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Condition-dependence in life history evolution

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Abstract

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Ageing is the progressive physiological deterioration that appears with increasing age and eventually leads to a decline in survival and reproduction. This physiological process is omnipresent across the tree of life, but the expected trajectory can widely vary between and within species. Classic theories predict that the evolution of senescence is strongly influenced by the level of extrinsic mortality. Furthermore, variation in early-life developmental environments can shape individual condition and thus lead to alternative life-history strategies. The interplay between early-life environment and individual condition might therefore predict the trajectory of ageing and is of importance when studying life history evolution. In this thesis, I focus on condition dependent life-history strategies and how this can translate in differential ageing patterns. Moreover, I specifically investigate the influence of early-life environment on key life history traits (i.e. survival and reproduction) and how this might eventually carry-over to future generations via nongenetic inheritance. First, I used an experimental approach involving lab populations of the nematode *Caenorhabditis remanei* to show that males, but not females, pay the cost for the evolution of increased lifespan (**Paper I**). Second, I used an empirical dataset based on 25 years of observations, to investigate the long-term effects of early-life environment on reproduction and survival (**Paper II**). Reproductive success of low-condition females in natural populations of collared flycatchers (*Ficedula albicollis*) peaks later in life, when high-condition females are already in steep reproductive decline and suffer from high mortality rates. Third, I used the neriid fly *Telostylinus angusticollis* in an experimental environment, to test whether condition-dependent investment in secondary sexual traits affects the life-history strategies of males (**Paper III**). High-condition males developed and aged faster than low-condition males, but interaction with rival males did not affect male reproductive ageing. Finally, continuing the *T. angusticollis* experiment, I also found that parental diet interacts with parental sex and offspring sex, ultimately affecting offspring life-histories. Parental effects can thus play an important role in shaping between-individual variation in reproductive and actuarial senescence (**Paper IV**). Overall, in this thesis I have explored the interaction between environment, condition and ageing in both experimental and natural settings.

Keywords: Ageing, senescence, nongenetic inheritance, sex differences, condition-dependence, life history, trade-off, Ficedula albicollis, Caenorhabditis remanei, Telostylinus angusticollis

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"[...] λοιπὸν δ΄ ἡμῖν θεωρῆσαι περί τε νεότητος καὶ γήρως καὶ ζωῆς καὶ θανάτου· τούτων γὰρ διορισθέντων τέλος ἂν ἡ περὶ τῶν ζῴων ἔχοι μέθοδος"

Αριστοτέλης, 350 π.Χ.

"It remains for us to discuss youth and age, and life and death. To come to a definite understanding about these matters would complete our course of study on animals."

– Aristotle, 350 BC

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I Chen, H-y.*, **Spagopoulou, F.*** and Maklakov, A. A. (2016) Evolution of male reproductive ageing under differential risks and causes of death. *Journal of Evolutionary Biology*, 29(4):848–856

II **Spagopoulou, F.**, Teplitsky, C., Gustafsson, L. and Maklakov, A. A. "Silver-spoon" natal conditions increase early-life fitness but accelerate reproductive ageing in a wild bird. *Manuscript.*

III Hooper, A. K., **Spagopoulou, F.**, Wylde, Z., Maklakov, A. A. and Bonduriansky, R. (2017) Ontogenetic timing as a condition-dependent life history trait: High-condition males develop quickly, peak early, and age fast. *Evolution* 71(3)671-685

IV **Spagopoulou, F.**, Hooper, A. K., Wylde, Z., Bonduriansky, R. and Maklakov, A. A. Early-life parental diet effects on ageing depend on the sex of parents and their offspring. *Manuscript.*

* Shared first authorship

The following papers were written during the course of my doctoral studies but are not part of the present dissertation:

Spagopoulou, F. and Lind, M. (2018) Editorial: Evolutionary consequences of epigenetic inheritance. *Heredity: In Press.*

Spagopoulou, F. and Blom, M. P. K. (2018) Digest: Life history evolution in Darwin's dream ponds. *Evolution: In Press.*

Spagopoulou, F., Vega-Trejo R., Head, M. L. and Jennions, M. D. (2018) Male response to mating competition unexpectedly lowers reproductive success: maladaptive phenotypic plasticity? *In Review*

Svensson, E., Bolanos, A., Goedert, D., Gomez-Llano, M., **Spagopoulou, F.** and Booksmythe, I. (2018) Sex differences in local adaptation: what have we learned from reciprocal transplant experiments? *Philosophical Transactions of the Royal Society Biology: In Review*

Wylde, Z., **Spagopoulou, F.**, Hooper, A. K., Maklakov, A. A. and Bonduriansky, R. Effects of age at breeding on descendants' lifespan accumulate over generations in matrilines and patrilines. *Manuscript.*

Spagopoulou, F. Teachers and student mobility: maximizing the learning outcome when faced with increased diversity in a classroom. *Manuscript.*

Contents

1. Introduction

1.1 A history of the Evolutionary Theories of Ageing

Ageing, or senescence, is a complex biological phenomenon that plays a fundamental role in shaping life histories (Stearns 1992; Shefferson et al. 2017). Across the tree of life, the process of ageing, is widespread and prevalent in most eukaryotic organisms (Jones et al. 2014; Shefferson et al. 2017). Ageing can be defined as the progressive physiological deterioration with increasing age, resulting in a decline of fecundity and survival (Abrams 1991; Rose 1991; Partridge and Barton 1993, 1996). However, even though ageing is a fitness impairing trait, it has not been eliminated by natural selection over time, and thus understanding its evolutionary origin and maintenance poses an interesting challenge.

> *"It is indeed remarkable that after a seemingly miraculous feat of morphogenesis[,] a complex metazoan should be unable to perform the much simpler task of merely maintaining what is already formed."*
>
> [Williams 1957]

Yet, the paradoxical evolution of ageing had been largely neglected by the scientific community until the late nineteenth century (Williams 1957). Such neglect occurred mainly because ageing was considered as a non-existing biological phenomenon in nature that was only observed in human populations or animal populations in captivity. This can be largely ascribed to the observation that most organisms in the wild will most likely succumb to extrinsic environmental hazards such as predation, accidents, or parasitism ("extrinsic mortality") and, therefore, will not survive until old age, when signs of senescence become prominent. As a result, populations in general have a lower frequency of old individuals, creating a window, termed "selection shadow", where natural selection has limited direct influence over the process of ageing (Haldane 1941; Medawar 1952). Even if a hypothetical "accelerating ageing" gene would exist, its late-life expression would be hindered by the low survival rates of organisms, and when expressed they would be further selected against by natural selection, due to their detrimental effect on individual fitness. Hence, it would not be possible for such

genes to be in equilibrium in a population, since any mutation that would block their expression would be beneficial, and thus go to fixation (Kirkwood 2002). Today we know that large population size and careful observation are required to document age-specific decline in life-history traits with advancing age in natural populations (Nussey et al. 2008, 2013).

August Weismann was the first to study the causes of ageing from an evolutionary perspective, separating it from the common physiological approach (Weismann 1891). He believed that *"physiological considerations alone cannot determine the duration of life […] [D]uration of life is really dependent upon adaptation to external conditions, that is length, whether longer or shorter, is governed by the needs of the species."* (Weismann 1891, p. 9). He proposed a well-received theory of senescence, using mechanical devices and their functional decline as an analogy for the ageing-related physiological deterioration. Weismann initially suggested that longer-lived individuals will accumulate injuries that would not heal properly, reducing their fitness in comparison to younger members of the population. Therefore, a selective advantage for death would be established in late life stages and natural selection would act on these old and worn out individuals via a specific mechanism resulting in death; a mechanism that remained undescribed. This idea was later abandoned because it was based on the group selection approach to trait evolution and does not explain when injuries cannot be fully repaired in the first place. Weismann's most important contribution to the evolutionary theories of ageing was his "germ-plasm" theory. He proposed that all cells of an organism can be separated in germ and soma cell lineages (Weismann 1891, 1892, 1893). The cells that constitute the soma will eventually die (at the death of the organism) and their purpose is to keep the germ cells in a good condition and reproducing. On the other hand, the *"germ cells are not derived at all […] from the body of the individual, but they are derived from the parent germ-cell"* and, thus, are immortal (Weismann 1891, p. 170). Despite criticism of the prediction that there is a need of a strict germ-soma distinction for senescence to occur (Shefferson et al. 2017), Weismann's theory has guided the field and motivated modern ageing research (e.g. the "Disposable Soma theory" – Kirkwood 1977).

Some years later, Ronald A. Fisher, one of the fathers of population genetics, developed important mathematical equations to describe these processes and set the foundation for the classical evolutionary theories of ageing. In his work "The Genetical Theory of Natural Selection" (Fisher 1930, 1958), he introduced the concepts of "Malthusian parameter" and "reproductive value". As Charlesworth described in his review (2000), Fisher (1930) showed that a sexually reproducing, age-structured population that reproduces in continuous time will reach an asymptotic exponential rate of population increase (i.e. r, or Malthusian parameter) with each individual having an

expected lifetime contribution to future generations at each age (i.e. $v(x)$, or reproductive value). As an example, he compared the age-specific changes in reproductive values and mortality rates of Australian women and argued that *"the direct action of Natural Selection must be proportional to this contribution"* (1930, p. 27), since it *"is probably not without significance […] that the death rate in Man takes a course generally inverse to the curve of the reproductive value."* (Fisher 1930, p. 29).

Almost a decade later, John B. S. Haldane in his work "New Paths in genetics" (1941)(1941) also used mathematical models to predict the genetic progress of selection and shed further light on the evolution of ageing. Haldane was inspired by observing the expression of Huntington disease, which is caused by a single gene and the existence of only one allele copy in the genome. What intrigued him was that the first symptoms commence after the age of 30. According to Haldane, Huntington disease, despite being very serious, has not been eliminated by natural selection, because the *"[…] present age of onset of that disease may merely mean that [in ancestral conditions prior to agriculture and civilization] primitive men and women seldom lived much beyond forty[,] so postponement of onset beyond this age had no selective advantage"* (Haldane 1941, p. 193).

The work of Weismann, Fisher and Haldane influenced Peter Medawar who developed the "Mutation Accumulation" theory (MA) in his essay "An Unresolved Problem of Biology" (1952). According to MA, *"[…] the force of natural selection weakens with increasing age – even in a theoretically immortal population, provided only that it is exposed to real [extrinsic] hazards of mortality. If a genetical disaster […] happens late enough in individual life, its consequences may be completely unimportant"* (Medawar 1952). Medawar, thus, suggested that the selective force on age–specific deleterious alleles that affect late life stages is weak, resulting in the accumulation of a large number of genes with small harmful effects on late-life survival which overall lead to senescence. Late acting alleles with major detrimental effects may also exist, but are less prevalent (i.e. Huntington disease). In his thought experiment, starting with a non-senescent population, sources of extrinsic mortality (e.g. accidents, parasites, predation) will eventually lead to a population with relatively fewer old individuals. Therefore, investment in somatic maintenance will not be selected for and for each individual the age-specific contribution to fitness will have to be weighted by the probability of survival up to each age point. Consequently, natural selection against emerging de novo mutations with deleterious late-acting effects will not be very strong, since individuals carrying such a mutation will most likely die before its expression. A hypothetical immortal population will thus accumulate mutations late-acting deleterious effects and will, eventually, evolve a senescent life history. *"Even in such a crude and unqualified form, this dispensation*

[i.e. late-acting deleterious mutations] may have a real bearing on the origin of innate deterioration with increasing age" (Medawar 1952).

Half a decade later, George C. Williams extended these ideas with his "Antagonistic Pleiotropy" theory (AP) (Williams 1957). In this theory, Williams focused on possible trade-offs between fitness and late survival. A mutation that has early-life beneficial but late-life deleterious effects, will be strongly favoured by selection, simply because early in life the contribution to fitness is higher. The fecundity of an individual, a major parameter of fitness, is maximized shortly after reproductive maturity, and declines with increasing age, as described by Fisher back in 1930. Williams suggested that since senescence is an unfavourable character and its development is opposed by natural selection, there must be *"[…] two opposing selective forces with respect to the evolution of senescence. One is an indirect selective force that acts to increase the rate of senescence by favoring vigor in youth at the price of vigor later on. The other is the direct selection that acts to reduce or postpone the "price" and thereby decrease the rate of senescence. The rate of senescence shown by any species would depend on the balance between these opposing forces"* (Williams 1957, p. 402). Hence, senescence emerges as a result of these late-life detrimental effects of pleiotropic genes that decrease survival probability later in life.

