Assessing ageing in natural populations

Michaël Rera
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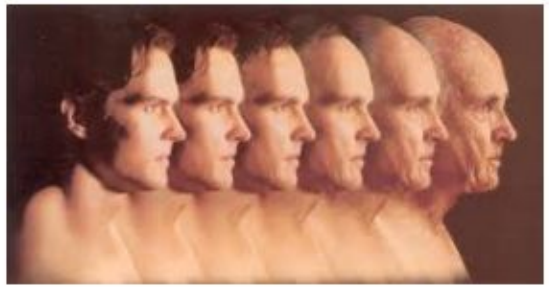
No time for ageing in the wild

Our expectations about aging in wild populations have been influenced by the classic evolutionary theories of aging and empirical shortcomings. The general hypothesis was that life in the wild is short, and hard, and that genes governing late life processes in the wild do not matter because few survive to old age. Evolutionary theories of aging suggest that aging exists because of the declining force of selection on late age-specific traits (Hamilton 1966, Medawar 1952, Williams 1957). Medawar (1952) suggested that aging could only be demonstrated in "captive," protected environments, in which animals are protected from natural hazards and can thus survive to ages never seen in the wild. This expectation, that aging cannot be found in the wild, has been quoted for the past 50 years (Kirkwood & Austad 2000), and empirically there were few demographic studies of individuals of known age to contradict this assertion. Recent theoretical work (Baudisch 2005, Williams et al. 2006) challenges some of these classic expectations, and long-term empirical studies of marked individuals demonstrate that the aging phenotype is an important phase of the life history in wild populations.

Zane et al., 2024

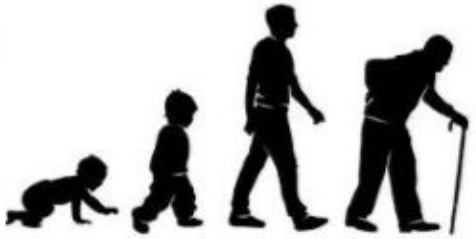
Intuitive definition of ageing







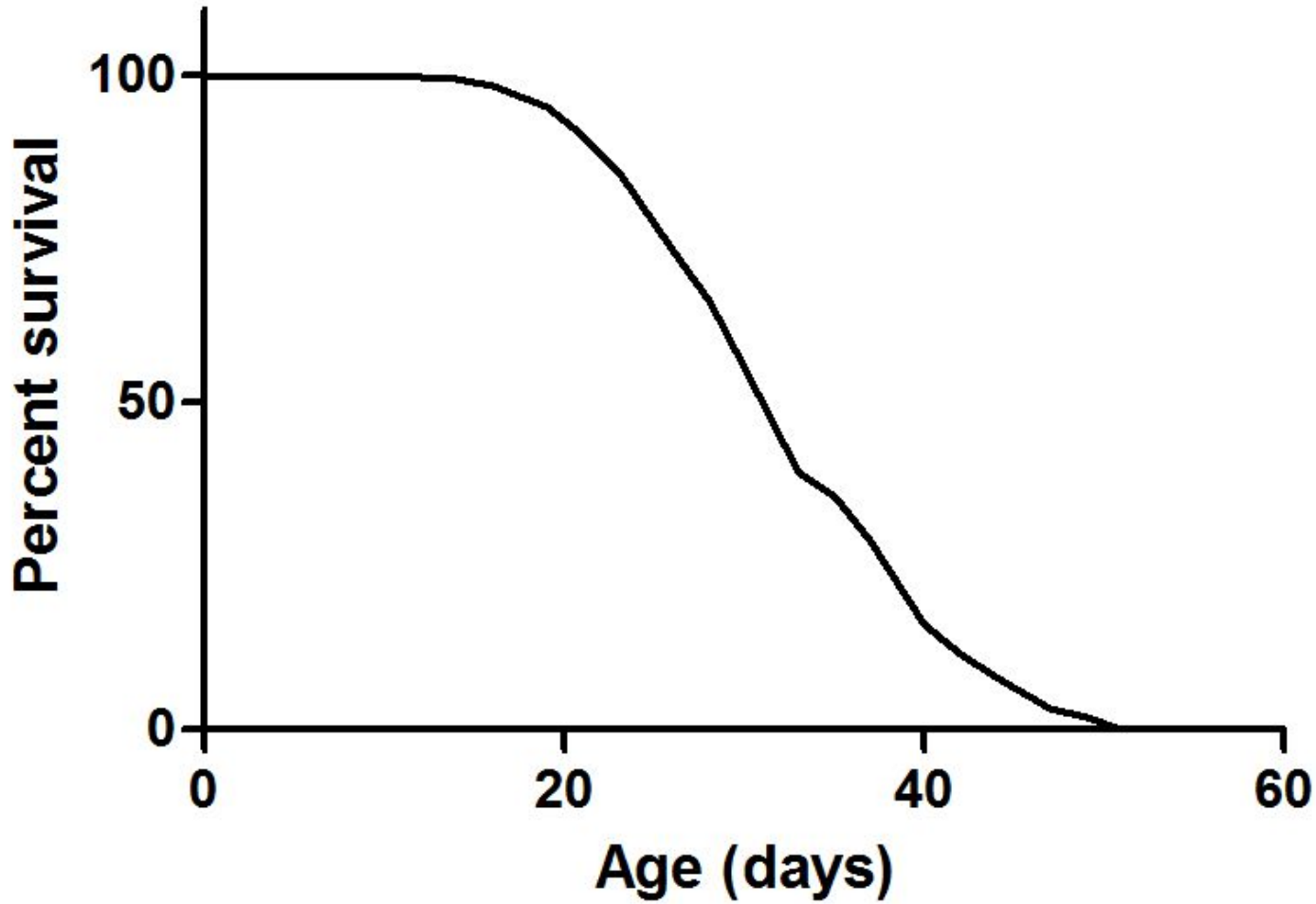








Classical approach for studying ageing



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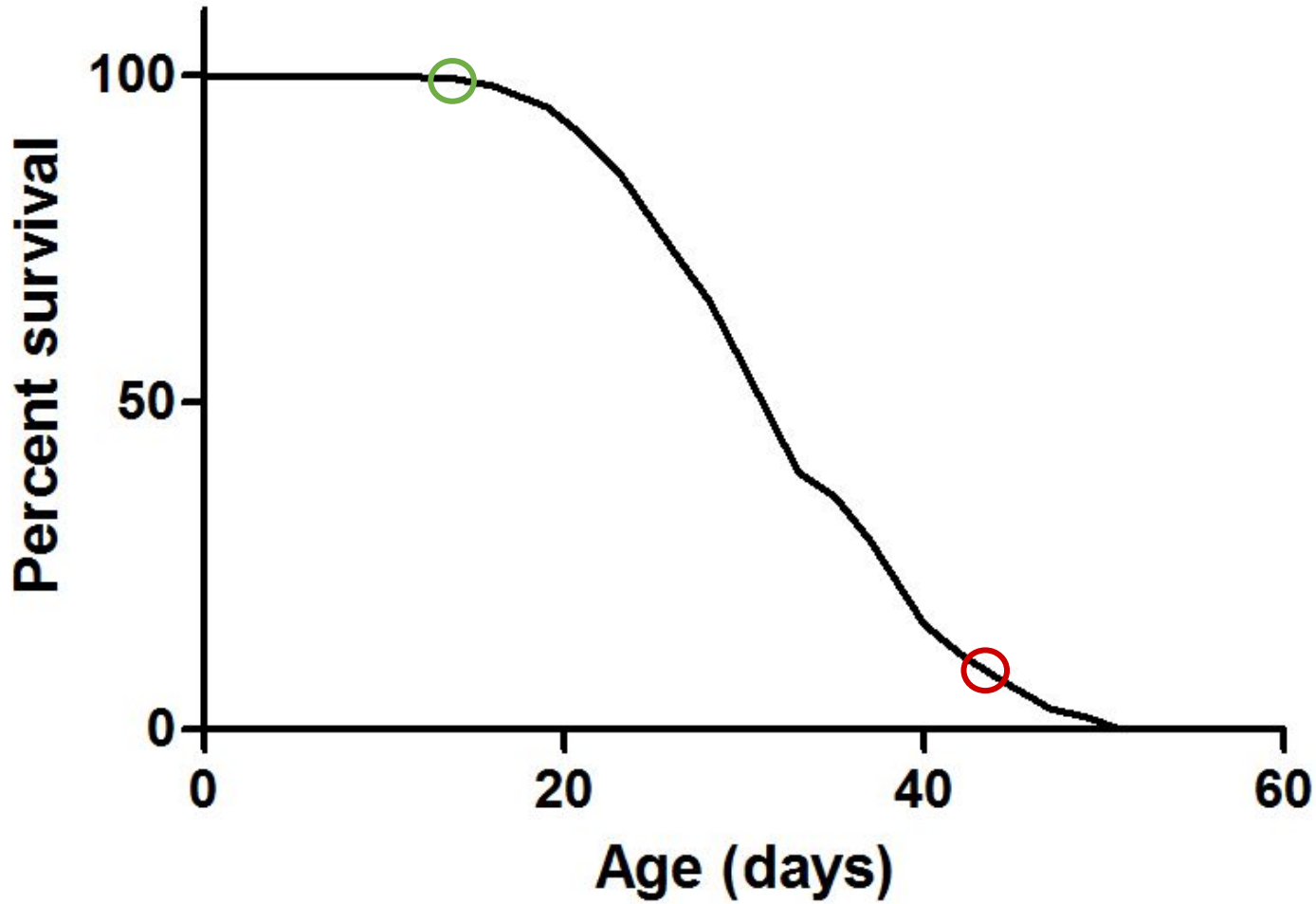
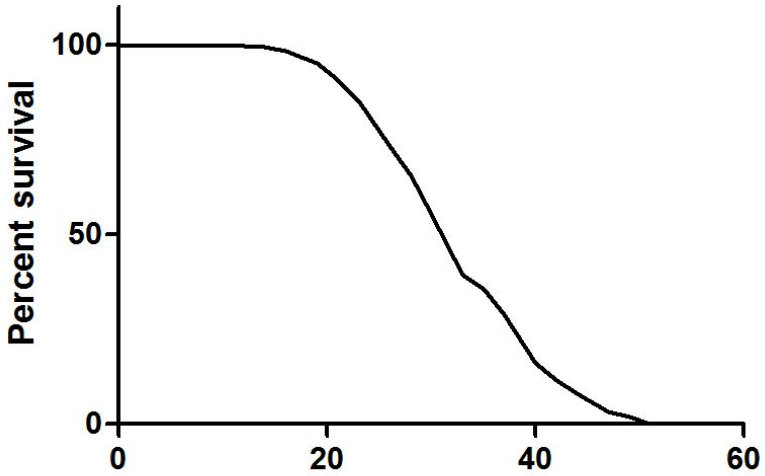
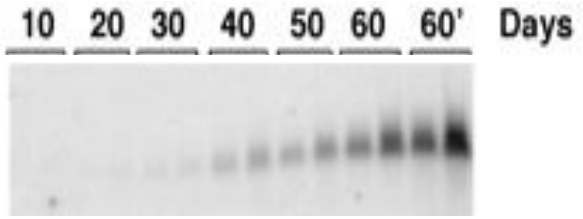


