**Bartlett, J. 1987. Filial cannibalism in burying beetles *Behavioural Ecology and Sociobiology* 21: 179-183**

In the case of *N. vespilloides,* brood reduction is shown here to be causedby adults killing and eating their own young duringthe normal raising of a brood

It is suggested that the consequent brood reduction can be interpreted as a means of optimising the eventual ratio of larvae to available carrion food.

*N. vespilloides,* the species used here, creates a burialchamber or crypt around the buried corpse andscatters its eggs up to several centimetres away

Both adults are normally present throughout larval development, feeding the young, repairing any damage to the chamber, and driving off insects which trespass on the crypt.

The number of *Nicrophorus* larvae a corpse can support increases with corpse size (Easton 1979; Wilson and Fudge 1984). However, the North American species *N. orbicollis* was found not to adjust its clutch size according to corpse size and to lay more eggs on a 15 g corpse than the corpse could support

Fifteen broods with a mean of thirty first stage larvae (to match the brood size found in the previous experiment) were created on 15 g mice by pooling the hatchlings of several families and dividing them between the mice.

experience suggested that adult *N. vespilloides* cannot recognise their own larvae and will raise a foster-brood,

Clutch size on 30 g mice is not significantly different from clutch size on 15 g mice, but subsequent survival of the brood is very different

On 15 g mice there is no significant difference between the mean number of eggs laid and the mean number of first stage larvae reaching the mouse but the difference between the mean number of first stage larvae and the mean number of larvae at dispersal shows that only about half of the larvae which reach a 15 g corpse are likely to complete development

significant fall in larval numbers between first and second instars but no significant mortality between second and third instars and up to dispersal

There was no mortality between first and second instars if the brood size was below about 15, but for broods larger than this numbers dropped sharply in the first 24 h on the mouse

In all the broods set up for observation the parents were seen to kill and eat first stage larvae

The main period of larval mortality on 10 g and 15 g corpses is at the first instar, during the first 24 h after the larvae have reached the corpse.

It is most unlikely that food is limiting at this time since only a small hole has been eaten in the skin of the mouse and the larvae have not begun to penetrate the

body.

Variable mortality of eggs or of hatchlings making their way to the corpse may explain why *Nicrophorus* lays many more eggs than are raised around a small corpse

or are bound by a physiological constraint such that they must lay a minimum clutch which is greater than the capacity of a small corpse.

In the laboratory N. *vespilloides* will lay 46.83\_+5.86 eggs on a 75 g corpse (n=18) and 18.44\_\_2.05eggs on a 5g corpse (n = 27), showing that some adjustment of egg number with clutch size is possible and that it is physiologically possible to lay a clutch smaller than the capacity of a 15 g corpse.

The strong relationship between brood size and mean larval weight at dispersal (Fig. 3) is found

even over a range of brood sizes less than that at which culling would be expected to occur

Intraspecific competition over corpses, the result of which is largely determined by body size (Wilson and Fudge 1984), means that small beetles have a greatly reduced chance of breeding

Small size also restricts the number of eggs a female can lay, both in a single episode on a large corpse and over several breeding attempts on a sequence of corpses

The adults cannot afford to let the members of an excessively large brood compete amongst themselves for the corpse and they therefore reduce the number by culling rather than by allowing some to starve

If filial cannibalism is to benefit *Nicrophorus* parents, then their total number of grandchildren must be greater, through the increased reproductive success of their surviving offspring, than it would have been through a larger brood of individually smaller young.

**Charlesworth, B. 2000. Fisher, Medawar, Hamilton and the Evolution of Aging. *Genetics* 156: 927–931**

THE idea that senescent decline in the performance ofmbiological systems must have an evolutionary basis traces back almost to the beginnings of evolutionary biology

At first sight, the nearly universal existence of senescence in species of multicellular organisms is paradoxical, given that natural selection supposedly causes the evolution of increased, not decreased, fitness.

But unicellular organisms, such as bacteria, which propagate simply by binary fission, and the germ lines of multicellular organisms, have been able to propagate themselves with- out senescence over billions of years, showing that biological systems are capable of ongoing repair and maintenance and so can avoid senescence at the cellular level

The large amount of variation among different species in their rates of senescence also clearly indicates that aging is subject to variation and selection (Comfort 1979; Finch 1990; Rose 1991; Wachter and Finch 1997).

Modern evolutionary theory has demonstrated that, in species with a clearcut distinction between parent and offspring, senescence is a virtually inevitable result of the fact that genes that affect survival or fecundity) only early in life have a greater selective impact than genes whose effects are manifest only late in life

It is probably not without significance in this connexion that the death rate in Man takes a course generally inverse s, to the curve of the reproductive value. The minimum of death rate curve is at twelve, certainly not far from the primitive maximum of the reproductive value; it rises more steeply for infants, and less steeply for the elderly than the curve of reproductive value falls, points which qualitatively we should anticipate, if the incidence of natural death had been to a large extent moulded by the at a given age, of differential survival. Fisher (1930) page 29

a hypothetical mutant gene that increases survival over a small time interval at an age when reproductive value is high would thus have a higher net effect on fitness than a gene acting at an age when reproductive value is low.

expectation that selection will be more effective in improving performance early in adult life than late in life

alleles with positive effects on performance early in life, but with negative effects because of physiological trade-offs later on, are more likely to be established by selection than alleles with the opposite pattern. This idea was more fully developed by Williams (1957) and is now known as the “antagonistic pleiotropy” theory of aging

if fecundity increases exponentially with age during adulthood, reproductive value also increases exponentially, so that its use would lead to the conclusion that selection opposes senescence

In contrast, Equation 6 implies that there is always a selective premium on early survival, although the rate of decline of the intensity of selection with age is greatly slowed if fecundity increases with age

Our understanding of the evolution of senescence is, at one level, very complete; we know that senescence is an evolutionary response to the diminishing effectiveness, of selection with age and that this explains many

aspects of the comparative biology of senescence (Williams 1957; Rose 1991; Charlesworth 1994; Ricklefs 1998).

On the other hand, it is at present hard to be sure which of the two most likely important mechanisms by which this property of selection influences senescence (accumulation of late-acting deleterious mutations or fixation of mutations with favourable early effects and deleterious late effects) plays the more important role, especially as these are not mutually exclusive possibilities

**Muller, J.K., Eggert, A. and Furlkroger, E. 1990. Clutch Size Regulation in the Burying Beetle *Necrophorus vespilloides* Herbst (Coleoptera: Silphidae). *Journal of Insect Behaviour,* Vol. 3(2): 265-270**

The buried carcass is the only food source for the larvae; it can be totally consumed by the larvae from a single clutch.

it would be selectively advantageous for them to adapt the number of eggs laid to the weight of the available carcass

Therefore we define clutch size as the total number of eggs laid before the female's first larva has hatched.

Clutch size was positively correlated with carcass weight

In contrast to Bartlett and Ashworth's (1988) study and Wilson and Fudge's (1984) study on *N. orbicollis,* our results indicate no correlation between female body size and clutch

Figure 1 – clutch size against weight of carcass buried – **useful**

Even on very small carcasses, some offspring could be raised. In all cases (n = 13) females on 2-g mice did raise some offspring that survived to pupation, the mean number being 4.1 (SD = 1.3). In nine undisturbed broods on 5-g mice, a mean number of 8.8 adults survived to the adult stage

When females cared for 50 larvae on 25-g mice, the survival rate was high (median, 96%; range, 88-100%). This result shows that females are able to care for 50 larvae on 25-g carrion, a number considerably larger than average clutch size on carcasses of this weight

Our data show that the number of eggs laid by *Necrophorus* females increases with the weight of the available carcass up to a carcass weight of 10g.

if the number of larvae is too small, females produce replacement clutches, either while feeding their larvae or after their larvae have left the carcass to pupate (Mfiller, 1987).

*N. vespilloides* lay all the eggs they mature only if the corpse is greater than 10 g and stated that some eggs are retained in the ovary on smaller corpses

Moreover, it is questionable whether *N. vespilloides* actually utilizes 75-g carcasses for reproduction in the field

On large carcasses females laid fewer eggs per gram carrion than on smaller carcasses, since there was no further increase in clutch size on mice heavier than 10 g.

Another explanation for the observed behavior may be that production of more than 35 eggs increases female mortality, or reduces their future productivity, so that their lifetime fitness is reduced

**Mair, W., Piper, M.D.W. and Partridge, L. 2005. Calories do not explain extension of life span by dietary restriction in Drosophila. PLoS *Biol* 3(7): e223**

Dietary restriction (DR), the extension of life span by reduction of nutrient intake without malnutrition, is often used as a benchmark comparison for interventions that extend life span [1–3].

some form of food restriction hasbeen shown to increase life span in commonly used model organisms such as yeast [5,6], nematodes [7], fruit flies [8,9], and mice [10], along with many species less often used for laboratory research such as water fleas, spiders, fish (see [3] for review), and dogs [11].

DR is often termed ‘calorie restriction’ because, in rodents, daily calorie intake per se has been implicated as the key determinant of life span, with the source of these calories (i.e., carbohydrate, protein, or fat) being considered irrelevant

Life span of female Drosophila was extended much more by reduction of yeast from control to DR concentration than by the equivalent reduction in sugar

In two independent experiments, reducing yeast concentration from control to DR levels whilst keeping sugar levels constant significantly increased life span

Flies fed food media with very similar caloric content showed marked differences in their life spans

This finding is in direct contrast to what would be predicted if ingested calories were the key mediator of life span in D. melanogaster and demonstrates that the nutritional composition of the diet affects life-span extension by DR in this species.

DR acts acutely to extend life span in Drosophila; it does not slow the accumulation of irreversible damage with age

The response of Drosophila life span to nutrition is not governed by calories, but rather by specific nutritional components of the food

Despite some reports in the literature that DR did not extend life span [38,41,42], the overwhelming majority of data support the idea that DR in some form extends life span across diverse taxa

The selective advantage of shifting resources from reproduction to maintenance when food is restricted could be the ‘‘public’’ factor shared between diverse organisms. However, the mechanisms by which extension of life span is achieved could be an example of convergent evolution, producing the same plasticity of life span in response to food shortage through mechanisms at least to some extent specific to different organisms, dependent upon their diet, experience of food shortages, and life history

**Fox, C.W., Czesak, M.E. and Wallin, W.G. 2004. Complex genetic architecture of population differences in adult lifespan of a beetle: nonadditive inheritance, gender differences, body size and a large maternal effect. J ournal od Evolutionary Biology 17: 1007–1017**

nonadditivity can cause the additive effects of alleles to change as the genetic composition of the population changes (i.e. the genetic variance–covariance matrices change in response to selection) and, as a result, the alleles that are favoured by selection, and the genetic relationships between traits, can change as the genetic background evolves

The evolution of lifespan, mortality rates and patterns of senescence is of substantial interest both because there is tremendous variation in these traits at all taxonomic levels (e.g. Promislow, 1991; Tatar, 2001) and because of the medical implications of genetic analyses of these traits.

studies of lifespan in D. melanogaster indicate that both dominance and epistasis may have significant effects on variation in lifespan

little is known about the genetic architecture of lifespan and senescence for organisms other than D. melanogaster and C. elegans

previous QTL studies with D. melanogaster have shown that the loci affecting lifespan differ between males and females and vary among rearing environments (Nuzhdin et al., 1997; Vieira et al., 2000; Harshman, 2002; Mackay, 2002;

Larval development and pupation are completed entirely within a single seed of their host species

adults have no access to food or water in a storage environment (they cannot feed externally on seeds) and there is little evidence that they feed as adults outside of a storage environment.

