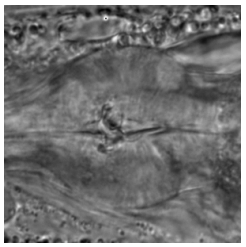

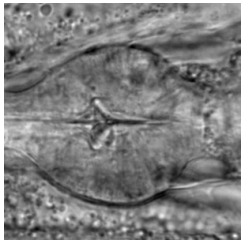

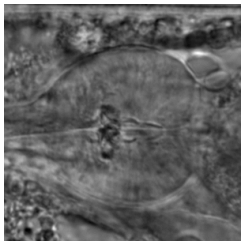

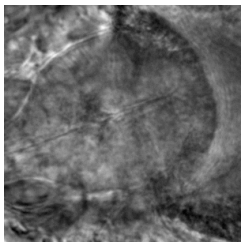

Quantitative morphological analysis of age-related degeneration in a model tissue system

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open microscopy environment

National Institute on Aging
Intramural Research Program

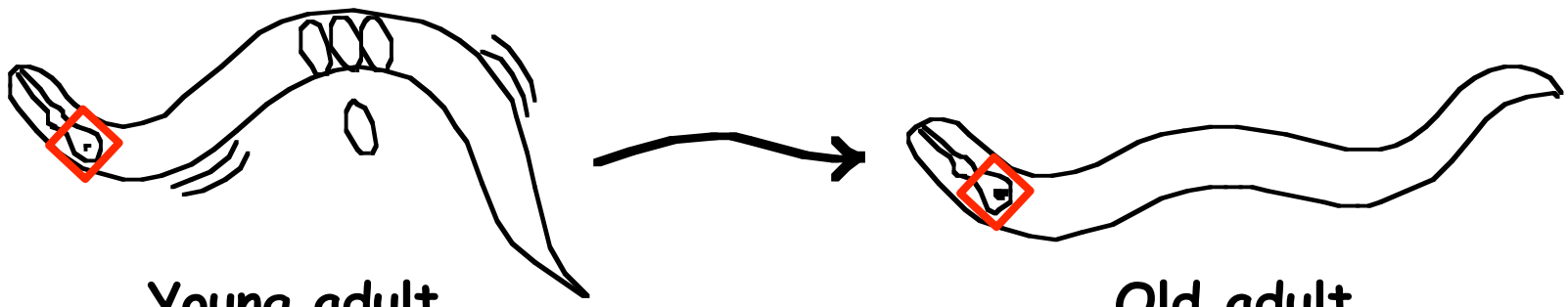
NATIONAL INSTITUTES OF HEALTH

DEPARTMENT OF HEALTH & HUMAN SERVICES • USA

Introduction

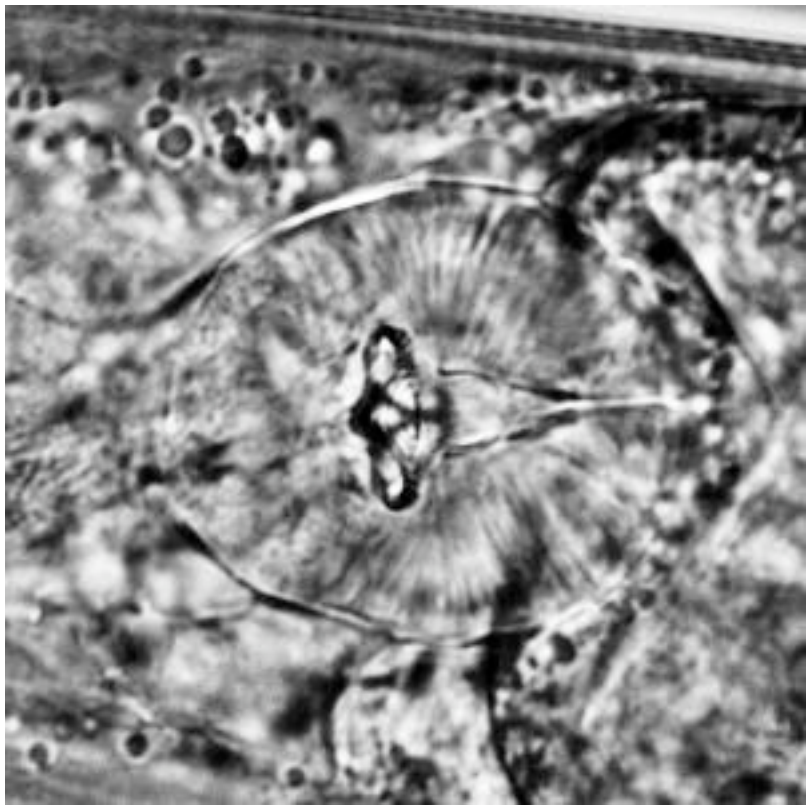
- Many tissues show age-related functional decline
- Goal: Use imaging to quantitatively assess structural decline
- Can we identify structural biomarkers corresponding to age, function or lifespan?