Hallmarks of ageing in a continuous ageing process



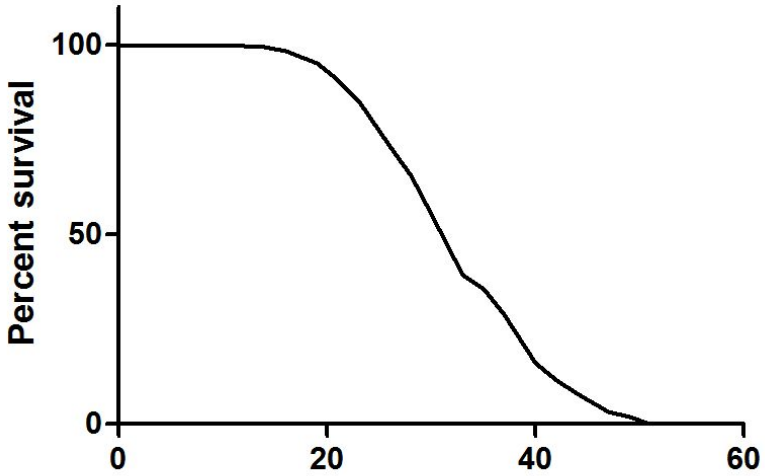
Death

Increasing systemic inflammation



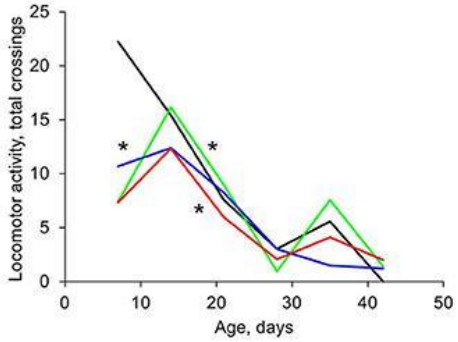
- Continuous changes

Hallmarks of ageing in a continuous ageing process



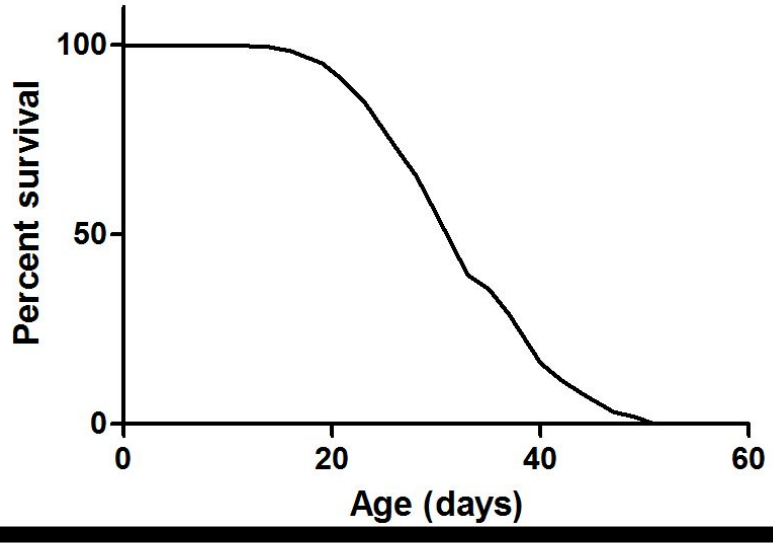
Death

decreasing motor activity



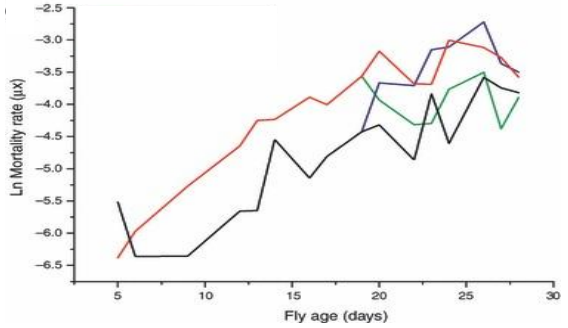
- Continuous changes

Hallmarks of ageing in a continuous ageing process



Death

exponential increase of mortality rates



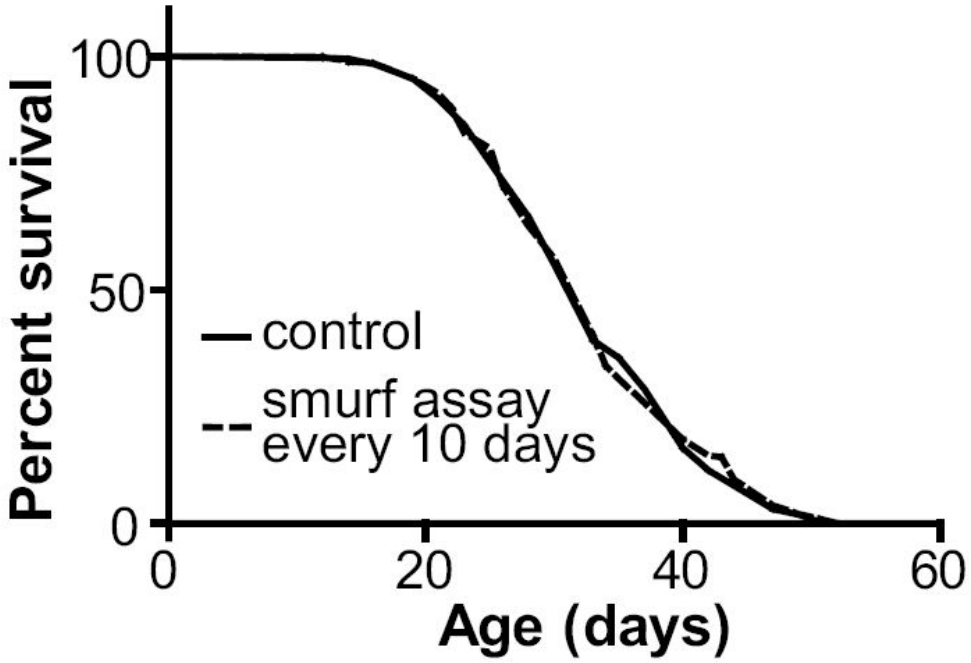
- Continuous changes

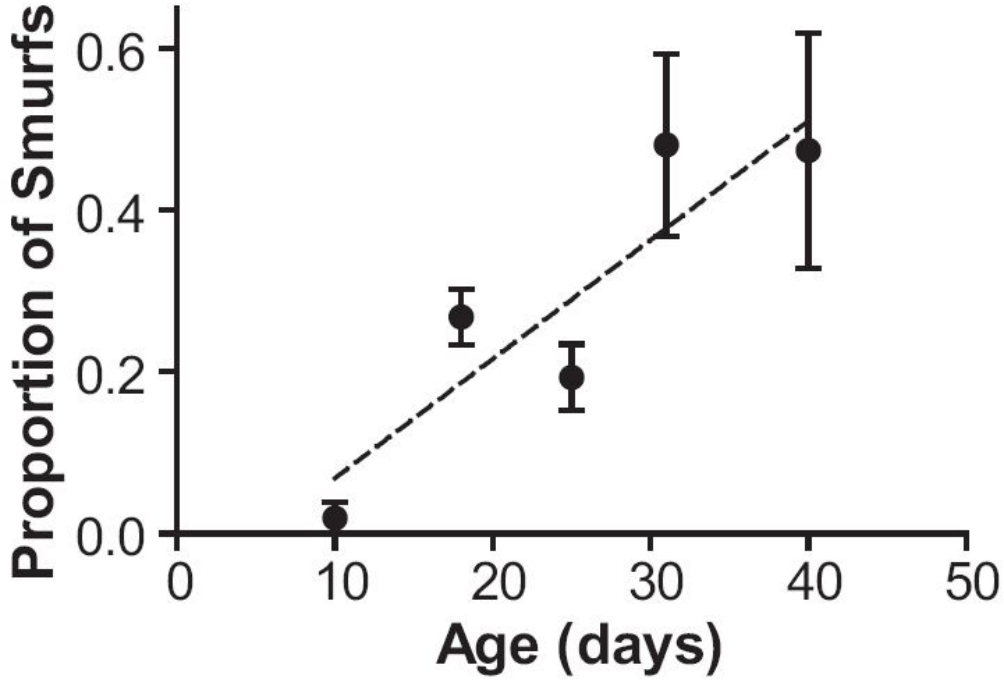
Studying ageing as a two-phase, discontinuous process

A Simple Assay To Identify Individuals About To Die Of Natural Causes

- *in vivo*
- measurement of intestinal permeability
- non-toxic food dye
- non-absorbed food dye
- ‘Smurf’ phenotype

