Quantitative morphological analysis of age-related degeneration in a model tissue system

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Introduction

• Many tissues show age-related functional decline
• Goal: Use imaging to quantitatively assess structural decline
• Can we identify structural biomarkers corresponding to age, function or lifespan?
C. elegans dataset

Young adult (day 0)

Old adult (day 12)
Analysis Overview

- Pharynx images
- Crop & align
- Training image sets
- Feature extraction
- Pattern recognition
- Trained Model
- Outputs:
  - Image similarity
  - Age predictions

Feature extraction:

- Test image sets

Analysis:

- Automated pattern recognition to assess morphological changes during aging
Unordered model predicts class order and identifies developmental stage.

Days since molting

0 2 4 6 8 10 12
Age predictions suggest three distinct morphological stages

Predictions made on every animal, sorted by known age and predicted age

Probability distributions of predicted age

Pearson’s Correlation Coefficient: 0.58, p-value: 7.18 E-55
Corpus analysis confirms Terminal Bulb findings

Corpus Age Predictions

TB Age Predictions

- During days 2 and 4, corpus prediction correlates with TB prediction twice as much as it correlates with known age.
- Change in structural state is repeated in a separate tissue.
Slow pumping mutant shows delayed aging

Predictions made on every animal, sorted by known age and predicted age

Probability distributions of predicted ages

Slow pumping mutant shows delayed aging
Serotonin deficient mutant resembles advanced aging

Predictions made on every animal, sorted by known age and predicted age

Probability distributions of predicted ages

Serotonin deficient mutant resembles advanced aging

Predictions made on every animal, sorted by known age and predicted age

Probability distributions of predicted ages
Mutants are indistinguishable from normal aging
Structural Biomarkers of Function

- Longitudinal data collection
- Measure Pump rate, Image, then Rescue day 6 animals
- Check pump rate and death state every few days thereafter

![Graph showing Lifetime Pumping Ability](image)
Structural Biomarkers at Day 6 correspond to sustained muscle function (LPA)

Experimental correlation: 0.40

Negative control correlation: 0.18 ± 0.08

Significance: 0.0017
Summary

• Validated approach of using imaging to assess structural states

• Currently applying to vertebrate models (Poster 15)

• Identified structural biomarkers of age that suggest distinct stages of aging

• Identified separate structural biomarkers of sustained muscle function (LPA)
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