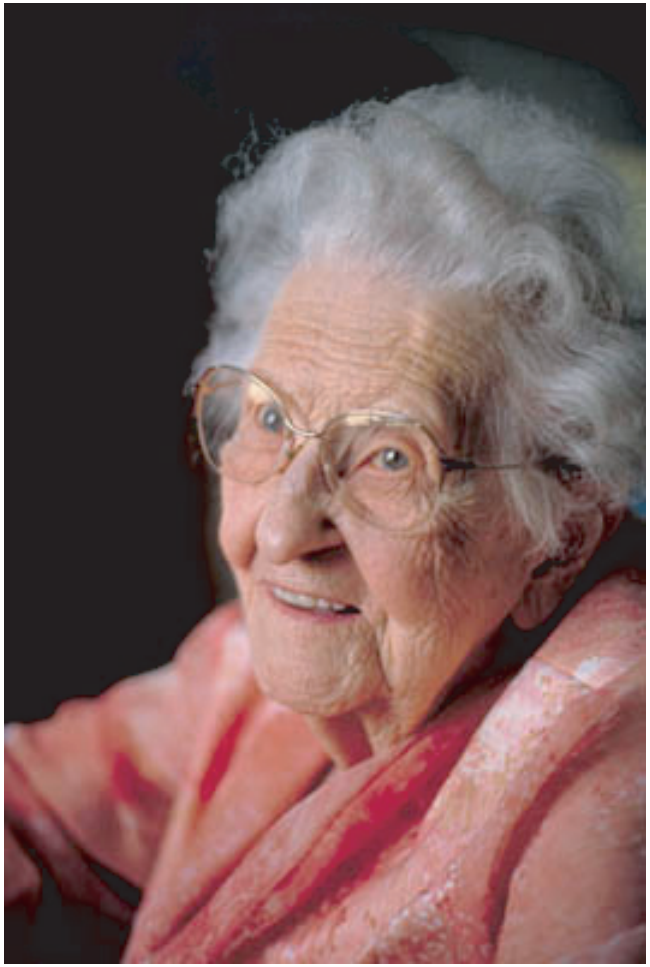
Questions about aging...



Why do we age?

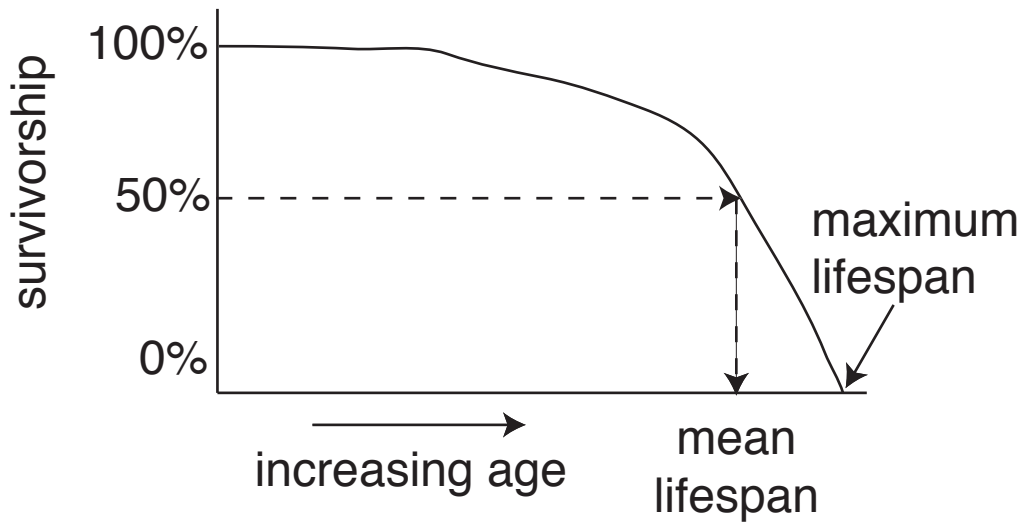
Why do bodily functions decline during aging?

Why is aging assiciated with certain diseases?

Can anything be done to avoid declines during aging?

What we know about aging

I. Mortality rate increases with increased age

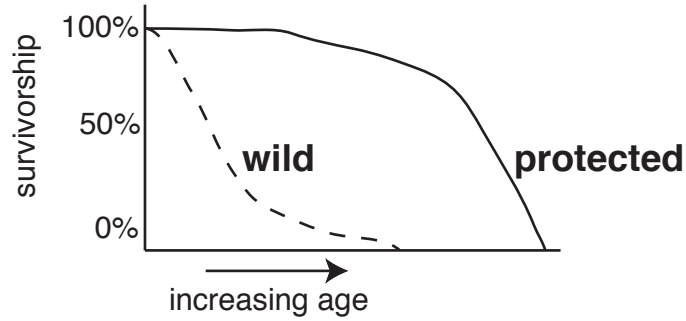


II. Different species have different lifespans

nematode	2-4 weeks
fly	1-2 months
mouse	2-3 years
human	80-100 years

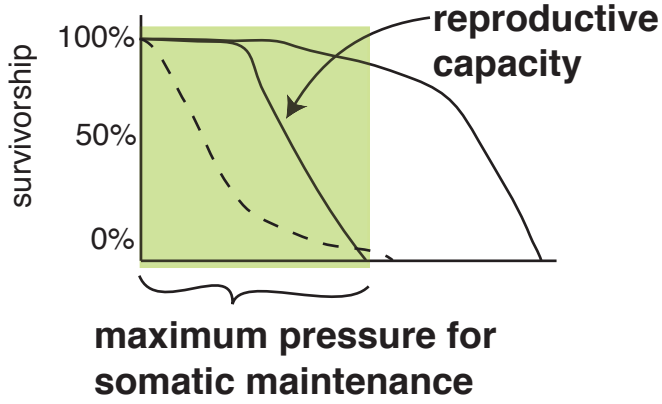
Theories of aging

1. Lifespan is not subject to natural selection, in general



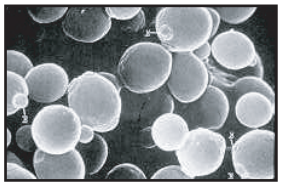
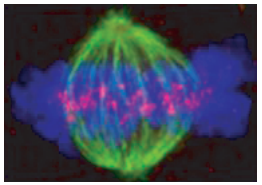
2. Antagonistic pleitropy

3. Disposable soma



see Kirkwood & Austad *Nature* (2000) **408**:233-8.