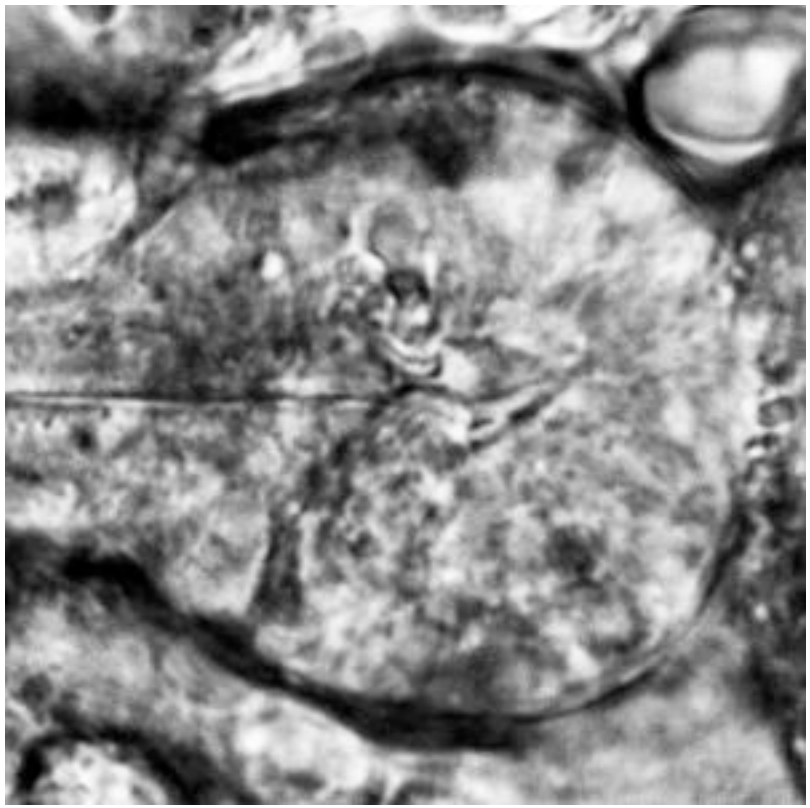
C. elegans dataset



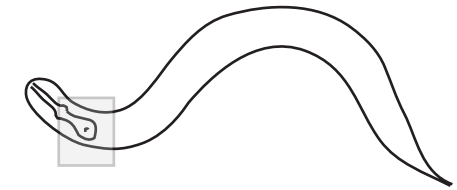
Young adult
(day 0)

Old adult
(day 12)



