Deep Learning Enabled Multi-Organ Segmentation of Mouse Embryos

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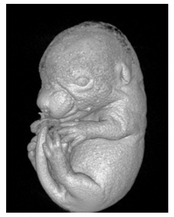
Introduction

- The IMPC has generated a repository of 3D imaging data from mouse embryos, providing a rich resource for investigating phenotype/genotype interactions
- Traditional image analysis requires significant computational resources, specialized equipment, and labor
- Manual annotation of multiple structures is very time consuming, prone to variability, and is typically not feasible in big data applications
- Atlas-based registration algorithms can improve speed but are still computationally intensive, require specialized hardware, and can introduce new sources of bias
- We introduce **MEMOS,** an open-source tool powered by a deep-learning model to be used in a semi-supervised pipeline for fast and highly accurate segmentations[1]
- MEMOS is deployed on the 3D Slicer platform, providing seamless access to tools for reviewing and editing the MEMOS segmentations.

Data

Knockout mouse phenotyping project (KOMP2)
- Generating mouse null mutants for each protein-coding gene in the mouse genome
- Comprehensive phenotyping of each mouse mutant to determine developmental, physiological, and biochemical parameters
- Provides an important baseline for exploring gene function

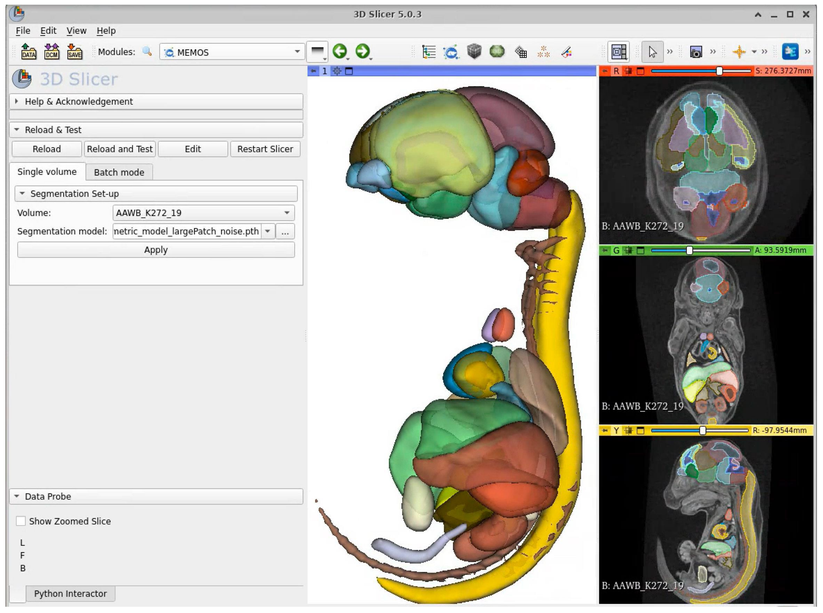
Imaging Data
- Whole body micro-CT scans collected at E15.5 from baseline and lethal/sub-viable knockout strains
- Low resolution scans have approximately 250x250x400 voxels
- Consensus population image previously calculated and manually segmented with 50 labels[2,3]



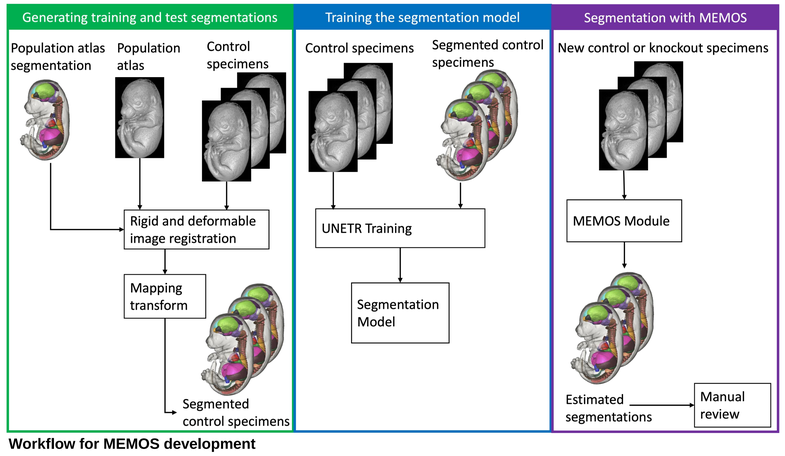
E15.5 stage mouse embryo

MEMOS

MOUSE EMBRYO MULTI-ORGAN SEGMENTATION



Methods



Workflow for MEMOS development

Generating labeled data for testing and training
- 50 labels from the E15.5 atlas transferred to 91 baseline scans from the KOMP2 dataset to produce a "ground truth" dataset.
- Atlas-based segmentation implemented using ANTS and ANTSR packages[4,5]

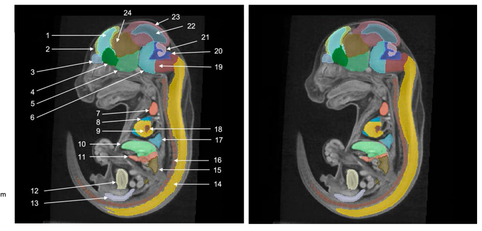
Training the deep learning model
- UNETR architecture for estimating 50 anatomical regions[6]
- Trained on a server with 512 GB RAM and A6000 GPUs
- Data divided into training (73), validation (18) and test (5) sets
- Input images randomly sampled with a volume of 128x128x128