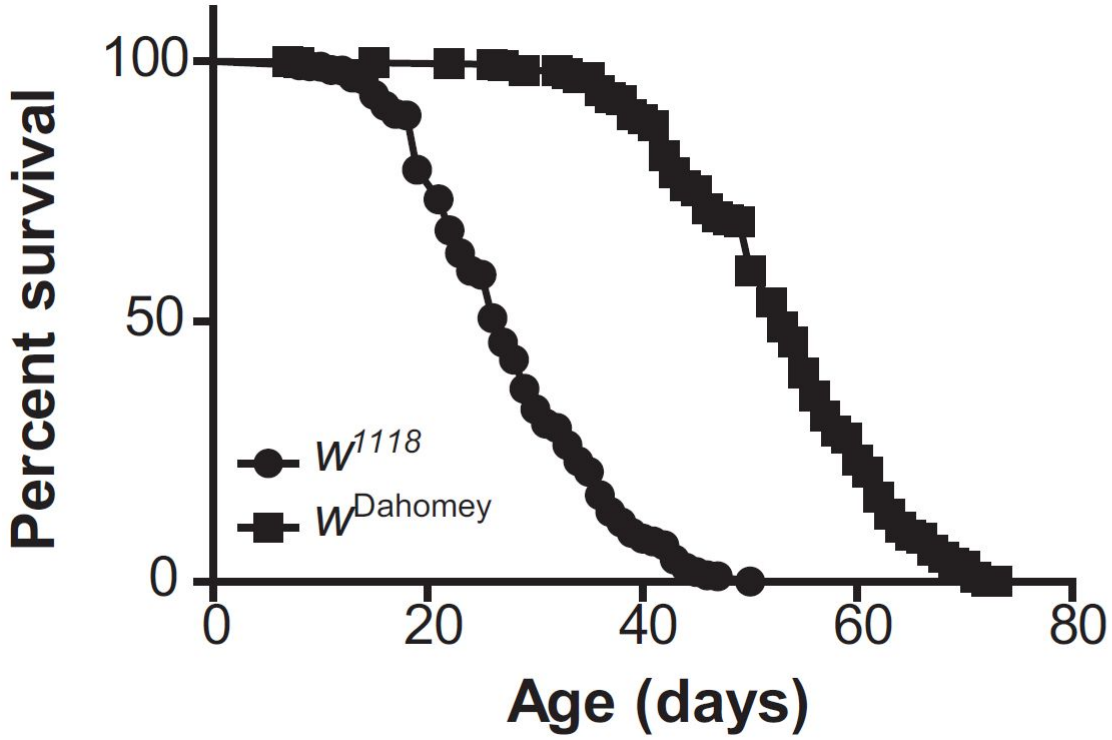
Smurfness is an age-dependent phenotype

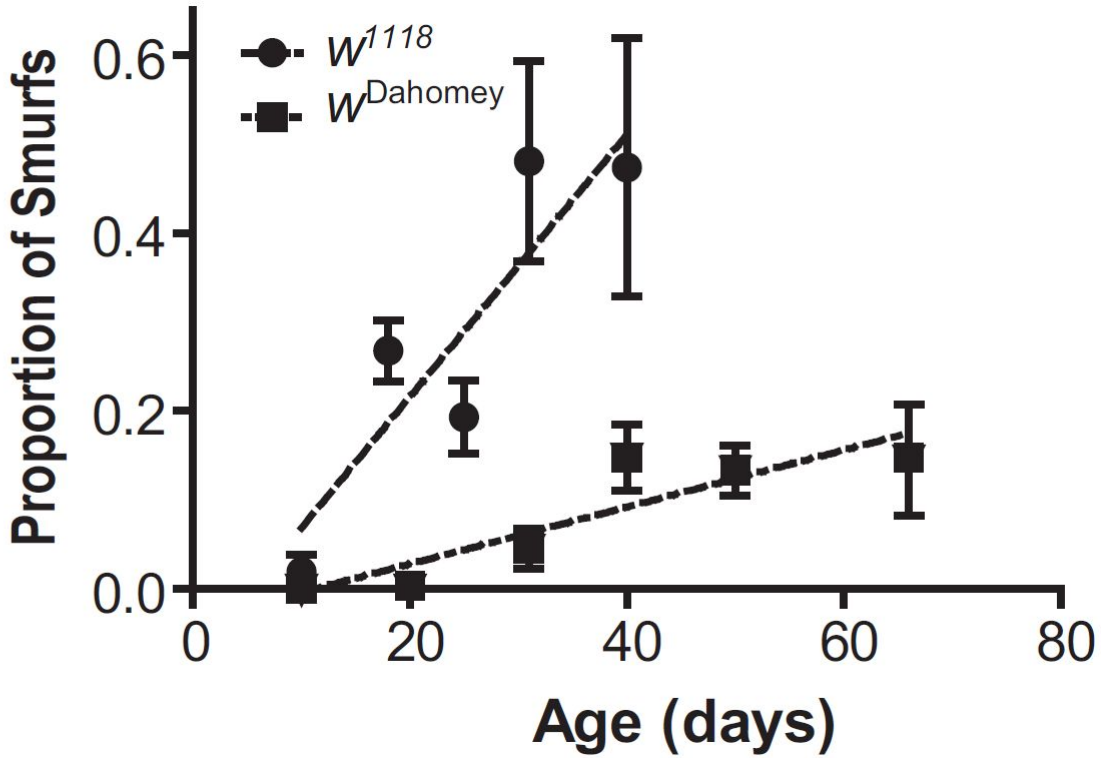




Rera et al., 2012 PNAS

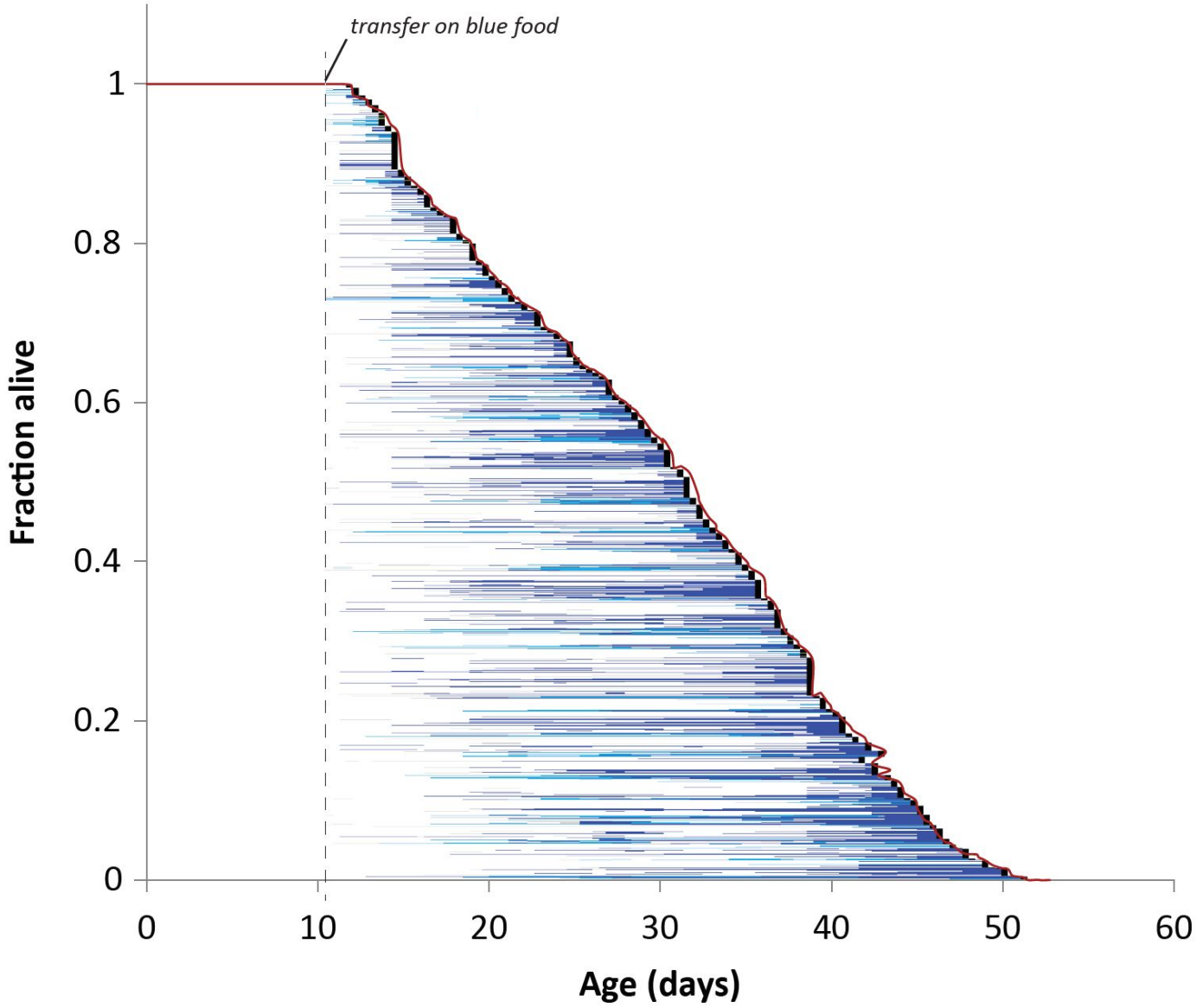
Smurfness is a « physiological age »-dependent phenotype





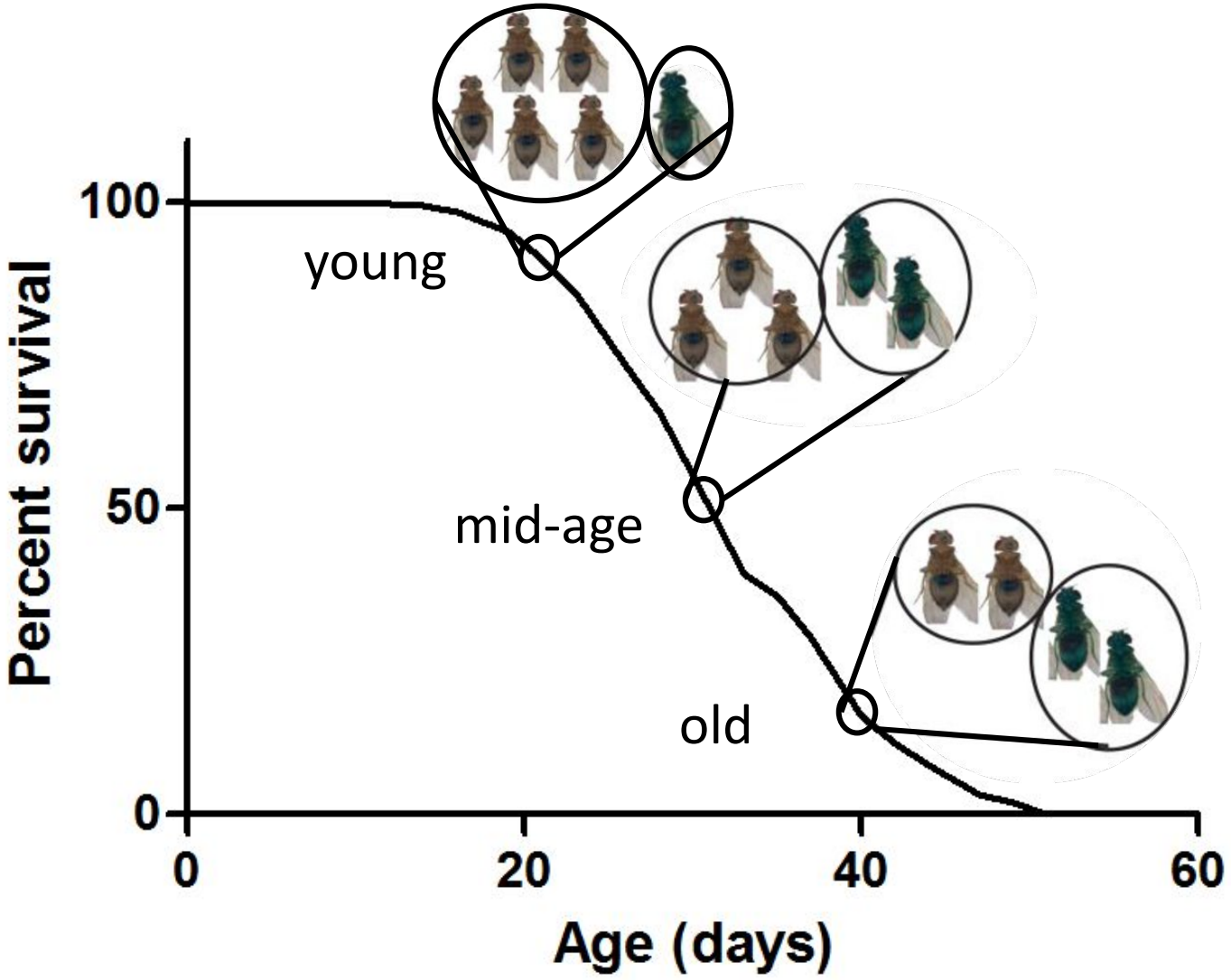
Rera et al., 2012 PNAS

Every individuals turns Smurf prior to death

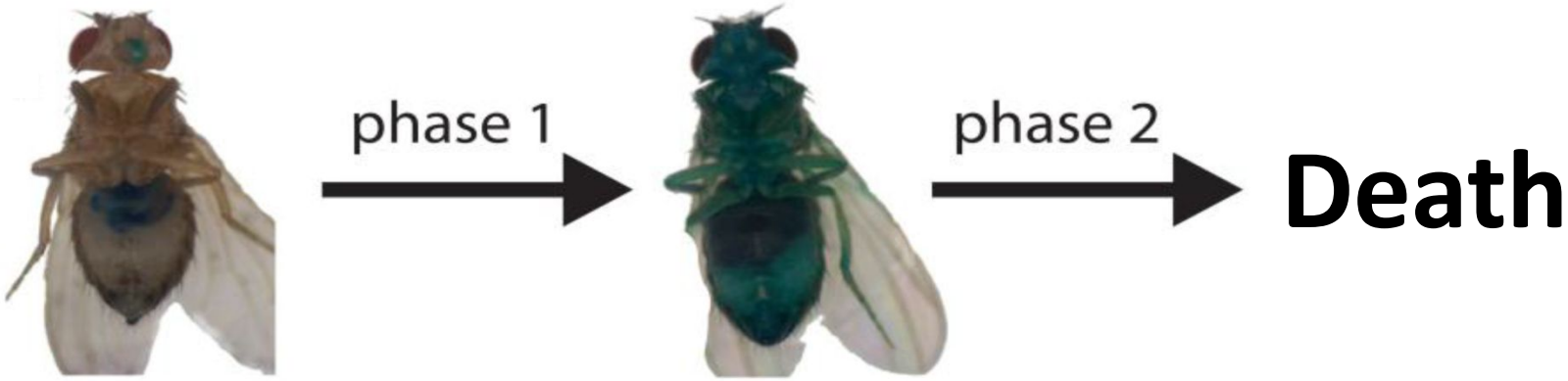


Tricoire and Rera, 2015 PLOS ONE

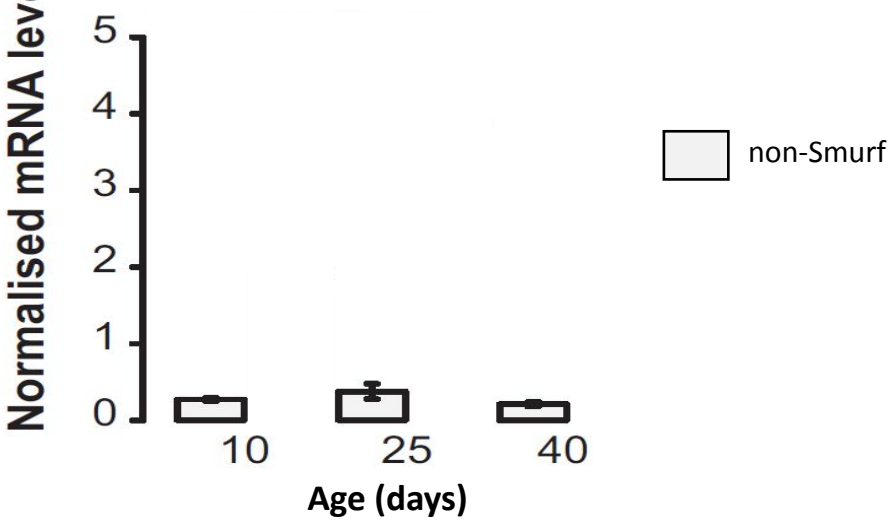
The 2-Phase Model Of Ageing



Hallmarks of ageing in the 2-Phase Model



systemic inflammation



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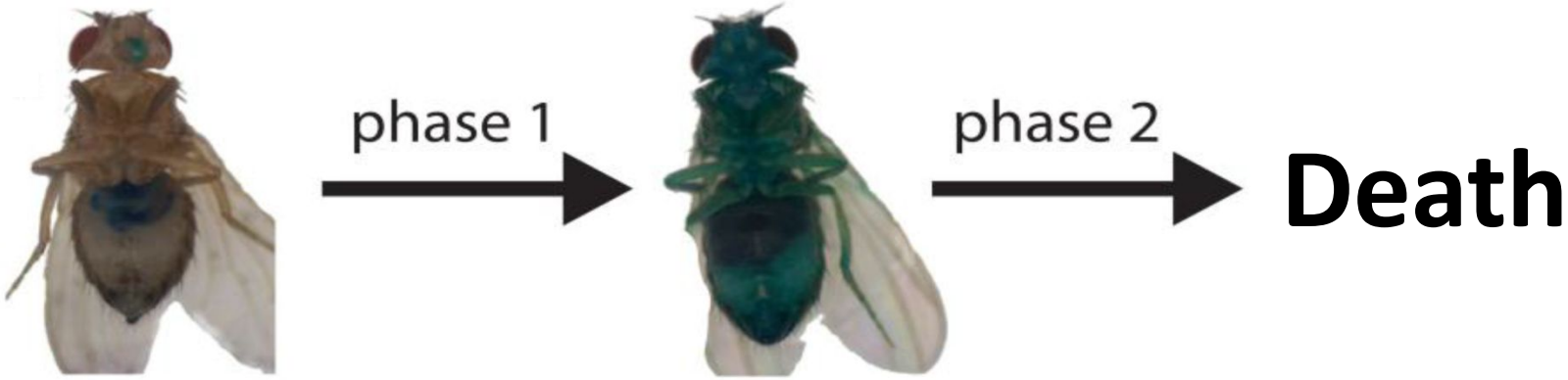