Life span and mortality rates of C. maculatus have been examined in numerous previous studies (Møller et al., 1989; Tatar et al., 1993; Tatar & Carey, 1994a, b, 1995; Fox et al., 2003a, b, 2004a).

The SI beetles lived longer than BF beetles by over 4 days in all sex–host combinations (Figs 1 and 2a,b; analysis of variance, F > 201, P < 0.001; for both sexes) and females outlived males by over 5 days in all population–host combinations

The SI beetles were significantly larger than BF beetles regardless of sex or rearing host (F > 741, P < 0.001) and in all population–host–sex combinations adult lifespan was positively correlated with adult body mass – larger beetles living longer

The mortality curves (hazard functions) for males and females were nonproportional within both populations, indicating that the mortality curves were not simply shifted between the sexes but that they actually differ in shape

For the SI population, males had both a faster rate of increase in mortality (b) and greater deceleration (s), but the baseline mortality rate (a) did not differ between the sexes – For the BF population, all three parameters of the logistic mortality curve differed between the sexes; males had a lower baseline mortality rate (a), but had a higher rate of increase in the mortality rate (b) and more rapid deceleration (s) than did female

For all sex–host combinations except females reared on cowpea, the slope of the mortality curve (b) was significantly greater for BF beetles than for SI beetles

In females, long lifespan alleles were generally dominant over short lifespan alleles – lifespan of hybrid female offspring resembled the lifespan of SI females. However, dominance was detected in only one of the two analyses for male lifespan and the composite genetic effect for dominance was smaller in both groups of males than in either group of females

the lifespan of male C. maculatus was influenced by a large maternal effect. In contrast, male lifespan was affected by a large and highly significant maternal effect that was not observed for female lifespan

some of the variation in lifespan among lines was explainable by differences in body size and, after correcting for body size variation, epistasis was detectable for the lifespan of females

In C. maculatus, the genetic correlation between the lifespan of males and lifespan of females is much less than 1.0 (e.g. Fox et al., 2004a) indicating that either different genes affect the lifespan of males and females or that these genes have different effects in the two sexes

offspring of older mothers lived longer than did offspring of younger mothers (Fox et al., 2003a) opposite the pattern commonly observed in other organisms (Priest et al., 2002).

Previous studies have found that patterns of mortality (e.g. Tatar et al., 1993; Messina & Fry, 2003) and the genetic architecture of lifespan (e.g. Leips & Mackay, 2002) both change when individuals are mated,

**Pérez, V.I., Bokov, A., Remmen, H.V., Mele, M., Ran, Q., Ikeno, Y. and Richardson, A. 2009. Is the oxidative stress theory of aging dead? *Biochimica et Biophysica Acta* 1790: 1005–1014**

The free radical theory of aging proposed in the 1950s by Denham Harman [1], postulates that oxygen free radicals formed endogenously from normal metabolic processes play a role in the aging process because of an increase in oxidative damage to macromolecules

The imbalance between prooxidants and antioxidants leads to an accumulation of oxidative damage in a variety of macromolecules with age resulting in a progressive loss in functional cellular processes, leading to the aging phenotype [2].

longer-lived animals show reduced oxidative damage and/ or increased resistance to oxidative stress

the observation that the experimental manipulations that increase lifespan in invertebrates and rodents correlate to increased resistance to oxidative stress or reduced oxidative damage provides strong evidence in support of the oxidative stress theory of aging. However, all of the experimental manipulations that increase lifespan also alter processes other than oxidative stress/damage; therefore, the increase in longevity in these animal models could arise through another mechanism.

Longevity or lifespan is the most acceptable parameter that has been used for several years to study aging

we do know that it is possible to retard aging in multiple animal models and simultaneously lengthen lifespan; for example, when mice and rats are fed restricted amounts of food, aging mechanisms appear to be delayed and the animals live longer

Longevity or lifespan is the most acceptable parameter that has been used for several years to study aging. Ideally, it would be better to determine other parameters involved in changes in the basic mechanisms of aging or healthspan. However, nowadays there is no consensus about how to define healthspan and how to measure this parameter in all of these model systems

we do know that it is possible to retard aging in multiple animal models and simultaneously lengthen lifespan; for example, when mice and rats are fed restricted amounts of food, aging mechanisms appear to be delayed and the animals live longer.

it is critical that lifespan be determined under optimal husbandry conditions to eliminate/minimize deaths from non-aging causes, e.g., infectious disease, inflammation, stress, etc

studies with invertebrates have given mixed results with respect to the effect of reducing antioxidant gene expression on lifespan

One of the problems in determining whether oxidative stress plays a role in aging using knockout mice to accelerate aging is that many manipulations can shorten lifespan that would not have any effect on aging.

Therefore, most gerontologists agree that a manipulation that increases lifespan gives the greatest insight in to the mechanism of aging. In other words, determining whether an increase in the antioxidant defense system would increase lifespan would be more powerful evidence for oxidative stress/free radicals playing a role in aging than showing that a reduction in the antioxidant system decreases lifespan.

In summary, our research with 18 different genetic manipulations in the antioxidant defense system show that only the mouse model null for Sod1 had an effect on lifespan that would be predicted from the oxidative stress theory of aging. One could argue that we failed to observe an effect on lifespan

we believe that the fact that the lifespan was not altered in almost all of the knockout/transgenic mice is strong evidence against oxidative stress/damage playing a major role in the molecular mechanism of aging in mice.

**J. Bartlett, J. 1988. Male mating success and paternal care in *Nicrophorus vespilloides* (Coleoptera: Silphidae). *Behavioural Ecology and Sociobiology* 23:297 303**

Burying beetles bury the corpses of vertebrates and use the carrion to feed their young.

If more than a single pair find the corpse, numbers are reduced by fighting, females with females, males with males (Pukowski 1933)

what is the benefit to those who help and are then driven away

Their larvae are fed with regurgitated carrion, they are defended from invertebrate predators, and any damage to the underground 'crypt' in which the corpse is buried is quickly repaired (Pukowski 1933).

In a fight the larger male could easily displace the smaller (unpublished observation).

A further sign was that males which were considered to have left were covered by a swarm of mites (carried by all burying beetles [Neumann 1943]) which had bred on the corpse and were now dispersing with the male. Males still in the crypt carry far fewer mites; most are still feeding on the corpse.

Small males, with little chance of winning another corpse, might stay more readily than larger males.

males tolerated one another on the corpse, signalled together in the evening and buried the corpse together overnight (if a female was then introduced, only the larger male and the female would later be found on the corpse).

often saw the smaller male mate with the female, although the larger male was the resident in the crypt. Once driven off, the loser stayed not far from the corpse and returned several times

The day on which males left the brood was not correlated with male pronotum width

nearly 80% of the males on the 5 g corpses had abandoned their broods by the fourth day and the rest were gone on the following day

The males from three of the 5 g broods were found dead. They had lost their antennae and one or more legs and had punctures along the abdomen. They had clearly been killed by the female with which they had been paired. Males only gradually left the 25 g broods, following the pattern usually seen for male care in broods used in other experiments. None of these males was found dead.

There was no significant difference in median lifespan between caring and non-caring males:

a single female seems to be able to feed a brood as efficiently as an adult pair.

males of any size seem always to stay until almost the end of larval development

**Partridge, L and Gems, D. 2002. Mechanisms of Aging: Public or Private? *Nature Reviews* 3: 165-175**

Ageing is a process of intrinsic deterioration that is reflected at the population level as an increase in the likelihood of death and a decline in the production of offspring1–3.

During ageing,macromolecules accumulate damage, including the PEROXIDATION of lipids, PROTEIN CARBONYLS and various forms of damage to DNA4,5

for work on these organisms (yeast, C. elegans and Drosophila) to be relevant to research in humans, their mechanisms of ageing need to be in common with those in mammals

We therefore need to know which mechanisms of ageing are ‘public’— those shared across distantly related evolutionary lineages — and which are ‘private’— those peculiar to particular evolutionary lineages13

ageing often occurs at different rates in different tissues and in different individuals, and seems to have a stochastic element16

Furthermore, no genes seem to have evolved specifically because they cause damage and, therefore, ageing. Ageing, and changes in its rate by genes and the environment, can be understood only as a side effect of something else

Calorific restriction, in which nutrient intake is restricted to 60–70% that of voluntary levels, slows ageing in many organisms,

21.A lower rate of reproduction also slows down ageing21,22; this so-called ‘cost of reproduction’ also occurs across a range of organisms

despite ageing’s deleterious nature, it occurs throughout the animal kingdom and is seen in natural populations in the wild25,26

Interestingly, among mammals, bats are long lived for their size27, which indicates that something about flight might lead to the evolution of a slower rate of ageing.

The key to the evolution of ageing lies in an observation by J. B. S.Haldane in the 1940s (REF. 29).Haldane was puzzled by Huntington disease — a genetic disease that causes severe mental illness and death

dominant lethal mutations can be maintained in a population by mutation if their effects are delayed until after reproduction

Is it possible that ageing itself is the result of mutations that strike very late in life, at ages beyond the control of natural selection

Two key theories had emerged: the mutationaccumulation theory and the PLEIOTROPY or trade-off theory (PLEIOTROPY

The capacity of different alleles of a gene to affect more than one aspect of a phenotype)

The evolutionary theories of ageing give us a clear, but stark, picture of the biological function of ageing: there is none. It is merely a nonadaptive epiphenomenon.

Species that lead a hazardous lifestyle or live in environments with high levels of external hazard from predators or disease will have high death rates, even in the absence of any intrinsic ageing process.