Reproductive lifespan

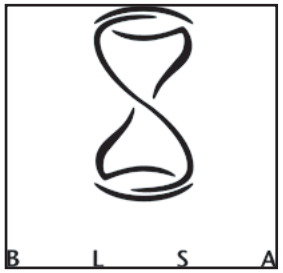



Invertebrates

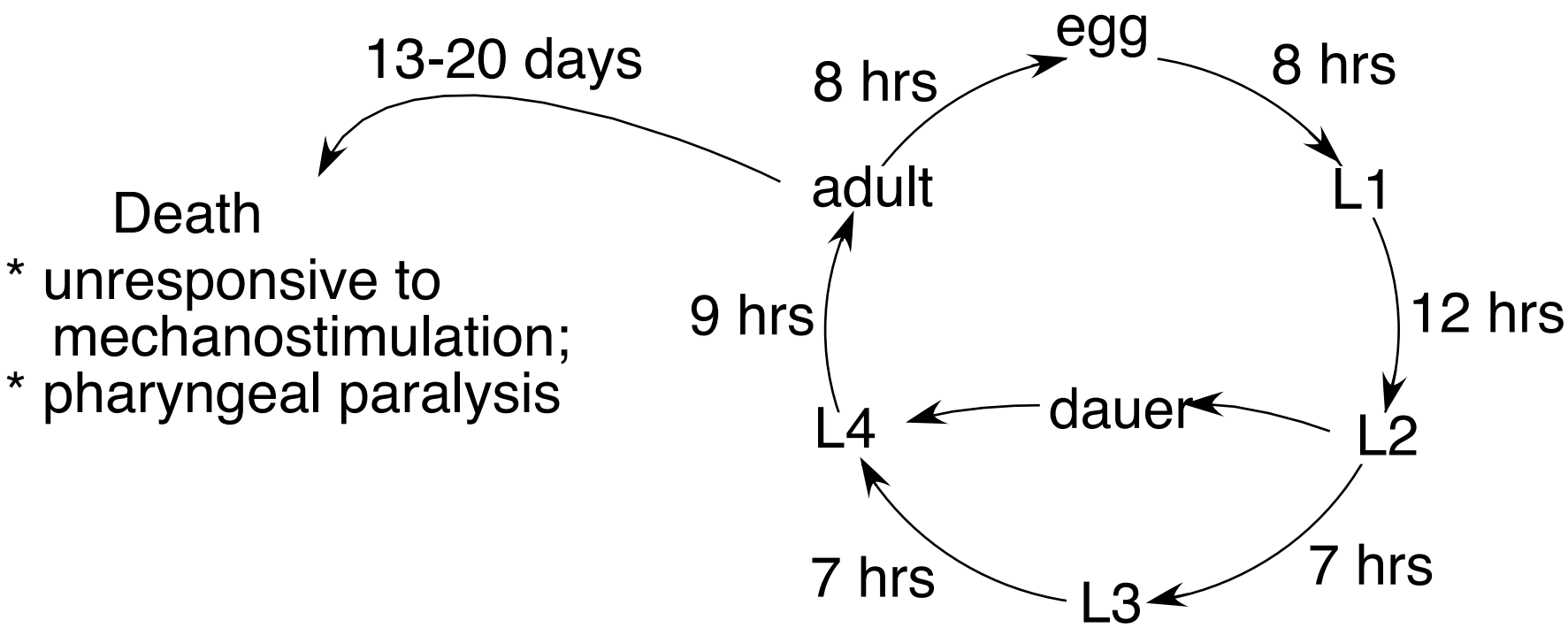
How can we study aging?

Mammals

Humans



Lifecycle of the nematode *C. elegans*

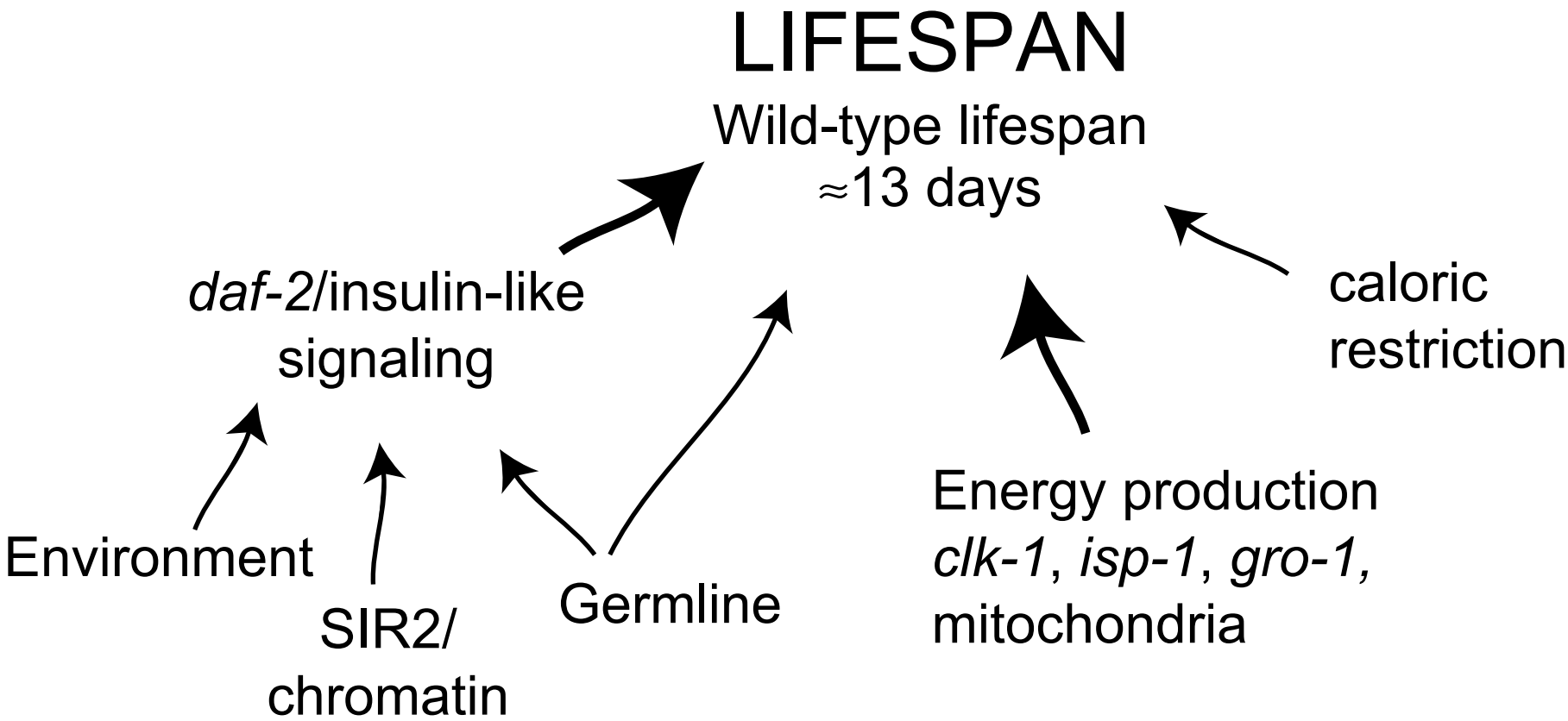


Aging in *C. elegans*

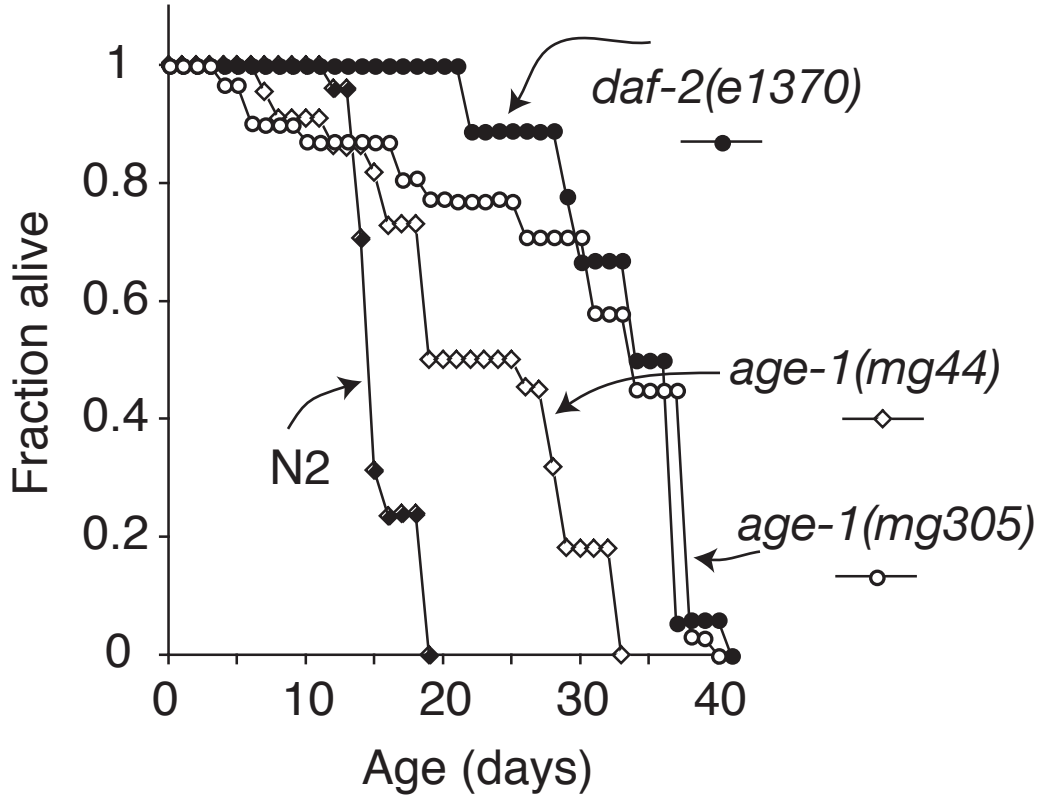
Why worms?

