3D Reconstruction and Multi-Organ Mapping of the Female Mouse Reproductive System as a Function of Age

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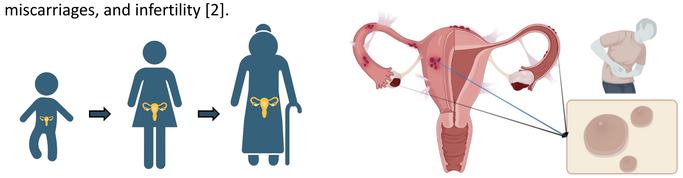
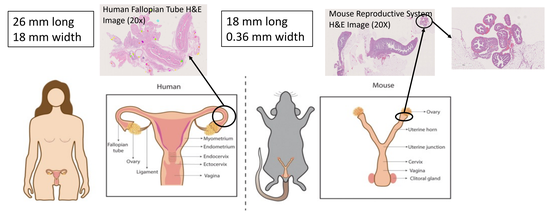
Motivation

Advanced maternal age is associated with infertility and a higher risk of experiencing adverse health complications. Menopause is a significant indicator of aging. After menopause, the uterus, fallopian tubes, and ovaries start to become smaller. Additionally, the vaginal wall, cervix, and uterine muscles tend to become looser due to the loss of muscle content. What's worse?, the accumulation of scarring and inflammation increases the likelihood of developing ovarian cysts, uterine fibroids, fallopian tube blockage, and raises the risk of gynecological cancers. These factors collectively contribute to the challenges faced by women as they age [1].

One common issue in the female reproductive system is the development of cysts, and cancerous cysts are more prevalent after menopause. Cysts can lead to health complications such as cyst rupture, ovarian torsion, abdominal or pelvic pain, vaginal discomfort, excessive bleeding, miscarriages, and infertility [2].



Conducting research on human reproduction presents challenges due to the complexities and limitations associated with investigating biological samples from women. On the other hand, the mouse model offers certain advantages in terms of accessibility and size, allowing for the exploration of interconnectivity between reproductive organs. Besides, studies have demonstrated that mouse models are crucial in uncovering patterns of cancer cell invasion and host immune responses in the reproductive system.



Objectives

Goal: Create 3D, multi-organ maps of the normal mouse reproductive system at a multi-cm³ scale to identify major changes to ovary, fallopian, cervix and vagina morphology and immune infiltration with age

Materials and Methods

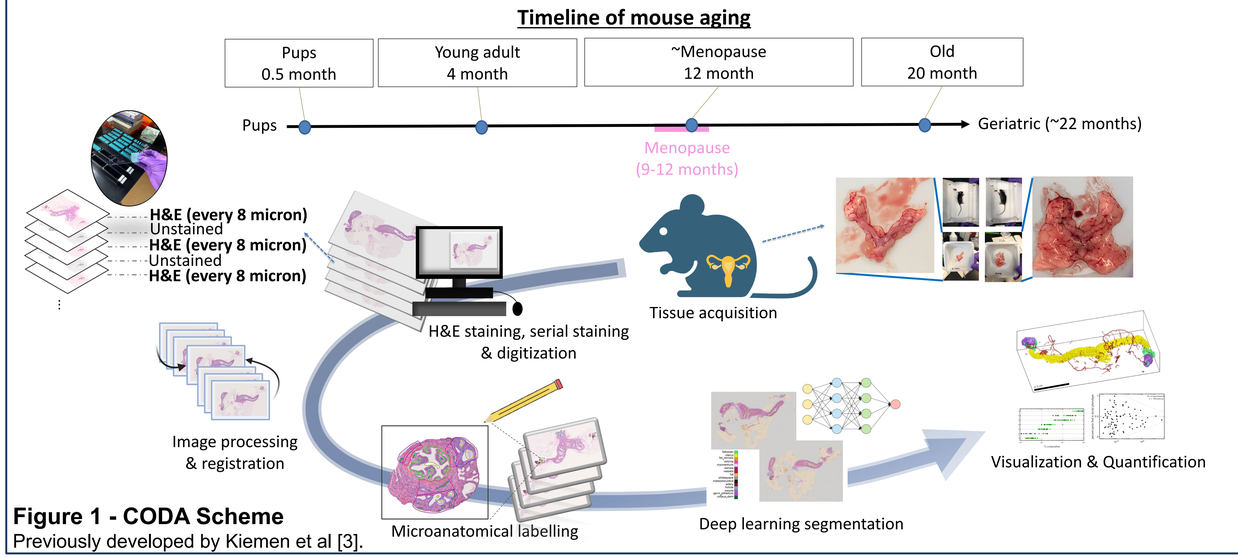


Figure 1 - CODA Scheme
Previously developed by Kiemen et al [3].