Late-acting deleterious mutations will therefore reach a higher frequency under the mutation–selection balance, and the latelife deleterious effects of pleiotropic mutations will weigh less heavily against their early benefits

Mutation accumulation might be expected to lead to lineage-specific, private mechanisms, because there is no reason for new mutations or their phenotypic effects to be shared across different evolutionary lineages

Under the theory of mutation accumulation, the heritable (additive) genetic contribution to death rates should increase in magnitude with age35

This theory also predicts that new mutations with late ages of onset should occur at a measurable frequency

the balance of experimental evidence is not strongly in support of mutation accumulation as a significant mechanism for the evolution of ageing. By contrast, pleiotropy/trade-offs and, in particular, a timelagged cost of reproduction, is implicated as an important general mechanism for the kind of delayed genetic effect that will lead to the evolution of ageing – (all experiments with drosophila which may not be a good species to use)

The evolutionary theories of ageing and the empirical tests of them indicate that differences in the rate of ageing between animal species might be partly due to a re-balancing of the trade-off between early reproductive rate and the subsequent rate of ageing in response to differing levels of extrinsic hazard

The key to understanding how the length of an organism’s life is specified is therefore to understand the mechanisms that generate latent damage and that determine the length of time between its occurrence and its expression as later mortality

findings from these model organisms, although somewhat different, hint at a possible mechanistic link between ageing and reproductive rates, through the response of both to variations in nutrient supply

The first-identified, long-lived *C. elegans*mutant carried a mutation in *age-1* (REF. 54). This gene encodes part of a lipid kinase enzyme (phosphatidylinositol-3 kinase)57 that transmits signals from DAF-2 (dauer formation constitutive) — a receptor that is thought to respond to insulin-like ligands — into the cell5

Mutant worms with defects in the chemosensory neurons that innervate the AMPHIDS show increases in mean lifespan of up to 121% (REF. 63). Studies of compound mutants have shown that these increases in lifespan result from reduced insulin/IGF signalling6

in wild-type *C. elegans*, ageing is accelerated by insulin/IGF signalling

The evolutionary theory predicts that the accelerated ageing is likely to be the downside of a trade-off with a fitness-enhancing trait, such as increased early reproductive output

The trade-off model is also particularly implausible in this instance because in *C. elegans*, unlike in *Drosophila*, egg-production levels have no discernible effect on lifespan54,55,72

if the germ line in C, elegans is removed by laser microsurgery, there are increases in lifespan68 and body size74 - a worm with a doubled lifespan might potentially be around for twice as long to reproduce

Strikingly, a mild reduction of *Inr* function increases mean female lifespan by up to 85% (REF. 78) and loss of function of *chico* by up to 52%

In contrast to studies in *C. elegans*, evidence from *Drosophila* studies provides some support for the hypothesis that the insulin/IGF pathway has a role in modulating a trade-off between fertility and longevity in response to changes in nutrition.

the hypothesis that trade-offs between fertility and lifespan are modulated by insulin/IGF signalling in response to nutrition, although more research is needed to confirm this hypothesis.

So, insulin/IGF signalling modulates the rate of ageing in two very distantly related animal species, and therefore represents a public rather than a private mechanism of ageing

There are many potential explanations for the increased lifespan of these dwarf mice: they are deficient in thyroid-stimulating hormone, growth hormone and prolactin, and have reduced fertility

in mammals, as in nematodes and probably insects, there exist powerful neuroendocrine modulators of ageing which shorten lifespan in wild-type animals

**Jang, Y.C. and Remmen, H.V. 2009. The mitochondrial theory of aging: Insight from transgenic and knockout mouse models. *Experimental Gerontology* 44: 256–260**

The free radical or oxidative stress theory of aging proposed by Denham Harman in 1956 states that the age-related loss of physiological function is due to the progressive accumulation of oxidative damage and that this ultimately determines the lifespan of an organism (Harman, 1956).

In subsequent years, the mitochondrial theory of aging was further refined suggested that the accumulation of somatic mutations in the mtDNA induced by oxidative stress is the major contributor of aging and age-related degenerative diseases.

reactive oxygen species (ROS) emanating from the mitochondrial respiratory chain damages macromolecules, especially

mtDNA. As a result, an accumulation of mtDNA mutations leads to production of defective mitochondrial respiration, further increasing ROS generation and oxidative damage

The core principle of the mitochondrial theory of aging is based on the fact that mitochondrial respiratory chain, mainly through complex I and complex III, is the major source of superoxide anion (O2\_\_)

oxidative damage to mtDNA has been the major focus of the mitochondrial theory of aging

Oxidative damage to DNA is to known to cause modification to purine and pyrimidine bases, single and double-stranded breaks, and cross-linking to other molecules

studies using long-lived mice and experimental manipulations that extend lifespan, such as calorie restriction, have provided a strong correlation between oxidative damage to the mitochondria and lifespan (Barja and Herrero, 2000; Trinei et al., 2002; Barja, 2004).

in Saccharomyces cerevisiae, deletion of the key antioxidant enzyme, manganese superoxide dismutase (MnSOD,Sod2), which, dramatically accelerates chronological aging and overexpression unambiguously increases the organism’s lifespan (Longo et al., 1996)

mammalian transgenic/knockout models with alterations in key mitochondrial antioxidant enzymes have produced mixed results and do not fully support the mitochondrial theory of aging.

Although reducing MnSOD activity in Sod2 knockout mice tests whether superoxide toxicity in mitochondria is limiting to lifespan, the alternative approach is to test the whether an increase in mitochondrial MnSOD activity can extend lifespan.

overexpression of MnSOD in Drosophila was shown to have a beneficial effect, extending lifespan, and supporting the mitochondrial theory of aging (Sun et al., 2002).

an Sod2 transgenic mouse line that overexpresses MnSOD in all tissues failed to show increased lifespan even when the transgenic mice generated less superoxide

Although peroxisome and nuclear overexpression showed a trend toward increased lifespan, only the mitochondrial targeted construct provided the maximal benefit, increasing both median and maximal lifespan by 20%

Data from the mCAT mice undoubtedly support the mitochondrial theory of aging

Interestingly, overexpression of thioredoxin 1 (the cytosolic form) has been shown to increase lifespan in mice (Mitsui et al., 2002)

mouse models of mtDNA instability have provided direct evidence of mitochondrial ROS role in the aging process

Recent studies using the transgenic/knockout strategies have challenged the core principles of the mitochondria theory of aging as well as its parent theory, the free radical or oxidative stress theory of aging

most studies do not support or remain inconclusive on whether mitochondrial dysfunction and oxidative stress determine lifespan

Interestingly, in S. cerevisiae and P. anserina, the deletion of a protein that promotes mitochondrial fission (dynamin related protein 1- dnm1p) extended lifespan without lowering fitness or reproduction (Scheckhuber et al., 2007).

**Lee, R.D. 2003. Rethinking the evolutionary theory of aging: Transfers, not births, shape senescence in social species. *PNAS* 100(16): 9637–9642**

In classical aging theory, as individuals age, their continued survival contributes less and less to reproductive fitness, because less of their lifetime fertility remains. Consequently, natural selection acts more weakly to reduce mortality at older ages

An alternative theory considers both fertility and transfers, including parental care and help from others such as older siblings or grandparents. It is shown that selective pressure to reduce mortality also depends on the cumulated investment needed to produce a survivor to a given age, including costs wasted on offspring who died earlier.

Fisher (11), noted that there would also be indirect effects on reproduction as when ‘‘a mother past bearing may greatly promote the reproduction of her children

In some species, postreproductive females make substantial contributions to their descendants, either through direct parental care or through grandparental care

the sex that mainly provides care to offspring tends to have

the higher life expectancy (18).

if there is continuing parental investment, then the force of selection against mortality should rise with juvenile age, and mortality should fall.

If higher fertility and less investment per offspring would improve fitness, then selection on mortality at a given age will be a weighted average of the classic and transfer effects, with positive weights on both. Lower mortality at younger ages would raise the growth rate, and lower mortality at younger and at older ages would economize on resources for investment, also raising the growth rate.

In the opposite case, where lower fertility and increased investments per birth would raise fitness, then lower juvenile mortality could actually reduce reproductive fitness by increasing competition for investments per surviving offspring. There would be strong selection for adult survival, but there might also be selection for increased juvenile mortality at early ages.

Most species that invest heavily per offspring, such as mammals, birds, and many insects, will have evolved an optimal allocation of resources between level of fertility and level of investment per offspring.

More rapidly growing populations are younger, with more juveniles per adult. At a given growth rate *r*, populations with lower mortality (higher survival) will be older with fewer juveniles per adult

Mutations affecting fertility and mortality are assumed to occur relatively frequently, mostly with adverse effects on fitness, which selection constantly tends to remove. A mutation–selection balance will be reached at each age, with stronger selection leading to lower mortality (31).

Lower mortality even at a postreproductive age reduces the ratio ofjuveniles to adults at any given growth rate, permitting higher consumption

Higher consumption raises survival, particularly of juveniles, so wastage of resources is avoided, and the adult\_juvenile ratio rises for a given population growth rate. (*ii*)Higher consumption raises productivity through larger body size and increased energy. (*iii*) Higher consumption may be associated with greater and longer investments in juveniles, which might have a high payoff for later production

The intuition is that higher mortality near age 0, for example at an early juvenile age, will thin out the number of surviving juveniles, permitting greater parental investment in each, which has a big payoff and raises the growth rate. Higher mortality is a poor substitute for lower fertility, and a more flexible model might instead imply situational infanticide as observed for birds in nature (32).

consider a mortality decrease at an intermediate age, between 0 and the cessation of fertility. Selection will be negative near age 0 and positive near the last age of fertility, with a crossover someplace between

Selection leads to a more efficient life history, permitting the species to equilibrate at a higher density by investing more in each offspring (higher \_), and in this way crowds out the original population even though the original population can replace itself (*r* \_ 0) at a lower level of consumption

For empirical work, measures of transfers would ideally include not just food but also such activities as warming, fanning, guarding, carrying, leading, and teaching, and would also reflect incremental mortality risks incurred in making these transfers.

Among the various approaches to the evolutionary theory of aging, including the classic theory, the disposable-soma theory, formal life-history optimizations based on it, and other recent variations on these themes, none incorporates the flow of resources transferred to offspring.

But for many others, continuing transfers to offspring are centrally important for survival, growth, and eventual reproductive success, and such organisms have evolved lower fertility, and plausibly optimize the quantity–quality tradeoff. The theory offered here shows how evolution shapes the life histories of such organisms for efficient use of parental and other resources and most strikingly shows that, in this case, only the transfer effect shapes mortality, explaining both postreproductive survival and why juvenile mortality declines with age

**Baldal, E.A., van der Linde, K., van Alphen, J.J.M., Brakefield, P.M. and Zwaan, B.J. 2005. The effects of larval density on adult life-history traits in three species of Drosophila. Mechanisms *of Ageing and Development* 126: 407–416**

The importance of longevity and starvation resistance to the mechanisms of ageing in part explains the interest in these traits.

Several authors working with D. melanogaster have found that longevity and starvation resistance are correlated

(e.g. Chippindale et al., 1993; Zwaan et al., 1991). Others found that selection on starvation resistance can increase longevity (Harshman et al., 1999; Rose et al., 1992) and vice versa (Zwaan et al., 1995)

environmental factors that affect life span and ageing (Tu and Tatar, 2003; Zwaan, 2003), including larval density (Miller and Thomas, 1958).