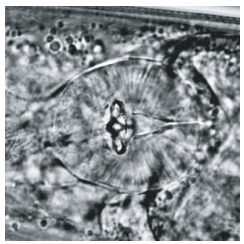


Analysis Overview



pharynx images

crop & align



Training image sets

Test image sets

Feature extraction

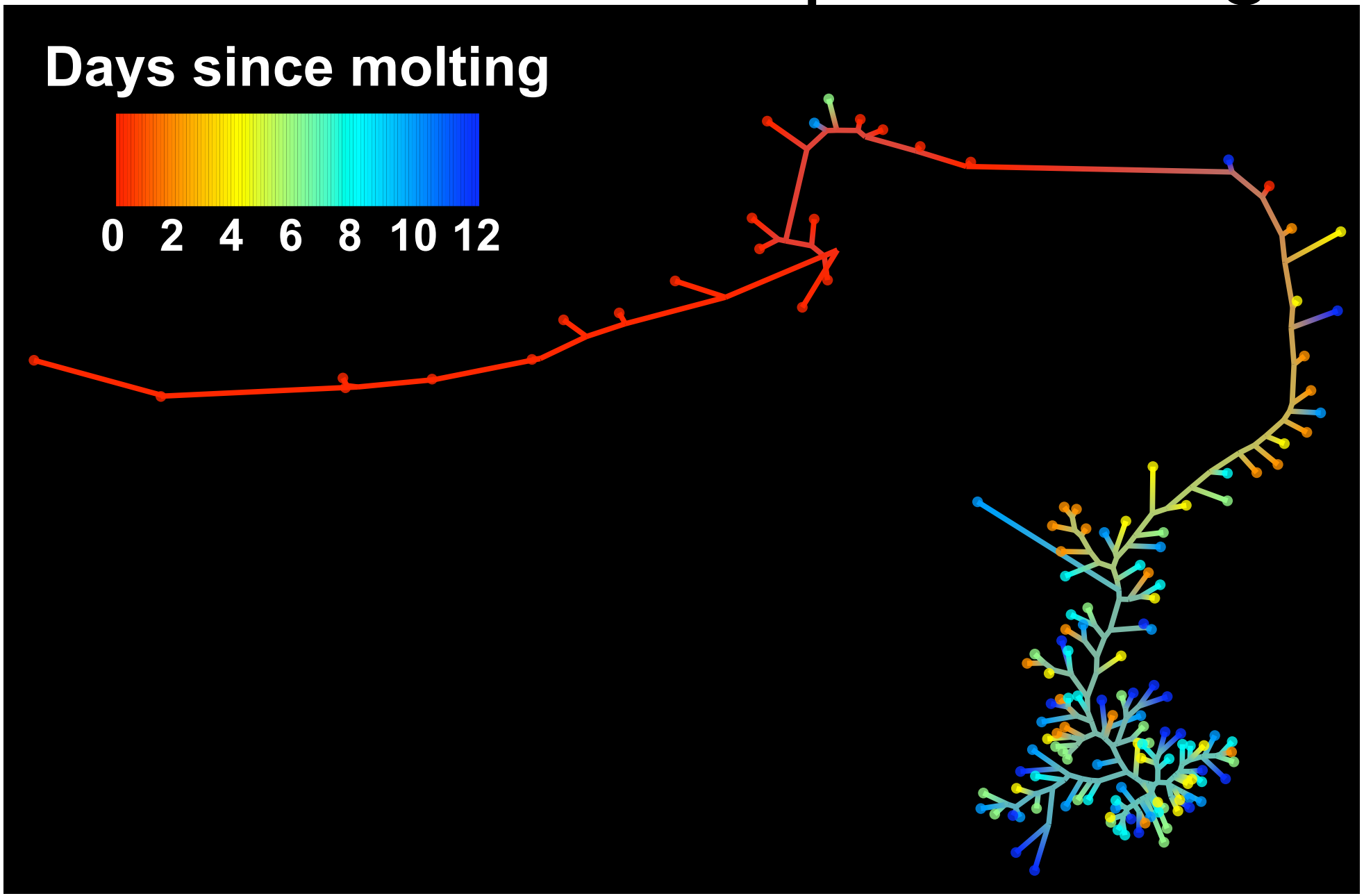
Feature extraction

Pattern recognition

Trained Model

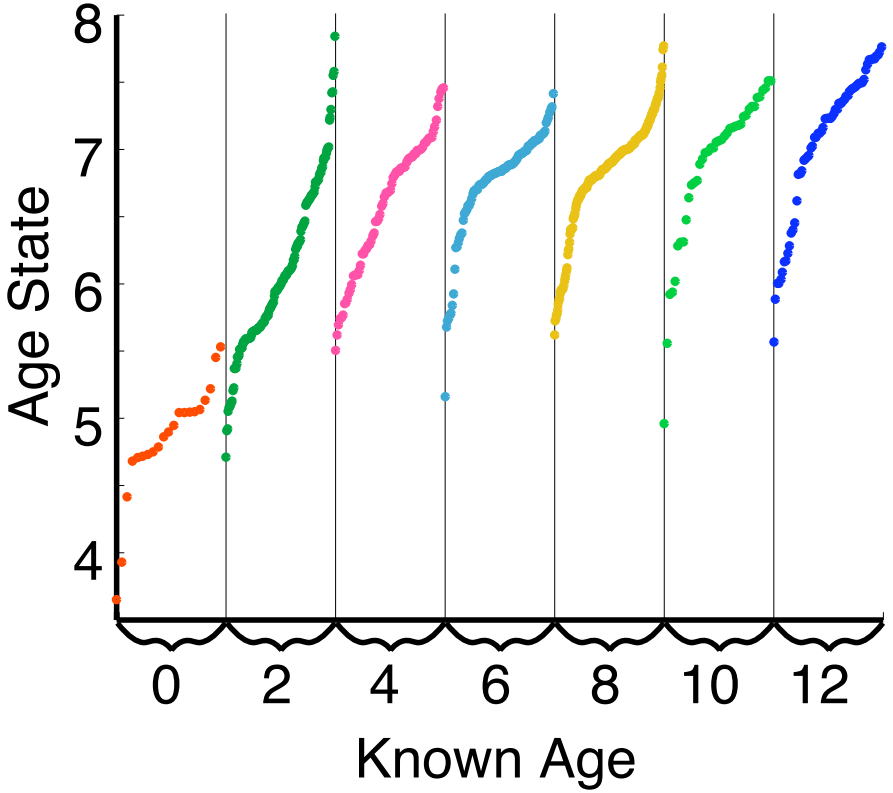
Outputs:
* Image similarity
* Age predictions