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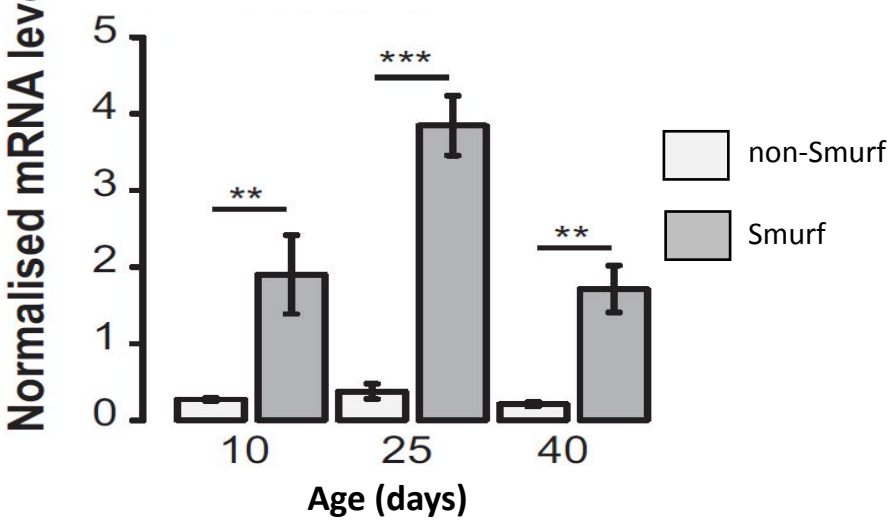


Rera et al., 2012 PNAS

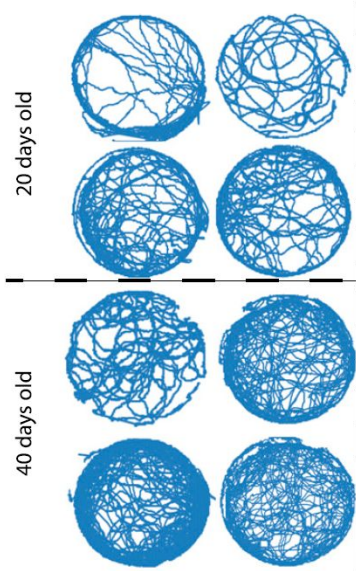
Hallmarks of ageing in the 2-Phase Model

phase 1

phase 2

Death

loss of mobility
non-Smurfs



Rera et al., 2012 PNAS

Hallmarks of ageing in the 2-Phase Model

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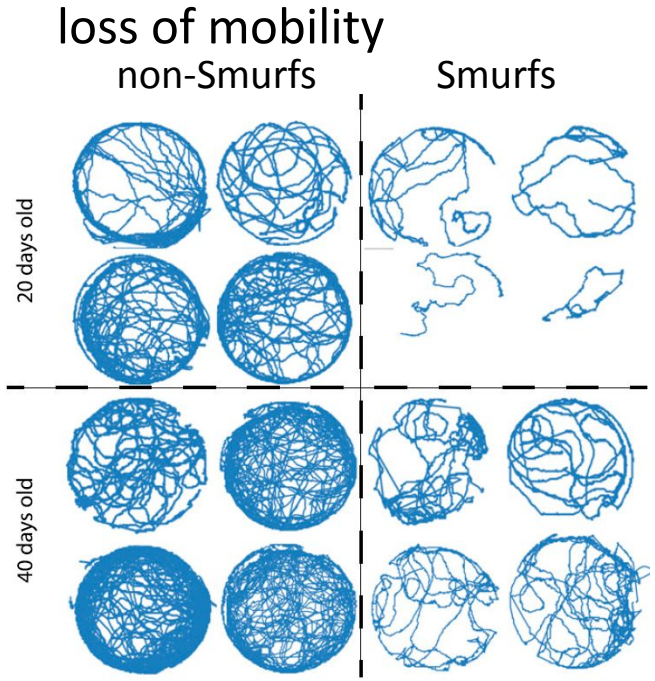
phase 2

Death



Rera et al., 2012 PNAS

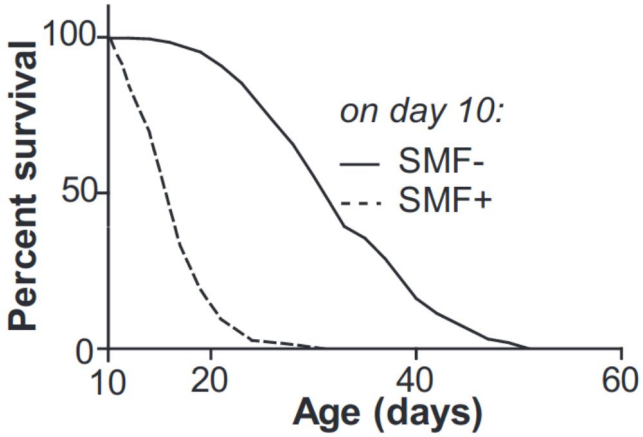
Hallmarks of ageing in the 2-Phase Model

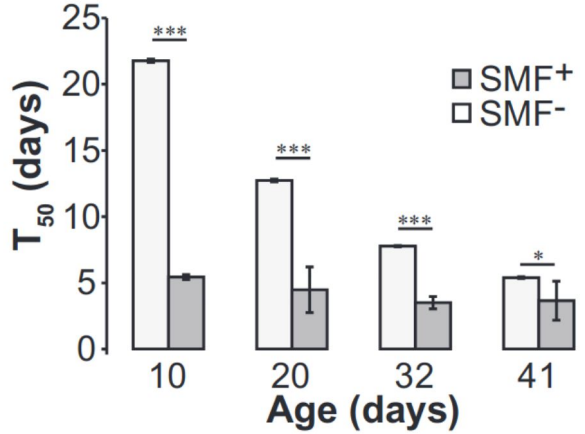
phase 1

phase 2

Death

mortality risk



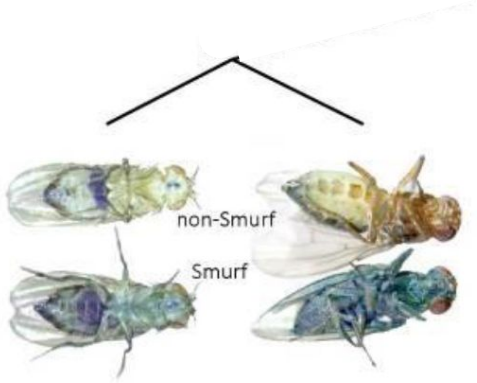


Rera et al., 2012 PNAS

A broadly relevant model of ageing

An evolutionarily conserved End-Of-Life phenotype

The 2-Phase Model of Ageing is evolutionarily conserved

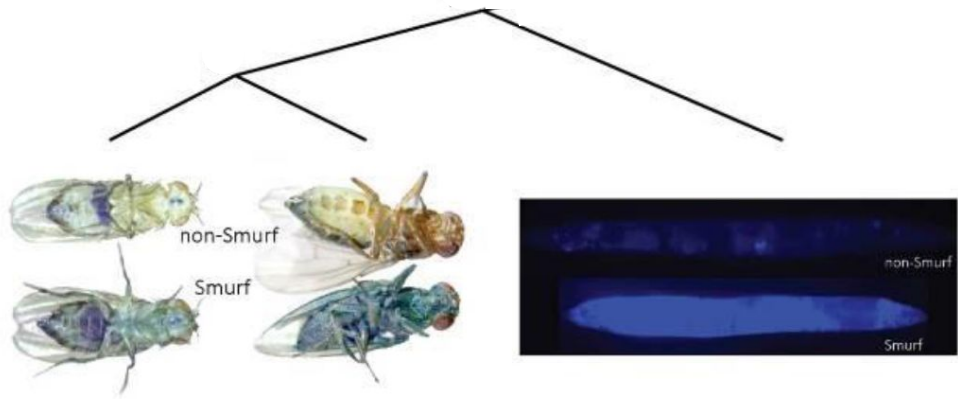


Drosophila

Adapted from *Dambroise et al., 2016* Scientific Reports

An evolutionarily conserved End-Of-Life phenotype

The 2-Phase Model of Ageing is evolutionarily conserved



Drosophila Nematode

Adapted from *Dambroise et al., 2016* Scientific Reports

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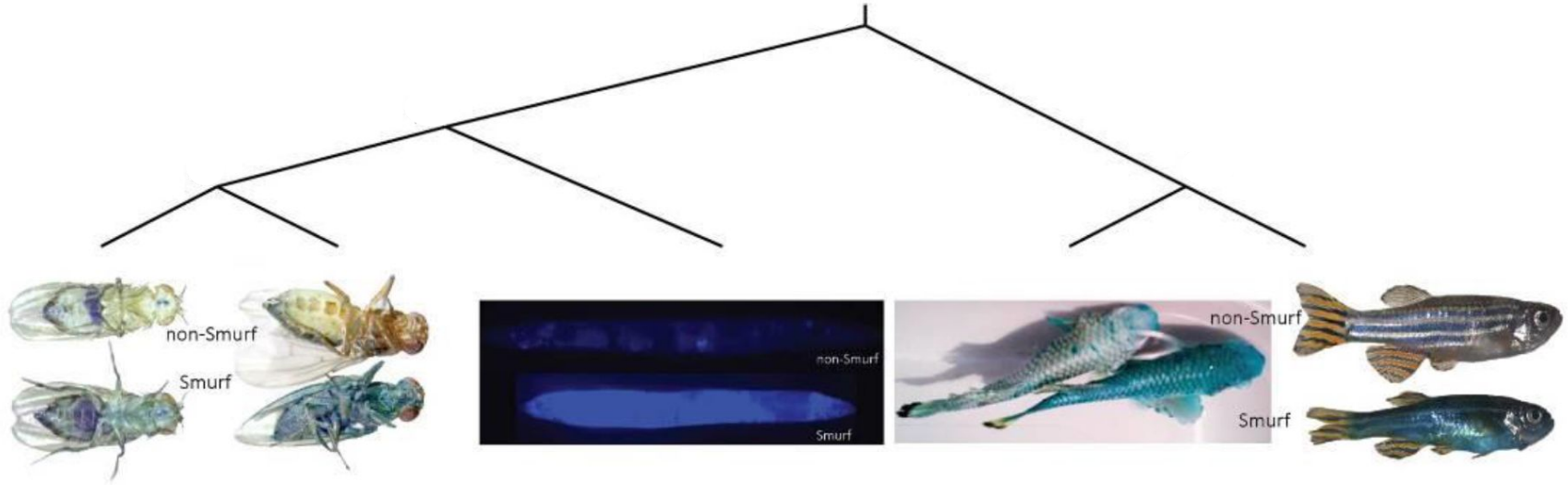