Longevity, starvation resistance and fat-content all show positive responses to higher larval density (Lints and Lints, 1969; Luckinbill and Clare, 1986; Miller and Thomas, 1958;Robinson et al., 2000; Sorensen and Loeschcke, 2001; Zwaan et al., 1991)

D. melanogaster lines reared at high densities showed higher starvation resistance than the same lines when reared at low densities

Selection lines for higher longevity in D. melanogaster showed elevated lipid content later in life (Djawdan et al.,

1996), and in general starvation resistance positively correlates with fat content (Djawdan et al., 1998; Graves et al., 1992; Zwaan et al., 1991).

starvation resistance and longevity are clearly related characters, and this relationship is modulated by larval density.

Longevity is the time between eclosion of the adult from the pupa and death of the adult under standard food conditions

The overall analysis shows a significant negative effect of increasing density on starvation resistance. The analysis of SR showed significant effects of species and density.

sexes behave differently among species. This is largely explained by the differences between males and females in D. melanogaster.

SR decreased significantly with increasing larval density in D. melanogaster, D. willistoni and D. ananassae

For longevity, both species and density were significant factors. However, sex differences were not found for this trait. The species–sex–density interaction showed a significant effect

Density was not important for D. melanogaster and D. ananassae longevity but was for D. willistoni

Larval density was important for SR2 in D. melanogaster and D. willistoni, but not for D. ananassae. In addition, D. melanogaster and D. willistoni showed significant sex–density interactions. D. willistoni males showed their highest starvation resistance at medium density whereas females showed their lowest starvation resistance at that density

The size of D. melanogaster and D. willistoni females declined with increasing larval density, whereas males showed no significant affect

In general, females of each species showed a stronger reduction in dry weight with increasing density than males. This effect on body size suggests that the animals were mildly stressed by higher larval density.

D. melanogaster and D. ananassae males showed effects of increasing larval density on adult fat content, whereas females did not

D. ananassae, D. melanogaster and D. willistoni showed significant effects of larval density on adult starvation resistance directly after eclosion and after 2 days of food

D. melanogaster is likely to allocate resources to reproduction rather than to somatic maintenance under laboratory circumstances

Female dry weight and fat-free dry weight declined in response to larval density. Males had a more uniform dry weight over different larval densities. Generally, fat content increased for all species and sexes with increasing larval density

animals from high larval densities showed the shortest starvation resistance.

We found that exposure to higher larval density reduces body size. This is in line with Santos et al. (1994), who found a decreased fitness and thorax length, and thus body size, at increasing densities

The effects of larval density in the present study tend to be small but are likely to reflect important responses to developmental conditions. Thus, we conclude that higher larval densities lead to smaller flies with a high relative fat content and reduced starvation resistance.

Starvation resistance is associated with longevity, suggesting that these traits share molecular pathways.

In the present study, relative fat content increases, and starvation resistance decreases with increasing larval density and vice versa

Responses of SR and longevity to larval density seem to follow a similar trend of reduced life span with increasing larval density in our experiments (Fig. 2) suggesting that these life-history characters share physiological mechanisms

**Leroi, A.M., Bartke, A., Benedictis, G.D., Franceschi, C., Gartner, A., Gonos, E., Feder, M.E., Kivisild, T., Lee, S., Kartal-O¨ zer, N., Schumacher, M., Sikora, E., Slagboom, E., Tatar, M., Yashin, A.I., Vijg, J. and Zwaan, B. 2005. What evidence is there for the existence of individual genes with antagonistic pleiotropic effects? *Mechanisms of Ageing and Development* 126: 421–429**

estimates place the heritability of longevity in western populations around 25% (Skytthe et al., 2003)

In 1957, George Williams proposed the ‘‘antagonistic pleiotropy’’ theory of senescence (Williams, 1957). Briefly, this theory held that ageing was due to the decline of the force of natural selection late in life, and that the fixation of alleles with positive effects upon fitness early in life also had deleterious effects late in life

lines of fruit-flies selected for late-life reproductive success became long-lived while also experiencing a decline in early-life fitness (fecundity, mating success) relative to lines selected for early-life reproductive success (Rose, 1984; Sgro` and Partridge, 1999)

human studies are association studies and so are always subject to the caveat that apparent pleiotropies (or even the main effect) may be due to linked loci

While it is certainly possible to measure fitness in laboratory populations of model organisms, such studies, if done at all, suffer from two objections: the alleles studied are often not natural polymorphisms but severe loss of function or even null mutants; and plush laboratory environments may obscure allelic effects that would be apparent in the wild (Zwaan, 2003)

five possible sources of antagonistic pleiotropy: gonadal signals, insulin-like growth factor signals, the control of free-radical production, heat-shock proteins and the control of apoptosis.

Among the many mutations that affect the fecundity of C. elegans, some of the most interesting are those that cripple glp-1, required for stem-cell proliferation in the germ. Such mutations produce few or no sperm and eggs and so are ~sterile. Interestingly, recently it has also been found that they are long-lived (Arantes-Oliveira et al., 2002).

Somatic maintenance (longevity) and gametes (fecundity) both require common, limiting, resources, proteins, lipids and the like

the gonads of the nematode worm, C. elegans, are the source of several molecular signals that regulate longevity (Hsin and Kenyon, 1999). Surprisingly, while the somatic gonad is the source of a signal that promotes longevity, the worm’s germ line is the source of a signal that represses it.

The evolutionary function of the germ-line signal, and whether or not it can explain the traditional ‘trade-offs’ detected by ecological experiments is a matter of debate (Leroi, 2001; Lessells and Colegrave, 2001; Barnes and Partridge, 2003)

loss-of-function mutations in the C. elegans insulin-like growth factor receptor homologue, daf-2 spectacularly increase longevity (Kenyon et al., 1993), a great deal of effort has gone into studying the effects of IGF signalling on longevity and health in a variety of organisms.

In C. elegans, insulin signalling appears to act at two stages in the life of the worm. First, during larval development it controls the formation of the stress-resistant dauer stage. Second, in adulthood it appears to regulate life-history as well, albeit in a more subtle way (Dillin et al., 2002).

A study of 16 independent daf-2 alleles shows a striking negative correlation between life time fecundity and longevity (Gems et al., 1998; Leroi, 2001) - as fine a demonstration of antagonistic pleiotropic effects between longevity and fecundity as one could hope to find

dwarfing mutations in drosophila leads to increases longevity and decreases fecundity

Perhaps the greatest surprise of recent years, has been the finding that insulin signalling also controls ageing in mammals

mutations (e.g., in the genes encoding pituitary specific transcription factors (Prop-1, Pit- 1) and growth-hormone-releasing hormone receptor (Ghrhr), cause mice to be dwarfed, long-lived with reduced fertility (Brown-Borg et al., 1996; Bartke et al., 2001a,b)

Why is antagonistic pleiotropy so pervasive in the IGF pathway? Many workers argue that IGF signalling is an ancient device to control alternate life-history strategies in the face of environmental vicissitudes

Under experimental conditions designed to mimic the natural environment, age-1 (phosphatidylinositol 3-OH kinase catalytic subunit) mutants suffered a 23% reduction in fitness relative to wild type worms (Walker et al., 2000); this had remained unnoticed under ‘‘standard’’ laboratory conditions

the Indy (I’m not dead yet, a membrane protein involved in the transport of Krebs cycle intermediates) mutation doubles the life time, but shows decreased fecundity only under caloric restricted adult food conditions (Marden et al., 2003).

The free-radical theory of ageing proposes that ageing is caused by the accumulated damage that reactive oxidative species inflict upon cells over the course of years

centenarians more commonly have the mitochondrial J haplotype than expected (De Benedictis et al., 1999; Ross et al., 2001; Niemi et al., 2003). Similarly, in the Japanese population the C5178A missense mutation (characterizing the Asian haplogroup D) has been reported to be associated with longevity (Tanaka et al., 1998). Do these longevity-associated haplogroups have any effect on early-life fitness?

it is hard to demonstrate the causal role of any given substitution on longevity, much less fitness. This is not the case for nuclear genes encoding mitochondrial proteins—and mutations in these genes frequently reveal antagonistic pleiotropic effects.

worms fed bacteria lacking coenzyme Q show an increase in late-life survivorship, but a decrease in early-life survivorship (Larsen and Clarke, 2002).

heat shock proteins seem to exhibit the sort of physiological relations that we might expect to give rise to alleles with antagonistic pleiotropic effects. Genetic experiments suggest that this is so.

Any system that regulates apoptosis might be expected to have antagonistic pleiotropic effects. Early in life, apoptosis is an anti-cancer mechanism; late in life, as stem cells no longer exist in sufficient quantity to maintain cell populations, it is supposed to contribute to the failure of tissue integrity. Any genotype, therefore, that increases late-life tissue integrity by repressing apoptosis does so at the expense of an increased risk of cancer

If, however, we consider the evidence for the existence of natural polymorphisms with antagonistic pleiotropic effects in the wild—the kind of polymorphisms most relevant to evolutionary theory and human health—the evidence becomes much thinner

**Trumbo, S.T. 1990. Regulation of Brood Size in a Burying Beetle, *Nicrophorus tomentosus* (Silphidae) *Journal of lnsect Behavior,* 3(4): 491-500**

Such adjustments of brood size should not maximize the number of offspring that will survive to reproductive age or the size of offspring but should maximize total fitness of the parents' offspring (Smith and Fretwell, 1974).

Burying beetles (Silphidae, *Nicrophorus* Fabricius) compete with rivals of the same sex for small vertebrate carcasses on which to reproduce.

*Nicrophorus* is known to regulate brood size by adjusting number of young to carcass size such that the mean mass of individual larvae at dispersal is similar on small and large carcasses (Wilson and Fudge, 1984; Kozol *et al.,* 1988; Scott and Traniello, 1990; Trumbo, 1989).

Bartlett (1987) has shown that parents can reduce brood size by cannibalizing firstinstar larvae.

*Nicrophorus* is an intriguing genus for a study of regulation of brood size and possible parental control of offspring size. Burying beetles use a wide range of carcass sizes (5-200 g), there is a 10-fold difference in body mass between the smallest and the largest species, body size is important in competitive interactions, and the mechanisms employed to assess resource size and brood size are poorly understood

The length of adult beetles was measured from the tip of the mandibles to the posterior edge of the elytra

The number of offspring was strongly related to carcass size but was not affected by the size of the female. Means mass of individual larvae, on the other hand, was not affected by carcass size nor by female size.

All eight pairs in Treatment 2 raised fewer offspring per gram of carcass in their second reproductive attempt

There was an inverse relationship between the number and the size of individual larvae. When the effect of total brood mass is removed, there is a strong partial correlation between number of larvae and mean mass of individual larvae on large carcasses

If parents are essential for regulation of brood size, larvae that develop on **a** limited resource without parental care are expected to be underweight. In the absence of parents, there was a trend for fewer larvae to mature on the small quantity of food

individual larvae produced on a smaller resource were of significantly lower mass than larvae produced on a larger resource

When food is abundant and accessible, larvae of *N. tomentosus* can develop to the final instar and disperse at the normal size without posthatching parental care. Because larvae do not grow to a normal size when food is limited and parents are removed, larvae do not appear to be able to regulate brood size on their own. This suggests scramble competition for the resource in the absence of parents.

