Why Do We Age?

A&S300-002 Jim Lund

The big questions about aging!

- **Why** do animals age?
- **What** causes aging?
- **How** does a young animal become an old animal?
- **Where** in the cell does aging occur?

Why?

Is aging inevitable? No.

No chemical or physical factor makes aging unavoidable.

Animals repair themselves.
If this repair worked better animals would not age.

Incorrect hypotheses: why animals age

- Death is good for the species.

- **Individuals make choices good for themselves not their species.**

Incorrect hypotheses: why animals age

- Animals age because of limited cell division.
  - Telomere length plays a role in cellular lifespan in cultured human cells
  - It is not the major factor in determining organismal lifespan.
  - Limited cell replication prevents cancer.
  - Plays a limited role in aging (part of the answer to the what and how questions).

Incorrect hypotheses: why animals age

- Rate of living theory
  - Plays a limited role in aging (part of the answer to the what and how questions).
  - Metabolism (burning oxygen) is damaging.
  - While there is a strong association of metabolic rate and lifespan in many animals there are also a number of exceptions.
  - Metabolism is part of the answer to the what and how questions.

Evolution

- "The major tenets of the Modern Synthesis (of genertics and evolutionary)
  - Populations contain genetic variation that arises by random (ie. not adaptively directed) mutation and recombination.
  - Populations evolve by changes in gene frequency brought about by random genetic drift, gene flow, and especially natural selection.
  - Most adaptive genetic variants have individually slight phenotypic effects so that phenotypic changes are gradual.
  - Diversification comes about by speciation, which typically entails reproductive isolation between populations.
  - These processes, continued for sufficiently long, give rise to changes of such great magnitude as to warrant the designation of higher taxonomic levels (genera, families, and so forth).

- Futuyma, D.J. in Evolutionary Biology, Sinauer Associates, 1986; p.12

Longevity quotient (LQ)

- LQ = longevity / expected lifespan given an animal's body size.

Animal	Max. lifespan	LQ
White-eared opossum	4.0	0.3
African lion	30	1.1
Hippopotamus	54	1.2
Southern flying quirrel	17	2.7
Vampire bat	19.5	3.5
Human	90	4.2
Little brown bat	32	5.8

Evolution

- Two main evolutionary factors:

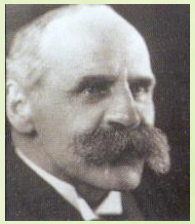
  Survival

  Reproduction

Evolutionary constraints

- Time to reproduce sets a minimum value on an animal's lifespan.
- Animals that don't live long enough to reproduce are out of the game.

Haldane's insight



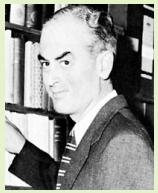
J. B. S. Haldane realized that alleles which give rise to traits after the reproductive period are not under evolutionary selection.

Haldane's insight

The consequence of this is that diseases with late onset are more common than they would be if they had earlier onset.

Huntignton's disease
onset typically between 30-40.
autosomal dominant disease
1:15,000 (European)

Medawar's theory



- Selection is strongest on alleles that express their effects in young animals.
- The later in life at which an allele acts, the weaker the selection it is under, either positive or negative.
- **Due to this, late acting alleles with deleterious effects accumulate in the genomes of animals.**

Evolutionary causes of aging

- Late acting alleles with deleterious effects accumulate in the genomes of animals.
- The case of genes with multiple biological or developmental roles: stronger selection on alleles that have positive effects early in development than on alleles which have negative effects late in life.

Resource trade-offs

- Reproduction is more important than maintenance of the animal's body.
- Evidence:
  - Testosterone suppresses the immune system
    - Castrated guinea pig resist infection better
    - Castrated dogs have lower cancer rates.
    - In *Caenorhabditis elegans*, mutations reducing sperm production extend lifespan 85%.
    - Human data from 20th century eugenics.
  - In many animals, females that don't reproduce live longer.
    - *Drosophila* female lifespan is shortened by increased egg production, receipt of male accessory fluid and courting.
    - In the nematode *Caenorhabditis elegans*, mating with males reduces the lifespan of hermaphrodites.

Evolutionary experiments

- Micheal Rose tested the effect of reproductive selection on lifespan of *D. melanogaser*.
- Steven Austad compared lifespans of a population of opossums on an island with few predators to mainland opossums.