Drosophila Nematode Killifish Zebrafish

Adapted from *Dambroise et al., 2016* Scientific Reports

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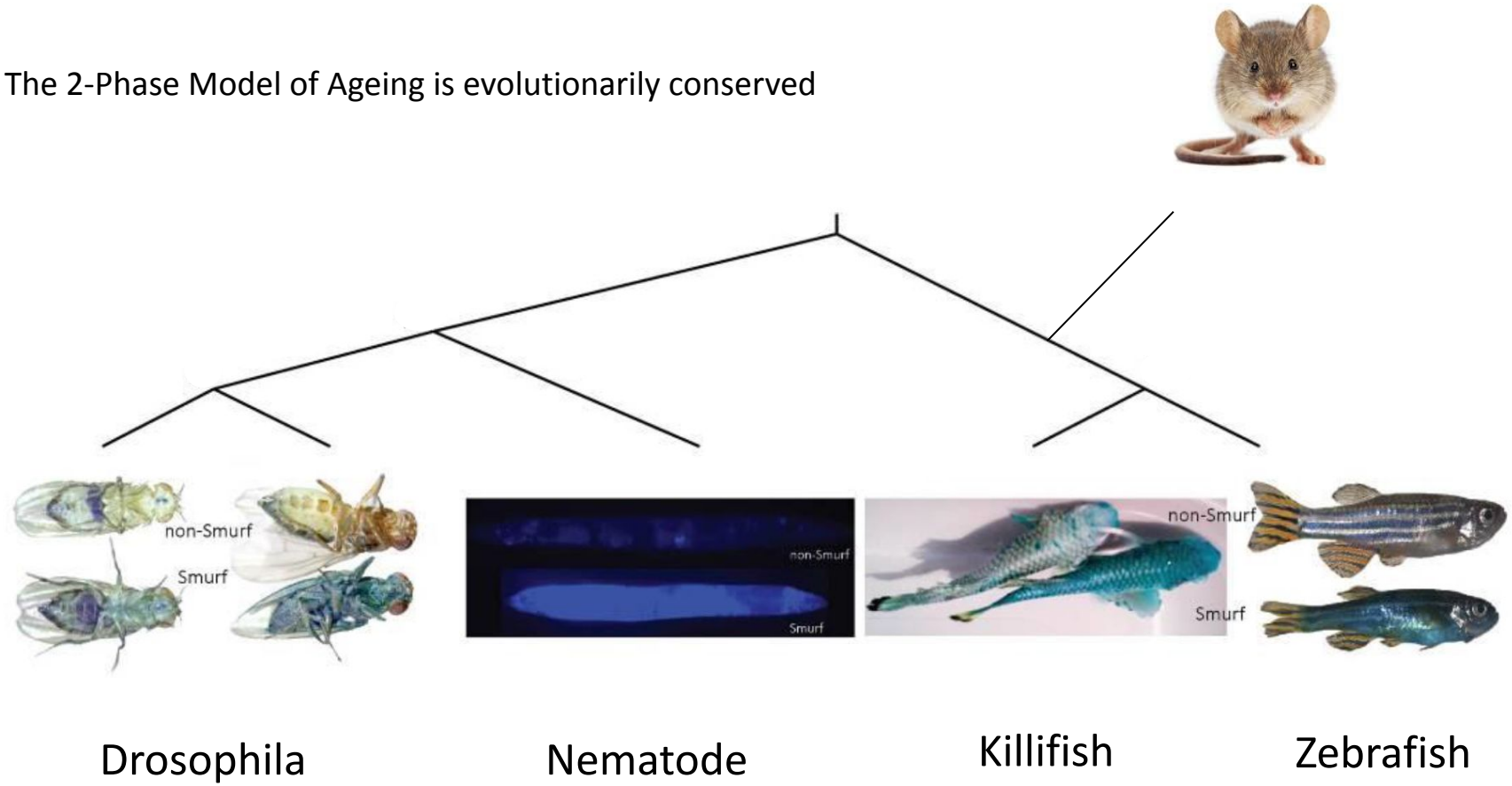

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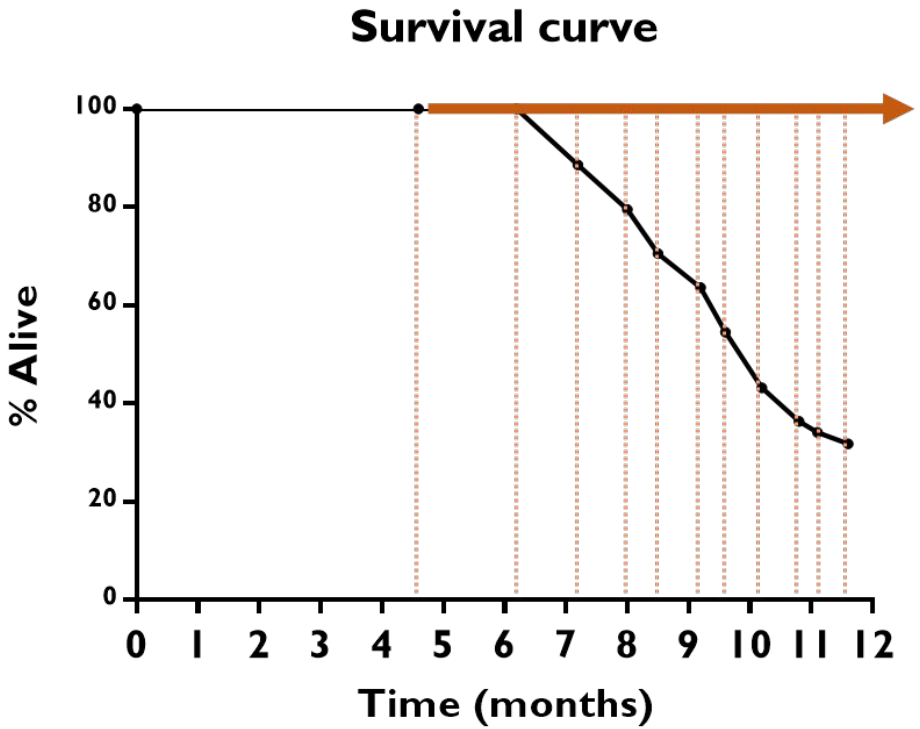
A “public” path to death: mice

Dr. Céline Cansell



-Intestinal permeability test

- ❑ Permeability T1h
- ❑ Permeability T3h

-Measurements :

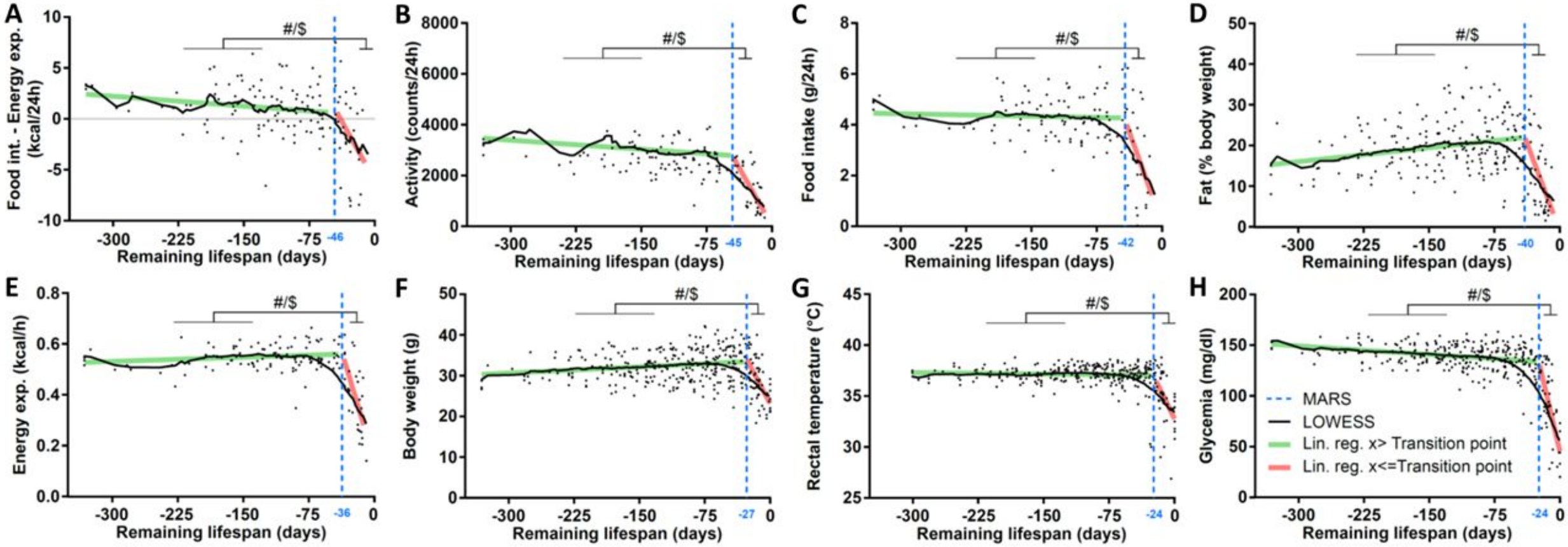
- ❑ Body Weight
- ❑ Fat and lean mass
- ❑ Body temperature
- ❑ Glycemia

-Metabolic recordings

- ❑ Food intake
- ❑ Locomotor activity
- ❑ Energy expenditure

Cansell et al., 2025

Smurfness in mice



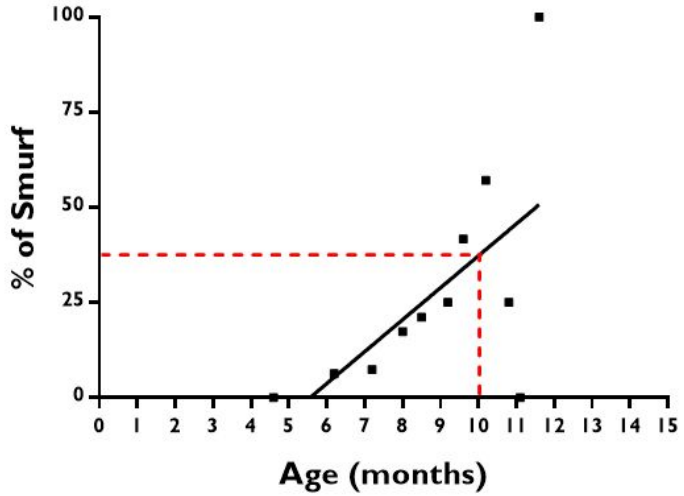
Cansell et al., 2025

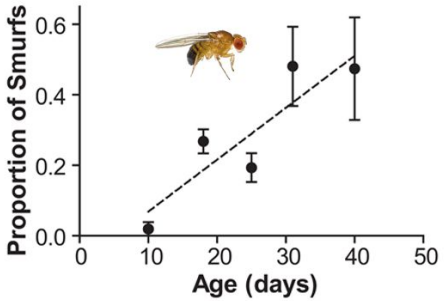
A “public” path to death: mice

Phase 1

Phase 2

Death





Cansell et al., 2025

A “public” path to death: mice

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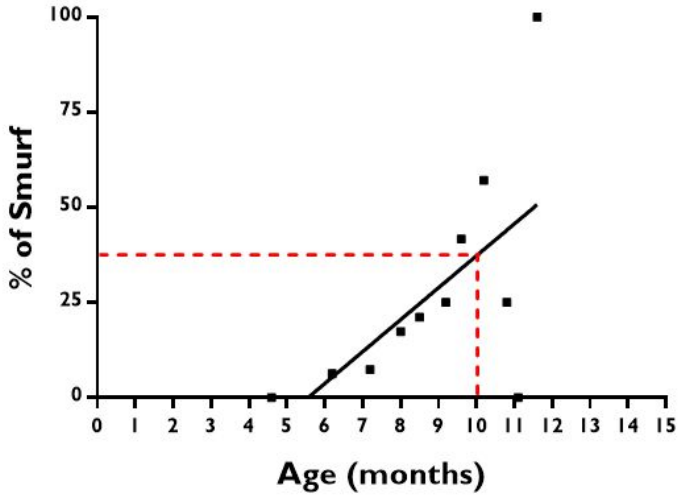
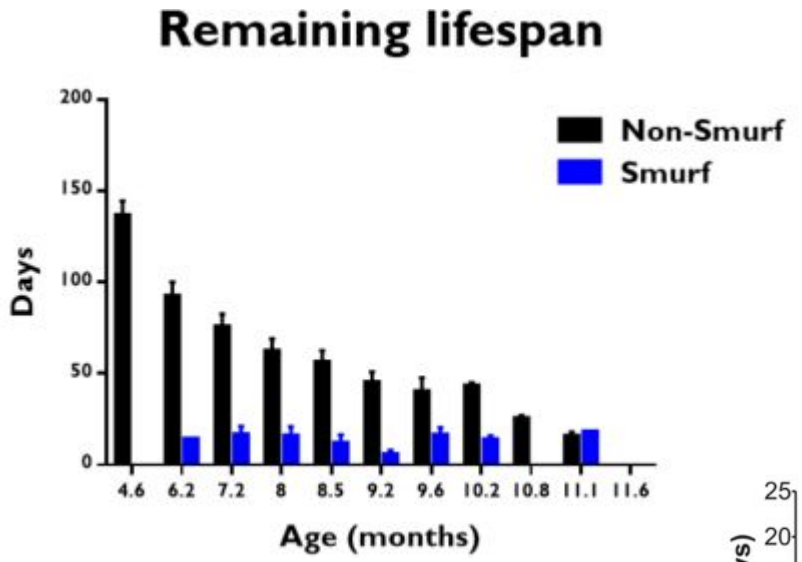
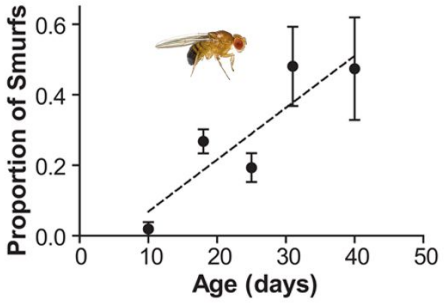
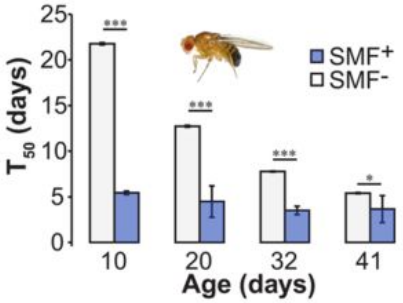