Using both *N. defodiens* Mannerheim and *N. orbicollis* in field studies, I found that parents consistentlyproduced many more larvae on large than on small carcasses (Trumbo, 1987;Trumbo, 1989).

This study demonstrates a trade-off between number of larvae in the brood and mean mass of individual larvae at dispersal. When the number of offspring is too large for the resource in broods without parents, larvae are considerably underweight

By regulating brood size, parents affect the body size of larvae and thus the eventual adult size and reproductive success that their young will achieve

**Priest, N.K., Mackowiak, B. and Promislow, D.E.L. 2002. The Role of Parental Age Effects on the Evolution of Aging. *Evolution* 56(5): 927-935**

The phenotype of an individual can be influenced not only by its genotype and the environment in which it is raised, but also by the genotype and condition of its parents

From the genealogical records of 8797 descendants of a colonial American family, Bell found that children from older mothers had 45% shorter lives than children from younger mothers repeated in: rotifers, duckweed, house flies, stink bugs, fruit flies, flour beetles, mealworms, nematodes, and yeast. This pattern is referred to as the "Lansing effect," after Albert Lansing's (1947, 1948, 1954)

Evolutionary theories of aging, which assume that parental age effects do not influence life span, predict that cultivating old females should produce offspring that are longer-lived, not shorter-lived (Hamilton 1966; Williams 1966; Edney and Gill 1968; Charlesworth 1994).

Still, the role of parental age in the response to selection on aging is unknown.

If the effect of parental age on offspring longevity varies among genotypes, then selection on the quality of offspring produced by parents of different ages can influence the evolution of aging

quantitative genetic studies have established Drosophila as an ideal model system in which to test evolutionary theories of aging

the strains were cultured in plastic half-pint bottles at a density of approximately 250 eggs/bottle for two generations.

Egg density can affect patterns of mortality (Clare and Luckinbill 1985).

for the wild-caught strain UGA98, daughters of older mothers were significantly shorter-lived than daughters from younger mothers, with a 12% decrease in longevity overall. In contrast, for the laboratory strain, Canton-S, daughters of older mothers were significantly longer-lived than daughters of younger mothers, with a 10% increase in longevity.

Maternal age effects on sons were in the same direction as the effects on daughters, but in this case, only Canton-S showed a significant correlation

For experiment II, older mothers produced daughters with shorter lives (longevity declined by 5% for 79L, 26% for 67L, 15% for 58S, and 18% for 35S; Table 1, Fig. 1). Maternal age was only weakly correlated with life expectancy of sons. The effect of maternal age on daughters was significantly greater than on sons

In experiment I, maternal age did not significantly alter mortality slope or the intercept for any particular sex in the two genotypes. In experiment II, maternal age significantly influenced the mortality intercept and slope of daughters in many of the inbred strains

The sex-specific maternal age effects on longevity resulted from changes in intercept (maternal age X sex, and not slope

This study shows that both maternal age and paternal age can influence offspring aging. Older mothers produced shorter-lived daughters in five of the six strains we examined. The effects on longevity were largely consistent with the Lansing effect studies conducted over the past 50 years

Overall, we found that paternal age had a much weaker affect on offspring longevity than maternal age, although both maternal and paternal age influenced offspring mortality trajectories

It is not surprising that maternal age has a greater effect than paternal age on offspring longevity because the mother contributes most of the mRNA, lipid, carbohydrate, and protein molecules in the zygote cytoplasm.

we would have expected older mothers to produce longer-lived offspring regardless of the age of the mate

Our findings of genetic variation in maternal age effects on adult mortality, together with Kern et al.'s (2001) finding of genetic variation for maternal age effects on juvenile mortality, suggest that parental effects may play a fundamental role in the evolution of aging

Both of these models (mutation accumulation and antagonistic pleiotrophy) have implications for the influence of maternal age on the evolution of aging. First, parental age effects can alter the rate of mutation accumulation by changing the age-specific decline in the force of selection. Second, parental age effects can influence the na-ture of life-history trade-offs. The life history of an individual may involve balancing resources not only for early-age and late-age fitness traits, but also for fitness traits of offspring (Trivers 1974).

inclusive fitness and parent-offspring conflict theories, as developed by Hamilton (1964) and Trivers (1974), respectively, may turn out to play a critical role in the evolution of aging

**Metcalf, C.J.E and Pavard, S. 2006. Why evolutionary biologists should be demographers. *TRENDS in Ecology and Evolution* 22(4): 205-212**

Demography, the study of survival, fertility and population dynamics, is a crucial tool for evolutionary biologists. In particular, survival and fertility at each age or life-history stage determine offspring production, which defines fitness.

if the mutation acts at a specific age, the degree to which it alters fitness depends on the survival and fertility of the affected individual at all other ages. For example, if mortality is such that few individuals are alive beyond a certain age, and the contribution of these individuals to lifetime reproduction is negligible, mutations acting after this age are effectively neutral

late-acting deleterious mutations are subject to less selection and their resulting accumulation is one possible explanation for the evolution of senescence

Using a single fitness component as a proxy for fitness can, consequently, be problematic

timing effects: if a population is growing, mutations for earlier reproduction are successful because the earlier offspring are produced, the more descendants they leave

Life span varies from a few hours (mayflies) to hundreds of years (trees)

mammals can be categorized along a continuum from species with late maturity, few offspring per reproductive event and a long generation time, to species that reproduce early, have large litters and a short generation time), are relatively well understood. Some however deviate from this trend.

For example, mortality in many species increases with age (senescence), although it can also remain constant (e.g. hydra [32]) or decrease (e.g. a monocarpic plant [1]).

the force of selection does not necessarily decrease with age if fertility and survival increase sufficiently with age. This might explain why some species do not senesce.

Humans (and many other animals – Mortality is high for infants and is then low until maturity, corresponding to the initial drop in survival. In late adulthood, mortality increases gradually (senescence) and survival continues to falls away. Maximum recorded age is 122. Fertility peaks at \_30 and then falls to zero at \_50 (the age of menopause

Hydra – Over a period of four years, mortality was low and showed no sign of increase with age; consequently, survival diminished gradually. Fertility (both asexual and sexual reproduction) remained approximately constant

In Drosophila [37] and other species, lifespan can respond plastically to caloric restriction: if resources become scarce, individuals reduce metabolism, allocating resources preferentially to survival

Average population survival curves flatten off at advanced ages. However, this flattening might not accurately reflect the survival trajectory of an individual, but might be observed only because ‘frail’ individuals die early, so that only individuals with overall lower mortality are present at late ages [38,39].

it is still not clear, even for humans, what fraction of variation in age trajectories of survival is heritable, what fraction is environmentally imposed and what fraction is due to plasticity.

**A. N. Clements, A.N. and G. D. Paterson, G.D. 1981. The Analysis of Mortality and Survival Rates in Wild Populations of Mosquitoes. *Journal of Applied Ecology* 18: 373-399**

It is generally accepted that in nature few organisms die of senescence, most being killed by predators, disease, and other hazards long before they reach old age (Krebs 1972), and as a corollary of that belief it is sometimes deduced that mortality rates are independent of age (Macdonald 1952)

field, Macdonald (1952) concluded that the full life span of females is measurable in months but that in nature few females survive to die of old age, most dying of one or other hazards of wild life

Two patterns of survival can be shown to be appropriate for adult mosquitoes. In one, the mortality rate does not vary with the age of the individuals, and the points of the log survivorship curve fall approximately on a downward-sloping straight line. In the other the mortality rate increases with age, and here the points fall on a curve which is concave below

The Gompertz survival function has the form of a curve that is concave below, and a plot of the logarithm of the instantaneous mortality rates against age yields a straight line that slopes upwards

This section presents techniques for analysing survival data, in particular for establishing whether mortality rates are constant or increase with age and, in the latter case, for establishing whether or not they accord with the Gompertz mortality function

The first step is to plot the numbers N. on a logarithmic scale against age on a linear scale, producing a survivorship curve for the population. If the points fall approximately on a straight line then the simple exponential model may be appropriate, implying that the mortality rate does not vary with age

Mortality rates in laboratory cohorts will be considered first. Such data are relevant to the present study because they provide patterns of mortality and survival under conditions in which many individuals may survive to die of old age; they therefore represent the base line state which is modified on exposure to natural condition

In an early experiment, Gillies (1961) estimated the survival of Anopheles gambiae from a mark-recapture experiment carried out near Muheza. Regression of numbers recaptured against age showed that the males had a constant loss rate, due to mortality and possibly to emigration, for 30 days after release (P > 0.9), with a daily 'survival rate' of 0.862. The females showed a constant loss rate for the period 4 to 23 days after release (P = 0.1), with a daily 'survival rate' of 0.853

There was a tendency for the female mortality rate to increase with age over the adult life-span as a whole, and the Gompertz model gave a satisfactory fit to the survivorship data

It can be seen that the longevity factor is a term compounded of probability of survival to a later age (x + n) and the life expectancy of survivors at that age

It is certainly widely believed, or at least assumed, that in wild populations of mosquitoes the adult female mortality rates are independent of age (Garrett-Jones & Shidrawi 1969; Weidhaas et al. 1974; Dietz, Molineaux & Thomas 1974; Molineaux 1978), although some workers have recognized that mortality rates are higher among the small percentage of older female

Survival records are available for adult females, of a number of mosquito species, when held captive and fed more or less normally with both sugar and blood. In all cases the mortality rates increased with age, and in the cases where they had been analysed appropriately it was found that the Gompertz mortality function provided an accurate description of the mortality rate

In species for which the mortality rates of both captive and wild populations are known, i.e. Aedes aegypti (Putnam & Shannon 1934; McDonald 1977a) and Culex quinquefasciatus (Briegel & Kaiser 1973; Samarawickrema 1967), it is clear that mortality rates are much higher in the wild than in captivity, confirming that predators and other hazards of the wild take a toll of mosquito life.

Gillies & Wilkes (1965) observed, with three species of Anopheles, that female mortality rates increased during the later gonotrophic cycles, but they stated that in An. gambiae and An. funestus the mortality rates remained constant

**Campisi, J. 2005. Senescent Cells, Tumor Suppression, and Organismal Aging: Good Citizens, Bad Neighbors. *Cell* 120: 513–522**

Multicellular organisms contain two fundamentally different cell types: postmitotic cells, which cannot divide, and mitotic (or mitotically competent) cells, which can divide.

In many simple organisms—for example, the nematode *Caenorhabditis elegans* and fruit fly *Drosophila melanogaster*—postmitotic cells are the predominant, if not exclusive, cell type in the somatic tissues of adults

The evolution of renewable somatic tissues very likely afforded organisms increased longevity. In spite of this, renewable tissues—unlike postmitotic tissues are susceptible to hyperproliferative disease, the most deadly of which is cancer

gate keeper tumor suppressors promote longevity by preventing the development of cancer. The apoptotic and senescence responses they implement can have cumulative deleterious effects, and thus may also limit longevity by contributing to aging and late-life pathology

senescent cells are dysfunctional and may actively disrupt normal tissues as they accumulate gatekeeper tumor suppressor mechanisms may be an example of evolutionary antagonistic pleiotropy (reviewed in Kirkwood and Austad [2000]; Campisi, 2003b).