Finally, two decades later, Thomas Kirkwood developed a mechanistic model, named "Disposable Soma" theory (DS – Kirkwood 1977, 1996; Kirkwood and Holliday 1979). DS is an extension of Weismann's "germ-soma" theory (1891, 1893) and relies on the same logic as William's AP theory. It highlights the importance of energy saving trade-offs resulting in errors in the molecular machinery underlying maintenance and repair of the somatic cells. *"Accuracy [in the translation apparatus] in the germ line is vital for the gene survival but a high level of accuracy in somatic cells may be a luxury our genes do better to forego"* (Kirkwood 1977, p. 303). Since individuals often do not reach an old age due to extrinsic mortality, the resources that are spent on the metabolically costly somatic maintenance and repair are only necessary for the period when survival probability is high. For instance, if the survival probability of a population to reach the second year is only 10%, then only 10% of this population will be able to benefit from any investment in survival mechanisms past the first year (Kirkwood and Austad 2000). At the same time, any of the limited resources that will be allocated to reproduction, will not be available for maintenance and repair mechanisms. This means that an allele that will allocate more resources to reproduction will enhance fitness, but will simultaneously have the pleiotropic effect of decreasing resource allocation to maintenance and repair of the somatic cells. Hence, the strategy of an organism to allocate sufficient resources to somatic maintenance and the remaining resources to growth and reproduction will provide a selective advantage. With such a strategy in

place, additional resources will increase fitness but simultaneously cause the accumulation of unrepaired somatic damage and eventually lead to the evolution of senescence. *"This strategy is evolutionary stable […] provided that the risk to the individual of accidental death is not too low[,] since the alternative of maintaining the high accuracy in all cells which might allow immortality would carry the penalty of an increased energy requirement. This penalty would mean that, other things being equal, an individual would grow and reproduce more slowly or would be subject to a greater risk of starvation or accidental death while seeking food"* (Kirkwood 1977, p. 303).

1.2 Extrinsic mortality and condition-dependence

Williams (1957) derived nine predictions that could be empirically tested and these predictions have greatly influenced ageing research over the years. The central and most widely tested prediction (termed "Williams' hypothesis") states that high levels of extrinsic mortality should lead to the evolution of rapid intrinsic senescence. In a high-mortality environment few individuals reach old age, resulting in a wider late-life "selection shadow" window, where more genes with late-acting deleterious effects can accumulate. Furthermore, organisms will shift resource allocation towards early-life reproduction, reducing overall investment in somatic maintenance and repair. Therefore, under protected conditions (e.g. in laboratory settings), populations with high levels of extrinsic mortality will exhibit a shorter intrinsic lifespan than populations with low extrinsic risks of death.

Williams' hypothesis has received substantial empirical support from studies using either a comparative or experimental laboratory selection approach (reviews by (Kirkwood and Austad 2000; Hughes and Reynolds 2005; Furness and Reznick 2017; Gaillard and Lemaître 2017). In a comparative study, Austad (1993) reported that a mainland opossum population that was subject to predation from larger mammals, showed rapid ageing and had a shorter lifespan in comparison to an island opossum population where such predators were lacking. In general, comparative research based on extrinsic mortality patterns have shown that adaptations that potentially decrease population mortality rates (e.g. flight ability, protective shells, defensive poison glands) are associated with slower senescence (Austad and Fischer 1991; Holmes and Austad 1995; Keller and Genoud 1997; Holmes et al. 2001; Blanco and Sherman 2005). Further experimental evidence for Williams' hypothesis comes from experimental evolution studies, with the evolution of longer lifespan when selecting for late-life reproduction. This approach is based on the premise that in populations with low levels of extrinsic mortality, individuals would have a higher probability to survive and thus would be

more likely to reproduce in later-life stages, highlighting the existence of a trade-off between survival and reproduction (Rose and Charlesworth 1980; Luckinbill et al. 1984; Rose 1984; Partridge et al. 1999; Buck et al. 2000). The strongest and most direct experimental evidence for Williams' hypothesis comes from an experimental evolution study conducted by Stearns et al. (2000). They applied selection via high and low levels of extrinsic adult mortality in multiple generations of *Drosophila melanogaster* populations, and found that flies kept under high adult mortality treatments evolved an earlier development time, increased early life reproduction and a higher intrinsic mortality rate in comparison with flies from the low mortality treatments.

Yet, the assumptions of William's hypothesis have also been challenged both empirically and theoretically over the years. For instance, Reznick et al. (2004) failed to produce similar results when comparing laboratory guppies from habitats that differed in mortality risk. They, found that high predation populations were long lived and had longer reproductive lifespan, contradicting the expected outcomes from Williams' hypothesis. Similarly, a study by Gray and Cade (2000) that focused on the effect of parasitism on the evolution of senescence in crickets and another by Morbey et al. (2005), that investigated senescence in Pacific salmon, did not provide any experimental support to the prediction proposed by Williams (1957). Thus, recent theoretical and empirical studies have expanded the theory and provided a broader framework that could explain such conflicting observations. They demonstrate that in situations where populations are faced with density-dependent growth or condition-dependent mortality, Williams' hypothesis does not hold (Abrams 1993, 2004; Williams and Day 2003; Reznick et al. 2004; Williams et al. 2006).

Williams and Day (2003) developed a theoretical model that highlights the importance of distinguishing between condition-independent and condition-dependent extrinsic mortality, for the evolution of senescence. Condition-dependence in mortality rates occurs when the probability of death due to extrinsic environmental hazards is higher in individuals with lower physical condition. This can result in a selection for more robust individuals and lead to the evolution of postponed ageing under high extrinsic mortality. This approach can be used to explain the longer lifespan found in guppies from high predation populations (Reznick et al. 2004). However, to bridge the gap between theory and empirical support it is important to control for population density and experimentally manipulate the rates of extrinsic mortality, rather than simply infer them based on the presence or absence of predators (Furness and Reznick 2017). This was done in an experimental evolution study by Chen and Maklakov (2012) on the dioecious nematode worm *Caenorhabditis remanei*, where the effects of the rates and sources of extrinsic mortality on the evolution of longevity could be disentangled. Chen

and Maklakov (2012) used a fuul-factorial design with build-in controls to expose replicated worm populations to four treatment regimes: i) high rates of mortality applied haphazardly (random), ii) low rates of haphazardous mortality, iii) high rates of mortality applied in a condition-dependent way (using heat shock), and iv) low rates of condition-dependent mortality. With this setting they were able to simultaneously test Williams' hypothesis (i.e. whether high mortality leads to rapid ageing) and the more recent condition-dependent hypothesis (i.e. whether condition-dependent mortality may lead to slower ageing). They found that under the random mortality regime, increased levels of mortality indeed led to the evolution of rapid ageing as predicted by Williams. However, high condition-dependent mortality led to the evolution of slowed senescence and longer lifespan, providing the first experimental evidence that condition-dependence is an important factor that shapes the evolutionary trajectory of ageing (Chen and Maklakov 2012, 2013).

Chen and Maklakov focused only on survival, actuarial senescence (i.e. mortality rate patterns) and reproductive success of females from each treatment (Chen and Maklakov 2012, 2013). While females from the randomly-applied mortality treatments showed the expected trade-off between survival and reproduction (i.e. lower survival with increased fecundity), females from the condition-dependent mortality treatments surprisingly demonstrated increased levels of both survival *and* reproduction. This result implied that, despite an increased investment in reproduction, robust individuals do not necessarily have to pay survival costs by reducing investment in somatic maintenance.

Yet, the lack of a trade-off between survival and reproduction, does not mean that trade-offs are completely absent. Increased selection for better condition can result in trade-offs with other life history traits, such as developmental time (Lind et al. 2017). Hidden trade-offs can also be found in sex-specific differences in life history traits. Sexes often have different phenotypic optima in the fitness landscape, due to anisogamy and sexual selection (Trivers 1972, 1985; Maklakov and Lummaa 2013; Fromhage and Jennions 2016), but face intra-locus sexual conflict over life-history traits due to their shared genome (Rice 1984; Rice and Chippindale 2001; Bonduriansky et al. 2008; Bonduriansky and Chenoweth 2009; Griffin et al. 2013; Connallon and Clark 2014). Thus, the costs of the evolution of delayed senescence could be invisible when focusing on one sex only. To address this issue, in **Paper I**, I explore potential sex-specific trade-offs by investigating male reproductive success of selection lines established by Chen and Maklakov (2012).

1.3 Life history trade-offs and condition-dependence

Across the tree of life, organisms use different strategies to optimize their fitness and this has led to the evolution of an incredible diversity in life history strategies (Shefferson et al. 2017). These strategies are needed to deal with constraints that organisms face in nature. Such constraints can lead to well-documented trade-offs, that in essence are *"the linkages between traits that constrain the simultaneous evolution of two or more traits"* (Stearns 1992 p. 72). Trade-offs can be commonly observed between life history traits, such as growth (size at birth and growth pattern), reproduction (age and size at maturity, reproductive investments and offspring number, sex and sex ratio) and survival (lifespan and mortality schedule) at any given point, or between current and future trait expression (e.g. current vs. future reproduction) (Stearns 1992).

Life history trade-offs emerge since the amount of available resources is finite at any given point in time. Throughout their lives, organisms accumulate metabolic resources (i.e. resource acquisition and assimilation), which subsequently are divided between various life history traits. However, allocating resources in one trait, will automatically result in a decrease in the amount of available resources for other traits. Thus, organisms are usually unable to maximise their investment to all fitness enhancing traits simultaneously, and will have to make strategic decisions (the so-called "Principle of allocation" – Levins 1968; Sibly and Calow 1986; Stearns 1992). These allocation trade-offs among life history traits (e.g. R and S traits in Fig. 1) have been described with the Y model of resource allocation (Fig. 1A; Noordwijk and de Jong 1986).

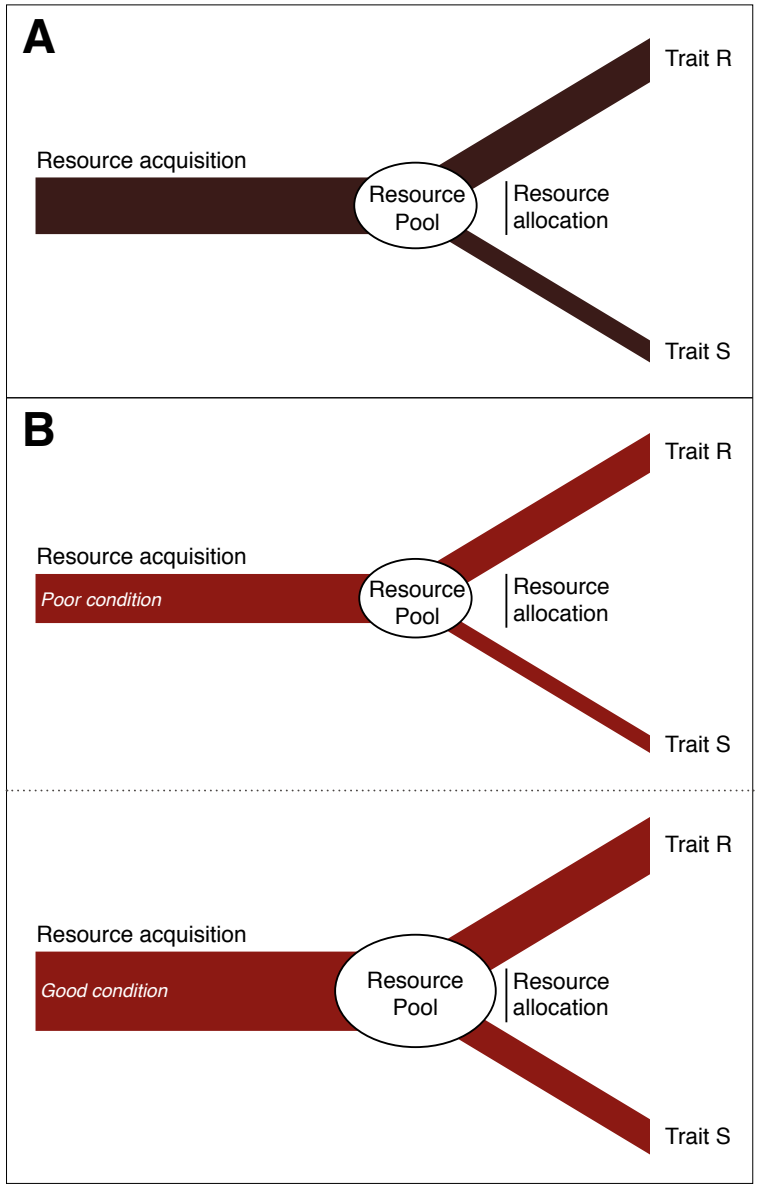

Figure 1. The Y model of resource allocation trade-offs. (A) Organisms accumulate resources in a resource pool (via resource acquisition and assimilation from the left), and these resources are subsequently allocated to competing traits R and S; (B) Individuals of different condition (up: poor condition; down: good condition) face the same trade-offs and follow the same allocation rules, but high-condition individuals can have increased expression of both traits.