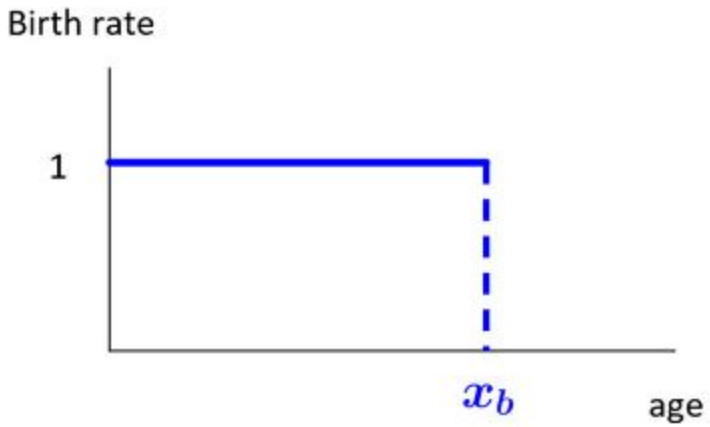


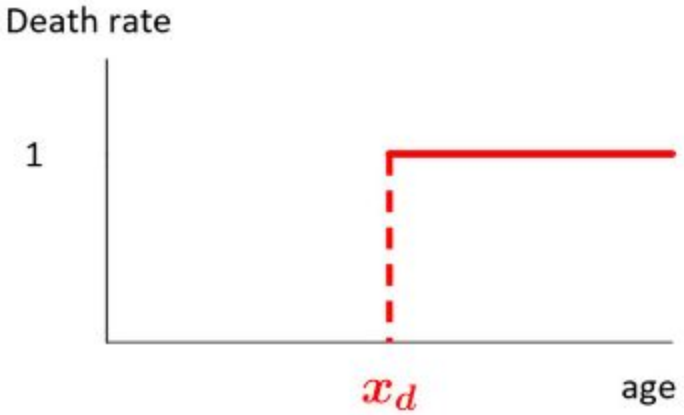




Cansell et al., 2025

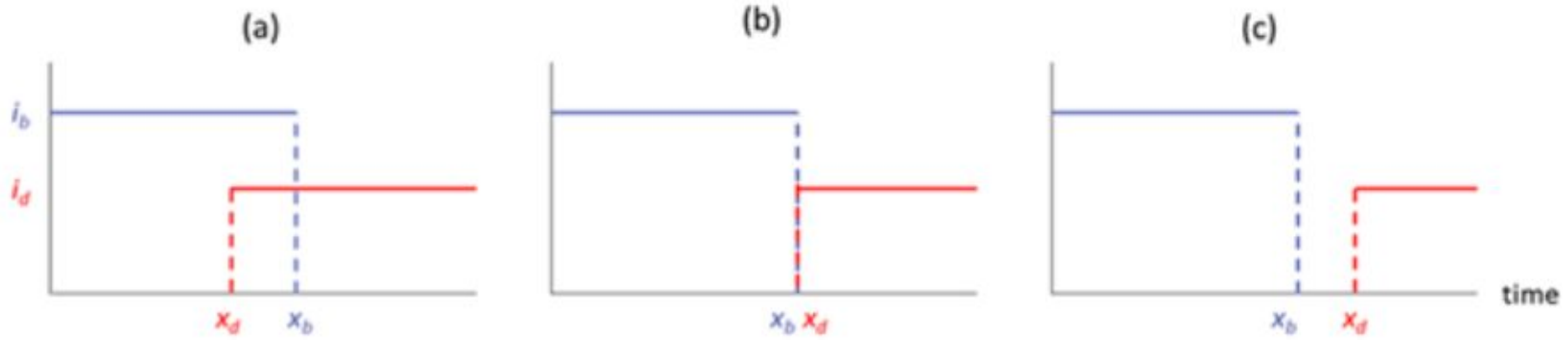
Proposing a simple birth-death model

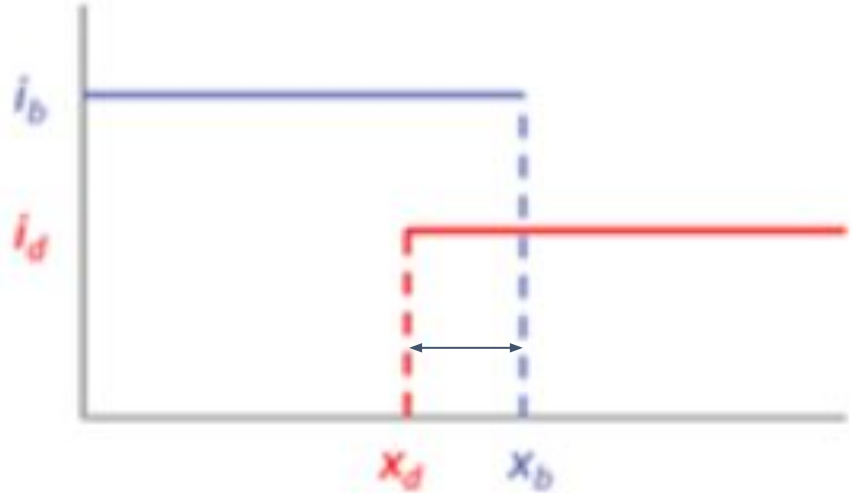




Roget, 2018; Roget et al., 2019

Evolution of the system





$$\lim_{t \to +\infty} (x_b - x_d)_t = \frac{\log(1+\frac{i_b + i_d}{i_d})}{i_b + i_d}$$

Roget, 2018; Roget et al., 2019; Roget et al., 2024

No time for ageing in the wild!?

Our expectations about aging in wild populations have been influenced by the classic evolutionary theories of aging and empirical shortcomings. The general hypothesis was that life in the wild is short, and hard, and that genes governing late life processes in the wild do not matter because few survive to old age. Evolutionary theories of aging suggest that aging exists because of the declining force of selection on late age-specific traits (Hamilton 1966, Medawar 1952, Williams 1957). Medawar (1952) suggested that aging could only be demonstrated in "captive," protected environments, in which animals are protected from natural hazards and can thus survive to ages never seen in the wild. This expectation, that aging cannot be found in the wild, has been quoted for the past 50 years (Kirkwood & Austad 2000), and empirically there were few demographic studies of individuals of known age to contradict this assertion. Recent theoretical work (Baudisch 2005, Williams et al. 2006) challenges some of these classic expectations, and long-term empirical studies of marked individuals demonstrate that the aging phenotype is an important phase of the life history in wild populations.

Zane et al., 2024

Searching for wild flies

Zane et al., 2024

A two-phase ageing process present in wild populations

5-8% smurfs

Zane et al., 2024

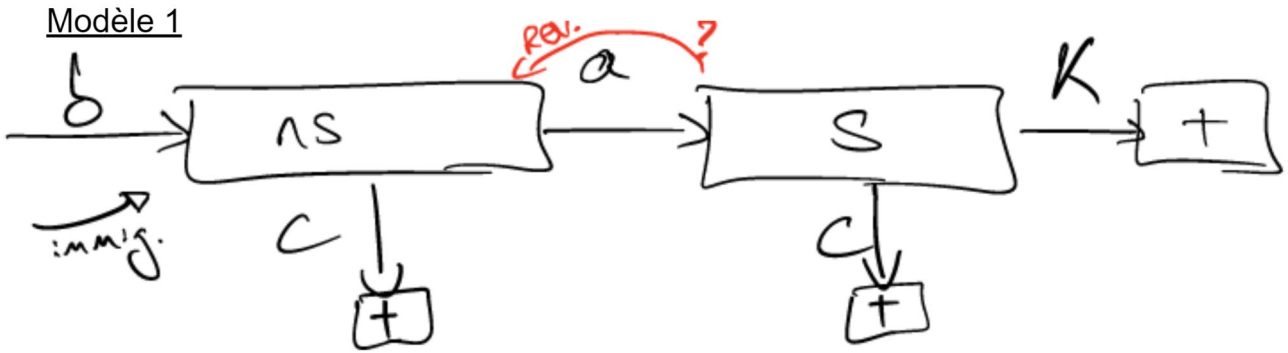
A two-phase ageing process present in wild populations

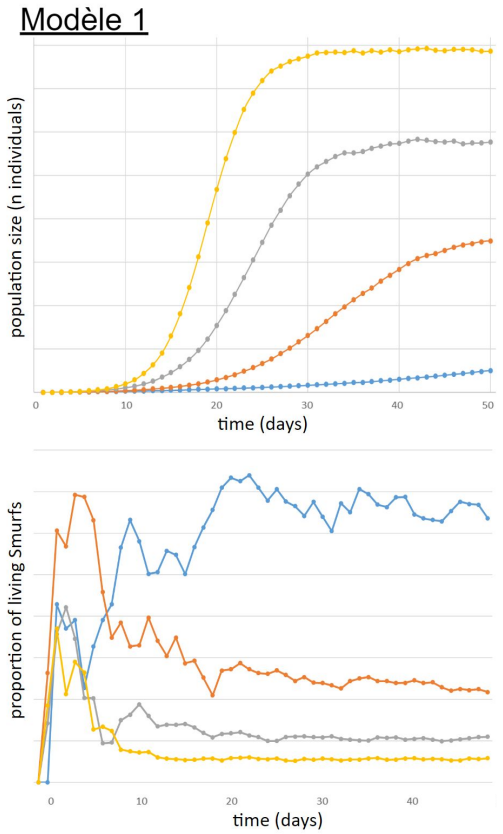
estimate the age pyramide of natural populations

