

The evolution of senescence

Attendance code

DJ-NB-AZ

Variation in reproductive patterns is tremendous



¹Public domain images: [Deer mouse](#), [Black bear](#), [Dandelion](#)

The perfect organism: A “Darwinian Demon”

An organism perfectly adapted for reproduction:

- ▶ Mature at birth
- ▶ Produce high fitness offspring
- ▶ Produce large numbers of offspring
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Question: Is such an organism possible? Why or why not?

Extreme reproductive strategies



¹Adactylidium image: Khaustov, A. A., & Abramov, V. V. (2021). A new species of Adactylidium (Acaria: Heterostigmata: Acarophenacidae) associated with Phlaeothrips sp.(Thysanoptera: Phlaeothripidae) from European Russia. *Acarologia*, 61(2):356-364. [\[Link\]](#)

²Brown Kiwi image: [Public Domain](#)

Trade-offs involving energy and time: two examples

Strategy 1: An individual can maximise size or condition at reproduction by allocating energy to growth for a long time.

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- ▶ Natural selection should favor individuals that allocate energy and time with an optimal balance between the benefits and costs so as to maximise lifetime reproductive success.
- ▶ Different balances will be optimal in different environments so we expect environmental variation (i.e., local conditions) to be the source of much life history variation among living organisms.

Life-History Analysis

The study of trade-offs involving energy and time

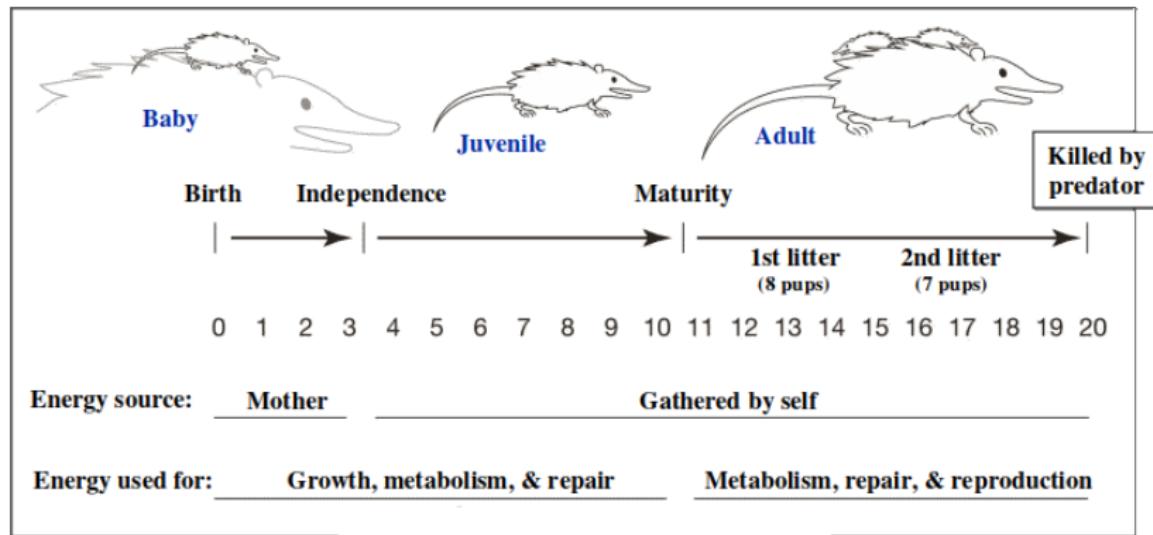
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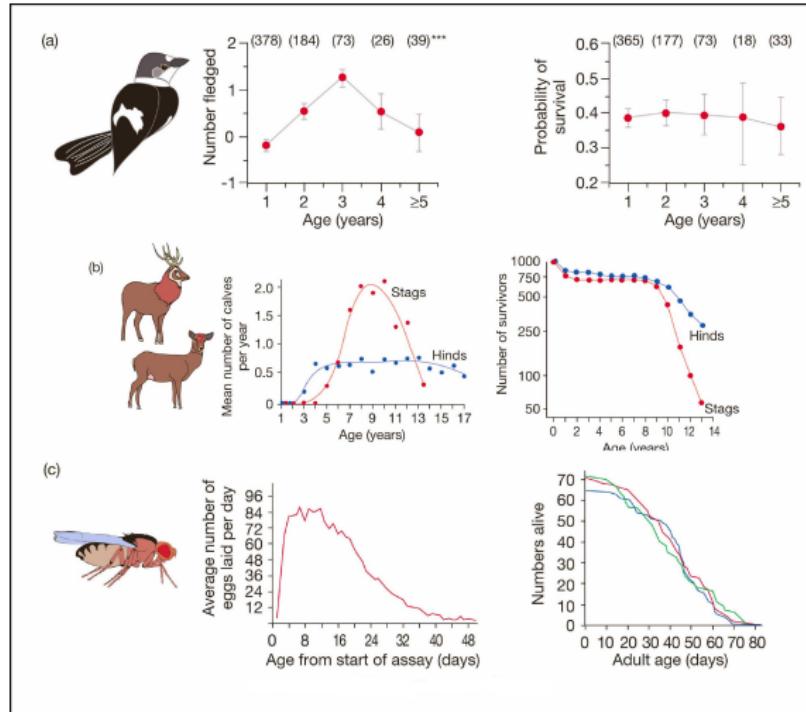
- ▶ Why do organisms age and die?
- ▶ How many offspring should an individual produce in a given year?
- ▶ How big should each offspring be?