Unordered model predicts class order and identifies developmental stage

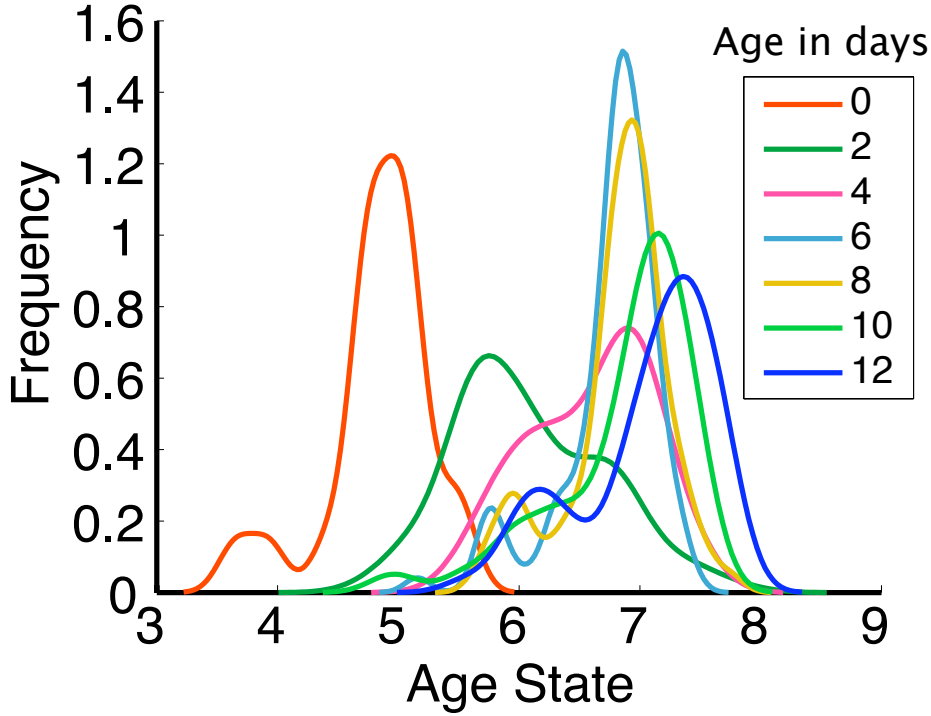


Age predictions suggest three distinct morphological stages

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



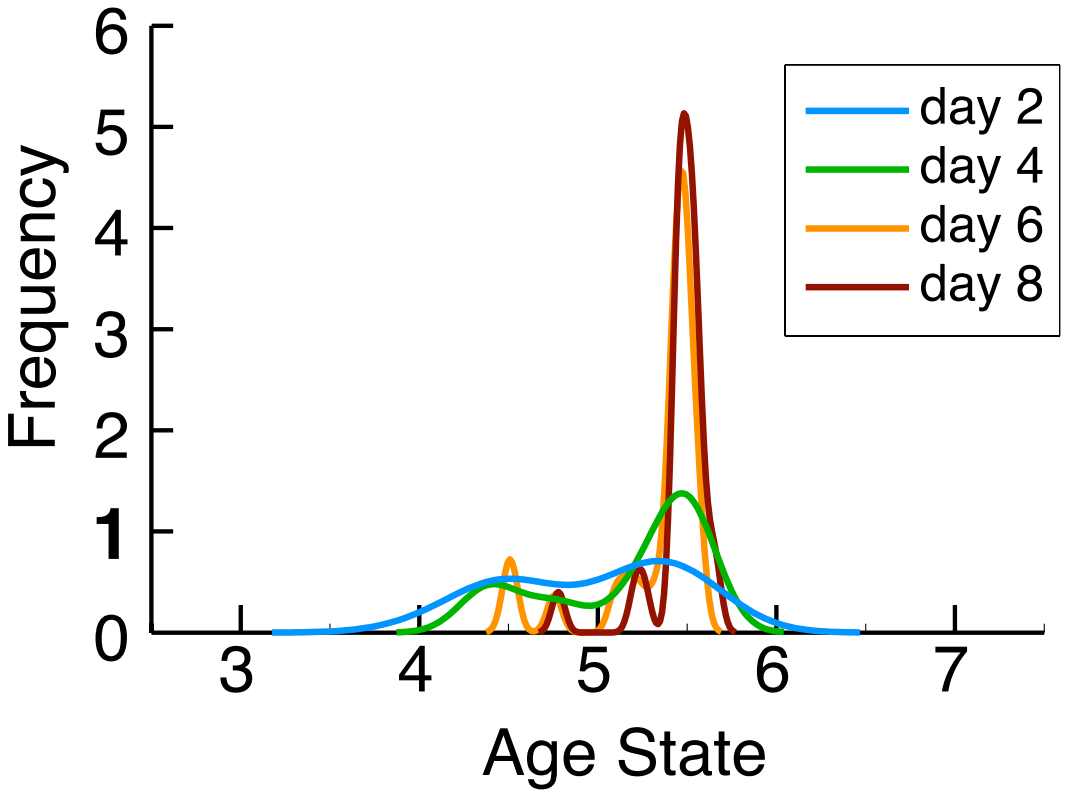
Probability distributions of predicted age



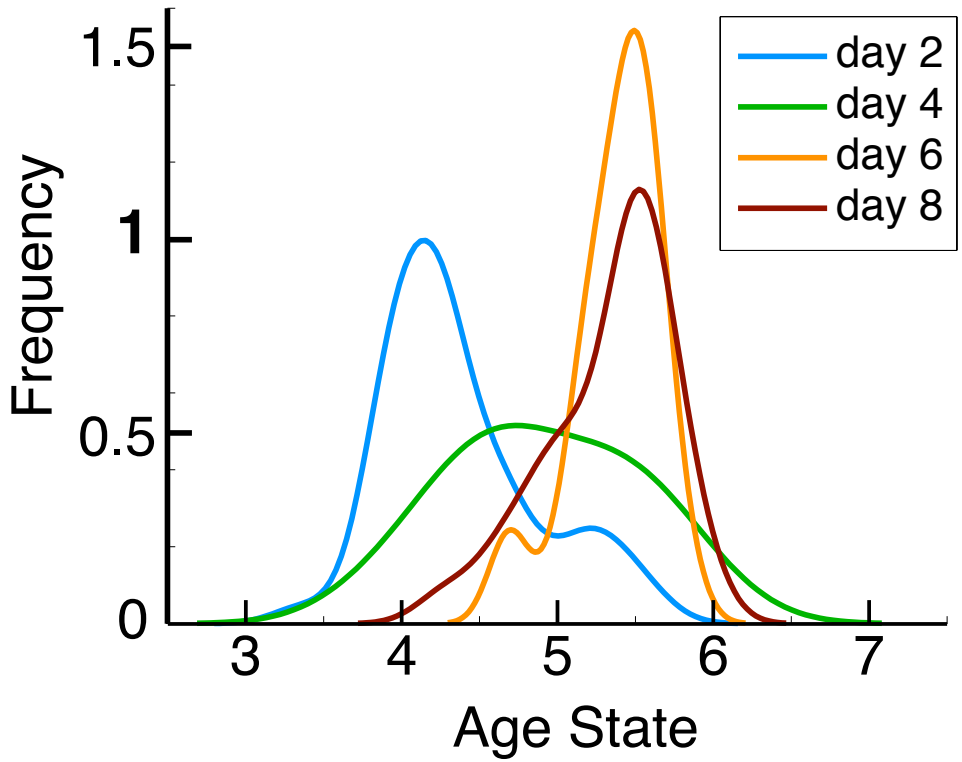
Pearson's Correlation Coefficient: 0.58, p-value: 7.18 E-55