estimate the “health” of natural populations

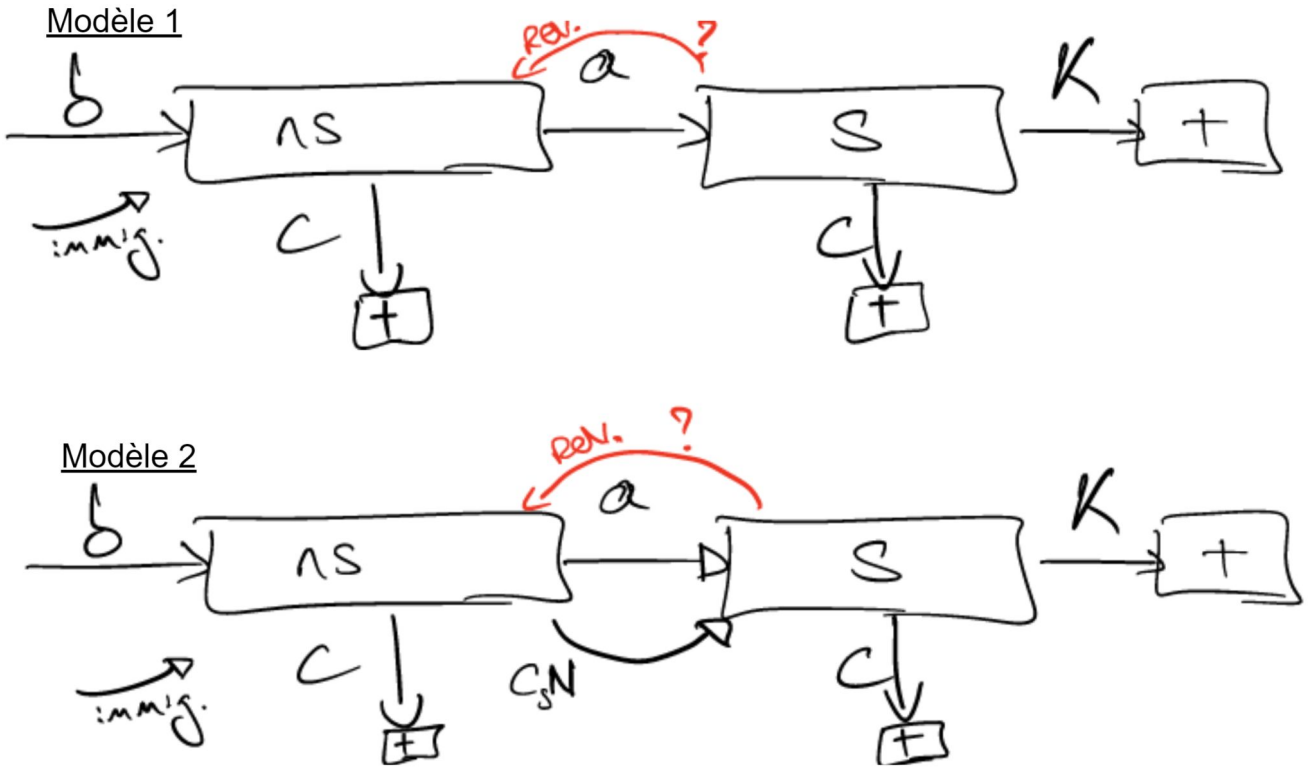
Zane et al., 2024

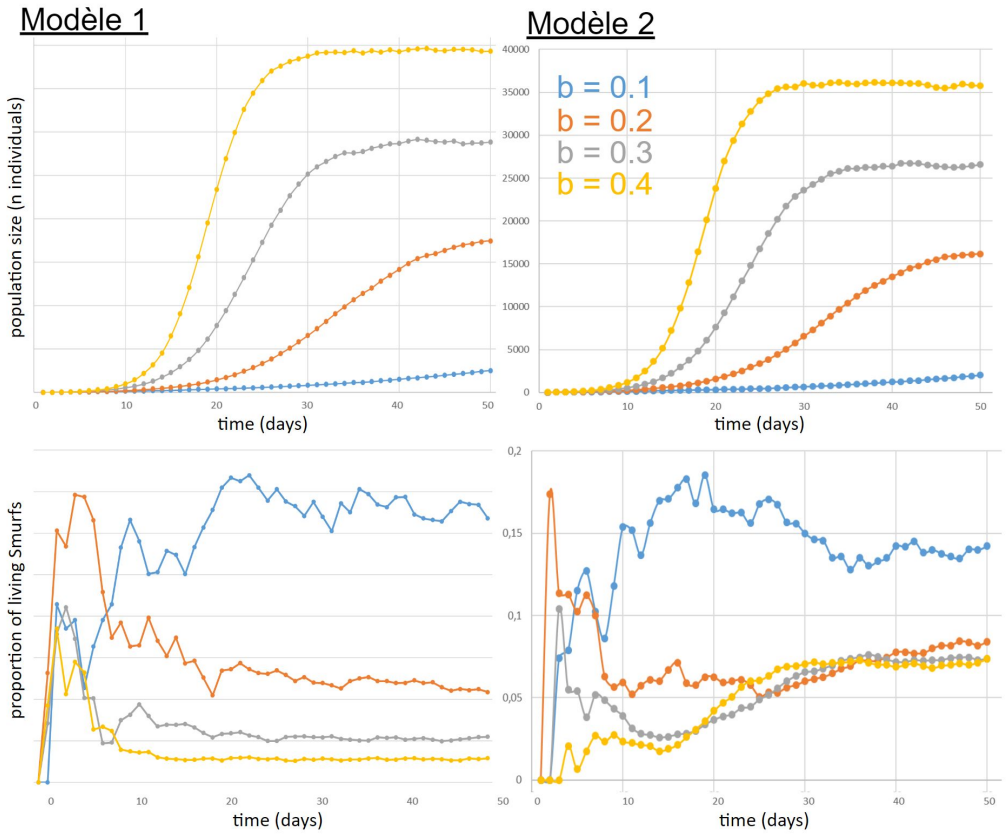
Modeling ageing in wild populations





Modeling ageing in wild populations





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Clément Dubost

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Tristan Roget (PhD)
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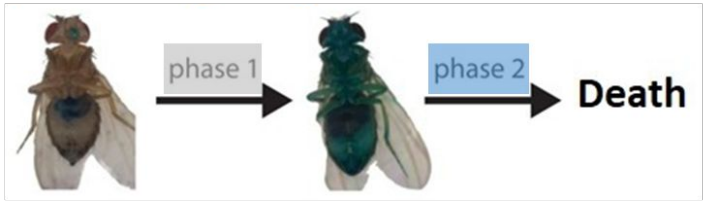
Jasmina Yeung (M1)
Isabel Berastain (M1)
Christina Fissoun (M1)
Julia Molina (M1)