Basic issues in life history analysis



¹Freeman S. & Herron J. C. (2007). *Evolutionary analysis* (Fourth). Pearson Prentice Hall. p. 485. Figure 13.2.

Why do organisms age and die?



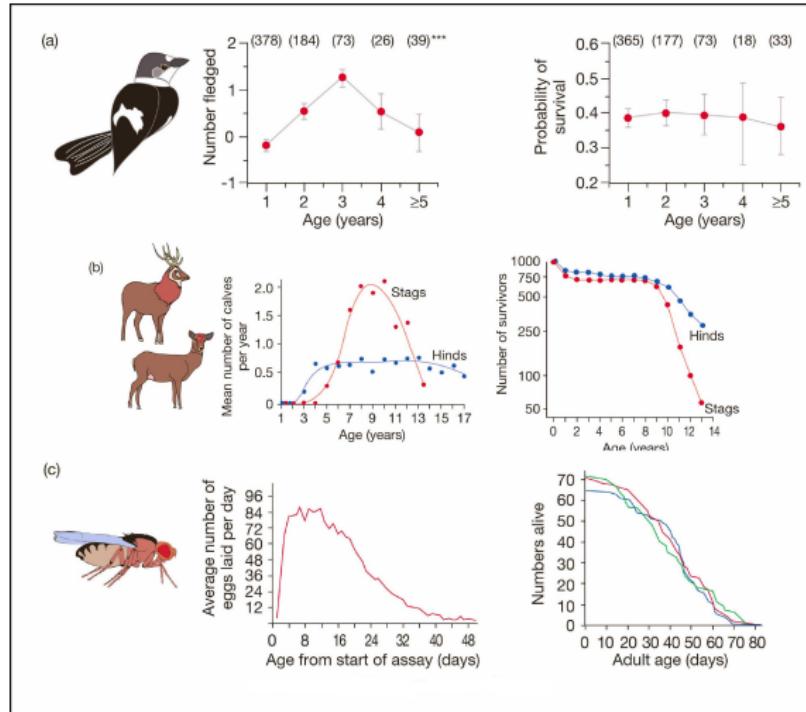
Aging in 3 animals

- ▶ Collared flycatchers
- ▶ Red deer
- ▶ *Drosophila melanogaster*

Declines in both fertility and survival (fitness)

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Aging should be opposed by selection, so why does it persist?

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Theories of aging

The rate-of-living theory of aging (Version A)

Senescence (aging) is caused by the irreversible damage to cells caused by the accumulation of poisonous metabolic by-products.