Dm selection for old reproduction produces long-lived flys

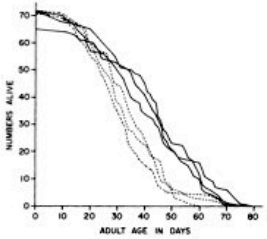


FIG. 1. Surviving numbers of females from the start of the adult life-history assay period. B population samples are shown as dashed lines, O samples as solid lines.

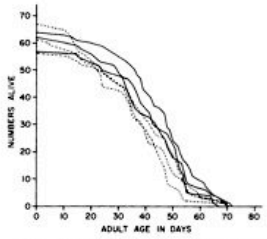


FIG. 2. Surviving number of males from the start of the adult life-history assay period. B population samples are shown as dashed lines, O samples as solid lines.

Laboratory Evolution of Postponed Senescence in Drosophila melanogaster. Michael R. Rose. Evolution, Vol. 38, No. 5. (Sep., 1984), pp. 1004-1010.

Dm selection for old reproduction

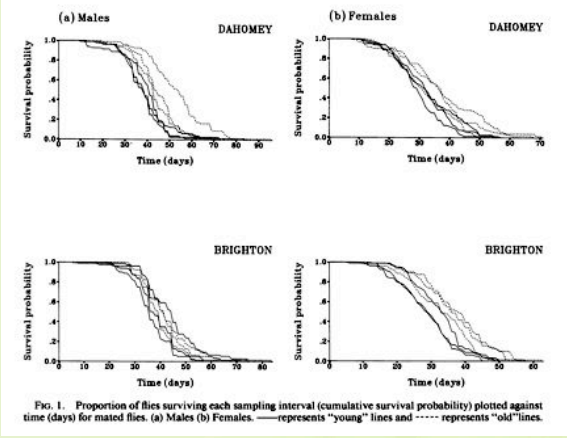


FIG. 1. Proportion of flies surviving each sampling interval (cumulative survival probability) plotted against time (days) for mated flies. (a) Males (b) Females. ——represents "young" lines and ----- represents "old"lines.

Direct and Correlated Responses to Selection on Age at Reproduction in Drosophila melanogaster. Partridge et al., 1992

Fly evolution experiments

- Later experiments by Micheal Rose selecting for late onset of reproduction:
  - Fly lines that begin reproduction when the baseline population is all dead.
  - Fly lines that live twice as long as the baseline population.

Opossum lifespan

- Steven Austad compared lifespans of a population of opossums on an island with few predators to mainland opossums.

Opossum lifespan

- Typically live under two years.
- Only survive long enough to have one litter of pups.
- Opossums are slow moving and easy target for predators: owls, coyotes, dogs, bobcats, cars…

Steven Austad's experiment

- Find a population of opossums living in an environment with few predators and measure their lifespan.
- Where to find this population: on Sapelo Island, a barrier island off the coast of Georgia.

Virginia opossums (*Didelphis virginiana*)

Steven Austad's experiment

- The island population:
  - Litters of 4-6 pups (6-9 pup litters in mainland population)
  - Lifespan:
    - Mean 25% longer
    - Maximum 50% longer
  - 50%+ live to a second breeding season!
  - Mortality rate increased half as fast.
  - Collagen aging slower.

Synthesis: why do animals age?

- Lifespan is under evolutionary selection to maximize reproduction. Animals must survive long enough to reproduce but aren't under selection to live longer.
- Animals with low survival due to predation or environmental conditions reproduce earlier.
- Animals with lower mortality rates can reproduce later or for a longer period and are under selection for survival to longer ages.
- Traits that have deleterious effects late in life are under weak selection; deleterious traits that express after reproduction are not under selection and accumulate in the genome.

Synthesis: why do animals age?

- Animals with low mortality live longer than expected:
  - Birds
  - Flying squirrels
  - Giant tortoises
- Animals experiencing heavy predation have short lifespans
  - Opossums
  - Mice.
- Generally, large animals have fewer predators than smaller animals and live longer.

Remaining big questions about aging!

- **Why** do animals age?
- **What** are the biological processes under selection that cause aging.
- **How** does the progressive action of these processes change an animal as it ages.
- **Where** in the cell does these aging processes act?