However, despite apparent trade-offs, some individuals have more metabolic resources to spend, and can thus increase allocation to all traits (Fig. 1B). Individuals that are able to invest more in multiple life history traits are identified as being in a better condition (i.e. having higher total amount of accumulated metabolic resources for allocation to different life history traits) than individuals with less resources to spend. Over the years, different definitions of the term "condition" have existed, but in this thesis I adopt the definition of Rowe and Houle (1996).

> *"We will refer to the pool from which resources are allocated as condition […]. […] Our view of condition is analogous to 'residual reproductive value' in traditional life history models, or 'state' in dynamic life history models, in that it is an internal property of the individual and accounts for a large portion of fitness."*
>
> [Rowe and Houle, 1996]

While individuals of different condition may follow the same allocation rules (Fig. 1), variation in condition can also lead to changes in allocation dynamics, since fitness optimization may be reached by using alternative allocation strategies. Thus, the fitness outcome depends on the relative variation between resource acquisition and resource allocation; a relationship that often can explain a lack of the expected life history trade-offs (i.e. positive relationships) (van Noordwijk and de Jong 1986). For example, a study in crickets (*Teleogryllus commundus*) found that high-condition males increased reproductive effort at the cost of shorter lifespan (Hunt et al. 2004), yet the expected trade-off between reproduction and survival was absent in a closely related species (*Gryllus pennsylvanicus*) where male condition, reproductive effort and longevity were positively correlated (Judge et al. 2008).

Overall, the Y model illustrates trade-offs between life history traits of individuals in different condition. However, the question is how condition eventually may affect age-specific trait expressions. For instance, focusing on the trade-off between reproduction and somatic maintenance (Kirkwood 1977; Kirkwood and Holliday 1979; Kirkwood and Rose 1991), individuals in different condition can show two contrasting patterns of age-specific reproductive change (Fig. 2). In both cases, high-condition individuals will have a higher reproductive value early in life, due to the increased resources they have in comparison to low-condition individuals. However, an overinvestment in reproduction early in life at the cost of somatic maintenance, may result in rapid deterioration with advancing age (i.e. trade-off between current and future reproduction), with only high-condition individuals being able to afford such a strategy (Fig. 2A – Bonduriansky and Brassil 2005).

Research in a variety of taxa have provided evidence for this pattern. For instance, male antler flies (*Protopiophila litigata*) that are in better condition (i.e. larger body size) have increased mating rate early in life but suffer from rapid reproductive ageing (Bonduriansky and Brassil 2005). Similarly, female red deer (*Cervus elaphus*) with increased early-life reproductive performance pay the cost of faster reproductive ageing rates in comparison with lower quality females (Nussey et al. 2006). Alternatively, reproductive rate may reflect condition and high-condition individuals may therefore always have a higher reproductive performance (Fig. 2B – Bonduriansky and Brassil 2005; Judge et al. 2008). In this scenario, the trade-off between reproduction and somatic maintenance is not absent, but it might be masked, if selection for example favours increased late-life reproductive effort. Females, for instance, may evolve a preference for older males in a population, because they possess "good genes" for viability (Kokko 1998; Brooks and Kemp 2001) and, thus, maintenance of their competitive advantage with age (i.e. condition) will be selected for. Reproductive rate may therefore become increasingly condition-dependent, since resources get depleted and it becomes more and more costly to maintain competitiveness with increasing age (Bonduriansky and Brassil 2005). For example, bighorn sheep (*Ovis canadensis*) with higher body mass have higher overall fecundity than low-condition males, without showing a trade-off between early- and later-life reproductive success (Bérubé et al. 1999). Similarly, high-condition male crickets (*Gryllus pennsylvanicus*) have a positive relationship with reproductive effort throughout their lives (Judge et al. 2008). In **Paper II**, I found that female collared flycatchers (*Ficedula albicollis*) that were raised in decreased nests (i.e. low sibling competition and thus high-condition), reached their reproductive peak earlier in life, but experience faster reproductive ageing than females from increased nests, following the first scenario (Fig 2A). Similarly, as shown in **Papers III** and **IV**, high-condition male neriid flies (*Telostylinus angusticollis*) have increased early-life but decreased late-life reproduction. They reach their reproductive peak earlier in life, but experience a faster reproductive ageing than low-condition males, following the first scenario (Fig. 2A).

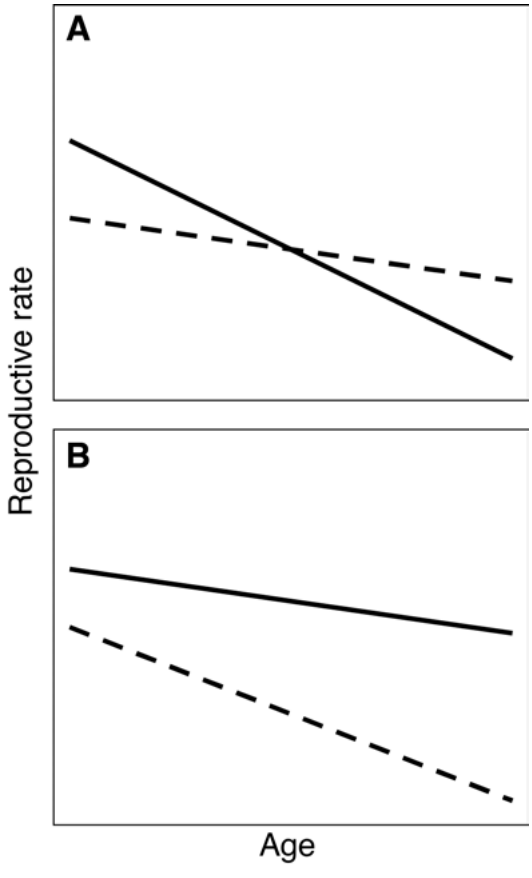

Figure 2. Contrasting patterns of ageing predicted by life history theory between individuals of different conditions: (A) trade-offs may cause individuals with high initial mating rates (solid line) to age faster than individuals with lower initial mating rates (dashed line); (B) alternatively, large individual variation in condition and increasing reproductive effort with age may enable individuals with high initial mating rates to maintain or increase their relative advantage with age (Figure and figure legend from Bonduriansky and Brassil 2005).

Often the expression of traits involves increased energetic costs for their production and maintenance, in addition to indirect ecological costs (e.g. increased predation risk or reduced foraging success) (Andersson 1994; Johnstone 1995). Condition-dependence is the mechanism that correlates condition with trait expression and evolves when trait expression has more costs than benefits (Andersson 1982; Nur and Hasson 1984; Grafen 1990; Houle 1991; Rowe and Houle 1996; Kotiaho et al. 2001). Furthermore, condition-dependence can maintain genetic variation in traits, such as sexually selected and life history traits (Rowe and Houle 1996; Tomkins et al. 2004). Sexually selected traits are the classic examples of fitness enhancing traits that develop condition-dependent expression (Mappes et al. 1996; Kotiaho 2000; Proulx et al. 2002; Getty 2006; Fitzpatrick and Lüpold 2014; Wigby et al. 2016; but see Cotton et al. 2004). In **Paper III**, I investigate whether condition-dependent investment in male secondary sexual traits leads to a

trade-off other life history traits, such as somatic maintenance and reproductive performance.

Overall, individual condition is determined both by the genetic quality of the individual (i.e. presence of "good" genes that increase fitness) and by the quality of its environment (i.e. resource availability and stressors in juvenile or adult environment) (Andersson 1982; Rowe and Houle 1996; Cotton et al. 2004; Tomkins et al. 2004; Hill 2011). Thus, to understand the causes of condition-dependent trait expression, it is important to manipulate genetic and/or environmental quality, to reveal how condition mediates these effects (Cotton et al. 2004; see Bonduriansky et al. 2015 for the interaction between genetic and environmental quality). In **Papers II, III and IV**, I measured the sensitivity of life history trait expression to changes in early-life environmental quality, and possible trade-offs among traits that emerge due to condition-dependence of their expression.

In this thesis, I address the topic of condition-dependence in the evolution and expression of ageing from different perspectives and in different study systems . I specifically aim to take advantage of both laboratory model organisms (**Papers I, III and IV**) and natural populations (**Paper II**), to shed further light on the importance of condition in life history trade-offs and, ultimately, in the evolution of senescence (**Paper I**). Such a holistic approach is needed, since previous studies have shown that experimental outcomes may depend on whether organisms were studied in wild or in laboratory conditions (Kawasaki et al. 2008).

> *"Field and laboratory studies on a broader range of organisms are needed to understand biological variation in the processes contributing to senescence."*
>
> [Monaghan et al. 2008]

1.4 Condition and early-life developmental environment

Early-life development is the period from conception to developmental maturity (Henry and Ulijaszek 1996), and can be of particular importance in determining individual condition (Monaghan 2008). Due to environmental stochasticity, individuals may experience different developmental stressors (i.e. increased population density, temperature deviations, or limited resource availability) that may constrain the development of an optimal phenotype. The fitness consequences of these stressors may not be straight forward and may depend on the ability of organisms to adjust their phenotype and avoid these negative effects (Monaghan 2008). Under mild environmental

changes, organisms usually show phenotypic plasticity and can maintain high fitness levels. Yet, when organisms develop in an environment with developmental stressors of greater intensity, they may be faced with detrimental fitness effects (Monaghan 2008). To minimize fitness decline, such individuals of poor-condition may strategically re-allocate their limited resources to different traits (i.e. trade-offs between traits) or alternative life stages (i.e. pleiotropic trade-offs between current and future trait expression) (Monaghan 2008). For example, organisms from a poor natal environment may be able to acquire a normal body size (i.e. similar to non-challenged individuals) by increasing growth rate early in life, even at the cost of reduced adult lifespan (Metcalfe and Monaghan 2001, 2003). This compensatory growth pattern, is a good example of pleiotropic trade-offs between early-life beneficial and late-life detrimental effects. Overall, such strategies may yield the maximal "best" fitness outcome, even in harsh natal environments, and thus be selected for in a population.

In contrast, organisms that develop in high quality early-life environments, may show different life histories with beneficial effects throughout life (Monaghan 2008), a scenario described as the "silver spoon effect" (Grafen 1988). Grafen defined the silver spoon effect *"[…] as positive correlations between characters in the adult that are positively associated with fitness, brought about by the common underlying cause of favorable […] environmental events during development"* (1988, p. 459). Thus, "silver spoon" individuals are of better condition and are therefore able to accumulate more resources for allocation to fitness-related traits than poor-condition individuals (i.e. developed in poor natal environments), with important fitness consequences for the individual.