Hayflick and colleagues first formally described cellular senescence as the finite replicative life span of human fibroblasts in culture

Telomeres are the DNA sequence and proteins that cap the ends of linear chromosomes damage and prevent their fusion by cellular DNA repair processes.

Because functional telomeres maintain the integrity and stability of the genome, they suppress the development of cancer.

Although diverse stimuli can induce a senescence response, they appear to converge on either or both of two pathways that establish and maintain the senescence growth arrest. These pathways are governed by the gatekeeper tumor suppressor proteins p53 and pRB (Bringold and Serrano, 2000; Lundberg et al., rest (Figure 1A). Consequently, although the senes2000;

Campisi, 2001).

p53 is a crucial mediator of cellular responses to DNA damage, including the senescence response (Wahl and Carr, 2001).

Many murine cells undergo only a few doublings in culture, despite long telomeres and expression of telomerase. These cells most likely arrest because standard culture conditions cause oxidative stress, which human cells resist much more effectively than mouse cells (Parrinello et al., 2003).

Recent findings suggests that p53, despite being a crucial tumor suppressor, also contributes to aging and does so at least in part by enhancing the senescence response

How might constitutively hyperactive p53 accelerate aging? Cells from these modified mice were more susceptible to both p53-mediated apoptosis (Tyner et al., 2002) and p53-mediated senescence (Maier et al., 2004)

There is no evidence yet that enhanced pRB function, analogous to the enhanced p53 function conferred by truncated p53 proteins, accelerates aging

The combined results from use of both p16 and SA-β-gal indicate that cells with characteristics of senescence accumulate with age in multiple tissues from both humans and rodents

The antagonistically pleiotropic effects of senescent cells suggest that aging is, at least in part, a consequence of gatekeeper tumor suppressor mechanisms

**Trumbo, S.T. 1990. Reproductive benefits of infanticide in a biparental burying beetle *Nicrophorus orbicollis.* *Behavioural Ecology and Sociobiology* 27: 269-273**

A male-female pair of burying beetles *(Nicrophorus* Fabricius spp.) will bury a small vertebrate carcass whichis used as a resource for their brood

Body length was measured as the distance from the tip of the mandibles to the edge of the elytra. Beetles were marked by clipping off a small part of the posterior edge of one of the elytra

The body size of beetles established on a carcass was related to their ability to retain ownership. In a large proportion of cases a male intruder was larger than the male resident replaced. The proportion was similar for female intruders and residents Male intruders were not significantly longer than resident single females they joined.

indirect evidence that intruders kill larvae they find on the carcass and then initiate their own reproductive attempt

When the larger intruder was a female, the roles of attacker and the pursued reversed as the encounter proceeded

Once infanticide began, larvae were not killed all at once but opportunistically as the intruder inspected the carcass.

In 22 of 28 trials in which an intruder was introduced into a container with a resident female and her brood, all the larvae in the initial brood died

Intrusions and takeovers, therefore, appear to be a regular feature of the breeding system of *Nicrophorus* in the field.

Intruders of both sexes kill larvae they find on the carcass and attempt to use the resource for their own reproduction

**Hämäläinen, A., Dammhahn, M., Aujard, A., Eberle, M., Hardy, I., Kappeler, P.M., Perret, M., Schliehe-Diecks, S. and Kraus, C. 2014. Senescence or selective disappearance? Age trajectories of body mass in wild and captive populations of a small-bodied primate. *Proceedings of the Royal Society B* 281: 20140830**

The increase in mortality probably results from functional senescence (FS, within-individual deterioration of physical or physiological functioning with advancing age), which, along with terminal disease or investment in reproduction at the expense of maintenance [5–8], can expose individuals to extrinsic hazards in a condition-dependent manner

Classic theories on life-history evolution [14] posit that populations with high extrinsic mortality (EM) rates (random mortality from environmental causes) should have a reduced lifespan and age rapidly, and support for this pattern has been found with experimental and comparative work [3,15–18].

In spite of the supposed significance of extrinsic factors in shaping life histories, ageing research is still largely biased towards captive animals living under standard, benign conditions (e.g. [16,19,20]).

the study of wild populations with high EM risk is essential for testing hypotheses on the evolution of lifespan and FS

The sexes often differ in their life histories, EM hazard and ageing processes [24–27], and female mammals typically enjoy longer lifespans than males [28

Therefore, a direct comparison of the sexes is essential for deciphering the evolutionary mechanisms behind senescence and lifespan determination.

BM broadly reflects resources available for allocation to physiological processes, making it a meaningful indicator of FS.

Given the high EM of M. murinus in the natural environment, we predicted average lifespan to be shorter in the wild than in captivity

however, extrinsic hazard selectively removes individuals in poor condition, evolutionary processes might instead lead to delayed FS or the survival of only the highest quality individuals (showing little senescent decline) to an old age.

As the same physiological processes presumably drive FS, senescent within-individual declines might nevertheless occur in both the wild and captivity.

Excluding juvenile mortality, captive males lived on average one season longer than females. By contrast, average minimum lifespan of wild females was on average seven months longer than that of males

An energy imbalance can quickly render an individual susceptible o disease [59] and predation [60] or lower their success in resource competition

However, our models indicated no support for sex differences in ageing in either captive or wild animals. It is possible that sex biases in mortality may lead to sex differences in FS, but these differences are masked by the strong seasonal effects and rapid terminal changes

As expected, the estimated lifespans of wild and captive M. murinus differ substantially: captive males live on average twice as long and females 50% longer than their wild counterparts

if lifetime fitness is sufficiently enhanced by living longer, selection may favour somatic maintenance and counteract the accumulation of damage [2,29,65]

**Bonsall, M.B. Longevity and ageing: appraising the evolutionary consequences of growing old. Philosophical Transactions of the Royal Society B 361: 119–135**

Senescence is a decline in physiological functioning that leads to a decrease in reproduction and an increase in mortality with age. Senescence appears maladaptive as it directly affects key life-history traits (such as the schedules of reproduction and survival) that influence fitness

Questions on the biology of ageing range from the molecular through to the whole organism- and population-level, and from the pathological through to evolution

Although, the general theory for the evolution of senescence is well established (Medawar 1952; Williams 1957; Hamilton 1966), the necessity for ‘improvement is long overdue’ (Williams 1992).

While no single gene can be credited as responsible for ageing, the mechanisms of ageing are clearly under genetic control

Harman (1956) hypothesized that endogenous oxygen radicals produced during aerobic respiration could cause cumulative oxidative damage resulting in senescence and eventual death (of cells, tissues and organs

It is important, at the outset, to distinguish between the causes and consequences of ageing

Reducing calorie intake, for example, has been shown to slow ageing in a variety of organisms spanning all the major phyla including mammals (e.g. rodents, McCay et al. 1935; primates, Lane et al. 2001), invertebrates (e.g. spiders, Austad 1989; Drosophila, Partridge et al. 2005) and fungi (e.g. yeasts, Lin et al. 2004).

Rate of living effects correlate with a range of abiotic variables. For instance, in the rockfishes, longevity increases with maximum depth (Cailliet et al. 2001)

assessment of the rate of living might also be confounded with body mass (Promislow & Haselkorn

2002) since size, metabolic rate and longevity may be tightly linked (West et al. 2001

The function of one gene, in particular, appears to have wide effects. Sir2 is a gene in yeast that regulates lifespan: in its absence the lifespan of Saccharomyces cerevisiae is shortened. This gene is highly conserved and is known to affect ageing across a broad range of organisms

Antioxidants such as SOD are widespread across all taxa and their role in reducing oxygen toxicity is undoubted. However, their role in reducing mortality rates and extending lifespan is more questionable

It is now well established that normal cells have a limited capacity to divide. This phenomenon is known as the ‘Hayflick limit’ (Hayflick 1965; Shay & Wright 2000

The importance of the Hayflick limit for understanding the mechanisms of ageing was discovered by

Olovnikov (1973, 1996). Olovnikov understood that the properties of DNA replication prevent cells from fully transcribing the ends (telomeres) of nuclear DNA

Telomeres are highly conserved regions of DNA (Ridley 1999) and the effects of telomere shortening have been shown to be correlated with lifespan in birds and mammals

First, is it appropriate to define lifespan or rate of ageing as a measure of longevity? Second, is it sufficient knowing the mechanisms of ageing to argue that the process of growing old is inevitable?

It has been known for almost two centuries that agerelated mortality trajectories follow an exponential increase (Gompertz 1825

Many organisms show determinate patterns of growth: i.e. organisms reach a fixed size at sexual maturity

In contrast, some organisms show indeterminate patterns of growth, where growth continues after reaching sexual maturity. These organisms tend to show no patterns of age-related dysfunction and age-dependent mortalities that are constant following sexual maturity.

suggests that even though, the mechanisms of ageing are under genetic control, the manifestations of senescence are as different as the difference between species

Medawar (1952) argued that the force of natural selection that maintains individual survival and fertility declines with increasing age. Medawar suggested that mutations acting early in life would be eliminated by natural selection. However, mutations that appeared at or around reproductive maturity would not be purged by natural selection (Partridge & Barton 1993), could accumulate and lead to a decline in survival and/or fertility

An alternative theory for the evolution of longevity, antagonistic pleiotropy, proposed by Williams (1957) suggests that there is a trade-off between early fecundity or survival and late mortality

The disposable soma theory proposes that resources are required to maintain cell integrity and, as such, there is a trade-off in reproductive capacity and physiological integrity.

More rigorously, in support of the mutation accumulation theory, Hughes & Charlesworth (1994) have shown that genetic variance in mortality rate increases with age in male D. melanogaster

As predicted by the mutation accumulation theory these late-onset genes with deleterious effects are not purged by natural selection (Hughes et al. 2002) and provide strong support for the mutation accumulation theory

Tests of the antagonistic pleiotropy theory have used artificial selection experiments on Drosophila. By selecting lines for late reproductive output, it has been shown, in general, that there is a trade-off: longevity and late fertility increase from lines initiated from ‘old’ adults (Rose & Charlesworth 1980) and there is a correlated decline in survival and fertility of ‘young’ adults (Rose 1984; Partridge & Fowler 1992).

It is postulated that the rate of ageing should increase, reproduction should start early and average lifespan decline as the rate of extrinsic mortality increases.

Using guppies, Poecilia reticulata, Reznick and colleagues showed that fish derived from different (high and low) mortality environments and reared at two different levels of resource availability showed different patterns in lifespan. Guppies from high-mortality environments began reproducing earlier, suffered significant decline in neuromuscular function but tended to have longer total lifespans

Given the variability in the manifestations of the molecular mechanisms of ageing, it is, however, entirely plausible that different patterns in mortality trajectories might arise through an interaction between genetic and environmental processes

it has been shown thatmeasures of age-specific mortality in plantain (Plantago lanceolata) depend on both fixed genetic characteristics and variable ecological and life-history factors such as temperature, rainfall and body size (Roach & Gampe 2004).