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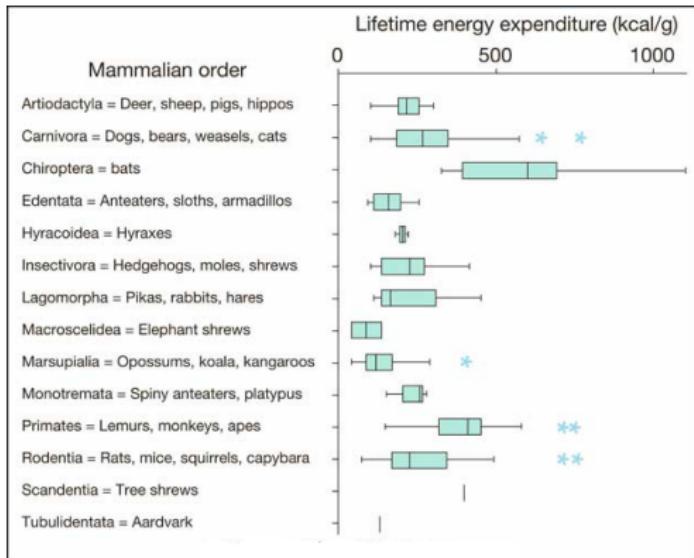
1. The rate of aging should be correlated to an organism's metabolic rate. All species should expend about the same amount of energy per gram per lifetime, whether they expend it slowly over a long lifetime or rapidly over a short lifetime.
2. Because of natural selection to resist and repair damage, species should not be able to evolve longer life spans (they are already living as long as is possible).

Variation among mammals in life energy expenditure

Prediction 1: Species should expend about the same amount of energy per gram per lifetime.

Data are not supportive:

- ▶ Bats have high metabolic rate but live 3x longer than similar size mammals.
- ▶ Marsupials have low metabolic rate but short life-spans relative to similar size mammals.



Not consistent with the Rate-of-Living Theory

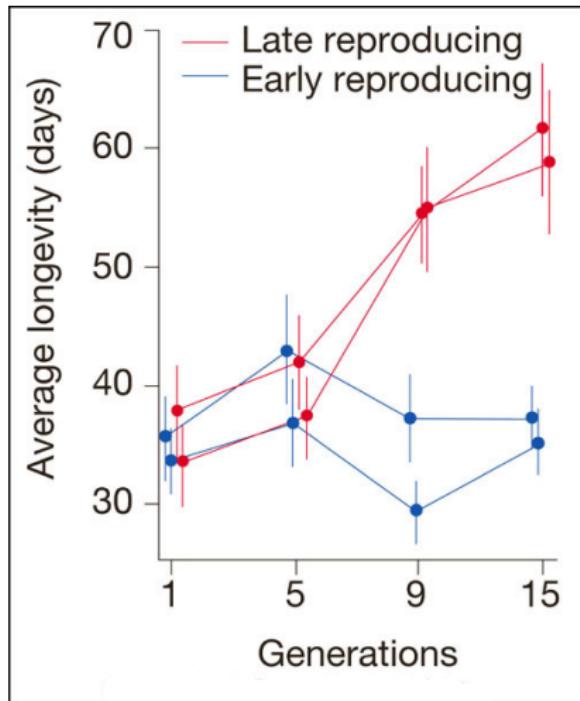
¹Freeman S. & Herron J. C. (2007). *Evolutionary analysis* (Fourth). Pearson Prentice Hall. p. 488. Figure 13.5.

Artificial selection increases lifespan

Prediction 2: Because of natural selection to resist and repair damage, species should *not* be able to evolve longer life spans.

Data: In *Drosophila*, longevity can be increased from about 35 days to 60 days.

Not consistent with the Rate-of-Living Theory of Aging



¹Freeman S. & Herron J. C. (2007). *Evolutionary analysis* (Fourth). Pearson Prentice Hall. p. 489. Figure 13.6.

Evolutionary theories of aging

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Question: What kind of mechanism might limit the number of divisions in a cell lineage?

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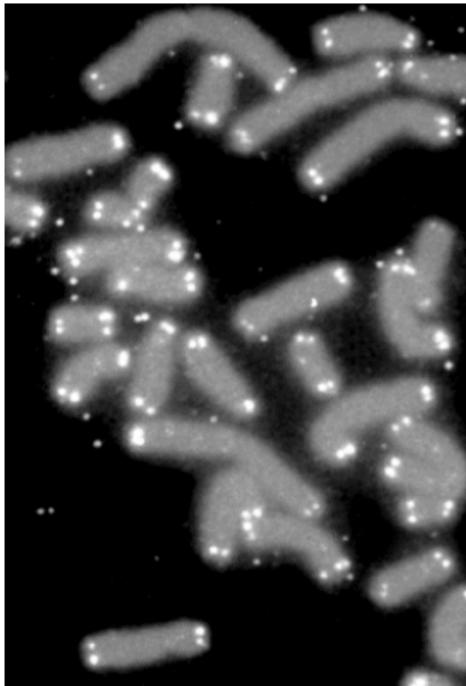
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Why do organisms senesce? Telomere damage?