Previous empirical studies have largely focused on short-term fitness consequences of early-life developmental environment. Individuals with a "silver spoon" development have increased early life performance, such as higher juvenile survival (Tinbergen and Boerlijst 1990; Magrath 1991; Perrins and McCleery 2001; Green and Cockburn 2002; Reid et al. 2003; Payo-Payo et al. 2016), natal dispersal (van der Jeugd 2001), and reproductive success (Gustafsson et al. 1995). However, stressful natal conditions can also have important long-term fitness consequences (review: Lindström 1999, birds: Harris et al. 1994; de Kogel 1997; Cam et al. 2003; Reid J. M. et al. 2003; van de Pol et al. 2006, reptiles: Marquis et al. 2008; Baron et al. 2010, mammals: Albon et al. 1987; Hamel et al. 2009), but the direction of such condition-dependent ageing trajectories show complex patterns. For example, zebra finches (*Taeniopygia guttata*) exposed to acute stress during the nestling period, via experimental elevation of glucocorticoids, showed a striking decline in lifespan (Monaghan et al. 2012), yet, increased glucocorticoid levels in grey partridges (*Perdix perdix*), caused by unpredictable food supply during the juvenile period, resulted instead in elevated adult survival

(Homberger et al. 2014). Persistent stressful conditions even after the developmental period can also affect adult lifespan in the same positive direction (Marasco et al. 2015).

Overall, while correlational studies can reveal associations between condition and life history traits, there is a need for experimental manipulations of the natal conditions, to be able to provide clear insights on the effects of early-life developmental environments in individual life histories. In **Papers II, III and IV**, I manipulate resource availability in natal environments both indirectly via brood size manipulations (**Paper II**) and directly with manipulations of nutritional content of developmental diets (**Papers III and IV**).

1.5 Nongenetic parental effects

The field of nongenetic inheritance has received an increase in attention during recent years. Initial molecular discoveries in plants revealed mechanisms of transgenerational epigenetic, cytoplasmic and small-RNA transmission (Jablonka and Lamb 1995; Johannes et al. 2008) that were subsequently also found in all other taxonomic groups (Bonduriansky and Day 2009). Nongenetic inheritance can be broadly defined as *"any effect on offspring phenotype brought about by the transmission of factors other than DNA sequences from parents or more remote ancestors"* (Bonduriansky and Day 2009, p.106). However, there is an overall lack in consistency with regards to the definitions used and similar mechanisms have been described as non-DNA-based inheritance, transgenerational epigenetic effects, non-Mendelian inheritance, carry-over effects, or most commonly, parental effects (Bonduriansky and Day 2009; Burggren 2016).

Traditionally, nongenetic parental effects were only recognized and studied via the maternal line. These studies revealed that maternal effects are widespread and influence offspring development across taxa (Mousseau and Fox 1998; Marshall and Uller 2007; Champagne 2008; Wolf and Wade 2009). On the other hand, paternal effects had for long been considered as rare, existing only in species where males provide parental care (Kokko and Jennions 2008; Crean and Bonduriansky 2014). This asymmetry can be largely explained by the lack of known transfer mechanisms for nongenetic molecular factors between father-offspring and the difficulty of differentiating between paternal and maternal effects, given that paternal influence is mediated by maternal responses (Crean and Bonduriansky 2014). However, an increasing body of research, such as evidence for the existence of sperm- and ejaculate-mediated mechanisms of transfer (sperm – cytoplasmic and epigenetic: Rassoulzadegan et al. 2006; Kumar et al. 2013; Casas and Vavouri 2014, ejaculate – proteins and lipids: Chow et al. 2003; Robertson

2005; Wong et al. 2007; Avila et al. 2011) have now highlighted that paternal effects can be as important as maternal effects (Jablonka and Raz 2009; Crean and Bonduriansky 2014).

Despite our limited understanding of the proximate mechanisms that underlie nongenetic parental effects, empirical studies have already revealed that chromatin modifications (i.e. DNA methylation and histone alterations), transfer of cytoplasmic molecules (i.e. small RNAs and proteins) and transmission of somatic factors (i.e. nutrients and hormones) are important components of nongenetic inheritance (Champagne 2008; Carone et al. 2010; Skinner et al. 2010; Daxinger and Whitelaw 2012; Holeski et al. 2012; Marré et al. 2016; Rando 2016; Houri-Zeevi and Rechavi 2017; Klosin et al. 2017; Rechavi and Lev 2017; Harvey et al. 2018). However, we can shed further light into the evolutionary and ecological consequences of nongenetic parental effects without focusing on the molecular machinery, but instead by investigating how parental condition influences the variation in offspring phenotypes (Day and Bonduriansky 2011; Bonduriansky and Day 2013).

> *"[F]rom an ecological or evolutionary perspective, the proximate mechanism mediating an effect might be of less interest than its pattern of transmission and its consequences for variation in phenotypic features and fitness."*
>
> [Crean and Bonduriansky 2014]

Nongenetic parental effects can be persistent and have important adaptive consequences, such as increasing the amount of heritable variation available for selection (Pál and Miklós 1999; Bonduriansky et al. 2012; English et al. 2015; Bonilla et al. 2016; Head et al. 2016). Thus, parental effects can contribute to population dynamics and life history evolution, by directly shaping the phenotypic variation of offspring (Mousseau and Dingle 1991; Benton et al. 2008; Uller 2008; Badyaev and Uller 2009; Wolf and Wade 2009; Crean and Bonduriansky 2014; van den Heuvel et al. 2016; Bonduriansky and Crean 2017). A number of hypotheses have been proposed to explain why influencing offspring phenotype could provide adaptive benefits to the parents (Bonduriansky and Crean 2017). The "anticipatory effects" hypothesis posits that in a predictable environment parents may anticipate the state of the future environment and adjust the phenotype of offspring to optimally prepare them for the conditions that they will encounter (Marshall and Uller 2007; Burgess and Marshall 2014). Such effects have been observed both when the offspring environment is predictably similar (Crean et al. 2013) or completely the opposite (Dey et al. 2016) of the parental environment. Yet, for the evolution of such anticipatory effects, parents must first develop a mechanism that would allow them to assess the environmental conditions and alter their offspring phenotype accordingly

(Bonduriansky and Crean 2017). A wrong estimation of the future environment can result in a mismatch between the expected (i.e. signalled by the parents) and the actual environment that the offspring experience, with detrimental fitness consequences. An alternative hypothesis termed "condition-transfer effects" maintains that individual condition will influence the levels of parental investment, with high-condition individuals being able to provide more resources (i.e. via parental care or nongenetic inheritance factors as mentioned above) to their offspring and increase their performance in any environment (contrary to the "anticipatory effects), thus receiving indirect fitness benefits (Qvarnström and Price 2001, reviewed in Bonduriansky and Crean 2017). Due to the associated costs in producing and maintaining such a transmission machinery, only high-condition individuals are able to transfer such beneficial resources, and thus this adaptive mechanism should be strongly condition dependent (Bonduriansky and Crean 2017; Macartney et al. 2018). However, these hypotheses do not necessarily exclude one another (Bonduriansky and Crean 2017), but can both co-occur and explain some of the observed transgenerational patterns.

In **Paper IV**, I investigated the condition-dependence of maternal and paternal effects on life history traits of female and male offspring, in neriid flies.

1.6 Sex-differences in life history evolution

Variation in resource allocation strategies can be particularly pronounced between the sexes. Female reproductive success is often limited by the resource availability and speed with which metabolic resources can be converted into offspring, while male reproductive success is often limited by the access to females. Therefore, males and females often follow different reproductive strategies and thus prioritize different traits when allocating resources. In a mating system where males are under strong sexual selection, females increase their fitness by investing in somatic maintenance and increased lifespan, since their reproductive success is often limited by the number of offspring they can produce per breeding attempt. At the same time, males often invest more in energetically costly secondary sexual traits to gain access to females, and forego long-term survival by focusing on short-term reproduction (Trivers 1972, 1985; Adler and Bonduriansky 2014). Such divergent reproductive strategies can result in sexual dimorphism in ageing (Bonduriansky et al. 2008; Maklakov and Lummaa 2013). It remains unclear, however, how differences in individual condition can affect sex-specific expression of life history traits. In **Paper IV**, I compared condition-dependent life history trade-offs between the two sexes in two generations.

2. Materials and Methods

2.1 Study systems

The nematode *Caenorhabditis remanei* (Paper I)

Caenorhabditis remanei is a free-living nematode (~ 1mm length) that can be found in decomposing plant material and compost soil where it feeds on bacteria. Its life cycle is described by four larval (L1-L4) and an adult life stage. However, if larval conditions become stressful (e.g. limited food availability) it goes through an alternative L3 stage, which is called "dauer" and is a form of diapause. Even though *C. remanei* is closely related to *C. elegans*, it is a dioecious species with no hermaphroditic forms. *C. remanei* show strong sexual dimorphism in life history, with males being smaller and reaching reproductive maturity earlier than females, while as in most *Caenorhabditis* species, males are the longer-lived sex (Fig. 3) (McCulloch and Gems 2003; Zwoinska et al. 2013).

With a very short generation time (3-4 days) and easy laboratory maintenance procedures, *C. remanei* is an excellent system for experimental evolution studies. The experiment described in **Paper I** was based on 16 populations (four replicates of each extrinsic mortality treatment) derived from an experimental evolution approach (Chen and Maklakov 2012), using the *C. remanei* wild-type strain SP8, provided by N. Timmermeyer from the Department of Biology at the University of Tübingen, Germany. This is a genetically heterogeneous strain created after crossing of three wild-type isolates: SB146 from Freiburg in Germany, MY31 from Tübingen in Germany and PB206 from Ohio in the United States (Fritzsche et al. 2014). During the experiment, *C. remanei* populations were maintained on agar plates seeded with a lawn of *Escherichia coli* OP50 and kept in climate chambers with 60% humidity and temperature constant at 20° C (Stiernagle 2006).

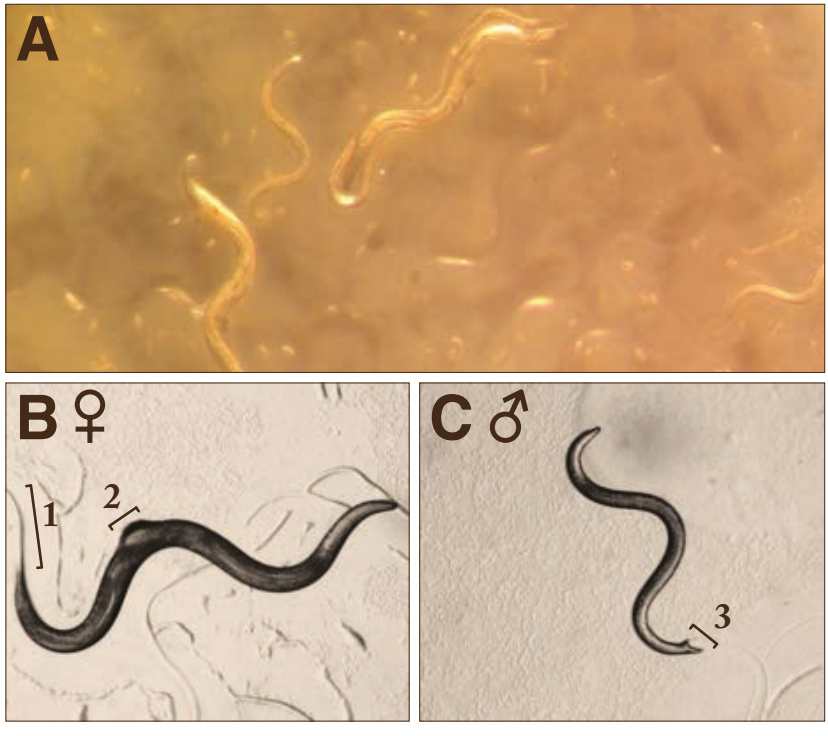

Figure 3. Nematode *Caenorhabditis remanei*; (A) Adult females (larger) and males (smaller) together with their eggs in a laboratory agar plate. The most characteristic difference among the sexes is tail morphology (1,3). (B) Adult mated female with copulatory plug visible (2). (C) Adult male. (*Picture A was taken at the Maklakov lab; Pictures B & C at the Bolund lab by Josefine Stångberg*)

The collared flycatcher *Ficedula albicollis* (Paper II)

Collared flycatchers (*Ficedula albicollis*) are small (~ 13g), migratory, insectivorous, cavity-nesting passerine birds (Fig. 4), that breed in deciduous and mixed forests in eastern and central Europe (and southwestern Asia). Breeding pairs tend to be socially monogamous, and only a small proportion of females have been observed with multiple males (i.e. < 5 %, Qvarnström et al. 2000). Females incubate four to eight eggs during a 14-day period and rear a single brood each year. Juveniles are fed by both parents and juveniles fledge 15 to 18 days after hatching (for further details on population and methods see Gustafsson 1989).