Results

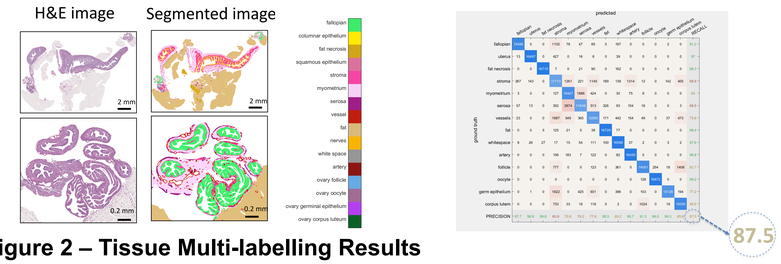
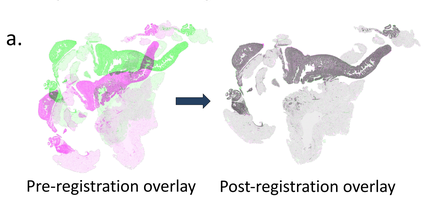


Figure 2 – Tissue Multi-labelling Results
Microanatomical components of the mouse reproductive system are reliably segmented and labeled by the deep learning model

Figure 3 – Image Registration Results
a. Images are aligned into a semi-continuous stack using global and elastic registration
b. Z-projections of the image stack



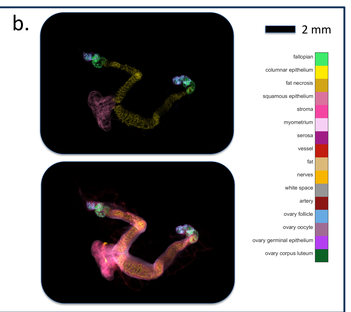
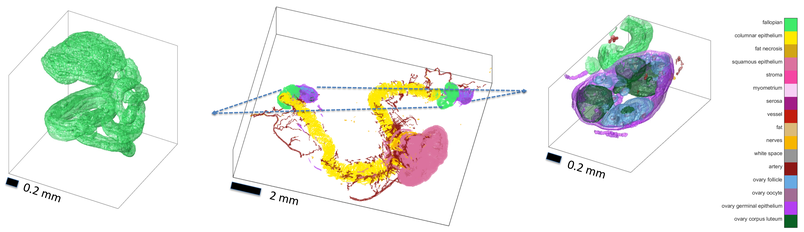


Figure 4 – Three-dimensional Reconstruction Results
Illustration of the fully-labelled 3D volumes of a young mouse sample at single-cell resolution



a.

	Volume (mm^3)	Volume percentage(%)
Total	50.5	100.0
Fallopian tube	0.7	1.4
Fallopian tube 1	0.4	0.8
Fallopian tube 2	0.3	0.6
Columnar epithelium	2.0	4.0
Squamous epithelium	5.0	9.9
Follicles	0.3	0.6
Oocytes	0.0	0.0
Corpus luteum	0.4	0.7

b.

Total	Number
Fallopian tube	2
Follicles	56
Oocytes	218
Corpus luteum	98

Figure 5 – Quantitative Results
Initial quantitative results corresponds to literature review a. volume and volume percentage pf each tissue compartment b. number of specific quantifiable tissue compartments

Future Directions

- Construct cellular-level 3D models of the mouse reproductive system at 4 different ages
- Perform IMC/IHC-based analysis to quantitively examine change in tissue morphology and cyst development under aging effect
- Further investigation and comparison with human reproductive tissue at corresponding tissue sections and ages

References

[1] Glick I, Kadish E, Rottenstreich M. Management of Pregnancy in Women of Advanced Maternal Age: Improving Outcomes for Mother and Baby. Int J Womens Health. 2021 Aug 10;13:751-759. doi: 10.2147/IJWH.S283216. PMID: 34408501; PMCID: PMC8364335.
[2] Mobeen S, Apostol R. Ovarian Cyst. In: StatPearls. StatPearls Publishing, Treasure Island (FL); 2022. PMID: 32809376.
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Acknowledgements

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