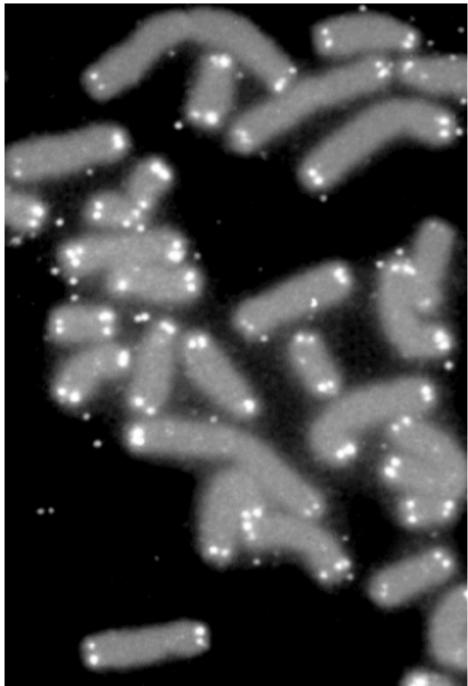
Questions about telomeres



Question: All cells contain the gene for telomerase so isn't it possible for cells to live longer by expressing this gene?

¹Image: Public Domain

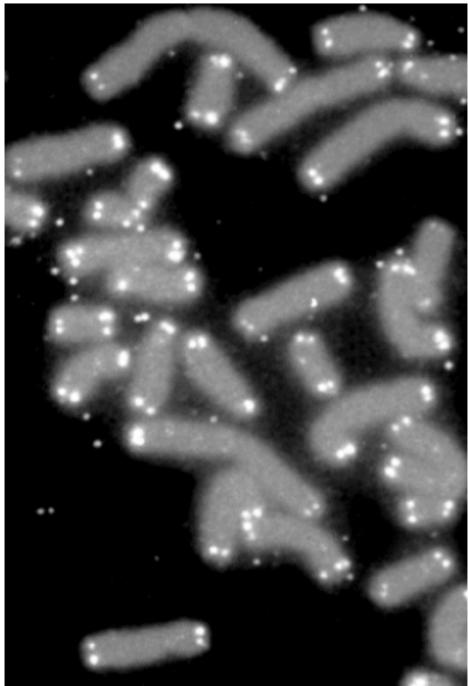
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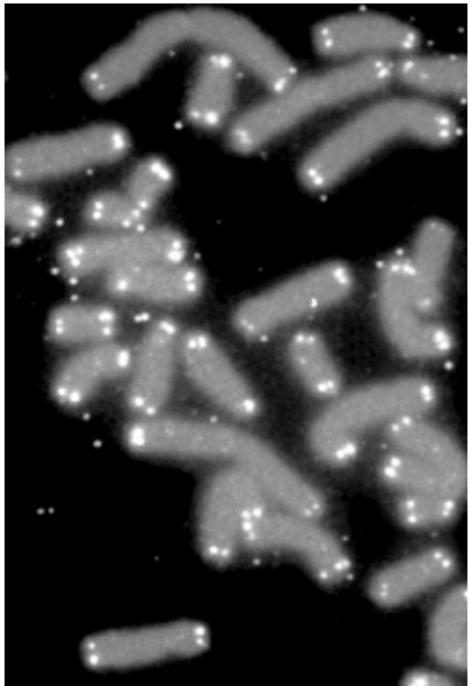
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- ▶ Yes: The life span of mammalian species (measured in years) is correlated with the life span of their skin and red blood cells.

¹Image: Public Domain

Telomere results: inferences

Telomere results are consistent with Version B of the rate of living theory, but also present a contradiction:

If expressing telomerase increases cell longevity and increased cell longevity causes an organism to live longer, then why doesn't natural selection act to increase individual fitness by increasing telomerase activity so that individuals can live longer?

Telomere results: inferences

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If expressing telomerase increases cell longevity and increased cell longevity causes an organism to live longer, then why doesn't natural selection act to increase individual fitness by increasing telomerase activity so that individuals can live longer?

The answer probably involves a trade-off between extending the longevity of cells (through telomerase activity) versus preventing the uncontrolled proliferation of cells (leading to cancer).