Figure 4. Collared flycatchers *Ficedula albicollis*; male (left) and female (right) (*Pictures taken by Johan Träff*)

Isolated from their main breeding grounds, additional breeding populations have been established on the Swedish islands of Gotland and Öland in the Baltic Sea. The collared flycatcher population on the island of Gotland (57° 10′, 18° 20′) has been well studied since 1980. Each year, new individuals (i.e. both adults and offspring) are measured and individually ring marked, to allow individual identification throughout their lifetime and enable the assessment of yearly reproductive success. The females are caught during incubation in nest boxes and the males during the chick provisioning period. Further details of the breeding region, and ecology have been collected using standard methods (Gustafsson 1989; Pärt and Gustafsson 1989).

Collared flycatchers in general and specifically the long-term studied Gotland population, are particularly suitable for the study of life history trade-offs in nature due to their high degree of site fidelity, limited dispersal and preference for nest boxes over natural cavities, which allows accurate age and survival estimation (Pärt and Gustafsson 1989). In **Paper II**, I used the long-term monitoring data collected between 1983 and 2009, to analyse reproductive performance and survival of female collared flycatchers.

The neriid fly *Telostylinus angusticollis* (Paper III and IV)

Telostylinus angusticollis is a dipteran insect with long, stilt-like legs, belonging to the neriidae family (Fig. 5). This Australian species that can reach up to 2cm in length, is native to New South Wales and southern Queensland. Adults aggregate and breed on decaying tree barks (Fig. 5A-D), such as the barks of *Acacia longifolia.* As many neriid flies, *T. angusticollis* show strong sexual dimorphism, with males having much longer legs, heads and antennae than females (Fig. 5A, B, I). Males engage in spectacular combats for access to high quality territories and to females (Bonduriansky 2006). They elevate their bodies, almost in a vertical position (Fig. 5E), and use their forelegs and antennae to strike (Fig. 5F) and occasionally headlock (Fig. 5G) their rival. After mating (Fig. 5H), males mate-guard the female (Fig. 5I), who oviposits eggs in the rotting tree barks (Fig. 5B, D, I). In the lab of Russell Bonduriansky, *T. angusticollis* is used for studies on life history, developmental plasticity, diet effects and non-genetic inheritance. When reared on a nutrient-rich larval diet, emerging adults show increased sexual dimorphism in morphology (i.e. males have elongated legs, head and antennae), in comparison with adults developing on a nutrient-poor diet (i.e. males look more like females) (Bonduriansky and Head 2007; Fig. 5H).

Hence, *T. angusticollis* is a highly suitable system to address questions on condition-dependence and sex-differences in life history traits (**Paper III** and **IV**). The flies I used for my experiments were collected from a naturally occurring population on trunks of *Acacia longifolia* trees in Fred Hollows Reserve in Sydney, Australia (33°54′44.04″S 151°14′52.14″E), and were bred in the laboratory for two generations to remove possible environmental transgenerational effects prior to the onset of the experiment. Laboratory populations were maintained with *ad libitum* food (brown sugar and dried yeast) at 25°C under a 12:12h photoperiod. In **Papers III** and **IV**, I used background individuals reared in a "standard" diet as companions for the focal housing containers and as "tester" virgins to collect focal reproductive performance data. All background individuals were separated by sex following emergence and housed in 2-L containers (20-30 flies per container).

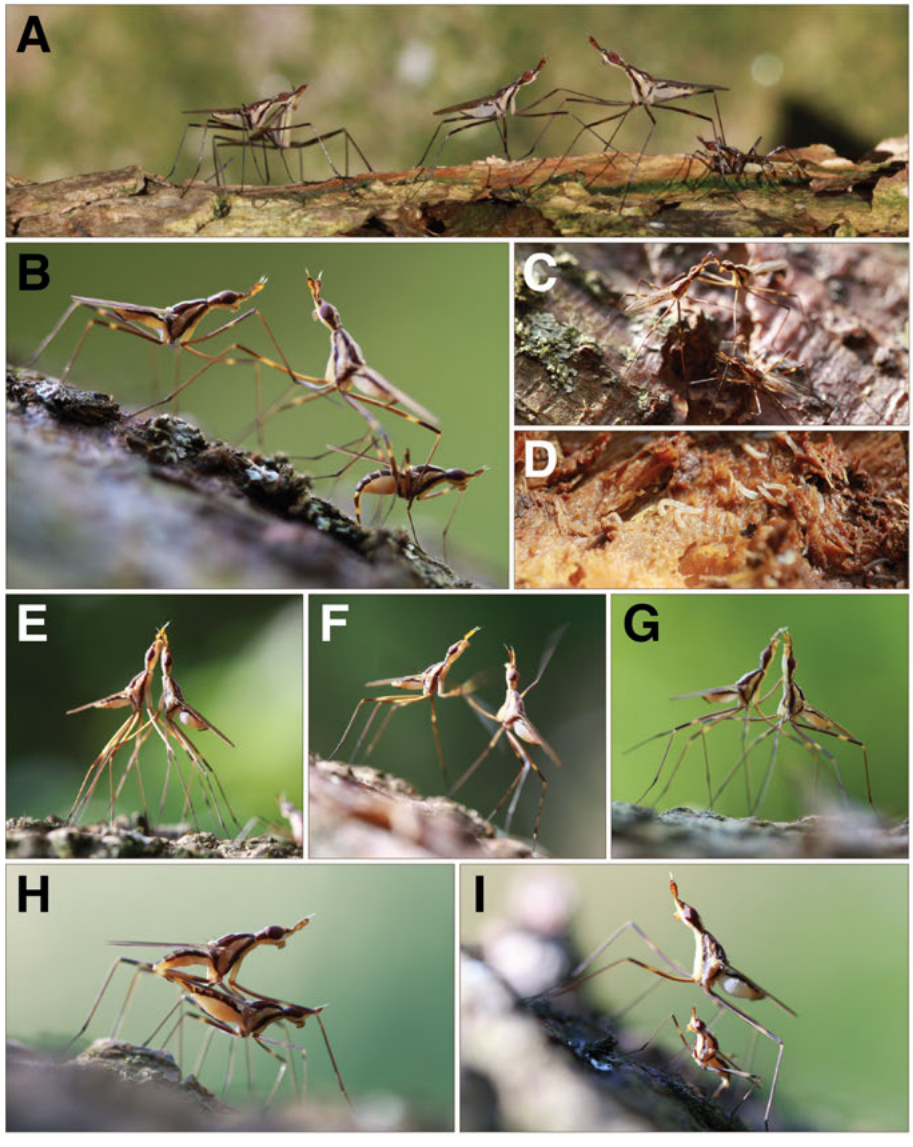

Figure 5. Neriid flies *Telostylinus angusticollis*. They aggregate (A-C) and breed (D, H) on tree barks, defend good quality territories (A-C, E-G) and males mate guard the females after mating (I). Females oviposit their eggs in rotten bark (B at bottom right, I at bottom), where the larvae develop (D).
(*Pictures taken by Russell Bonduriansky*)

2.2 Methods used

Brood size manipulation (Paper II)

Since 1983, multiple brood size manipulation experiments have been conducted in the Gotland population of collared flycatchers (Gustafsson and Sutherland 1988; Nordling et al. 1998; Doligez et al. 2002; Forsman et al. 2008; Pitala et al. 2009), to examine various aspects of parental investment, such as hormone-mediated maternal effects, the costs of increased reproductive effort and the trade-off between reproductive investment and immune function. To investigate the effects of early-life natal conditions on individual life histories, data was collected from individuals raised in brood-size manipulated nests (i.e. nests of origin), where clutch size was increased or reduced by two offspring. In addition, possible translocation effects were accounted for by including a control treatment, in which offspring were swapped between nests without alteration of the initial number (Figure 6). For each female, the survival and the number of recruits (i.e. offspring that returned to Gotland to breed the following years, after overwintering in Africa) during each reproductive season (i.e. nests of annual reproduction) was analysed, to investigate how reproduction changes with increasing age (age-specific reproduction).

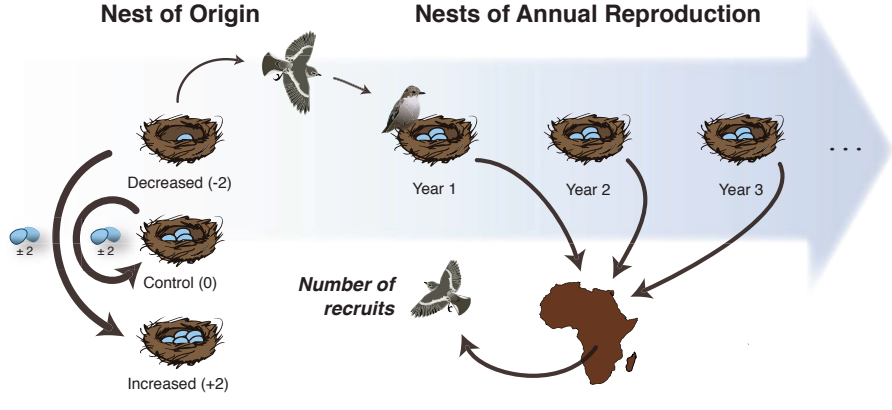

Figure 6. Brood size manipulations of female collared flycatchers in Gotland. Age-specific reproduction (i.e. number of recruits from each nest of annual reproduction – right) of females raised in manipulated nests of origin (left).

Larval diet manipulation (Papers III, and IV)

To achieve high- and low-condition treatments in the neriid fly, I reared the focal individuals on either a nutrient-rich or a nutrient-poor diet during larval development and thus experimentally manipulated the amount of resources available (Fig. 7A). All diets were selected from Sentinella et al. (2013) with the aim of maximising body size differences between treatments, but keeping the degree of viability selection during larval development and the protein to carbohydrate ratio (1:3) constant. The body sizes of the experimental individuals were all within the range of the natural variation, as observed in the wild (Bonduriansky 2006). For all diets I used a "base" of 600ml of reverse osmosis water and 170g of coco peat (i.e. shavings from coco husks), mixed with protein (Nature's Way soy protein isolate, Pharm-a-Care, Warriewood, Australia) and carbohydrates (brown sugar, Coles brand, Bundaberg, Australia). The high-condition treatment was provided with the nutrient-rich ("rich") larval diet containing 32.8g of protein and 89g of carbohydrate per "base" and the low-condition treatment was provided with the nutrient-poor ("poor") larval diet containing 5.5g of protein and 14.8g of carbohydrates per "base". For rearing background individuals of intermediate size (i.e. "companion" or "tester" individuals), I used a nutrient-intermediate ("standard") larval diet that was containing of 10.9g of protein and 29.7g of carbohydrates per "base" (Sentinella et al. 2013; personal observations). Larval medium was thoroughly mixed with a hand-held blender until complete homogenisation and then frozen at -18°C until the day of use.

In **Paper IV**, the males and females of the second generation (F_2) were obtained from the eggs produced during the first reproductive assay (see below) of the parents (day 15) and were reared on standard larval medium, as described above (Fig 7D).

Adult housing and male competition (Papers III and IV)

Upon emergence of the flies, focal adult males and females were individually marked on the thorax with enamel paint (Model Master, Testor, Rockford, IL; Kawasaki et al. 2008) and then transferred to separate 400ml containers (Fig. 7B), where they were kept throughout their lives. The housing containers were covered with mesh stockings to allow ventilation, had moist coco peat at the bottom to provide water and a tube filled with a mixture of brown sugar and dried yeast to provide *ad libitum* access to food. Furthermore, focal individuals were provided with a small petri dish (35mm diameter) of oviposition medium (rich larval medium) as an additional source of adult food, and were housed together with a background companion individual of

the same sex. Throughout the experiment the position of all containers was changed every two days, to avoid possible spatial effects of variation in the laboratory environment (i.e. light intensity, ambient temperature).

