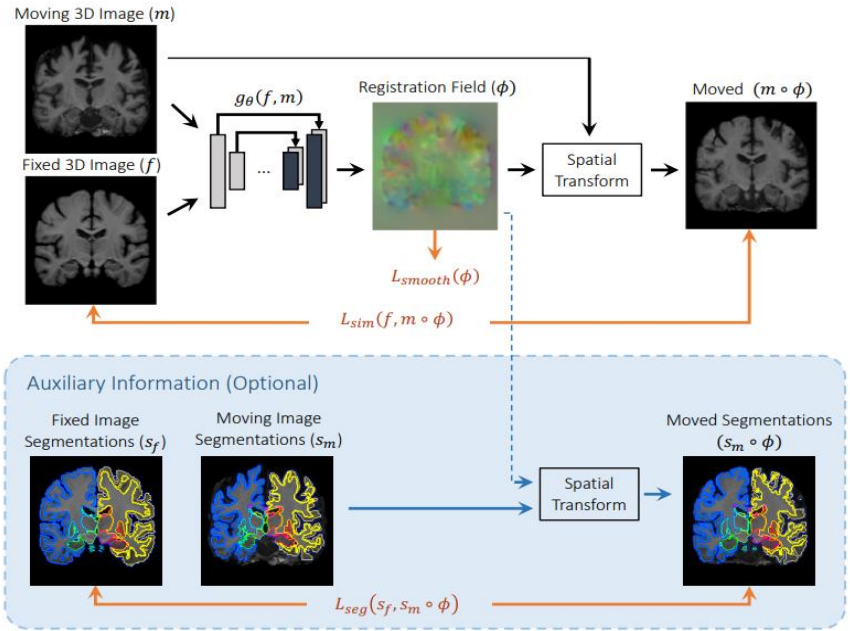
- In total, 1 template scan and ~1000 larval brain scans from
  - Department of Genetics, University of Leipzig, Leipzig, Germany.
  - Janelia Research Campus, Howard Hughes Medical Institute, Ashburn, VA, USA.
- Evaluation performed on test data and compared with *larvalign.*

	Number of scans	Original Resoultion	Scaled Resolution
Department of Genetics, Univesity of Leipzig	100	980x1440x81	256x512x64
	052	512x512x104	
	200	592x800x102	
Janelia Research Campus	200	977x1428x69	
	200	981x1428x76	
	200	973x1434x79	
Larvalign (Test Data)	021	973x1434x79	
	020	981x1430x79	
	025	977x1432x77	

Concepts

- Unsupervised method.
- Feed auxiliary information to the network to guide it in the right direction of learning.

- Base model: **Voxelmorph**
  - A learning framework for deformable medical image registration.
    - It is proven to work: Comparable performance to state-of-the-art medical image registration.
    - Can be combined with auxiliary information to improve the accuracy (e.g., segmentation map).



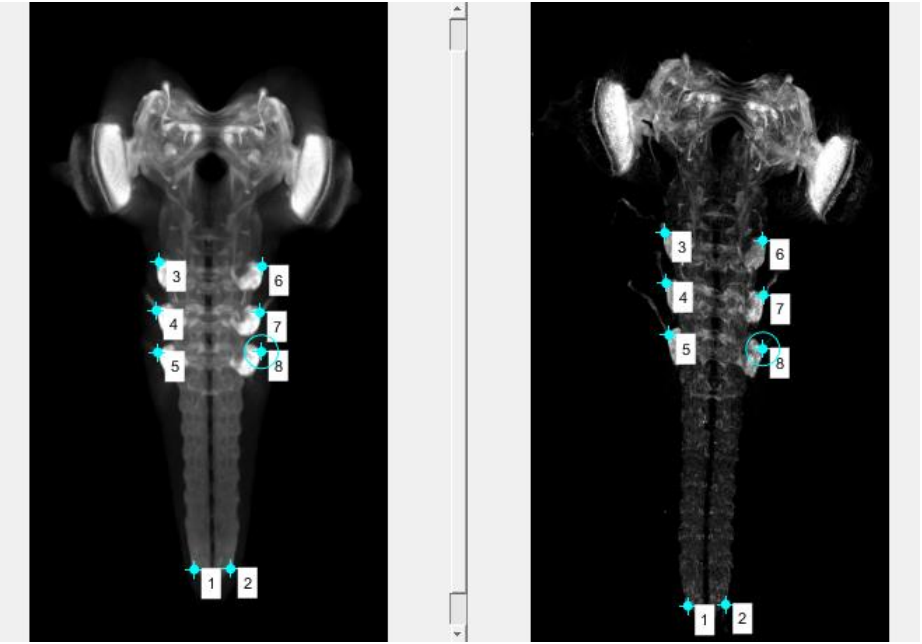
Voxelmorph: Balakrishnan et al., IEEE Transactions on Medical Imaging, 2019.