A novel framework for studying ageing

Changing paradigm

Classic framework

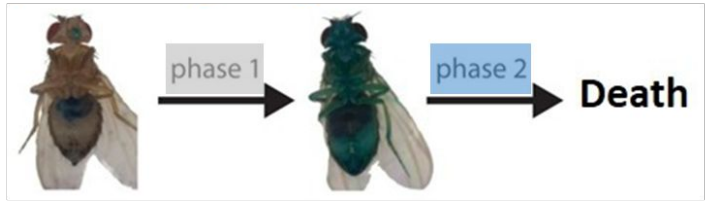
2-phase ageing framework



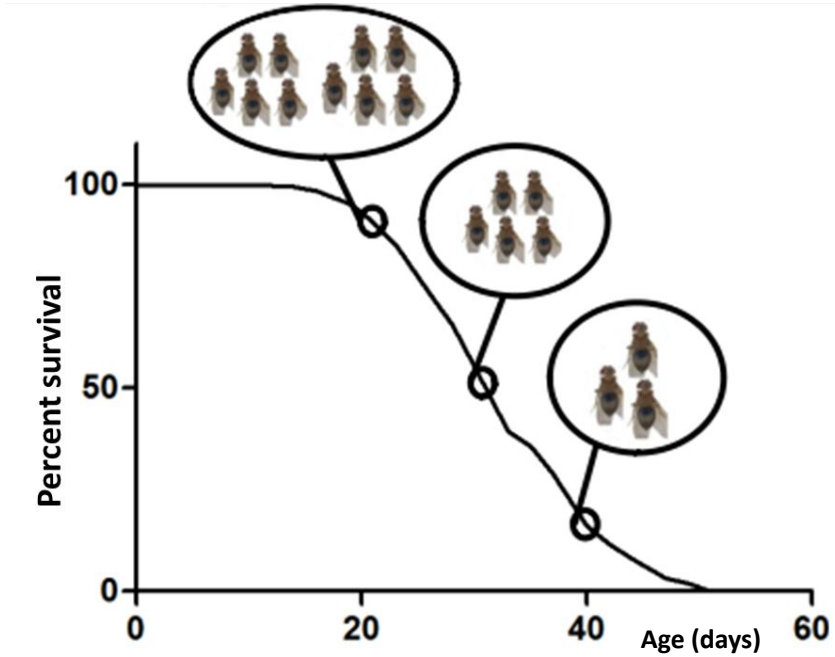
Changing paradigm

Classic framework

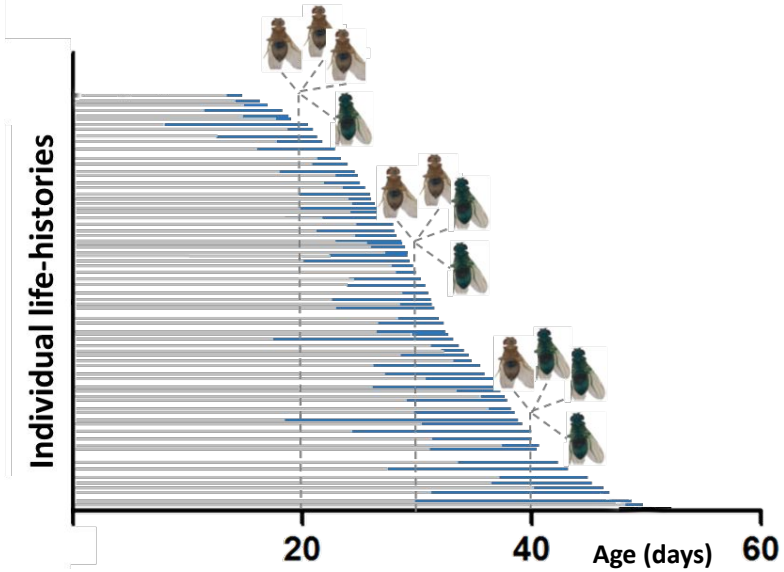
2-phase ageing framework



Chronological age



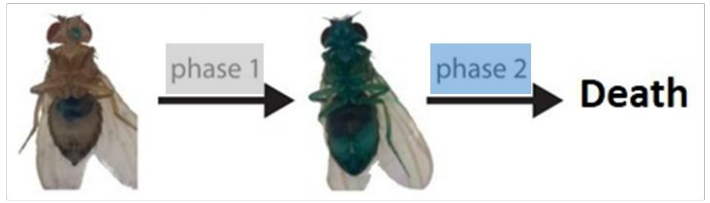
Physiological age



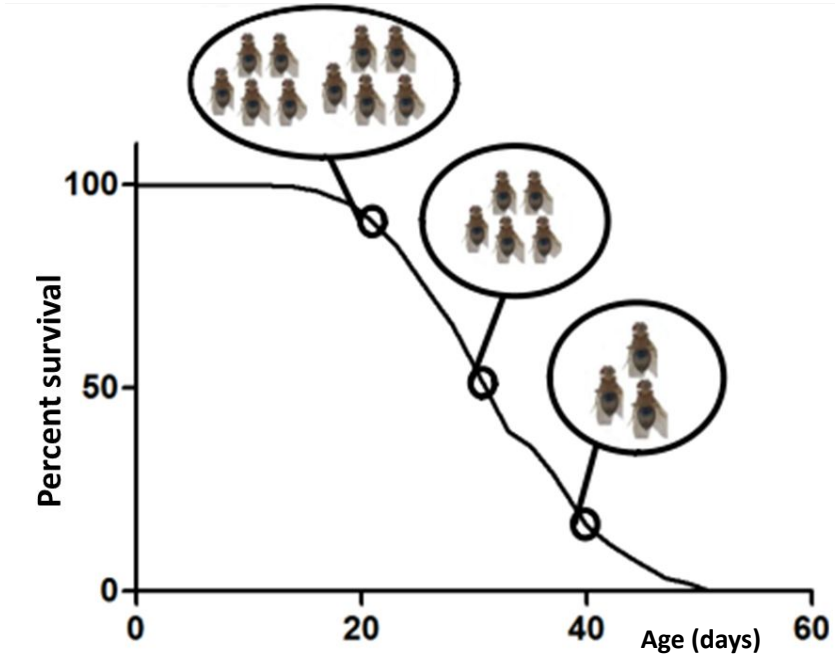
Changing paradigm

Classic framework

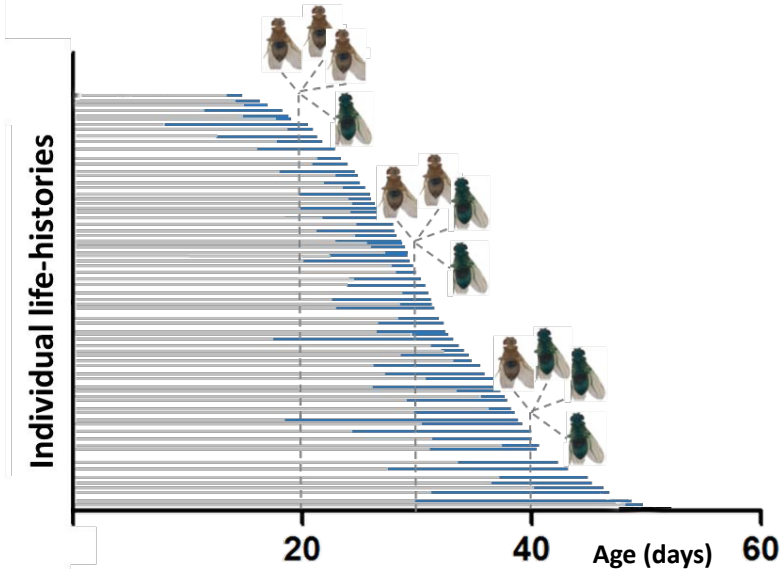
2-phase ageing framework



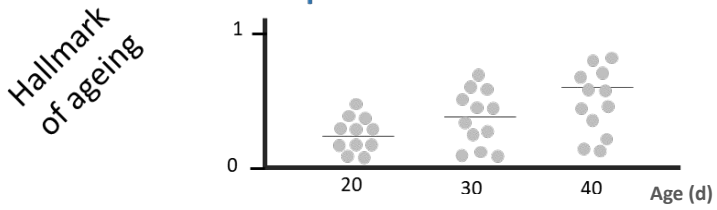
Chronological age



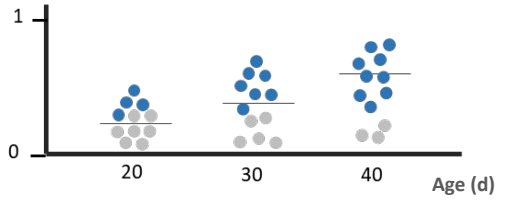
Physiological age



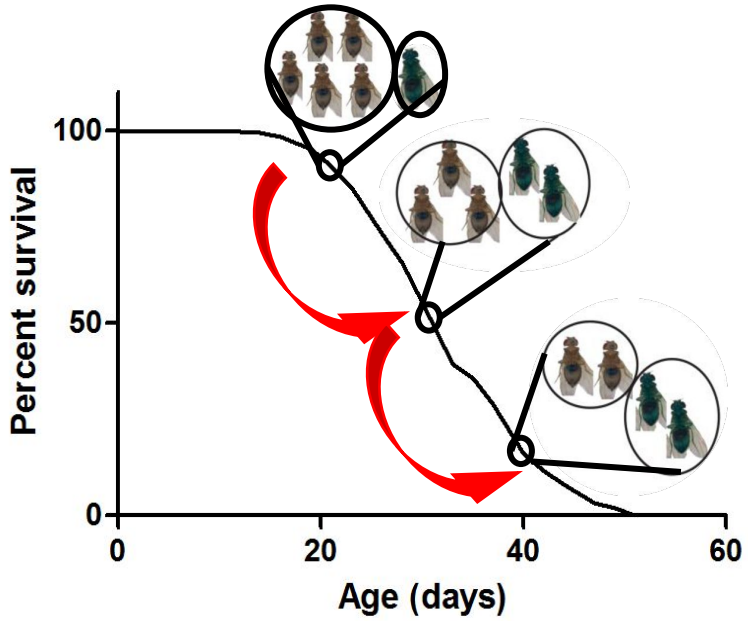
Population-based



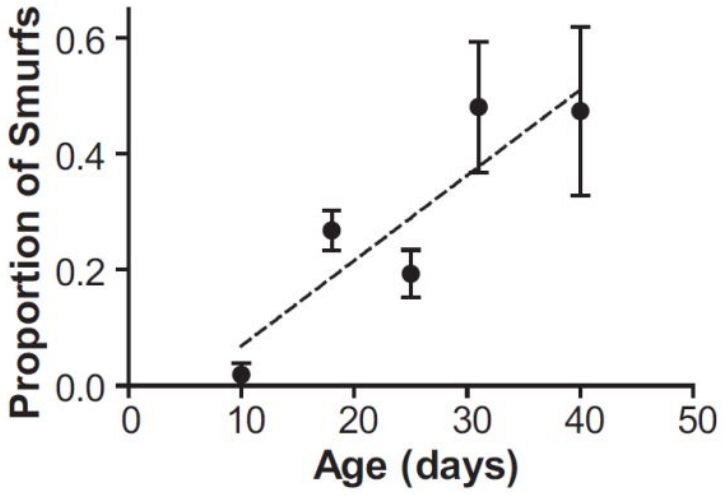
Individual-centered



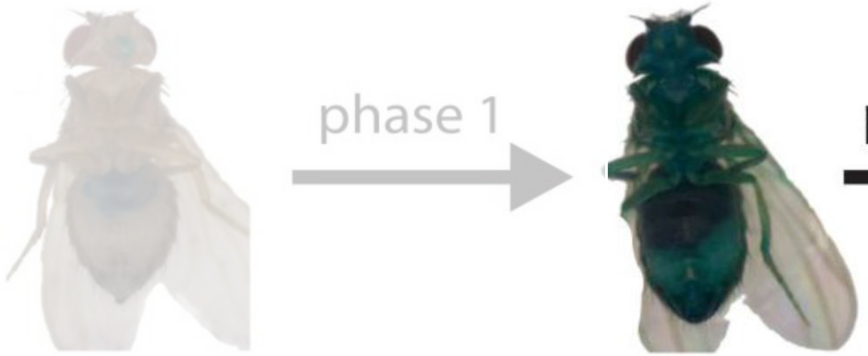
Our approach separates chronology and physiology



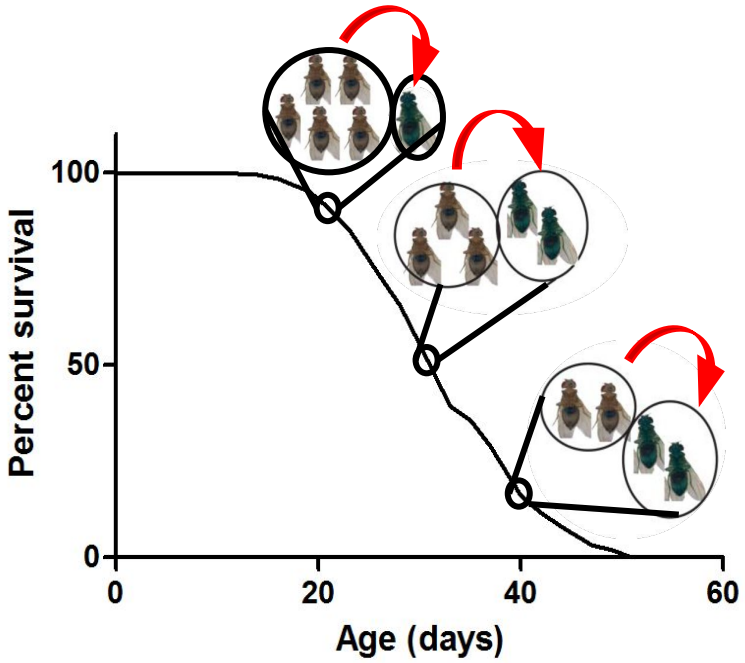
Understanding the increase in age-dependent risks



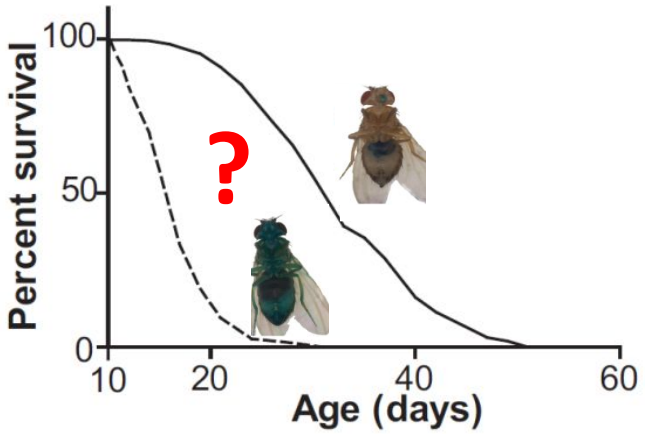
Our approach separates chronology and physiology



Death

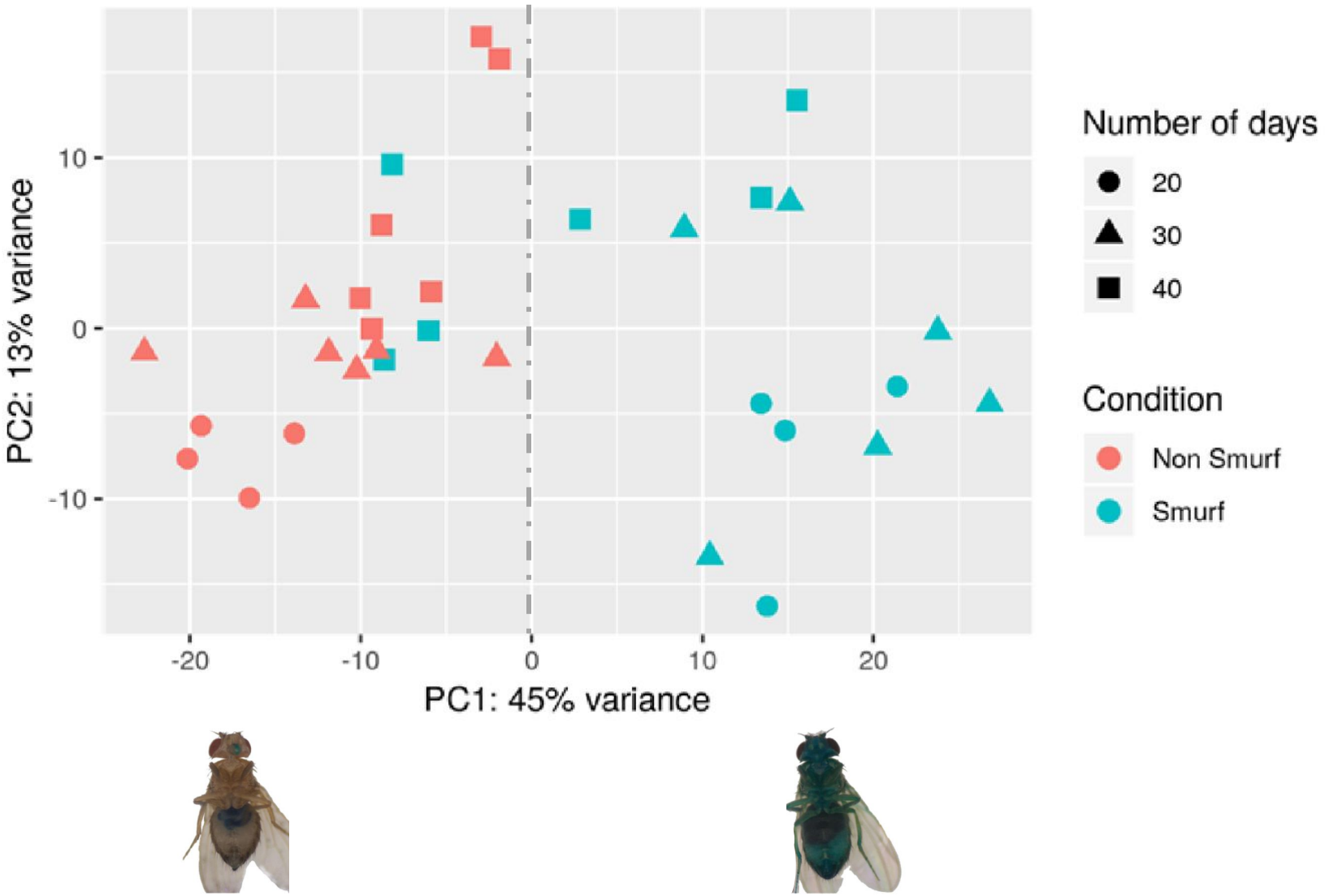


Understanding the
high risk of impending death

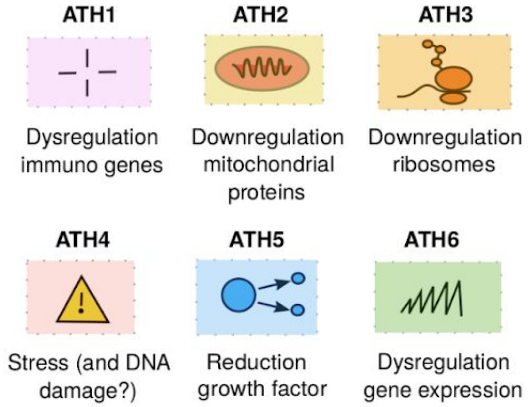


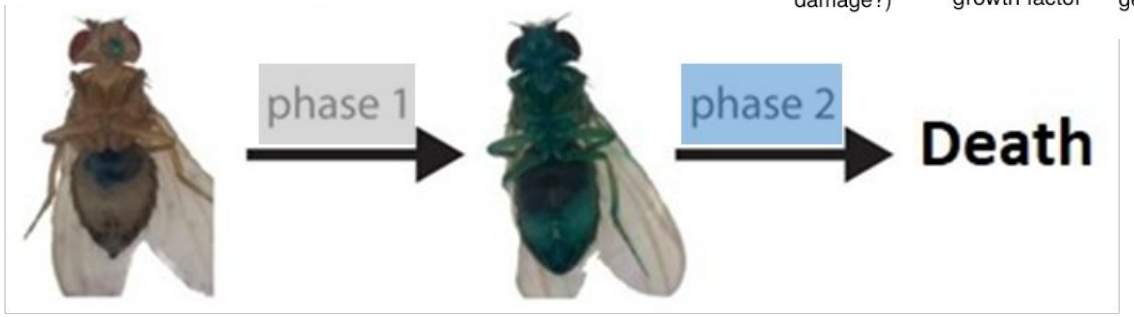
There is a Smurf-specific signature

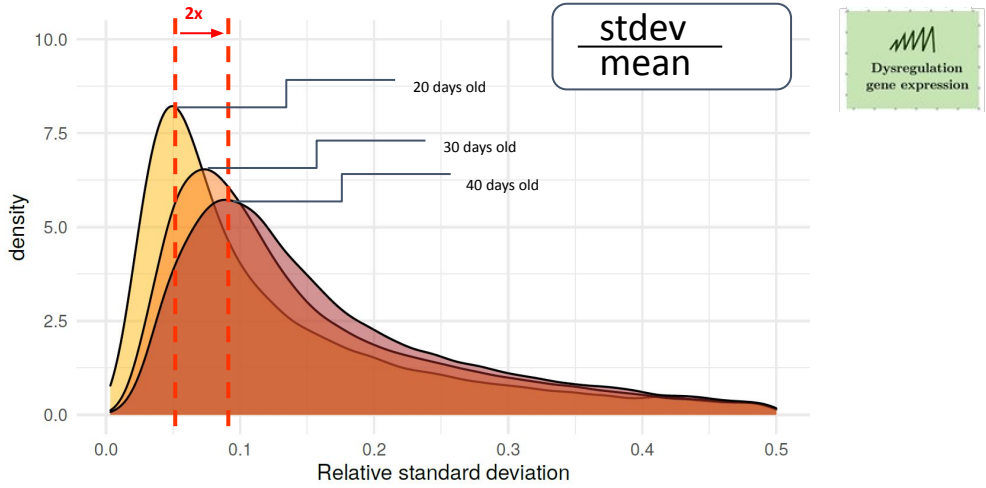
Flaminia Zane
PhD 12/05/22



Zane et al., 2023 Aging Cell







Zane et al., 2023 Aging Cell