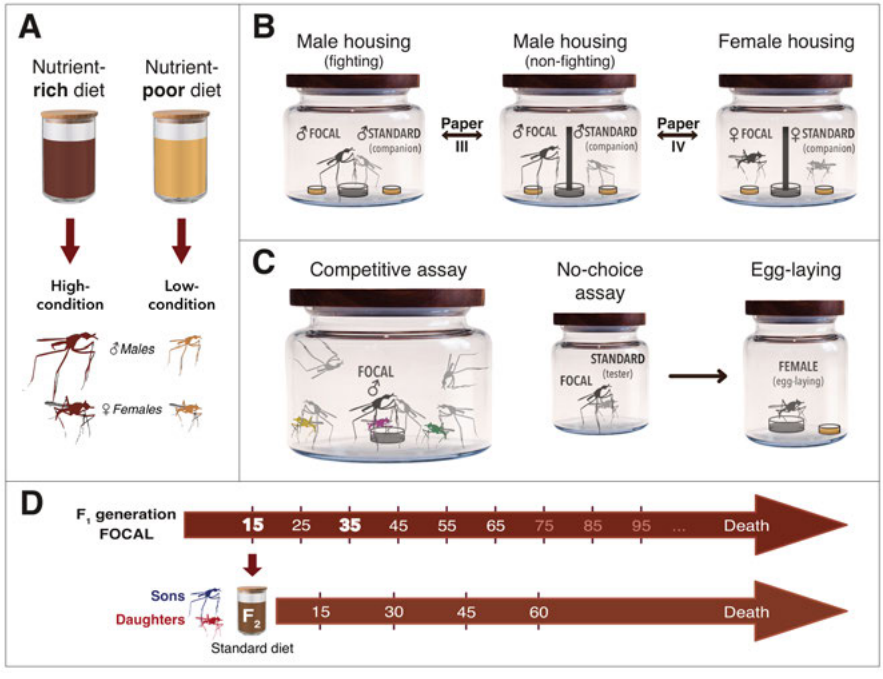

Figure 7. Experimental design in Papers III and IV. (A) Larval diet manipulation produced individuals of high- and low-condition. (B) Housing setup of focal individuals for Papers III and IV. Male "fighting" treatment in Paper III was lacking the black divider. (C) Male competitive assay with three females and five competitors and no-choice reproductive assay for both male and female focal individuals. After the no-choice reproductive assay, females were transferred to an egg laying container with an oviposition medium for 96h. (D) Timing of reproductive and competitive assay in the F_1 parental and F_2 offspring generation.

Competitive treatment (Paper III)

To manipulate male opportunity to engage in male-male contest behaviours in *T. angusticollis*, focal males were randomly allocated to one of two social treatments: fighting or non-fighting (Fig 7B). In the fighting treatment, focal males and the companion male were allowed to freely interact and engage in contests for control over the oviposition dish in the centre of the container. In the non-fighting treatment, a barrier of fly mesh with a solid black surface in the middle was placed in the centre of the housing container, splitting the

area and the oviposition site in two. This housing setup allowed each focal individual to receive overall visual and olfactory cues from the companion individual, without being able to engage in tactile interactions while defending its own oviposition site. Without the solid black divider in the middle of the oviposition dish, *T. angusticollis* males would engage in highly-energetic aggressive interactions to defend oviposition sites (i.e. their "territories). This design provided males in each social treatment with the same amount of space, food, and oviposition medium per male. As males in the non-fighting treatment could sense each other through the fly mesh, both visually and chemically, social cues across treatments were similar; the only difference between the two treatment groups was the opportunity to engage in physical contact, and incur mechanical damage and allocate energy to combat. If the companion individual died prior to the focal, it was replaced with a new background individual of similar age.

Males and Females (Paper IV)

The "non-fighting" males from **Paper III** (i.e. males in the housing with the barrier) were also used in **Paper IV**. Female flies were housed in containers with the same setup as the non-fighting males (Fig. 7B), allowing for visual and olfactory cues from the companion female, without being able to engage in physical interactions.

Second generation F_2 (Paper IV)

The focal flies of the second generation were obtained from the first reproductive performance assay (i.e. day 15) of the F_1 parental generation, when mothers and "non-fighting" fathers were "young". I randomly selected a male and a female from the day-15 emerging offspring and marked them on the thorax with a different colour paint than the F_1 parental individuals (Fig. 7D). The housing containers of the F_2 offspring generation were the same as described above for the females and the "non-fighting" males, and all sons and daughters were kept with a background companion of the same sex (Fig 7B).

Reproductive assays (Papers I, III, and IV)

Male reproductive assay – *C. remanei* (Paper I)

At the beginning of the assay, I isolated 10 focal males synchronized at the last larval stage from each of the 16 experimental populations. Age-specific fertility was measured every third day throughout male lifespan, from day one of adulthood (i.e. the next day of isolation) until death. Specifically, one focal male was paired for three hours with five virgin "tester" females (approximately two-days old) derived from SP8 populations. After three hours of mating, the focal male was removed, and the five females were transferred to a separate fresh plate and were left to lay eggs for three hours. The number of eggs produced by the five females within this three-hour egg-laying period was used as an estimation of the focal male's age-specific fertility. Each of the focal males was paired with one mature SP8 'holding' female in-between the assays to reduce males' mate-search behaviour (i.e. males wander around in search of females when kept alone and may die when stranded on the walls of the petri dish) and to standardize their mating status. These "holding" females were replaced after each assay to avoid mixing with progeny nematodes. All assays were performed on 60-mm Petri-dishes with standard medium and handling (Stiernagle 2006).

No choice reproductive assays – *T. angusticollis* (Paper III and IV)

To test the reproductive performance of all focal individuals at different ages, I paired them with a background tester individual of the opposite sex in a glass scintillation vial for one hour (Fig. 7C). During this hour, latency to first mating, number of matings that occurred during the hour and duration of each mating were recorded. In all assays the tester individuals were virgin and reproductively mature (15±1 days old). The first assay was done when the focal individuals reached maturation at day 15 and they were subsequently assayed repeatedly every 10 days until their death. At the end of the mating hour the females (i.e. focal females for the female reproductive assays and tester females for the male reproductive assays) were transferred to a 250ml container with ad libitum food and an oviposition petri dish (35mm diameter) for egg laying (Fig. 7C). The females were allowed to lay eggs for 96 hours and were provided with a fresh oviposition dish after the first 48h. Depending on the availability of eggs, 20 randomly selected eggs were transferred, either 48h or 96h after the reproductive assay, to an incubation container with 100g of standard larval medium. All available eggs were collected, when there were less than 20 eggs present on the oviposition dish. From the date of first adult emergence the flies were allowed to emerge for 10

days and then were euthanized by freezing. Incubation containers that did not contain any adult flies 10 days post adult emergence of the last container with the same egg transfer date, was scored as having zero emergence. After each reproductive performance assay, I also recorded the number of eggs laid in each oviposition dish (i.e. at 48h and at 96h) and the egg-to-adult viability (proportion of adults emerging) of the resulting offspring.

For the second generation (F_2) in **Paper IV**, I followed the exact same no-choice reproductive procedure, with the change that focal individuals were assayed every 15 days until day 60 (Fig. 7D).

Male-male competition (Paper III)

Competitive assays

As male flies frequently compete with other males for access to females (Fig. 5), male ability to achieve matings under the pressure of competition was investigated in **Paper III**. Male performance in competitive arenas was tested when males were 15 and 35 days old to gain a measure of performance at young and old ages for each individual.

Males were placed in an arena with five competitor males and an oviposition dish (Fig. 7C). Competitor males were derived from a stock founded by *T. angusticollis* individuals collected in Brisbane, Queensland (Cassidy et al. 2013), and were reared on a standard larval diet and housed in large population cages before and between assays. The Brisbane stock was preferred to facilitate paternity assignment (which was not undertaken as part of this study), since offspring from the Brisbane competitors would give different molecular signal that the focal individuals. To allow males to establish dominance hierarchies, all males were left in the competitive arena for at least 8 hours before any behavioural observations.

At the beginning of the competitive assay, three standard females (individually marked) were introduced into the arena, resulting in a high-competition environment for the focal male (Fig. 7C). Competitive arenas were then observed for one hour. The total number of matings that occurred were recorded, differentiating between mating attempts by the focal and the competitor males. All contest interactions involving the focal male were also noted. The definition used for a contest interaction was the physical encounter between two males that ended with a clear retreat by one male. These were further classified as either a full combat (which occurs when males lock together in a characteristic vertical contact posture and strike each other with their bodies, heads and forelegs; Fig. 5E), or a non-combat contest interaction (i.e. not involving vertical contact posture). Chasing behaviour,

measured as when there was a clear approach and retreat between two males without touching, was also recorded. Where possible, the initiator of the contest was recorded (i.e. focal individual or competitor) as well as which male retreated (i.e. "lost" the contest). As a measure of resource defence strategy, the contest location (i.e. on or next to the oviposition dish) was also noted. After the observational hour was completed, focal and competitor males were returned to their respective enclosures.

Male competitive interactions in housing containers

Before each "no-choice" reproductive assay at each age up until 45 days old (i.e. days 15, 25, 35, 45), male behaviours in the fighting social treatment were followed for 30 minutes and all contest interactions recorded. This was done, to determine the relative rates of contest behaviours experienced by high- and low-condition males in their housing containers.

Body size morphology (Papers III and IV)

The housing containers of the focal flies were checked every second day for survival, and after death, each focal individual was photographed with a Leica DFC digital camera mounted on a Leica MS5 stereomicroscope. From the photos thorax length, which is a reliable proxy of adult body size (Bonduriansky 2006), was measured, using the software ImageJ (Abràmoff et al. 2004).

3. Results and discussion

3.1 Condition-dependence and extrinsic mortality

Accelerated ageing and shorter lifespan is predicted to evolve under higher extrinsic mortality (Medawar 1952; Williams 1957; Abrams 1993; Williams et al. 2006). Furthermore, elevated extrinsic mortality should also drive the evolution of increased investment in early life reproduction (Williams 1957; Kirkwood 1977; Kirkwood and Rose 1991). However, when the extrinsic hazards are not affecting all individuals in a population equally, but depend on individual condition (i.e. low-condition individuals are less likely to survive), selection should favour more robust individuals with better condition and prolonged intrinsic lifespan (Abrams 2004; Williams et al. 2006; Maklakov 2013). Chen and Maklakov (2012) used an experimental evolution approach, to test this prediction and found that high levels of condition-dependent mortality, imposed by heat-shock, indeed resulted in the evolution of physiologically robust phenotypes with elevated resistance to heat stress (Chen and Maklakov 2013), longer lifespan in both sexes and increased female fecundity. The latter outcome was surprising, since it did not reveal the expected trade-off between reproduction and survival in females.

The aim of **Paper I**, was to investigate whether such trade-offs may instead be revealed in male *C. remanei*, by studying the reproductive success of males from the same experimental populations established by Chen and Maklakov (2012). The results highlighted that male age-specific reproduction did not evolve under differential rates of extrinsic mortality. There was no difference in male fertility between selection regimes of high and low rates of mortality (Fig. 8A). While, the disposable soma theory predicts that there should be an increased investment in early-life reproduction under high rates of extrinsic mortality, males of this experiment did not show such a pattern. However, the source of extrinsic mortality had a strong effect on male reproduction (Fig. 8). Males that evolved under condition dependent mortality had lower overall fitness (Fig. 8B) resulting from a reduced early-life fertility (Fig. 8A). In summary, increased condition-dependent mortality caused by heat-shock resulted in increased longevity (Chen and Maklakov 2012) and resistance to heat stress (Chen and Maklakov 2013) in both sexes, greater lifetime fecundity in females (Chen and Maklakov 2012) and a re-

duction in early fertility as well as individual fitness in males (Fig. 8). These results suggest that male reproductive performance trades-off directly with heat-shock resistance rather than longevity, because even low level of heat-shock resistance (i.e. low rate of condition-dependent mortality) that was not associated with increased longevity, resulted in a reduction of male fertility (Fig. 8B). These findings further highlight the key role of condition-dependence in extrinsic mortality that can shape not only the evolution of longevity and ageing, but also the evolution of sexual dimorphism in life history.