Corpus analysis confirms Terminal Bulb findings

Corpus Age Predictions



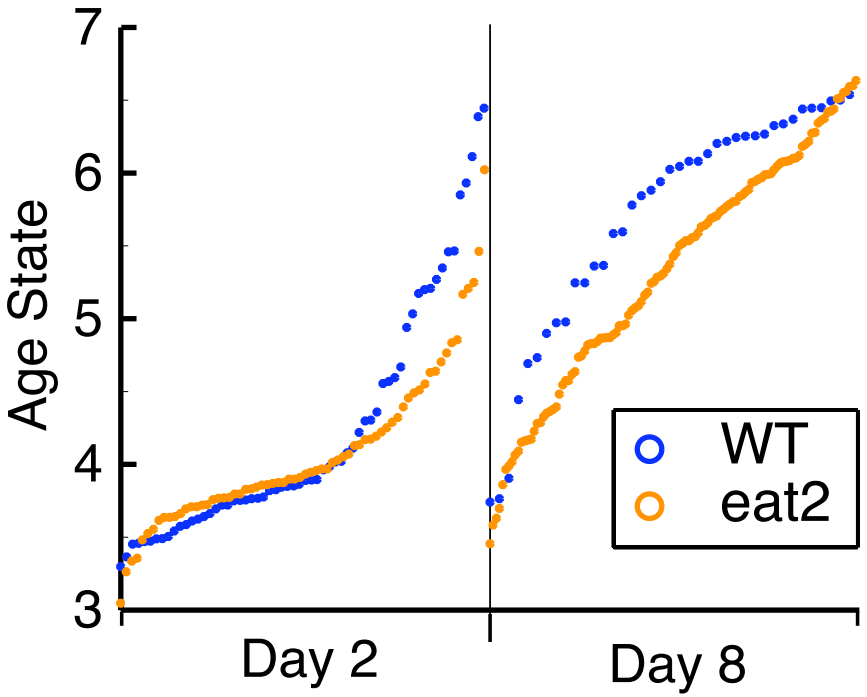
TB Age Predictions



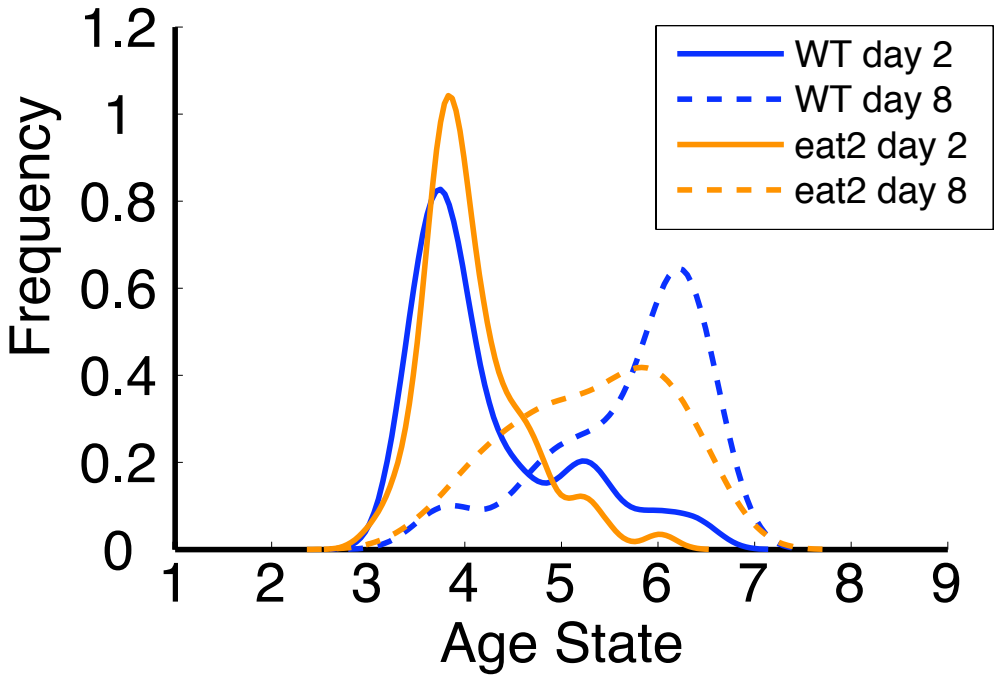
- During days 2 and 4, corpus prediction correlates with TB prediction twice as much as it correlates with known age
- Change in structural state is repeated in a separate tissue