Deployment of the MEMOS module
- Trained segmentation module deployed as an extension of the open-source 3D Slicer platform
- Can be installed with a single click and used to estimate segmentations on new data from the GUI
- Segmentations can be edited within the same application

Results

Segmentation accuracy:
- Average Dice coefficient between the MEMOS-generated and state-of-the-art atlas-based segmentations for the test data set is **0.91**.
- 48 out of 50 segments had an average Dice score over **0.8**

1. Left ventricular zone
2. Left neopallial cortex and amygdala
3. Left olfactory bulb
4. Left septal area
5. Left hypothalmus
6. Pons
7. Left thymic rudiment
8. Right ventricle
9. Left ventricle
10. Medial lobe of liver
11. Left lobe of liver
12. Bladder
13. Rectum
14. Spinal cord
15. Caudate lobe of liver
16. Vertebrae
17. Accessory lobe
18. Left ventricle chamber
19. Medulla oblongata
20. Fourth ventricle
21. Right cerebellar primordium
22. Mesencephalic vesicle
23. Midbrain
24. Left thalamus



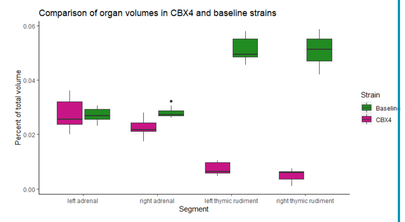
Computational Efficiency
- Manual segmentation of 50 segments in a fetal mouse scan takes approximately **40 hours**
- Using a high-performance server, 50 structures can be segmented using an atlas-based method (ABM) in approximately **6 hours**
- MEMOS can perform the same segmentation in under **22 seconds**

Platform specific performance for MEMOS and ABM

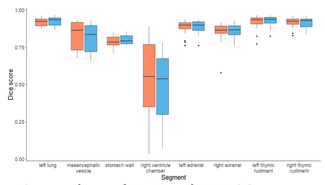
System	Compute platform	Memory	Average MEMOS segmentation time	Average ABM segmentation time
Linux server	NVIDIA A6000 GPU, AMD Ryzen Threadripper PRO 3995WX, 64 cores	512 GB RAM	21.9 seconds	6 hours
Linux server, CPU only	AMD Ryzen Threadripper PRO 3995WX, 64 cores	512 GB RAM	412.0 seconds	NA
Windows desktop	Intel Xeon W-2125	64 GB RAM	1719.9 seconds	NA

Results

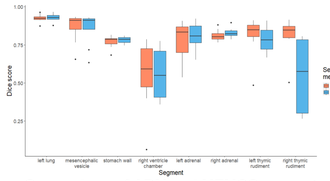
Segmentation sensitivity
- Validated for the Cbx4 knockout strain, with previously reported volume reductions in the adrenals and thymic rudiments.
- Statistically significant volume decrease for the right adrenal (p=0.001), left thymic rudiment (p<0.001) and right thymic rudiment (p<0.001) in the Cbx4 knockout group
- Volume decrease in the left adrenals is not statistically significant



Comparison to manual segmentation
- MEMOS is designed as a replacement for gold standard ABM approaches frequently used in big-data applications
- Manual segmentation would not be feasible for this dataset
- To quantify the relationship between ABM, MEMOS, and manual segmentation, we manually segmented a subset of 8 structures from 22 baseline and 8 CBx4 knockout mice for comparison with to the two automated methods
- For the baseline specimens, there are no statistically significant differences in the Dice overlap scores for the two automated methods
- In the Cbx4 knockout group, with known abnormality in 4/8 sampled segments, only the right thymic rudiment shows a significant difference in the MEMOS segmentation



Comparison of ABM and MEMOS-generated segmentations to manual labels for baseline



Comparison of ABM and MEMOS-generated segmentations to manual labels for Cbx4 knockout

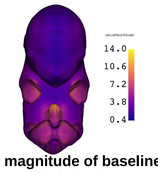
Conclusions

- **MEMOS** is an accessible, fully open-source, deep learning-enabled tool to segment micro-CT scans of embryonic mice.
- Accuracy comparable to gold-standard methods requiring multiple orders of magnitude more computation time and resources.
- Sensitivity supports use of this tool with the KOMP2 database on both baseline and knockout strains
- Can be retrained and deployed for custom applications/datasets
- Available on GitHub: **https://github.com/SlicerMorph/SlicerMEMOS**
- One-click installation from the 3D Slicer App: **https://download.slicer.org/**

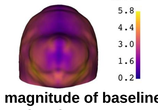
Next Steps

Extending the MEMOS module
- Train with knockout strains and manually edited labels for improved accuracy and robustness
- Provide models for additional developmental stages and strains through a model browser in the MEMOS module

Deep phenotyping of shape and asymmetry
- Use surface models extracted from the KOMP2 volumetric scans in a pipeline to create dense assessments of asymmetry and shape abnormality across the surface
- Identify knockout strains with asymmetric phenotypes
- Select candidate genes that will be explored for associations between asymmetric growth and orofacial cleft risk



Average magnitude of baseline asymmetry, whole body



Average magnitude of baseline asymmetry, head

References

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