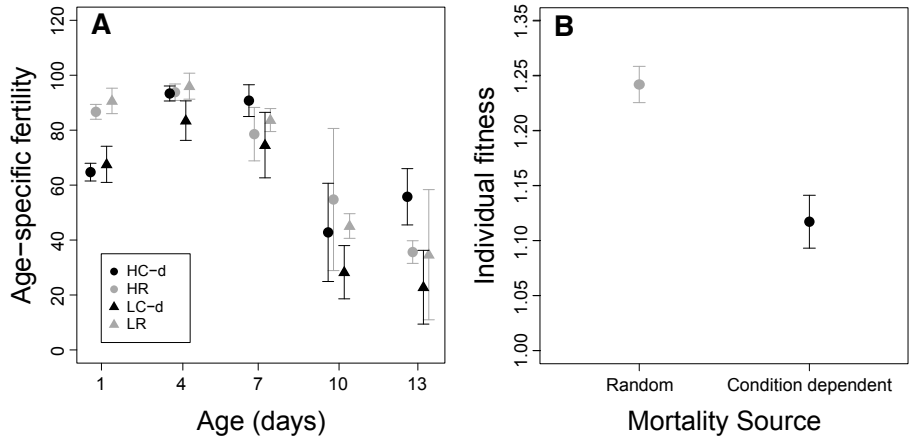

Figure 8. (A) Mean (± SE) age-specific fertility of males evolved under high (H – circles) or low rate (L – triangles) of mortality imposed by different mortality sources (Condition dependent: C-d – black; Random: R – grey). (B) Mean (± SE) individual fitness (λ_{ind}) of males evolved under condition dependent mortality (black) or random mortality (grey).

3.2 Condition-dependence in a natural population

Early-life environment can have substantial consequences on individual condition and thus life history strategies (Monaghan 2008). To maximise their fitness, individuals strategically allocate their limited resources not only between different fitness-enhancing traits but also between current and future trait expression (Stearns 1992). Diverse ageing patterns have been observed between and within species, yet the direction of these relationships among individuals of different condition remain unclear. In **Paper II**, I used data from a long-term study on a natural population of collared flycatchers (*Ficedula albicollis*) from the Swedish island of Gotland. The brood size at nest was manipulated across the breeding seasons from 1983 until 2009, by either adding or removing two offspring and thus creating either artificially increased (low-condition) or reduced (high-condition) broods. Individuals from nests with a reduced brood size experienced a "silver spoon", less stressful environment and grew to a larger body size at fledgling. This allowed me to directly test whether experimentally improved developmental conditions decelerate or increase reproductive and demographic ageing.

I found that females experiencing a low-competition natal environment (high-condition) fledge at higher body mass, start to reproduce at higher rate, have an earlier reproductive peak (Fig. 9) and lower acceleration of mortality rate (Fig. 10B) than their low-condition counterparts raised in high-competition nests. However, high-condition females also show earlier signs of reproductive senescence (Fig. 9) and suffer from increased mortality rate in the last years of their lives (Fig. 10B). These results demonstrate that "silver spoon" effects can increase female early-life performance at the cost of faster reproductive ageing and increased late-life mortality. To my knowledge, this is the first experimental demonstration of condition-dependent ageing in a natural population and supports the evolutionary theory of ageing.

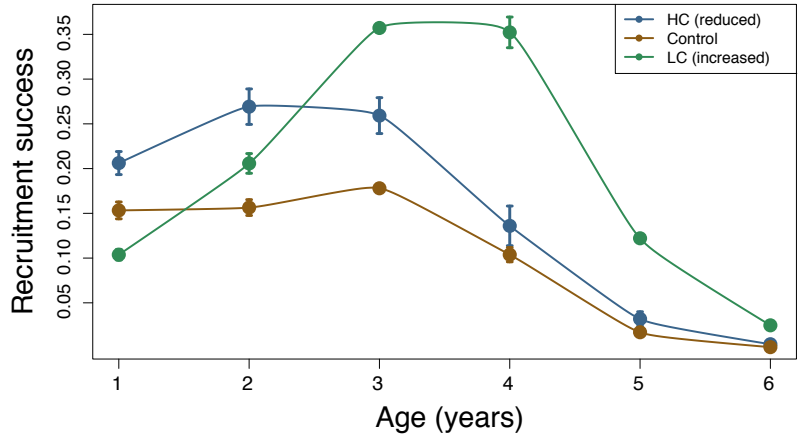

Figure 9. Age-specific reproduction of the three manipulated natal environments (means ± SE of model predictions). Green lines represent the low-condition (LC) treatment, yellow represent the control treatment and blue represent the high-condition (HC) treatment.

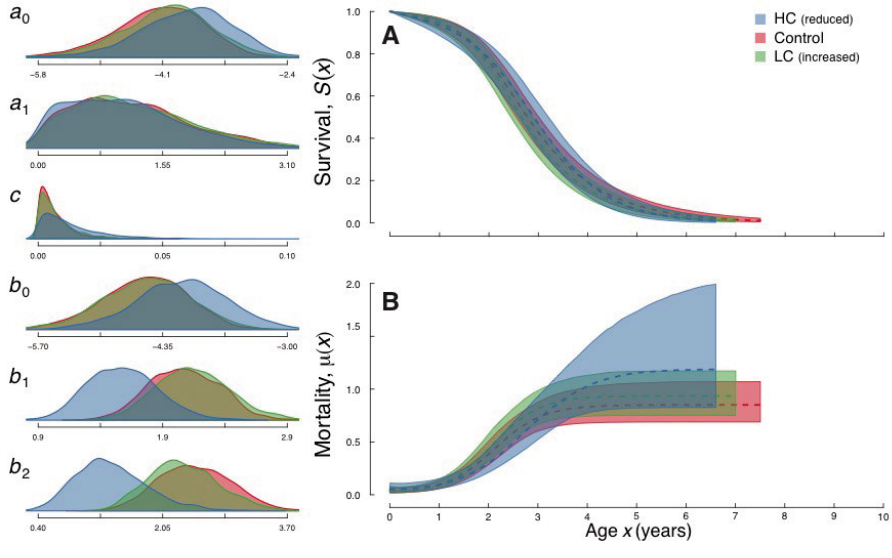

Figure 10. Survival (A) and Mortality (B) curves with 95% confidence intervals for each treatment as fitted by the bathtub Logistic mortality model. On the left are the posterior distributions of the six model parameters. Green lines and distributions represent the low-condition (LC) treatment, red represent the control treatment and blue represent the high-condition (HC) treatment.

3.3 Condition-dependence and male competition

Variation in resource allocation strategies can be particularly pronounced between the sexes. Males and females often follow diverse reproductive strategies and thus prioritize different traits when allocating resources (Adler and Bonduriansky 2014). Life history trade-offs may be especially pronounced in males, since increased condition is often associated with increased investment in secondary sexual traits, such as sexual displays and weapons (Mappes et al. 1996; Emlen 1997; Hunt et al. 2004; Judge et al. 2008). Yet, predicting the age-specific ageing patterns between individuals of different condition can be challenging, because increased resource allocation to the production and maintenance of sexually selected traits may be associated with high latent costs.

In **Paper III**, I used the neriid fly, *Telostylinus angusticollis*, to investigate how the costs of condition-dependent secondary sexual traits influence male ageing patterns. This species is characterized by pronounced developmental plasticity in response to nutrient concentration in larval diet, which results in much smaller individuals when reared in a nutrient-poor medium than when reared in higher nutrient concentration (Bonduriansky and Head 2007; Sentinella et al. 2013). Furthermore, females of this species oviposit their eggs in rotten tree bark and males often extensively defend territories in high quality oviposit locations. Larger males engage more often in battle and tend to be more successful in defending such territories. While body size is highly condition dependent, investments in condition-dependent morphological and behavioural traits are likely to impose costs and might potentially affect the rate of ageing. To test this hypothesis, I manipulated nutrient concentration during larval development to create males in different condition, simulated male-male contests environments and evaluated ageing patterns, in a full factorial design.

High-condition males developed more quickly and reached their reproductive peak earlier in life, but also experienced a faster decline in reproductive ageing and died earlier than low-condition males (Fig. 11). However, while interactions with rival males reduced male lifespan, this did not affect male reproductive ageing. High-condition in early life is therefore associated with rapid ageing in *T. angusticollis* males, even in the absence of damaging male–male interactions. These findings are in line with the situation in nature, where extrinsic mortality is high and early-life reproduction would, thus, substantially increase fitness.

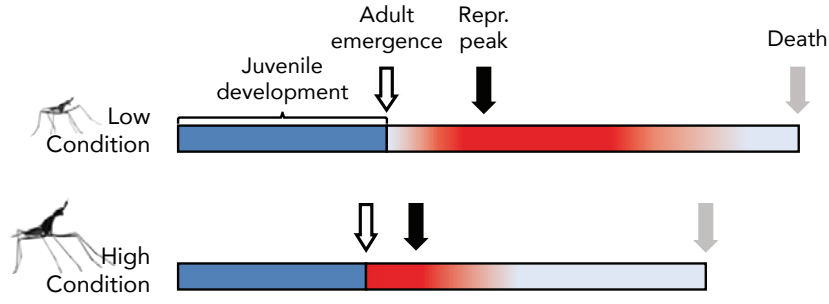

Figure 11. Ontogenetic timing of high- and low-condition males. High-condition males experience accelerated ontogeny but age faster and die sooner compared to low-condition males. The lengths of developmental and adult ontogenetic phases are based on observed means for low- and high-condition males. Although the precise positions of reproductive performance peaks cannot be determined from our data, the approximate relative portions of these peaks in high- and low-condition males are shown.

3.4 Condition-dependence in males, females and beyond

Early-life developmental environment can have persistent adaptive effects on individual life history and offspring phenotypic variation across multiple generations (Mousseau and Dingle 1991; Pál and Miklós 1999; Badyaev and Uller 2009; Bonduriansky et al. 2012; Head et al. 2016; Bonduriansky and Crean 2017). Maternal and paternal condition can strongly influence offspring phenotype via parental effects (Mousseau and Fox 1998; Marshall and Uller 2007; Champagne 2008; Crean and Bonduriansky 2014) and high-condition parents will be able to provide more resources to their offspring, via parental care or nongenetic inheritance factors (i.e. epigenetic, cytoplasmic or somatic). Yet, the direction of parental effects on reproductive and demographic ageing of offspring remains poorly understood. Parents can shape offspring phenotype, by either directly transferring their condition to their offspring ("condition-transfer effects" – Qvarnström and Price 2001; Bonduriansky and Crean 2017) or adjusting their parental investment based on environmental cues ("anticipatory effects" – Marshall and Uller 2007; Burgess and Marshall 2014).

In **Paper IV** I investigated how parental condition may affect reproductive and demographic senescence of parents and their offspring in the neriid

flies *Telostylinus angusticollis*, by manipulating the parental larval environment to create high- and low-condition parents. Larval diet contains proteins and carbohydrates that might differentially affect ageing rates of the two sexes. Indeed, sexes exhibit strong sexual dimorphism in size only on rich nutrient diet and it is possible that sexual dimorphism in ageing is also condition-dependent (Bonduriansky and Head 2007). My results showed that high-condition fathers developed faster but suffered from rapid reproductive (Fig. 12) and actuarial (Fig. 13) senescence (i.e. higher mortality rates). Their sons had a similarly fast reproductive decline (Fig. 14A), but were more long-lived (Fig. 15A) and had decreased mortality rates (Fig. 15B) than their low-condition equivalents. Daughters of high-condition fathers also had lower mortality rates (Fig. 15B) but their reproduction was unaffected (Fig. 14A). High-condition mothers developed faster and had better survival early in life, but lower late-life survival compared to low-condition mothers (Fig. 13). In sharp contrast to paternal effects, sons of high-condition mothers did not suffer from rapid reproductive ageing (Fig. 14B), but showed higher mortality in late-life (Fig. 16B), compared to sons of low-condition mothers. Remarkably, there were few effects of maternal diet on the age-specific life histories of the daughters (Fig. 14B, 16). These results do not fully support the hypothesis that parents transfer their own condition to their offspring, but instead suggest that parental diet interacts with parental sex and offspring sex to affect offspring life-histories. Thus, this study highlights that parental effects can play an important role in shaping inter-individual variation in reproductive and actuarial senescence.