Concepts: Auxiliary Information

- Landmark points, spatial correspondences between f and m.
  - commonly known as the gold standard in the field of image registration.

- We quantify perfect registration of landmark points using mean squared error function.

$$\mathcal{L}_{ldm}(l_f, l_m, \phi) = \frac{1}{K}\sum_{k=1}^{K} MSE(l_f^k, l_m^k - \phi_{f,m}^k)$$



Voxelmorph: Loss Functions

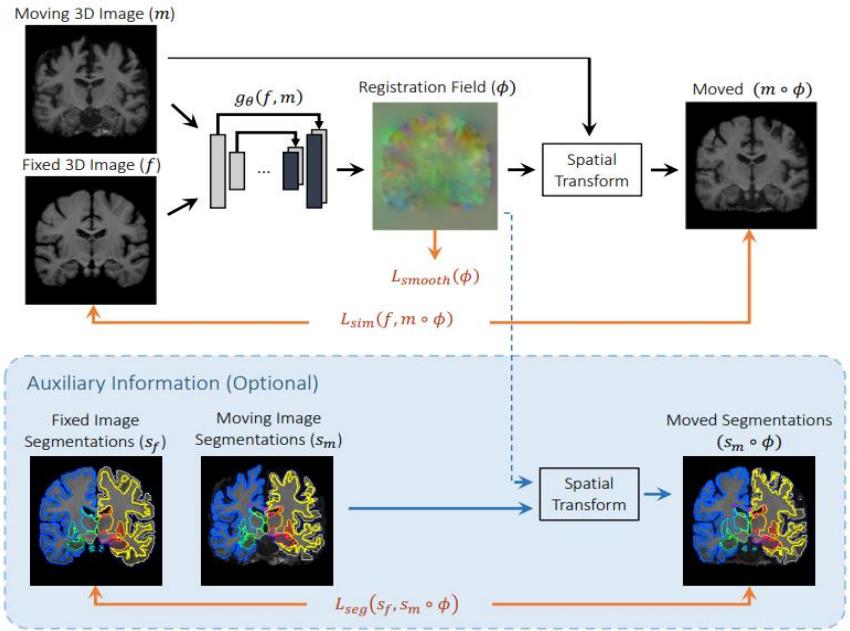
- Two losses:
  - Unsupervised loss.
  - Supervised loss.

- Unsupervised loss:

$$\mathcal{L}_{us}(f, m, \phi) = \mathcal{L}_{sim}(f, m \circ \phi) + \lambda \mathcal{L}_{smooth}(\phi)$$

  - Experiment is done with **MSE**, CC, MI as the similarity loss functions.
  - $\mathcal{L}_{smooth}(\phi)$ penalizes local spatial variation in ϕ.

$$\mathcal{L}_{smooth}(\phi) = \sum_{\mathbf{p} \in \Omega} \|\nabla \mathbf{u}(\mathbf{p})\|^2$$



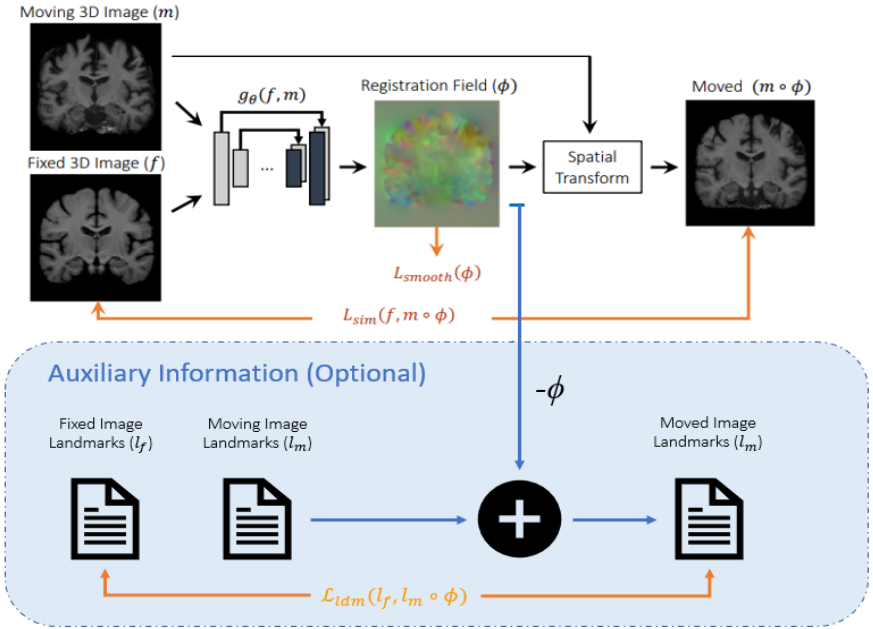
Voxelmorph: Balakrishnan et al., IEEE Transactions on Medical Imaging, 2019.