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Aging is caused by the irreversible damage to DNA caused by the division of cells and chromosomes.

Available data better support Version B

Evolutionary theory of aging

Given that organisms contain the genetic information needed to make complex tissues and organs, then, in principle, basic maintenance and complete repair ought to be physiologically possible.

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Actually, organisms are pretty good at repair at whole part level yet the job is often incomplete at cellular level.

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Predictions

Under Evolutionary Theory of Aging, failure to completely repair damage is ultimately caused by:

- ▶ Deleterious mutations.
- ▶ Trade-offs between repair and reproduction.

Evolutionary theory of aging: a null model

Life histories from birth until death (e.g., due to accidents, predation, disease).

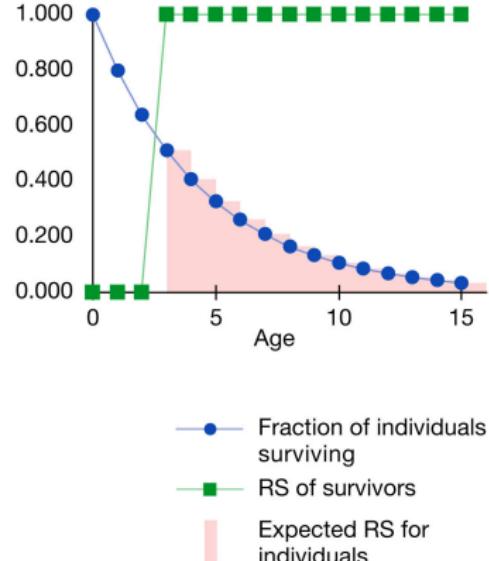
- ▶ Prob survival is $p = 0.8$ each year
- ▶ Maximum age is 15 years
- ▶ Reproductive success (RS) is 1 from age 3
- ▶ Age-specific expected RS = $\text{Pr}(\text{Survival}) \times \text{RS}$
- ▶ Expected lifetime RS is RS accumulated lifetime.

Evolutionary theory of aging: a null model

(a) Wild type matures at age 3 and dies at age 16; prior to age 16 annual rate of survival = 0.8

Age	Fraction of individuals surviving	RS of survivors	Expected RS for individuals
0	1.000	0	0.000
1	0.800	0	0.000
2	0.640	0	0.000
3	0.512	1	0.512
4	0.410	1	0.410
5	0.328	1	0.328
6	0.262	1	0.262
7	0.210	1	0.210
8	0.168	1	0.168
9	0.134	1	0.134
10	0.107	1	0.107
11	0.086	1	0.086
12	0.069	1	0.069
13	0.055	1	0.055
14	0.044	1	0.044
15	0.035	1	0.035

Expected lifetime RS: 2.419



¹Freeman S. & Herron J. C. (2007). *Evolutionary analysis* (Fourth). Pearson Prentice Hall. p. 493. Figure 13.10.

The mutation accumulation hypothesis

Concept: Mutations that decrease survival or reproduction late in life will accumulate in populations because they have relatively small effects on fitness.

Suppose a lethal mutation causes death at age 14 instead of 15 (everything else stays the same).

How strong will it be selected against?

- ▶ Expected lifetime RS w/o mutation = 2.419
- ▶ Expected lifetime RS w/ mutation = 2.34

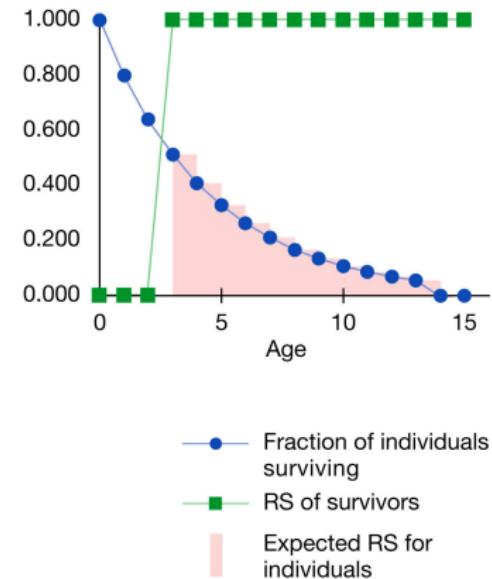
Mutant has 96% of the fitness!