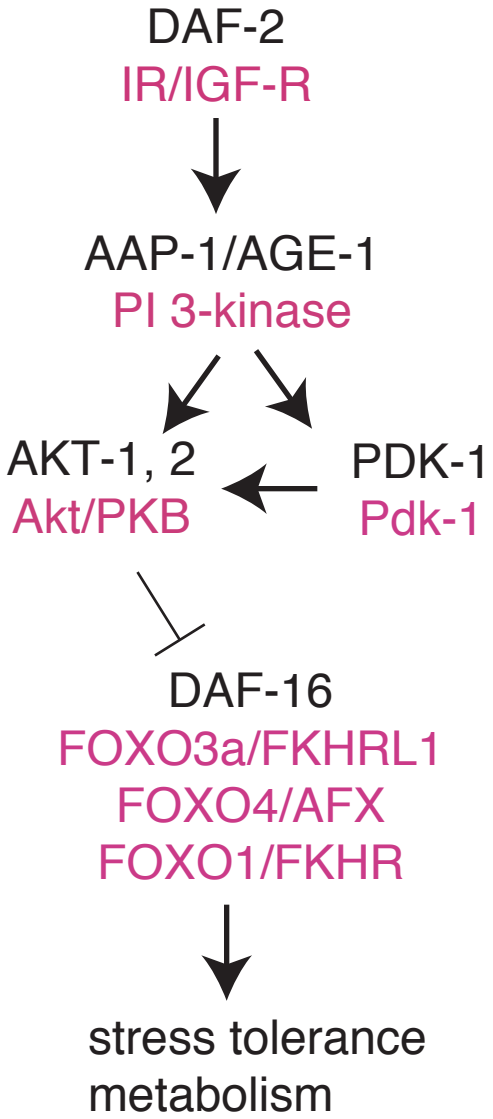
1. Short lifespan
2. Genetics
3. Genome
4. Anatomy

C. elegans lifespan pathways

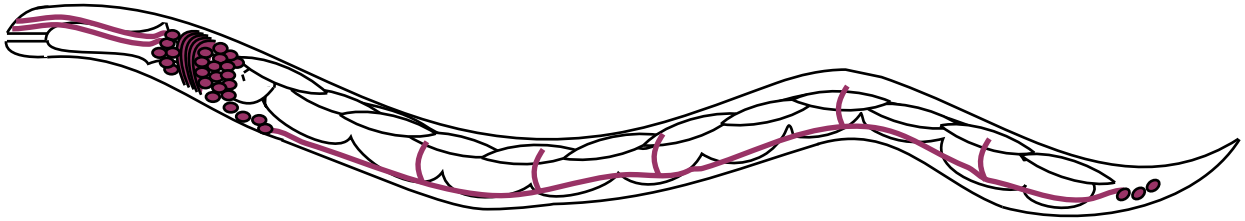


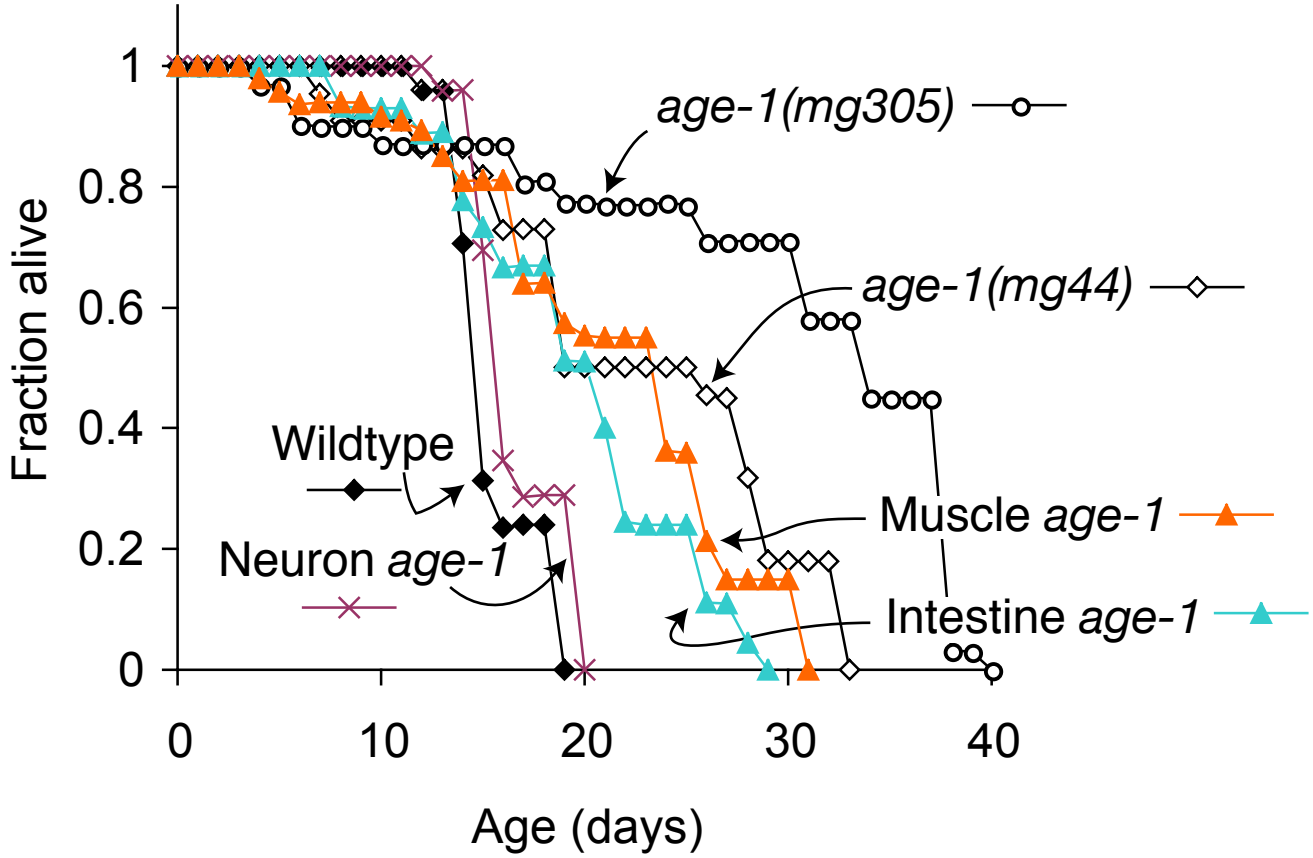
Mutants lacking DAF-2/insulin signaling function live longer