Slow pumping mutant shows delayed aging

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

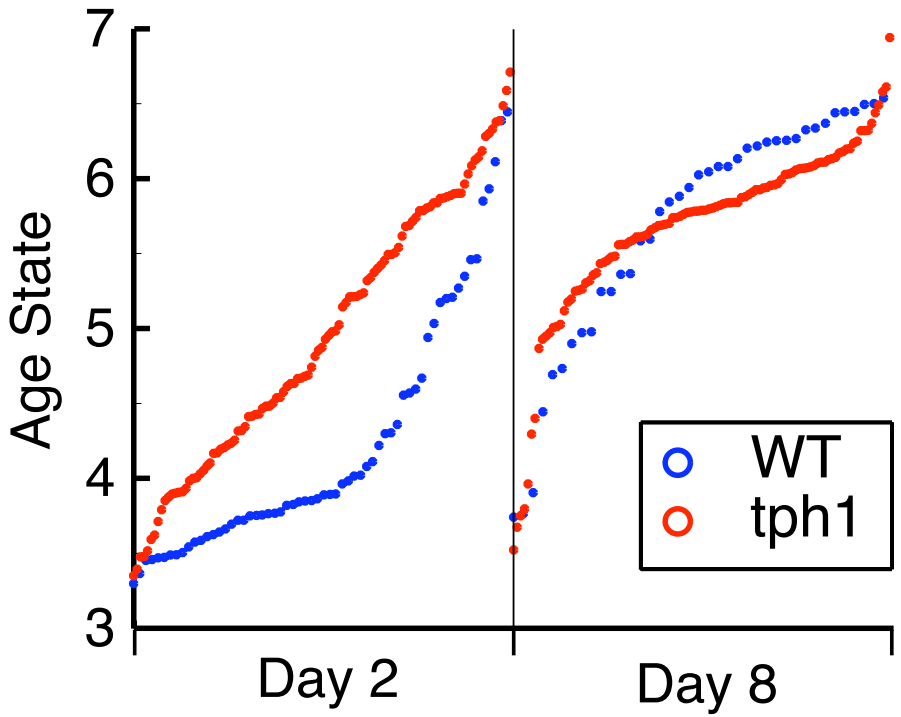


Probability distributions of predicted ages