The mutation accumulation hypothesis

(b) Mutation that causes death at age 14; prior to age 14 annual rate of survival = 0.8

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Expected lifetime RS: 2.340



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- ▶ Would a mutation at age 13 be more strongly selected against? Ages 10 or 2?
- ▶ What is the expected frequency of mutations that are selected against only weakly? (remember equilibrium frequency of deleterious recessives at mutation selection balance)

Mutations that cause death in an advanced age?

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Example in Humans

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Example in Humans

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If there are germ-line mutations in the genes that code for these enzymes, the result can be the accumulation of mismatch errors in other genes, which in turn can result in cancer.

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Example in Humans

- ▶ Germ-line mutations in DNA mismatch repair genes in humans can cause colon cancer
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Such mutations persist because they reduce survival only late in life, have small effects on fitness.

Trade-offs and aging: Antagonistic pleiotropy hypothesis

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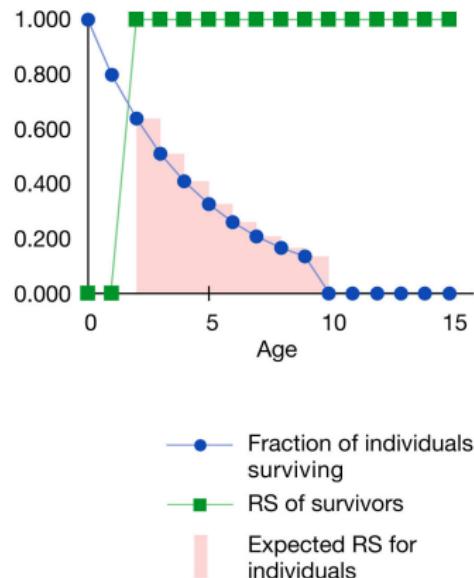
Do such alleles exist in nature?

Trade-offs and aging: Antagonistic pleiotropy hypothesis

- (c) Mutation that causes maturation at age 2 and death at age 10; prior to age 10 annual rate of survival = 0.8

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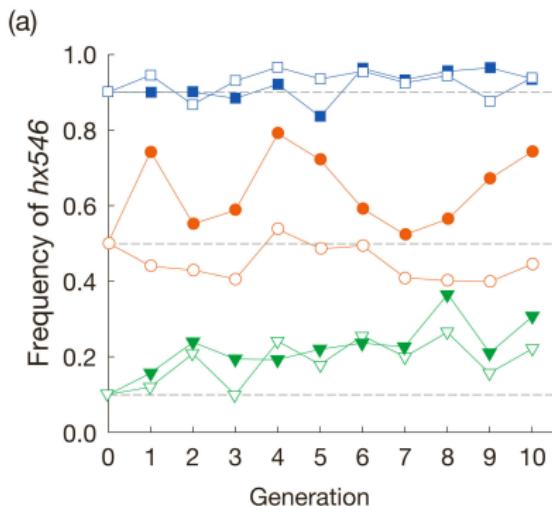


¹Freeman S. & Herron J. C. (2007). *Evolutionary analysis* (Fourth). Pearson Prentice Hall. p. 493. Figure 13.10.

Trade-offs and aging: age-1 gene in nematodes

Mutations in the age-1 gene can increase life by 80% in *C. elegans*

- ▶ Mutant hx546 allele
- ▶ Carriers of hx546 appear fine
- ▶ hx546 should be advantageous?
- ▶ No evidence of selection in lab



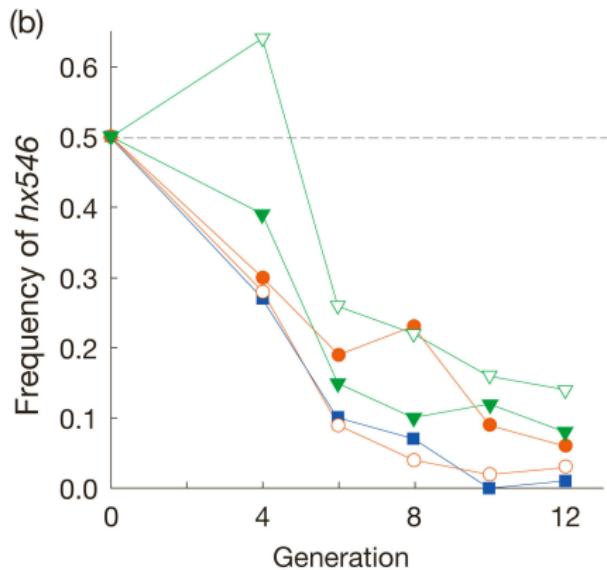
Suggests no fitness benefits to extra longevity.