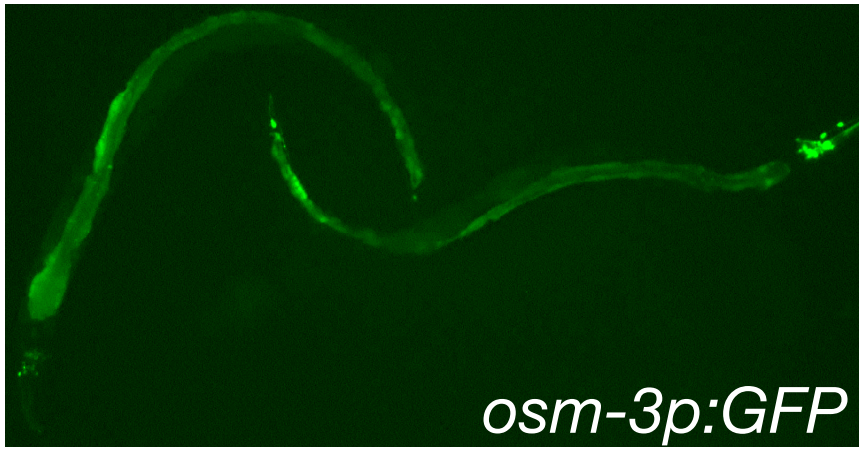


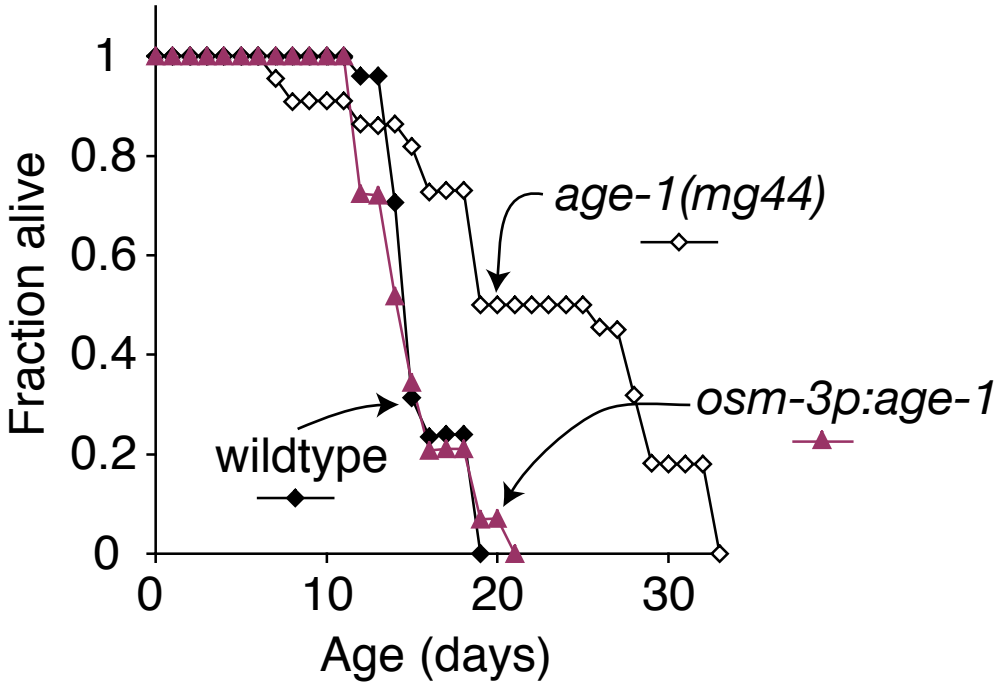
Identifying cells where insulin-like signaling controls lifespan



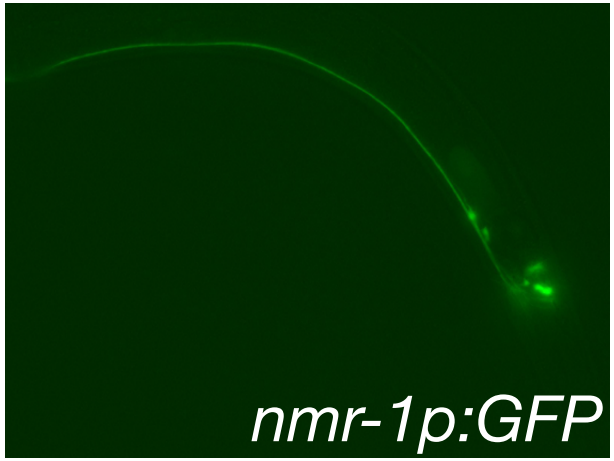


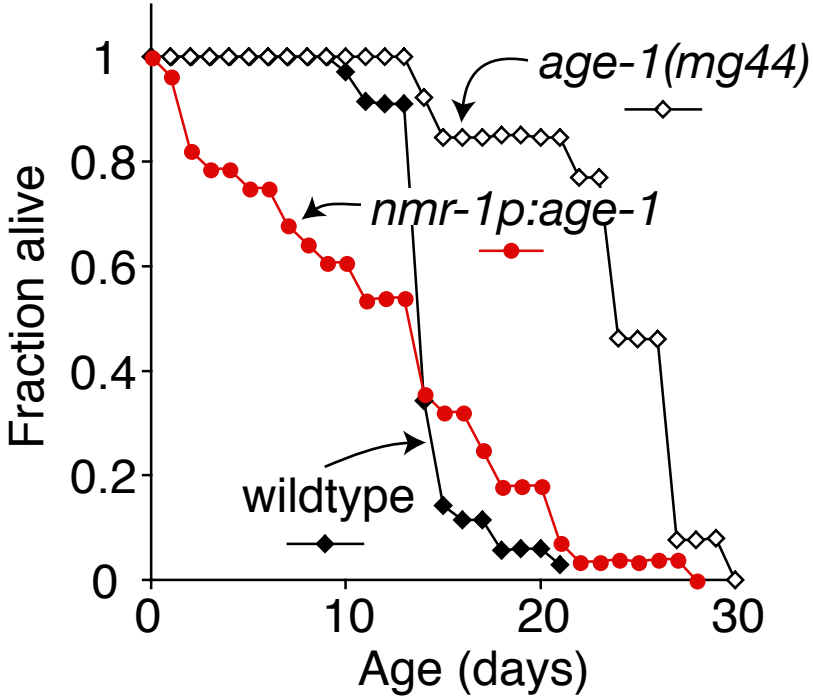
Lifespan with AGE-1/PI3K in sensory neurons