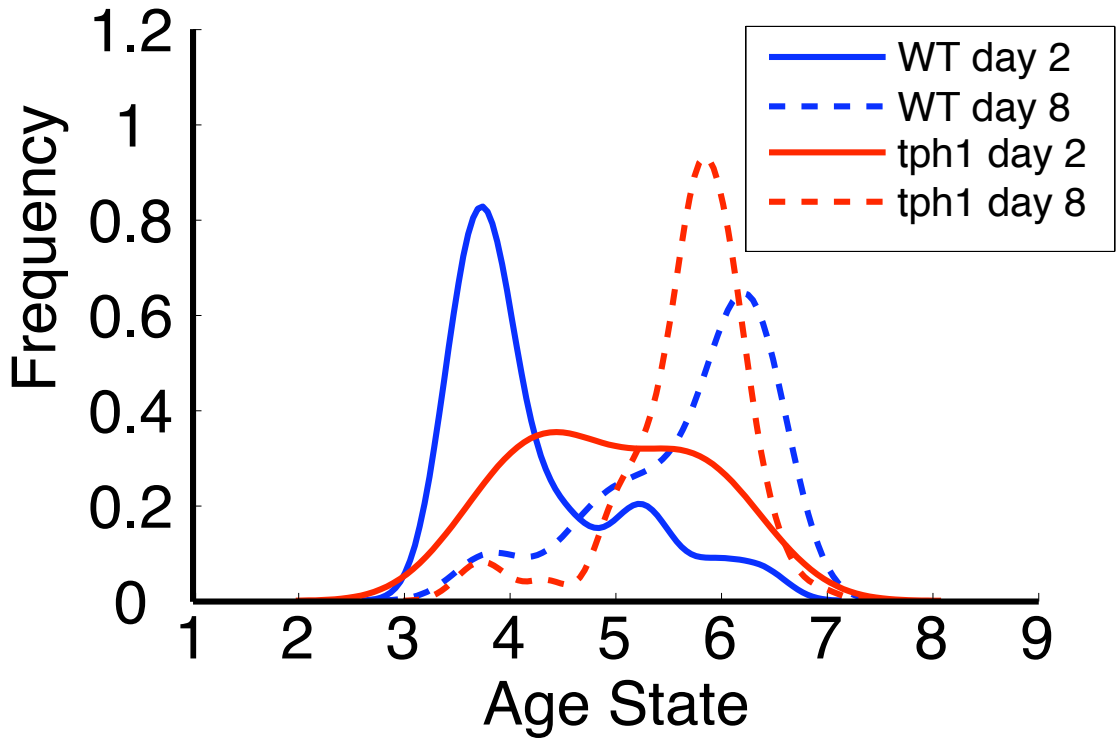


Seratonin deficient mutant resembles advanced aging

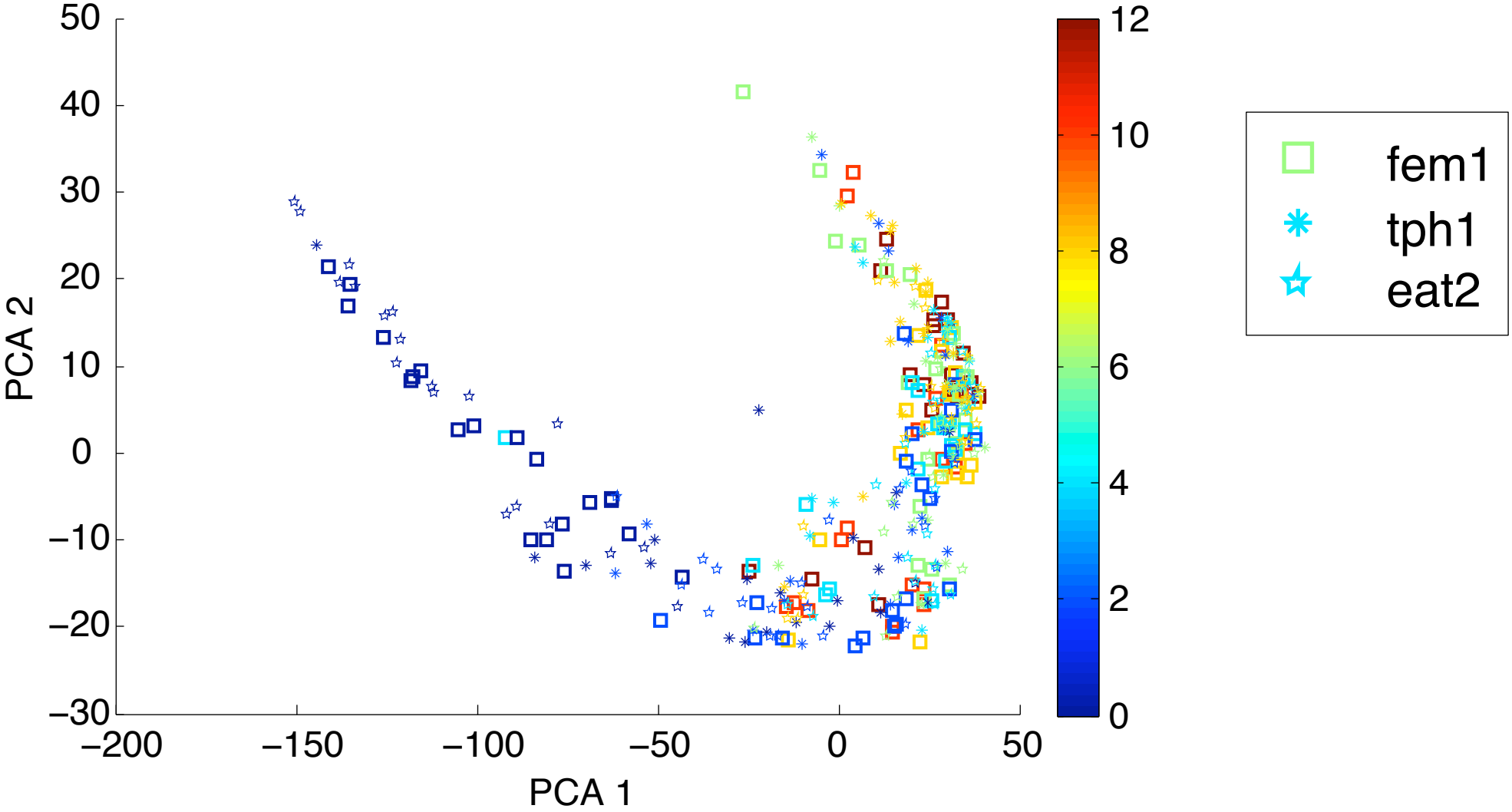
Predictions made on every animal, sorted by known age and predicted age