If extrinsic mortality risk is high, less resource is allocated to repair (and more to growth), the greater the degree of intrinsic mortality (cellular damage) and the lower the probability of surviving to a given age

Individual mortality is the product of natural selection acting on behaviour, growth and reproduction, and of the physiological processes acting across the life of an organism

changes in the population dynamics of Drosophila subobscura (figure 3), are principally determined by changes in mortality rate. These changes in mortality operate in a density-dependent manner such that there is higher mortality at higher population sizes and lower mortality at lower population sizes.

intense competition for limiting resources, rapid development and sustained metabolic damage are more likely to be manifest when population sizes are large.

If there is parental investment in offspring, then significant and often lethal conflict can occur among siblings, despite the close degree of genetic relatedness.

the patterns of age- and stage-dependent food transfers are important in affecting caste function and ageing (Amdam & Page, 2005).

there might be a link between genome size and lifespan (Monaghan & Metcalfe 2000; Griffith et al. 2003) which, given our understanding of the molecular machinery of ageing, is entirely plausible. in birds, a significant positive relationship exists between genome size and longevity (when corrected for body size; Monaghan & Metcalfe 2000

Genes often have several functions each controlled by different regulatory mechanisms with multiple pleiotropic effects. Redundancy or specialization can take a number of distinct forms such that the expression of gene duplicates occurs in different tissues or in novel developmental stages (Force et al. 1999).

Ageing is a deleterious trait. In some respects this is a conventional evolutionary puzzle, in others it is not.

Understanding why and how fertility and survival decline through time should be a relatively straightforward problem. However, the multitude of mechanisms by which ageing and senescence occur leaves a bewildering array of potential explanations for the longevity problem

**Carey, J.R. and Judge, D.S. 2001. Life Span Extension in Humans Is Self-Reinforcing: A General Theory of Longevity. *Population and Development Review* 27(3): 411-436**

if model species are so similar to humans in molecular makeup that they can serve as models, why do mice age as much in 2 years as humans do in 70 years?

Despite the arguments by Sacher and others (e.g., Hayflick 2000) in support of developing a longevity-oriented theory of the finitude of life, no such theory has ever been published

from environmental factors associated with the evolution of extended longevity in insects (Carey 2001a, 2001b

First, whereas senescence is a byproduct of evolution (Medawar 1955), life span is an evolved life-history trait that results from positive natural selection

Second, unlike the evolutionary theory of senescence, which is based solely on individual natural selection (Williams 1957), this theory includes processes of sexual selection and kin selection, bringing life-history theory more fully to bear on questions concerned with the latter portion of the life cycle

animals that possess armor (e.g., beetles; turtles) or capability of flight (e.g., birds; bats) are often long- lived (Austad 1997; Kirkwood 1992)

The evolutionary theory of senescence suggests that animals better able to escape sources of stochastic mortality such as predators (e.g., via armoured defences or effective escape mechanisms) live longer, and thus the force of natural selection at older ages is increased and the evolution of longer pre-senescent life span is possible

the observation that flight ability and extended longevity are correlated does not provide any insight into why within-group differences in life span exist (e.g., among birds), nor does it account for the variation in longevity in insects where adults of the majority of species can fly.

Across a wide taxonomic spectrum, many long-lived species appeared to cluster within one of two general ecological and/or life-history criteria: (1) species that live in either unpredictable environments (e.g., deserts) or where food resources are scarce (e.g., caves; deep water); or (2) species that exhibit extended parental care and/or live in groups with complex or advanced social behaviour

intensive parental care is linked to flight capability in birds and bats,7 which, in turn, is also linked to extended life span

Nesting behavior and sociality result in improved micro-environmental conditions, which foster greater survival; and greater survival improves conditions for increased provisioning and more-intensive social organization

Medawar ( 1957) proposed that if deleterious hereditary factors are expressed at some intermediate age of an individual, and if the age of this expression is both variable and heritable, then selection will weed out earlier expressions more effectively than later expressions, delaying the average age of expression and increasing longevity

longevity. As the force of selection is reduced by the declining reproductive value9 of increasingly older individuals, those deleterious traits will accumulate-resulting in a mosaic and variable pat- tern of age-specific infirmity and thus senescence (Kirkwood 1997

deterioration. As more individuals live longer, the force of selection increases at later ages, weeding out later-expressing deleterious alleles; selection for somatic maintenance is prolonged; and senescence is delayed

Increased per capita investment in offspring decreases juvenile mortality, increases the health and well-being of offspring, and thus improves adult health and survival

Selection for longevity also increases the return on higher levels or prolonged periods of investment

allocation of energy to reproduction removes its availability for somatic growth and repair and thus is reflected in increased mortality

increased survival from birth to sexual maturity improves energetic efficiency to the parent by decreasing reproductive waste and allows parents either to produce more young or to invest more per capita in existing young

forgone. Increased resources available for reproduction can have any of the following effects depending on which age classes can access them: (1) in- crease the number of young, (2) increase the survival of the young, (3) de- lay maturity of the young by allowing the parental generation to support overlapping sets of offspring, (4) reduce the cost of reproduction to moth- ers through "grandmothering" (Hawkes et al. 1998).

Parents experiencing fewer births but unchanged levels of reproduction be- cause of higher rates of child survival remain healthier. Consequently par- ents themselves experience higher survival and can invest more of their resources in a smaller number of "high-quality" offspring-healthier, larger, more competitive (Clutton-Brock 1994

First, the life spans of nearly all primate species are greater than those predicted by body mass alone

a theory of longevity raises questions about the interpretation of studies on the biological mechanisms of aging that rely on model species such as fruit flies, laboratory rodents, and nematode worms, all of which are solitary (nonsocial) species

example, the aging re- sponse to caloric restriction (Sohal and Weindruch 1996; Weindruch 1996) in solitary species, which must survive independent of a social group, may be fundamentally different from the mechanisms in social species with evolved behaviors for helping, sharing, and food storage

Whereas the aging-oriented question assumes that age-specific improvements in survival exert their impact only at older ages, the self-reinforcing model argues that age-specific decrements in late-life mortality can also have a positive effect on early survival and productivity through selection, inter- generational transfers of resources and information, and increasing innovation from specialization

**Fox, C.W. and Czesak, M.E. 2000. Evolutionary Ecology of Progeny Size in Arthropods. *Annual Review of Entomology* 45: 341–369**

progeny size is subject to selection in both the parental and progeny generations. This selection often varies in direction and/or magnitude among generations (parental versus offspring), among environments, and even among siblings within

a family, such that understanding the factors that influence the evolution of progeny size can become quite a challenge

The number of grandprogeny a female will produce depends on both the number of progeny she produces and the fitness of those progeny

there is a trade-off between the number of progeny a female can make and the amount of resources allocated to each of those progeny. If a female makes larger progeny, IYoung increases and N decreases.

If an individual has a fixed amount of resources available, those resources can be divided into three basic functions—growth, somatic maintenance, or reproduction.

For a trade-off between egg size and number to be evident, we must assume that the quantity of resources allocated to reproduction (ITotal) is constant. Yet ITotal is often not constant

larger individuals generally lay both more and larger eggs, leading to a positive correlation between egg size and number. In this case, the relationship between egg size and number will be negative only when body size is controlled

Smaller-than-average young have three developmental options: *(a)* mature at a smaller-than-average size, *(b)* extend development to fully or partially compensate for their small starting size, or *(c)* increase their rate of growth to mature at a normal size.

Most arthropods exhibit some degree of developmental plasticity by which progeny partially compensate for their small hatchling/birth size by extending development time

Progeny hatching from larger eggs can often better withstand environmental stresses such as larval competition (7), starvation (38, 89, 145, 199, 212), desiccation (201), oxygen stress (97), cold stress (36, 105), nutritional stress (27, 74, 78, 219), and environmental toxins (62).

shifts in the abundance of hosts may result in a change in optimal egg size, even without changes in the relationship between egg size and progeny fitness (183).

for organisms that exhibit parental care, large clutches may be less easily tended/defended than smaller clutches, such that progeny survivorship decreases with increasing maternal fecundity even if progeny size is constant.

For terrestrial insects size-selective egg predators and parasites impose selection on egg size that will vary with predation intensity.

The commonness of these latitudinal clines is often interpreted as evidence that large eggs are selectively favored at low temperatures. However, environmental effects of temperature on egg size often mimic the geographic clines observed in nature (larger eggs at lower temperatures; see below).

Within populations, larger females tend to lay larger eggs (Table 2), suggesting some morphological constraints on egg size.

Theoretical models generally predict that, as food availability decreases, and thus progeny mortality increases, females should shift to laying larger eggs (46, 189).

In some crustaceans females produce larger progeny at low food concentrations (Daphnia: 23, 24, 34, 58, 87–89, 92, 153, 173, 179; *Euterpina:* 93; and one isopod: 32), although progeny size may decrease at very low food levels (22, 213, 215). This increased progeny size often results in higher survivorship under food stress (89; references in 22

Females reared at high densities often lay eggs that are smaller than those of females reared at low density (73, 76, 79, 154; but see 65, 185), likely due to effects of competition on female size or nutritional status

Many studies show that females lay larger eggs when reared (104) or ovipositing (4, 5, 63, 101) at lower temperatures (232), although some arthropods lay larger eggs when reared at intermediate temperatures (10), lay larger eggs at high temperatures (110), exhibit variable responses to temperature depending on other environmental conditions

In many arthropods, progeny size varies throughout the year

In most arthropods, however, progeny size decreases with maternal age (Table 3), although an increase is commonly observed in orthopterans and heteropterans

**Partridge, L. and Barton, N.H. 1993. Optimality, Mutation and the Evolution of Aging. *Nature* 362: 305-311**

death is often proceeding by imitations of mortality, in the form of a decline in fertility and most aspects of biological performance, a characteristic of senescence or aging

aging is an evolutionary paradox if organism ca function well in youth why not when older?

aging reduces the contribution of older individuals to future generations

the rate of aging is highly variable

mechanistic accounts of aging invoke various forms of damage, to DNA, cells, tissues and organs. From this perspective the rate of aging could be determined solely by the level of exposure to damaging influences: the process would be inevitable and in no need of evolutionary explanation. not seen as even captive populations senesce.