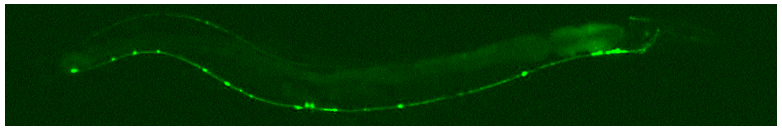
...AGE-1/PI3K in interneurons



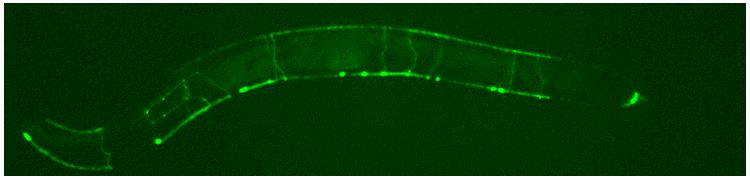


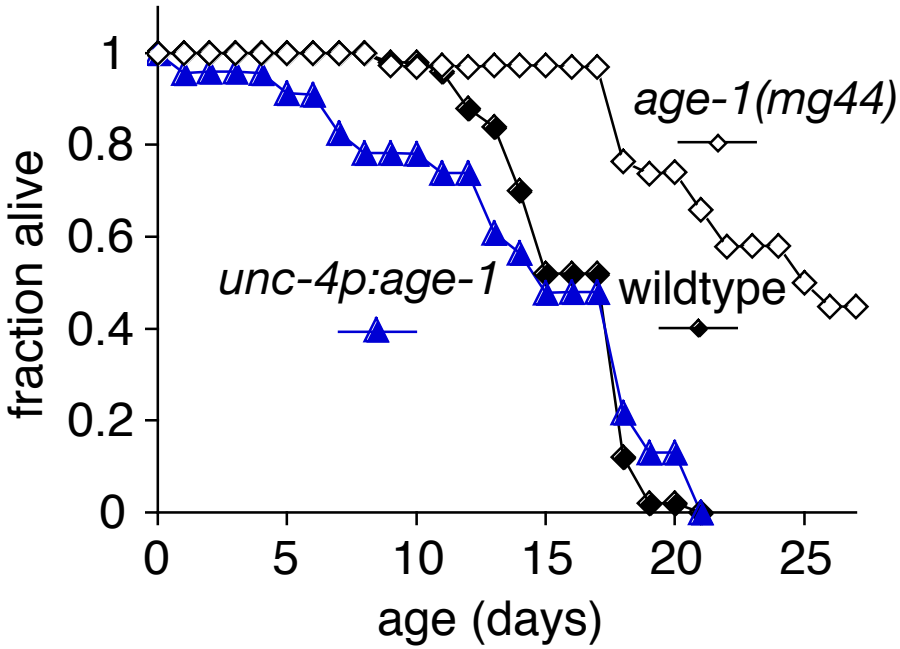
Lifepan with AGE-1/PI3K in motor neurons

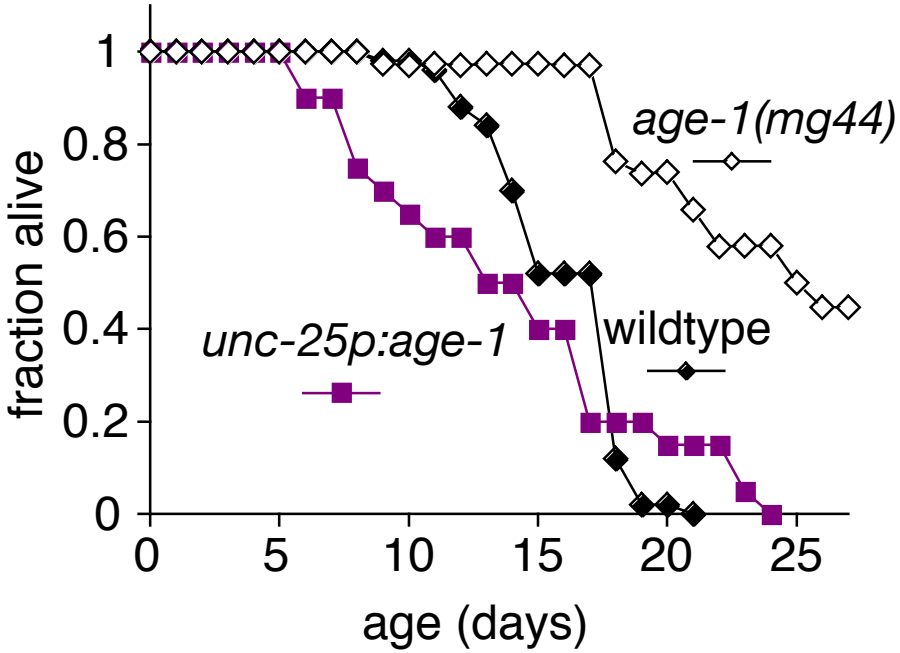
unc-4p:GFP



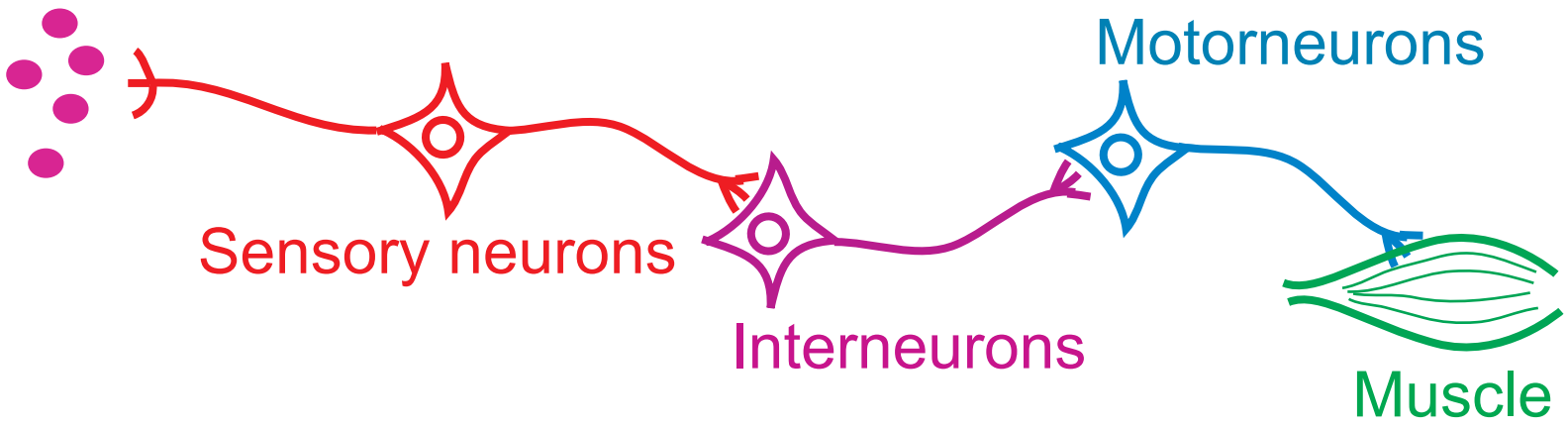
unc-25p:GFP



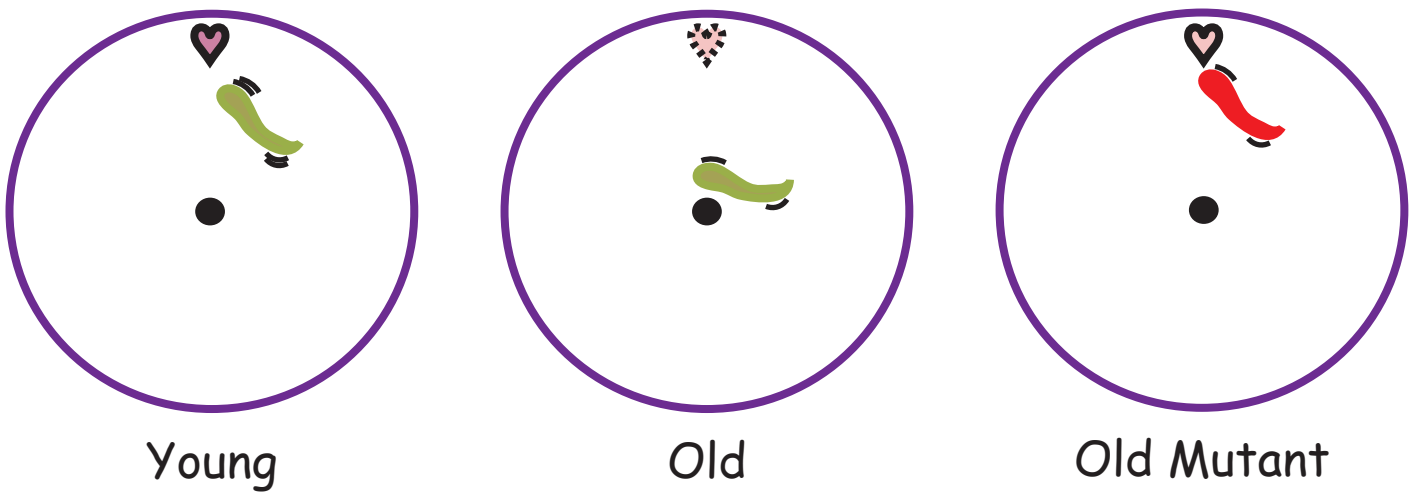




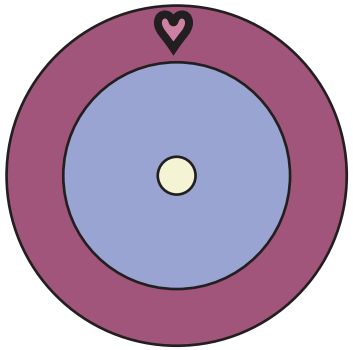
If neurons control lifespan, how does aging affect neuron function?