Probability distributions of predicted ages

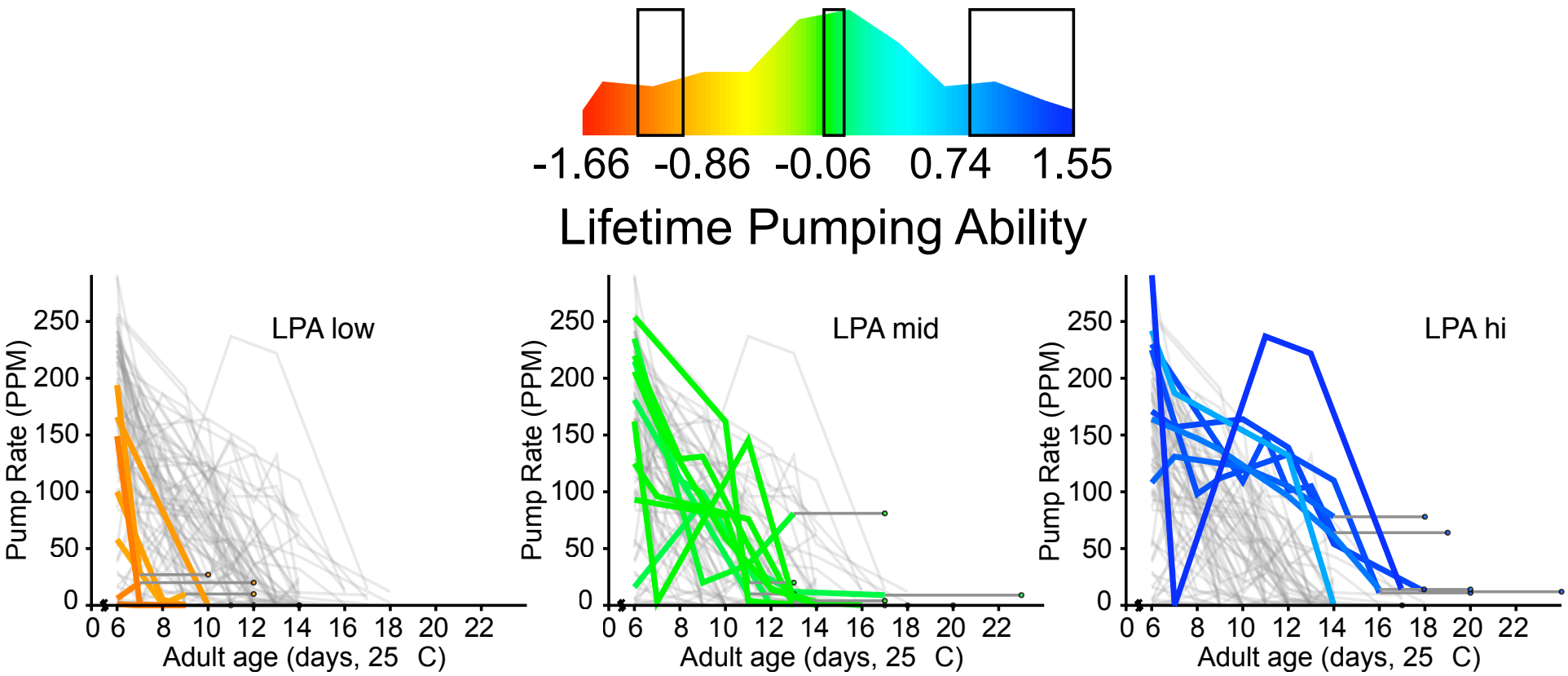


Mutants are indistinguishable from normal aging

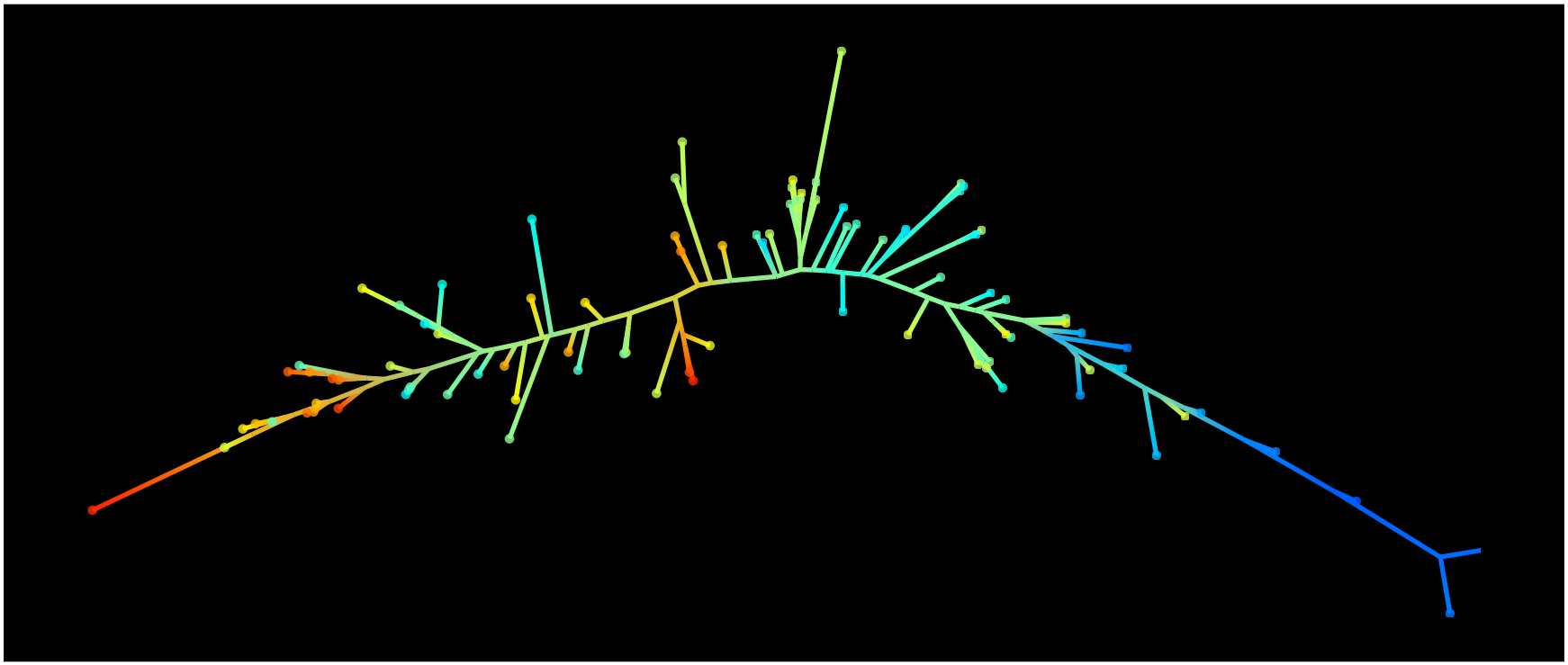


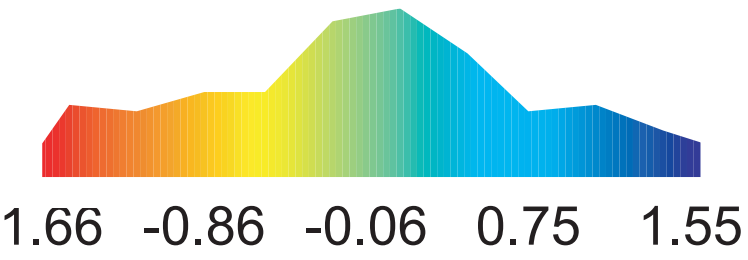
Structural Biomarkers of Function

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



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)

Acknowledgments

IICBU / LG

- Mark Eckley
- Tomasz Macura
- Nikita Orlov
- Lior Shamir
- Ilya Goldberg

IMGU / LNS

- Wendy Iser
- David Chow
- Michael Chen
- Cathy Wolkow

Related Posters

Age Map: Thursday afternoon, #15

Cell-based RNAi Screening: Thursday afternoon, #7

Lymphoma: Friday morning, #51