¹Freeman S. & Herron J. C. (2007). *Evolutionary analysis* (Fourth). Pearson Prentice Hall. p. 497. Figure 13.13a.

Trade-offs and aging: age-1 gene in nematodes

Exposed *C. elegans* to repeated starvation

- ▶ hx546 allele frequency plummeted
- ▶ Fitness of hx546 less than 80%

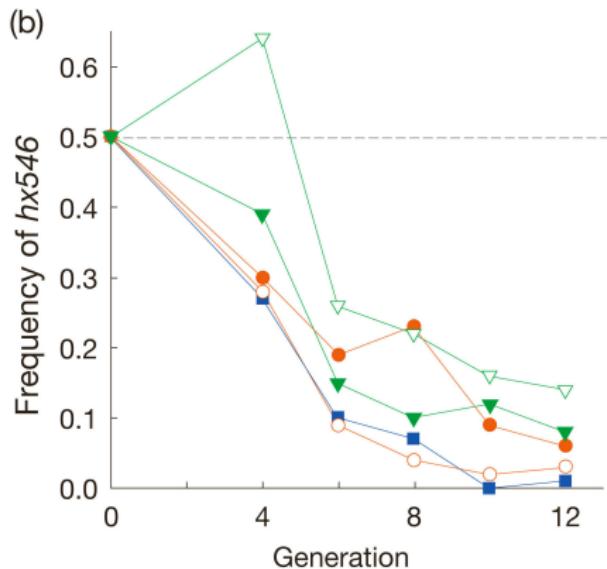


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Just as the antagonistic pleiotropy hypothesis predicts: Early reproductive success at cost of shorter lifespan.

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Trade-offs and aging: Collard Fly Catcher

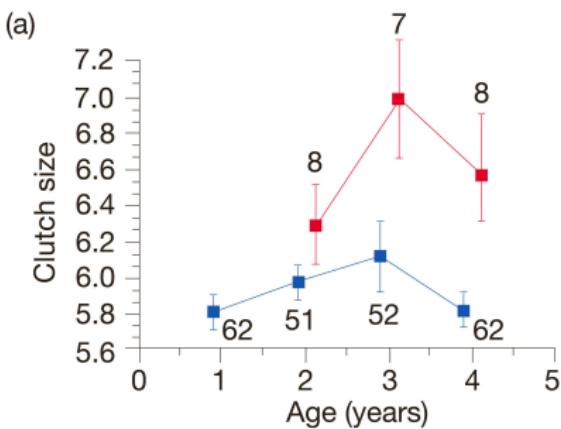
- ▶ Females that breed in their first year have smaller clutches in years 2, 3, and 4 than females that do not breed until year 2
- ▶ Females given extra eggs at age 1 have progressively smaller clutches each year at ages 2, 3, and 4.
- ▶ Control females do not show a decline in egg production until age 4.
- ▶ Supports the antagonistic pleiotropy hypothesis?



¹Image: Frank Vassen, [Creative Commons Attribution 2.0](#)

Trade-offs and aging: Collard Fly Catcher

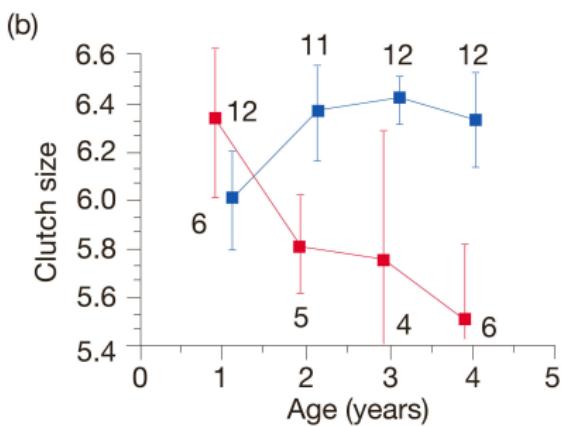
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- ▶ Senescence evolves because natural selection is weaker late in life.
- ▶ Late-acting deleterious mutations can persist under mutation-selection balance.
- ▶ Selection can favour reproduction early in life at the expense of repair later.