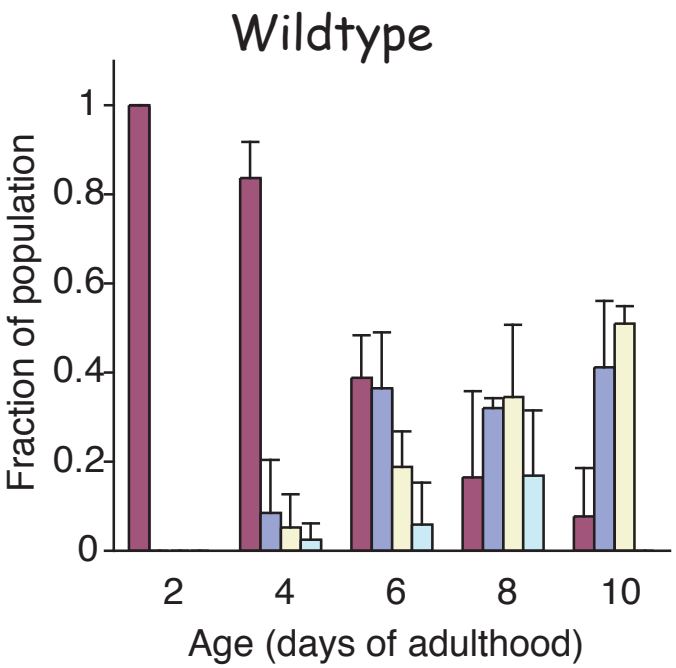


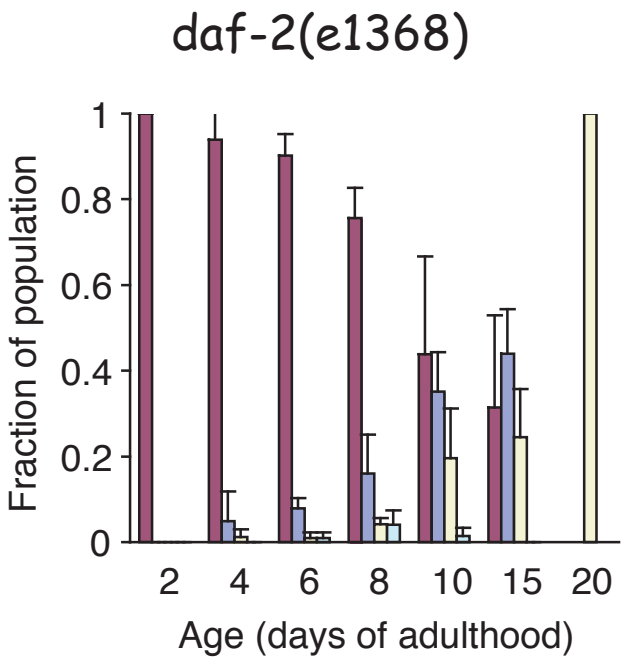
...examine behavioral responses during aging



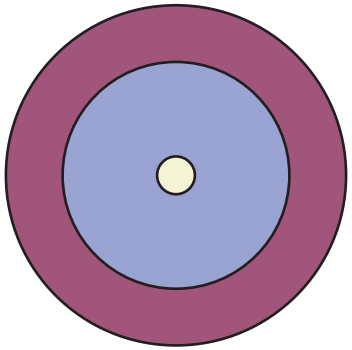
Chemotaxis towards an attractant over lifespan