Voxelmorph: Loss Functions

- Two losses:
  - Unsupervised loss.
  - Supervised loss.

- Supervised loss:
  - If landmark points are available, then for *K* landmark points.

$$\mathcal{L}_{ldm}(l_f, l_m, \phi) = \frac{1}{K}\sum_{k=1}^{K} MSE(l_f^k, l_m^k - \phi_{f,m}^k)$$



Voxelmorph: Balakrishnan et al., IEEE Transactions on Medical Imaging, 2019.

Experimental Setup

- Registration is always done against the fixed template image.
- 7 nerve entry points in the inferior ventral nerve cord are chosen.
- More such landmarks can be added to further assist the network.

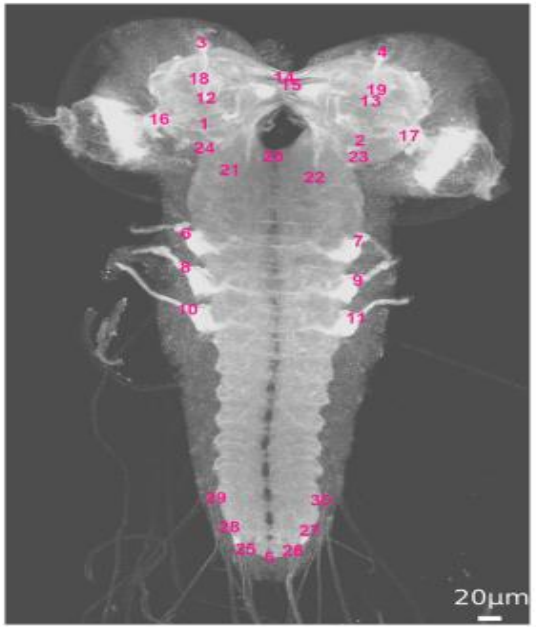
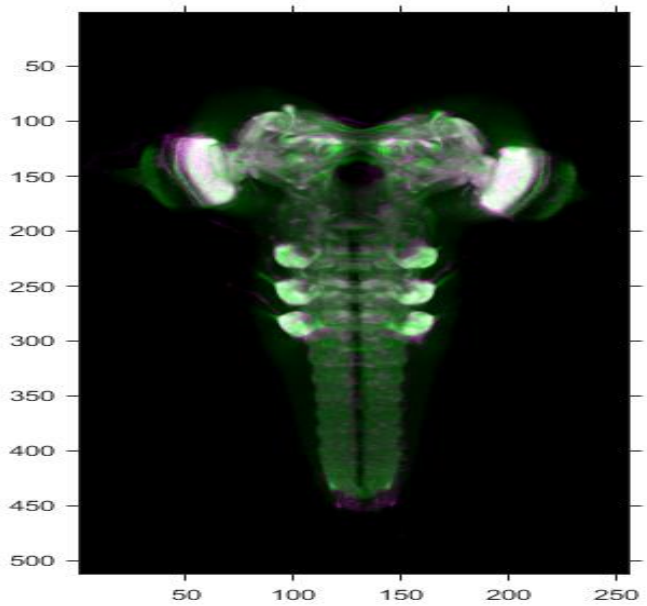


Image: Muenzing, Sascha E A et al. *Neuroinformatics* vol. 16,1 (2018): 65-80.

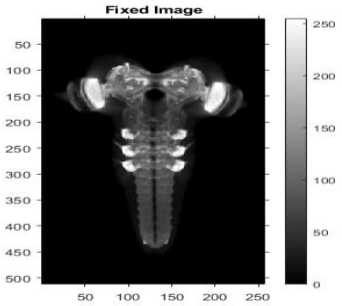
Assessment

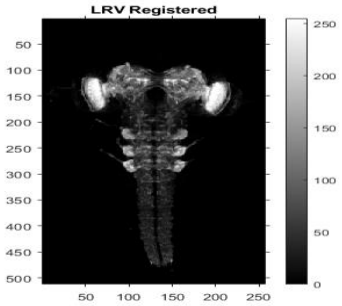
- Qualitative assessment.
  - The registered scans are merged with the template in different colors (green and magenta) to then visually inspect deviations.

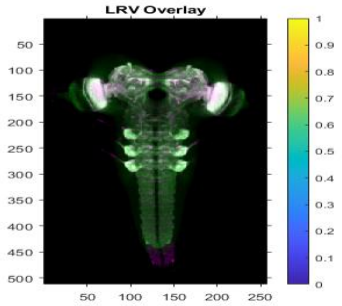
- Quantitative assessment.
  - Global Registration Error.
  - VNC Terminal Error Indicator (VI).
  - Thoracic Nerve Error Indicator (TI).
  - Landmark Registration Error (LRE).