Organisms vary in the extent to which they avoid or combat damage if it is a major factor – comparisons of birds and mammals of same size; turtles and other reptiles etc

because aging reduces the genetic contribution of individuals to the next generation it is opposed by natural selection.

but the selection that that maintains fertility and survival becomes weaker throughout life – even without aging organisms are at risk of death and impaired fertility from disease, predation and accidents

gnes that influence later life will be under weaker selection because by the time they take affect more of the original carriers will already have died or become infertile

problem of senescence one general question: to what extent does the degree of adaptation reflect the strength of selection?

aging could evolve as part of an optimal life history. On this view, senescence arises from the deleterious side-effects late in life of processes that are favourable early on (antagonistic pleiotrophy)

early reproduction may impair survival or future fertility by consuming resources causing somatic dmage or exposing the organism to environmental injury. The disposable soma theory is an optimal account of aging in which allocation of resources to reproduction jeopardizes somatic repair mechanisms and hence longevity

The optimisation theory of aging has become known as the ‘plieotropy theory of senescence’ because it is often developed in terms of genes with effects on more than one aspect of the phenotype, in this caseon the survival and fertility at different ages.

mutation pressure could lead to aging because the intensity of selection on later-acting mutants declines with age, alleles with deleterious effects will reach a higher frequency in a mutation selection balance the later the age at which they reduce fitness.

surprisingly, minor mutations reduce fitness just as much as those with larger effects, because they rise to higher frequency in a mutation slection balance

because a given change in performance has less effect later in life, we expect deleterious mutations to cause a greater frop in fertility and survival probability later in life assuming the same mutation rate for each age

the same argument can explain why different functions often decline with similar age: synchronous collapse does not imply a single mechanism of senescence

for empirical tests we must distinguish between predictions that are common to all evolutionary theories and those that can distinguish between optimality and mutation-accumulation.

because we know that there is a substantial input of deleterious mutations to populations and that it is impossible for individuals to combine indefinably high survival and fertility both the optimality and the mutation –accumulation theories of senescence must apply.

the two theories are difficult to separate as can both be tied to the same patterns – both e presence and absence of genetic variation could mean either theory is at work

if senescence is primarily due to late-acting deleterious mutations then one would expect the additive genetic variance to for survival and fertility to increase with age – not found in studies of drosophila

inbred lines of drosophila which are liable to give different colorations that actually occurring and are unsuitable for the evolution of aging

selection of breeding amoung older adults would be expected to reduce aging because of selection for higher longevity and fertility at older ages

misleading gene-environment interactions can occur in an environment other than in which the life history evolved. may apply to most published studies and a genral problem with experiments

environmental manipulations have the considerable advantage that they can be used in wild populations and they are also relatively quick

evidence for the mutation acculamaltion theory in drosophila – selected for early breeding for 120 generation s led to increased aging

affects of aging must have evolved – primordial soup replicators could ot have evolved if not immortal (genes are immortal) and senesce could be prevented with contious binary fission.

senescence of clones is probably cuased by the accumulation of deleterious mutations

**Leips, J. and Mackay, T.F.C. 2000. Quantitative Trait Loci for Life Span in *Drosophila melanogaster*: Interactions With Genetic Background and Larval Density. *Genetics* 155: 1773–1788**

Despite this near universal property, the potential life span of individuals varies a great deal among species (Finch 1990; Austad 1997; Gagny *et al.* 1997; Lass *et al.* 1997; Martı´nez 1998; Vaupel *et al.* 1998) and populations (Austad 1996; Ricklefs 1998).

Understanding the genetic basis of life span variation that and how the genetic components interact with environmental

influences to limit life span is not only of practical importance to the medical community, it is fundamental for understanding how the process of aging itself has evolved

Both theories of aging are based on the assumption that the strength of selection declines with increasing age following the onset of reproduction (Hamilton 1966; Charlesworth 1994).

Evaluation of these hypotheses requires identifying the genes that contribute to variation in aging, determining their age- and environment-specific effects, and the pleiotropic effects of these genes on traits directly related to fitness (*e.g.*, age-specific fecundity, age at maturity)

the effects of specific genes on aging and life span limitation are mediated by environmental variation (Kenyon *et al.* 1993; Gems *al.* 1998). Second, there is increasing evidence that many genes that contribute to variation in life span have pleiotropic effects on other traits and interact epistatically with other genes to influence life span (Gems *et al*1998; Tissenbaum and Ruvkun 1998).

Larval density varies a great deal in natural populations and is known to affect life span (Miller and Thomas 1958; see review of Graves and Mueller 1993) as well as a number of traits directly related to fitness (*e.g.*, age and size at eclosion; Miller and Thomas 1958; Barker and Podger 1970; Prout and McChesney 1985). Differences in larval density also affect the amount of heritable variation in life span that is expressed (*e.g.*, Clare and Luckinbill 1985; Buck *et al.* 1993a). Thus, larval density is an important ecological variable with potentially important effects on the evolution of life span.

On average newly eclosed male and female flies fromthe low density density vials were 15 and 16% heavier, respectively, than those that emerged from the high density vials

No other main effects (sex and density) or their interactions significantly affected life span.

the main effect of sex was significant, and females lived z20% longer than males in both densities.

For males, the only significant effect on life span was due to the cross-by-line interaction, which occurred in both density treatments. This interaction explained 9 and 11% of the total variation in life span in the low and high density treatments

6 QTL contributed to the variation in life span among lines, but different QTL were identified as important in each sex and larval density

Five QTL affected the sensitivity of life span to variation in larval density, but none were common to both sexes

In general, genetic differences among RI lines were evident for both males and females after exposure to high larval densities;

our finding that genetic variation for life span is more prevalent in high than in low density is consistent with the observation that selection for increased life span is more effective when flies are reared in high larval densities (*e.g.*, Clare and Luckinbill 1985;

genetic differentiation among lines in their general stress response may be reflected by differences in life span

Higher larval density generally leads to longer life span in *D. melanogaster* (Miller and Thomas 1958; Zwaan *et al.* 1991; Buck *et al.* 1993a), although in our experiment the response to density depended on sex and genotype

Oxidative damage from ROS is thought to be a major factor in aging (Harman 1956) and life span and several studies support this hypothesis (*e.g.*, Orr and Sohal 1994; Dudas and Arking 1995; Deckert-Cruz *et al.* 1997; Hari *et al.* 1998; Parkes *et al.* 1998).

Our finding that the effects of QTL genotypes on life span depend on genetic background, sex, and larvalenvironment is surprising

Life-history theory predicts that little, if any, genetic variation should persist for these traits because natural selection should fix the genes that produce the optimal phenotype in a given environment.

**Maklakov, A.A., Fricke, C. and Arnqvist, G. 2007. Sexual selection affects lifespan and aging in the seed beetle. *Aging Cell* 6: 739–744**

Theory suggests that senescence evolves because the intensity of natural selection declines with age (Medawar, 1952; Williams, 1957; Partridge & Barton, 1993; Charlesworth, 1994; Hughes & Reynolds, 2005).

Increased rates of extrinsic mortality should lead to accelerated rates of intrinsic mortality (i.e. senescence) under both of these scenarios (Partridge & Barton, 1993; Hughes & Reynolds, 2005), and this prediction has been supported experimentally (Stearns *et al*., 2000

However, it has also been suggested that a high extrinsic mortality rate can select for increased investment in somatic maintenance, which can in turn result in decelerated senescence (Abrams, 1993; Williams & Day, 2003; Williams *et al* ., 2006)

In theory, increased levels of sexual selection may either elevate or depress adult survival rates

the sexual conflict theory of aging predicts that higher rates of sexual conflict lead to the evolution of higher rates of senescence. However, it is theoretically plausible that increased level of conflict will reduce age-related deterioration as a byproduct of increased investment in somatic maintenance

However, the effect of selection interacted with sex, such that females from monogamous populations lived longer than females from polygamous populations while there was no difference in lifespan between males from the two selection regimes.

The analysis of the rate of senescence showed that males generally senesce faster than females, while we found no effect of selection

Our experimental removal of reproductive competition among males and conflicts of interest between males and females triggered the evolution of decreased rates of mortality and elevated lifespan in monogamous females, presumably as a direct response to a release from a sexual selection load

This finding is consistent with the general trend that differences in lifespan between populations are often attributable to differences in baseline mortality rather than to differences in the rate of senescence (Promislow *et al* ., 1996; Pletcher *et al* ., 2000; Bronikowski *et al* ., 2002; Maklakov *et al* ., 2006b; but see Fox *et al* ., 2004a).

The sex differences in lifespan and mortality rates are generally consistent with previous studies in *C. maculatus*: males lived shorter and senesced faster than females (e.g. Fox *et al* ., 2003, 2004a),

**Reznick, D.N., Bryant, M.J., Roff, D., Ghalambor, C.K. and Ghalambor, D.E. 2004. Effect of extrinsic mortality on the evolution of senescence in guppies. *Nature* 431: 1095-1099**

Medawar’s1 ‘mutation accumulation’ theory predicts that populations with high mortality rates should accumulate deleterious mutations that reduce fitness late in life

Williams’2 ‘antagonistic pleiotropy’ theory predicts that high mortality rates will select for earlier maturity and a higher rate of investment in reproduction early in life, which incurs a cost in the form of reduced investment in maintenance and reproduction late in life

Increases in extrinsic mortality rate may be accompanied by decreases in population density and increases in resource availability to survivors5. When such complexities are included, increased extrinsic mortality may cause the evolution of earlier senescence, later senescence, or no change in patterns of senescence, depending on these additional factors

There is a striking discrepancy between the diversity of theory on the evolution of senescence and its treatment in the literature. Empirical evaluations of the evolution of senescence focus almost exclusively on the classical theory7–16, as do recent reviews17,18

Two generations of lab rearing removes confounding environmental effects

Low predation localities tend to have lower levels of food availability23, reflected in the lower growth rates and smaller asymptotic body sizes of guppies from those sites

Whereas theory is clear in making predictions about how senescence should evolve, it is less clear about how one should quantify senescence. We have taken literally the definition of senescence as any age-specific decline in variables associated with individual fitness, specifically mortality, reproduction and physiological performance.

The rate of ageing13 is lower in the high predation localities in all four paired comparisons (drainage by food) between guppies from high and low predation localities

Guppies from high predation localities begin reproduction at an earlier age20, cease reproduction at a later age (Fig. 1) and hence have a longer reproductive lifespan. They also have longer total life spans (Table 1) but there are no differences among treatment groups in post-reproductive lifespan (data not shown).

A second way of evaluating senescence is through changes in the

rate of production of offspring with age

Whereas these analyses do not provide statistical support for differences among predator communities in reproductive senescence, they also do not comply with the prediction for delayed senescence in guppies from low predation communities.

guppies from high predation environments experience a more rapid deterioration in physiological performance with age than do their counterparts from low predation environments

Our results do not comply with the classical Medawar–Williams theory when senescence is evaluated in terms of survival, fecundity or reproductive value. Guppies from high predation localities have lower rates of ageing and do not differ in reproductive senescence relative to those from low predation localities

If older age classes benefit more than younger age classes from higher resource availability, then higher mortality can cause the evolution of delayed senescence, even though increased mortality without an indirect effect of density predicts the evolution of earlier senescence

Luckinbill and Clare30 showed that selection on late-life reproductive success causes the evolution of later senescence if larval density is high, but has no effect on the evolution of senescence if larval density is low

Stearns et al15. successfully selected for later senescence and the evolution of other life history traits by decreasing adult mortality rates, but only after increasing larval density and decreasing food supply