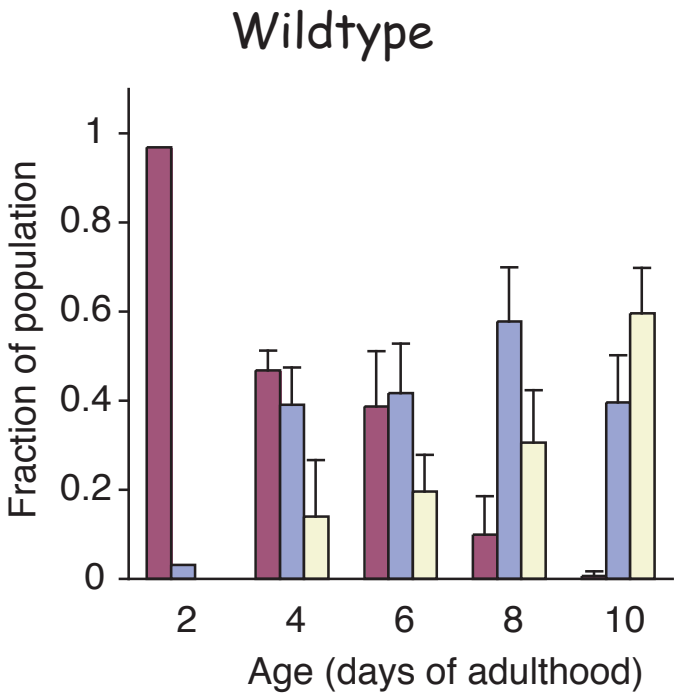


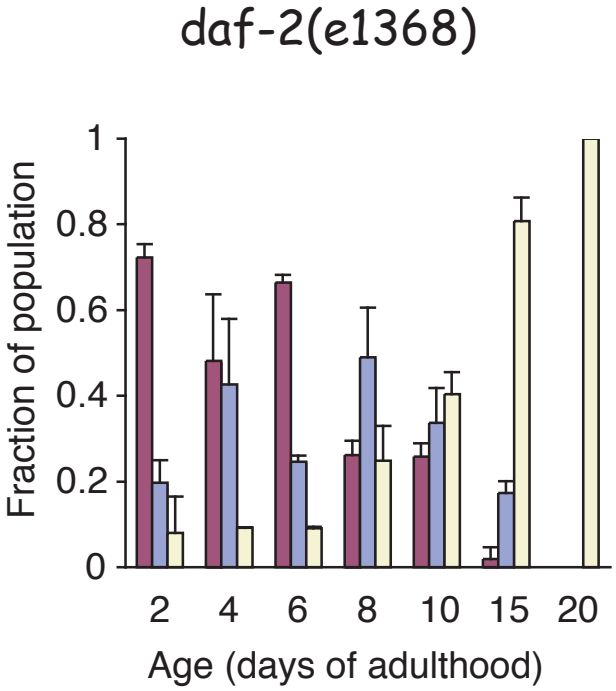




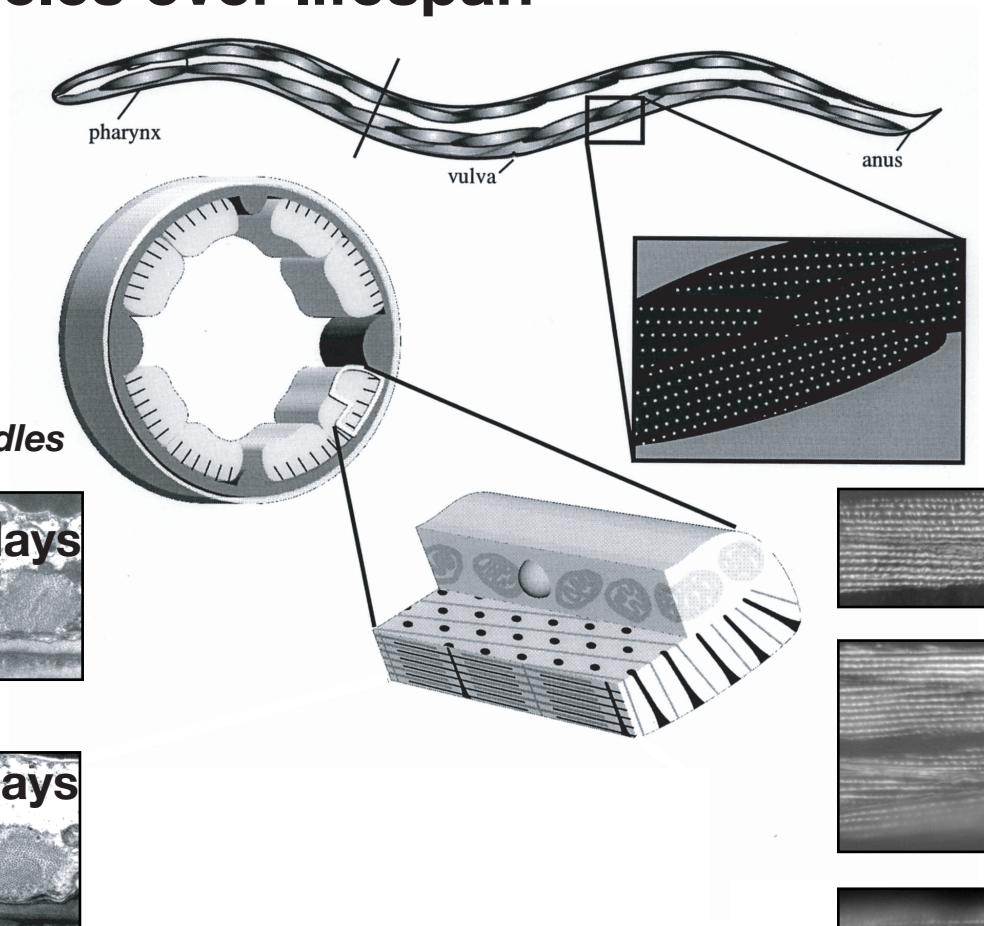
Locomotion declines with chemotaxis during aging