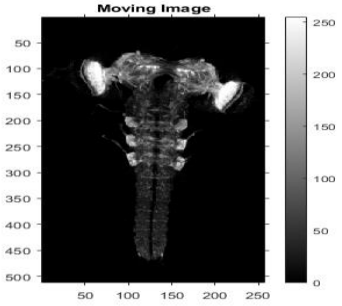


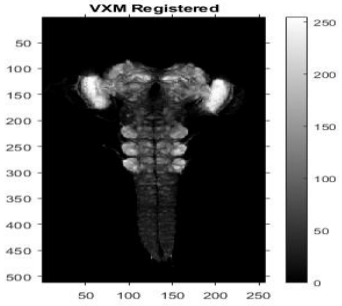
Results | Voxelmorph registration without auxiliary information

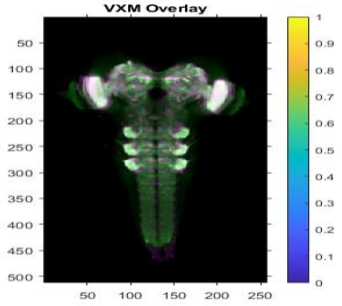












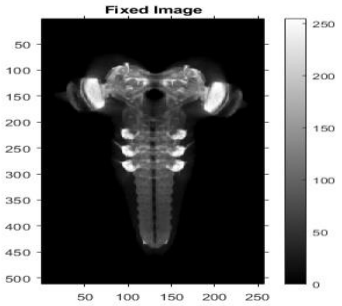
Quantitative Measure

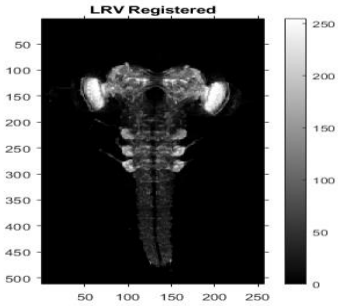
Quantitative LRV	
Global Registration Error	46
VNC Nerve Error	24
Thoracic Nerve Error	57

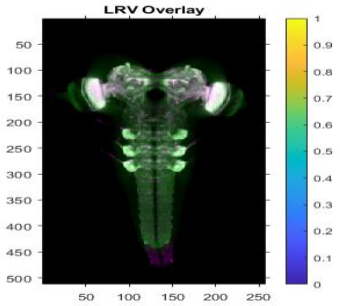
Quantitative Measure

Quantitative VXM	
Global Registration Error	44
VNC Nerve Error	18
Thoracic Nerve Error	60

Results | Voxelmorph registration with auxiliary information

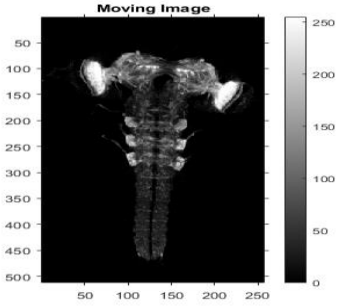


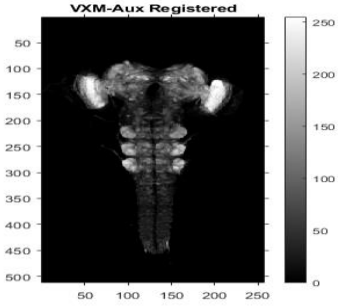


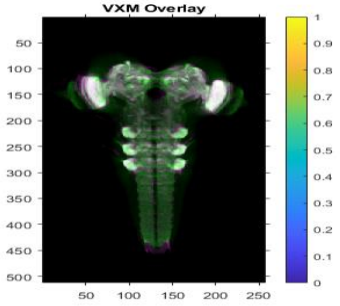


Quantitative Measure

Quantitative LRV	
Global Registration Error	46
VNC Nerve Error	24
Thoracic Nerve Error	57







Quantitative Measure

Quantitative VXM-Aux	
Global Registration Error	45
VNC Nerve Error	44
Thoracic Nerve Error	64

Results

Generalizability

- To evaluate the robustness of the network, the following test was performed.
  - Experimental configuration_1:
    - Train on larvalign dataset
    - Test on larvalgin dataset
  - Experimental configuration_2:
    - Train on janelia_dataset.
    - Test on larvalign_dataset

- The qualitative and quantitative assessment of configuration_1 is comparable with configuration_2 in both the respective scenarios of with and without auxiliary information.

Work to do

- In many examples, the quantitative score of larvalign is higher than that of voxelmorph.
- And in a few examples, the VNC error score of the network trained without landmarks is higher than that of its counterpart trained with landmarks.
- Data augmentation: flipping in horizontal direction.
- Work with large scale images.
- Include more landmark points.

Vielen Dank
für Ihre Aufmerksamkeit