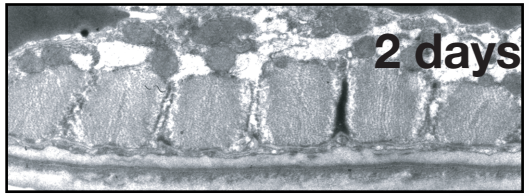


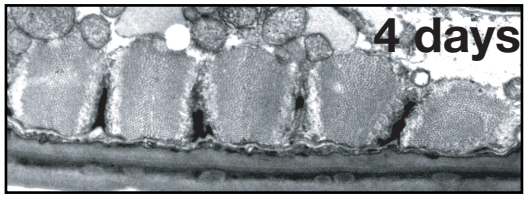


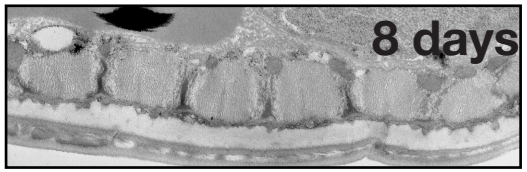
Examining muscles over lifespan



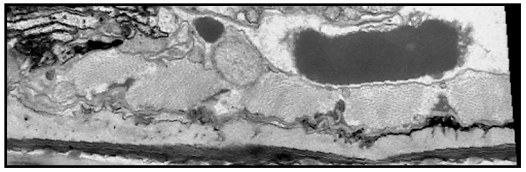
Muscle sarcomeric bundles







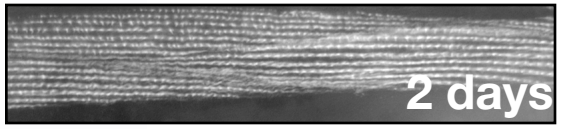
7/8 animals

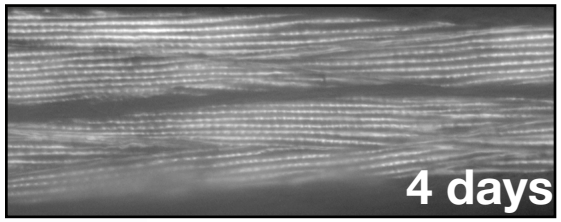


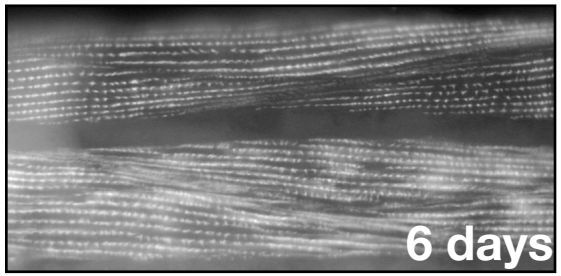
1/8 animals

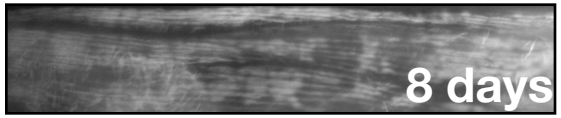
2 microns

Muscle actin

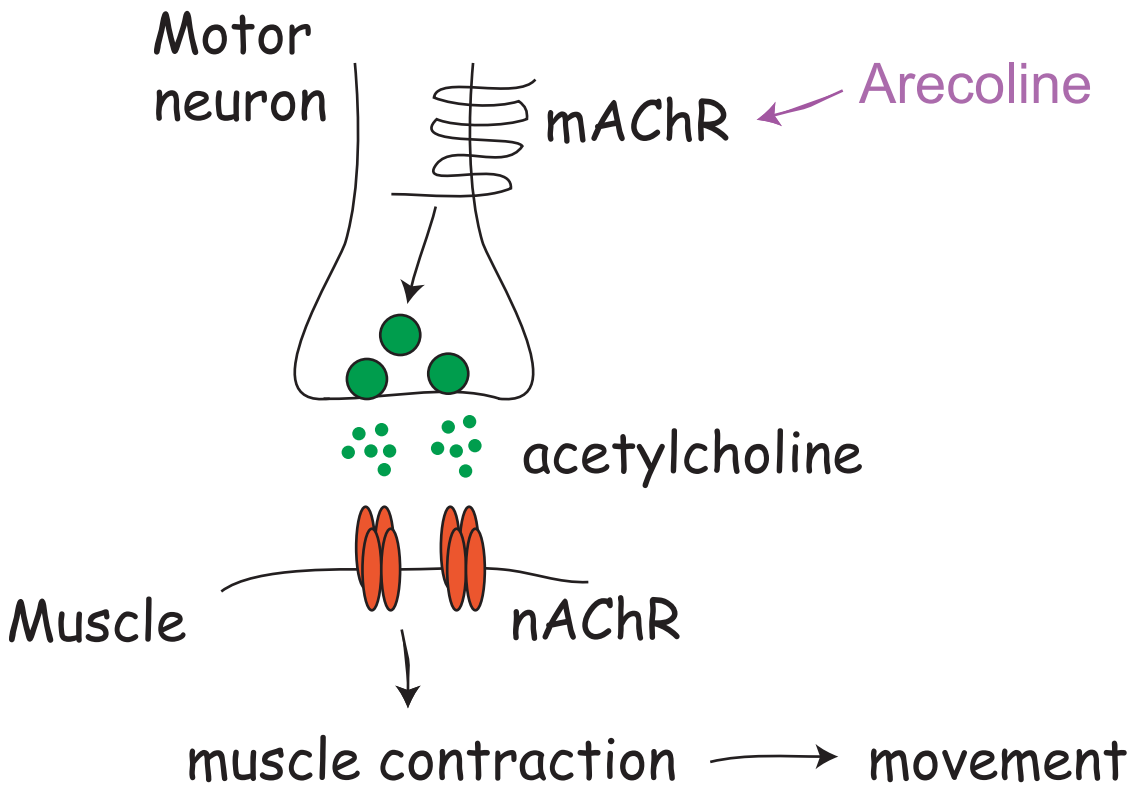




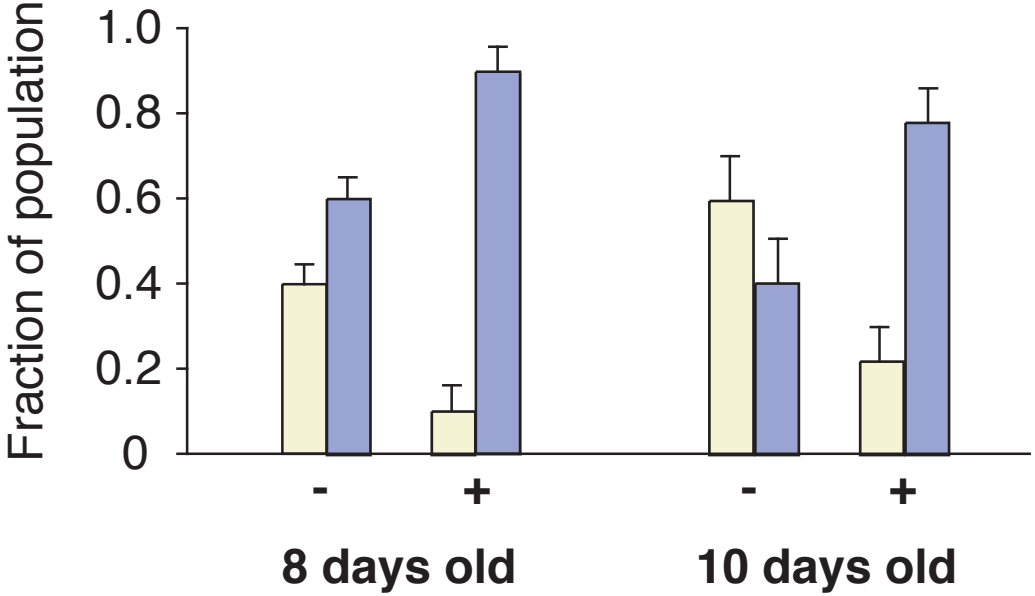




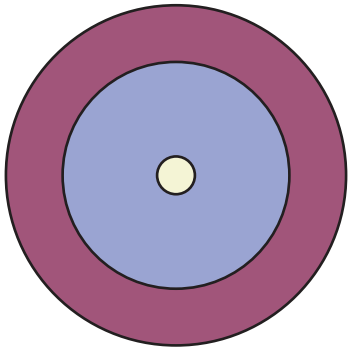
Acetylcholine regulates movement in C. elegans

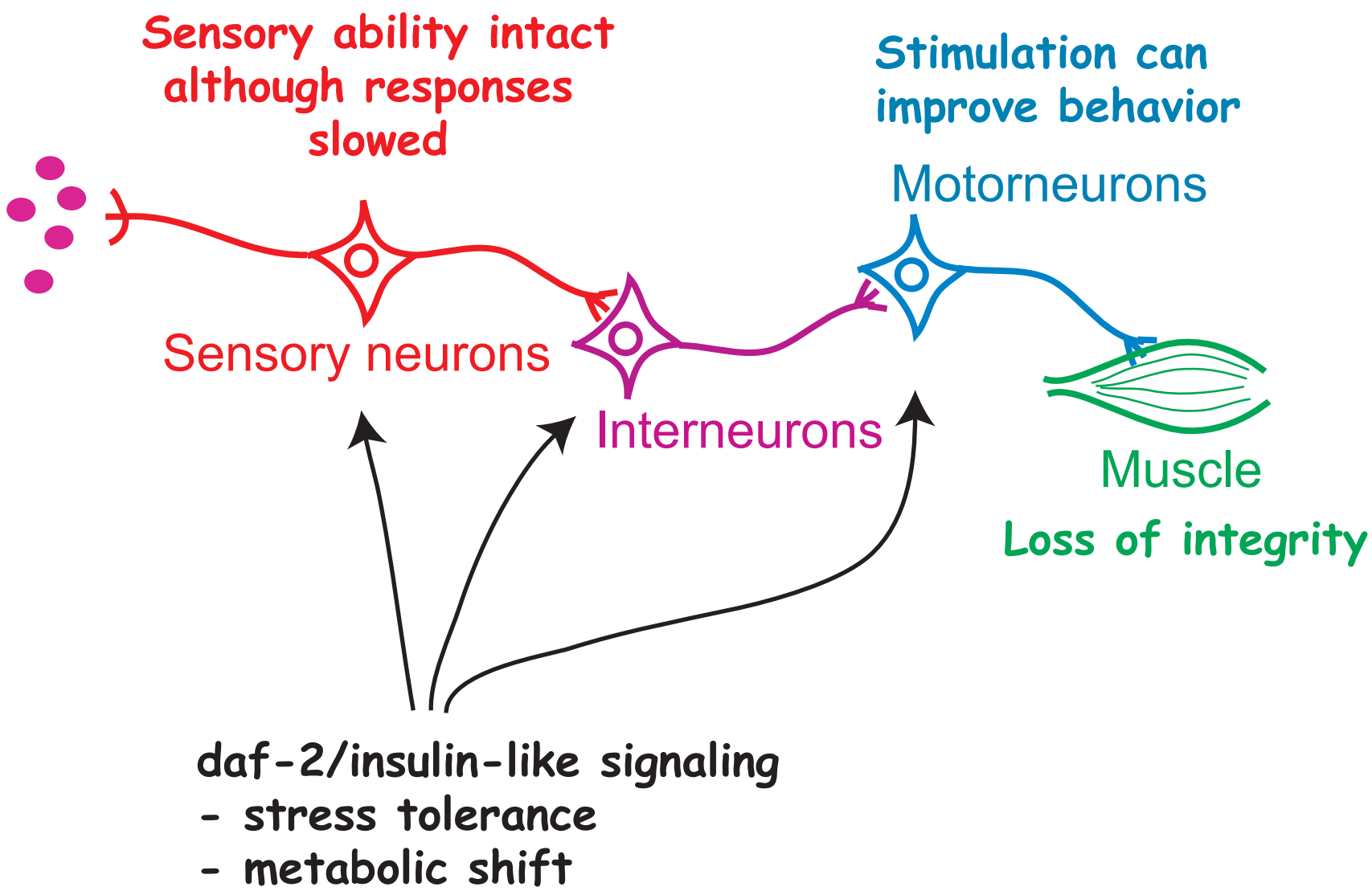


Locomotory behavior in old animals can be improved by cholinergic stimulation



1 hour displacement



Arecoline
(muscarinic agonist)

Impact of age on the *C. elegans* nervous system