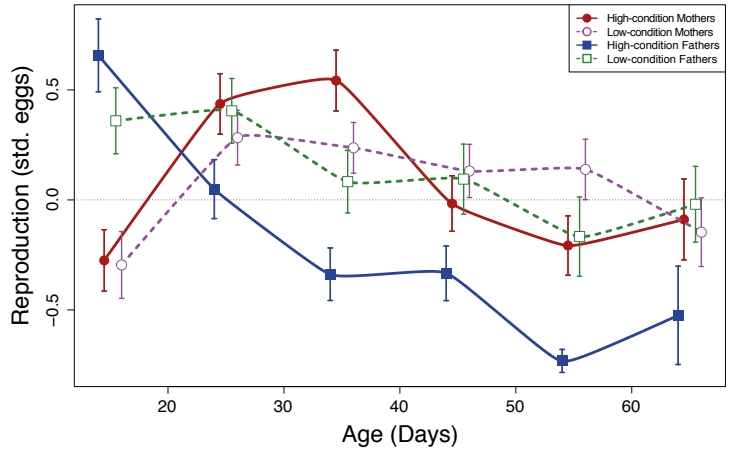

Figure 12. Age-specific reproduction (means ± SE) of high-condition (solid lines and filled symbols) and low-condition (dotted lines and empty symbols) parents (mothers: circles and fathers: squares). Blue lines represent the high-condition fathers, green represent the low-condition fathers, red represent the high-condition mothers and purple represent the low-condition mothers.

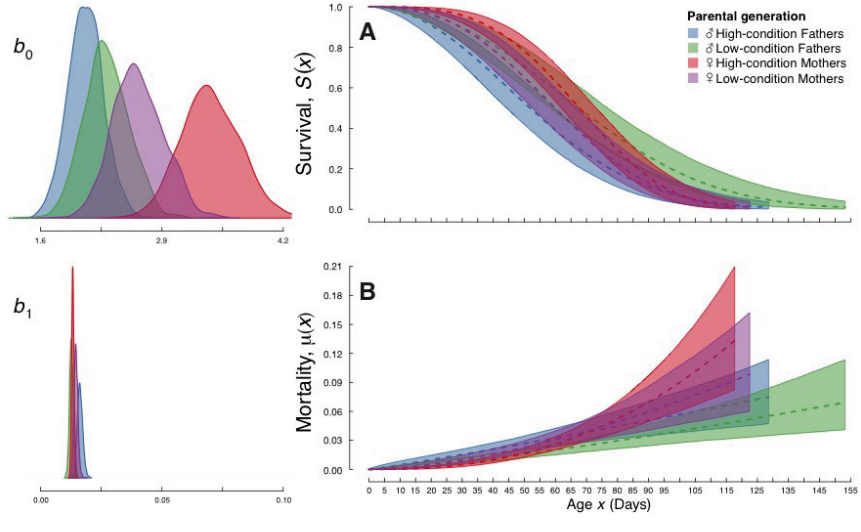

Figure 13. Survival (A) and Mortality (B) curves with 95% confidence intervals for each parental treatment as fitted by the simple Weibull mortality model. On the left are the posterior distributions of the two model parameters. Blue lines and distributions represent the high-condition fathers, green represent the low-condition fathers, red represent the high-condition mothers and purple represent the low-condition mothers.

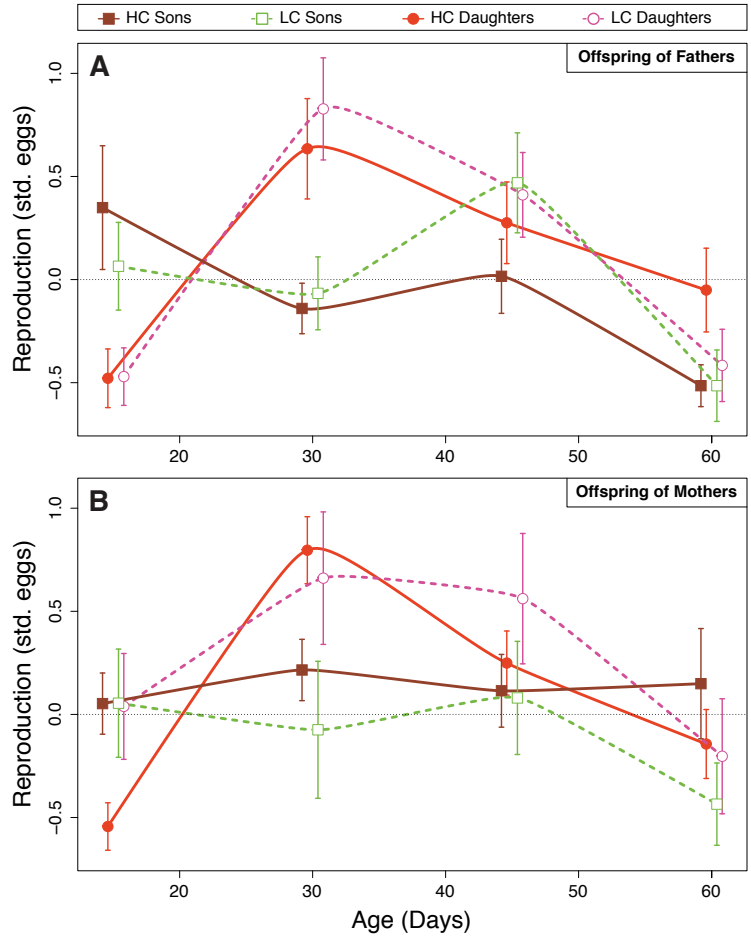

Figure 14. Age-specific reproduction (means ± SE) of the sons (squares) and daughters (circles) of high-condition (HC – solid lines and filled symbols) and low-condition (LC – dotted lines and empty symbols) fathers (A) and mothers (B). Brown lines represent the sons of high-condition parents, green represent the sons of low-condition parents, orange represent the daughters of high-condition parents and pink represent the daughters of low-condition parents.

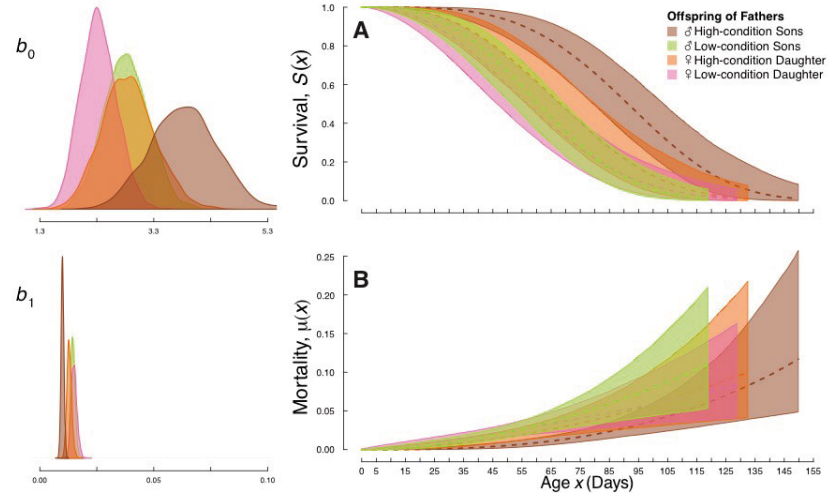

Figure 15. Survival (A) and Mortality (B) curves with 95% confidence intervals for sons and daughters of fathers as fitted by the simple Weibull mortality model. On the left are the posterior distributions of the two model parameters. Brown lines and distributions represent the sons of high-condition fathers, green represent the sons of low-condition fathers, orange represent the daughters of high-condition fathers and pink represent the daughters of low-condition fathers.

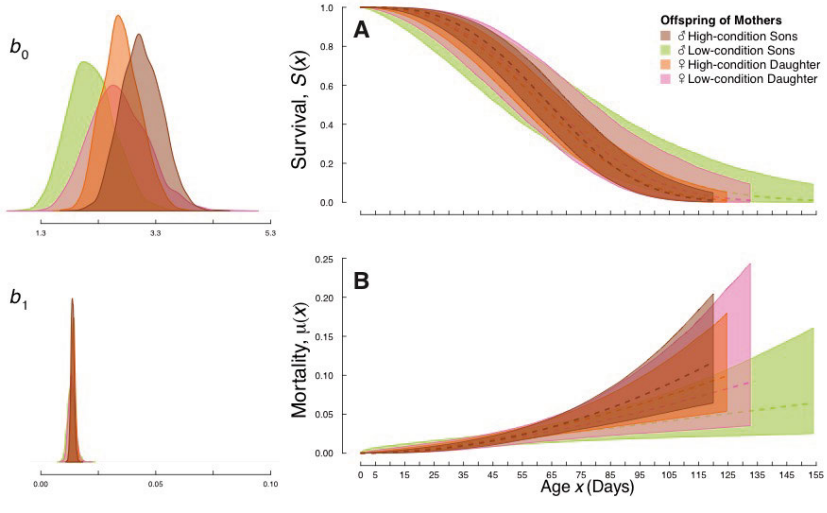

Figure 16. Survival (A) and Mortality (B) curves with 95% confidence intervals for sons and daughters of mothers as fitted by the simple Weibull mortality model. On the left are the posterior distributions of the two model parameters. Brown lines and distributions represent the sons of high-condition mothers, green represent the sons of low-condition mothers, orange represent the daughters of high-condition mothers and pink represent the daughters of low-condition mothers.

4. Conclusions

Ageing is a complex trait that is likely influenced by many factors. In this thesis I have explored the role of condition-dependence in the expression and evolution of ageing. My results show that variation in early-life developmental environment can determine individual condition and thus have profound consequences for the life history of individual organisms (**Papers II, III** and **IV**) and populations (**Papers I**). By mediating the resource allocation among traits and life stages, individual condition can extensively influence, over multiple generations (**Paper IV**), the current and future expression of life history traits and, ultimately, fitness (**Papers II, III** and **IV**). Furthermore, individual condition determines the probability of surviving an extrinsic environmental hazard, when such a hazard is only targeting low-condition individuals. Thus, variation in individual condition in a population combined with such condition-dependent environmental pressures can lead to the evolution of delayed ageing in nature (**Paper I**). Yet, sex differences in reproductive strategies and life history trade-offs can result in sex-specific responses to changes in individual condition and it is, therefore, crucial to include both sexes in the study of condition-dependence in life history evolution (**Papers I** and **IV**).

Sammanfattning på svenska

Åldrandet är ett utbrett biologiskt fenomen som spelar en viktig roll för att forma livshistorier hos olika organismer i livets träd. Åldrande kan definieras som den progressiva fysiologiska försämringen som uppträder med ökande ålder, vilket leder till en minskning av reproduktion och överlevnad. Trots åldrandets negativa effekter på en organism har åldringsprocessen inte eliminerats via det naturliga urvalet och forskare har fascinerats av åldringsprocessen alltsedan antiken. Till exempel argumenterade den stora grekiska filosofen Aristoteles att:

> ”*Anledningarna till att vissa djur är långlivade och andra kortlivade, och i ett ord, orsakerna till livets längd och korthet kräver efterforskning. [...] Vi finner att denna skillnad [dvs. att vara långlivad eller kortlivad], påverkar inte bara hela släkten jämförda som helheter med varandra, utan även kontrasterade grupper av individer inom samma art*”
>
> [Aristoteles, 350 f. Kr., egen översättning från G. Ross Engelska version]

Sedan antiken har många andra försökt att förklara den otroliga mångfalden av åldrandemönster, men det var inte förrän i slutet av 1800-talet som de första sammanhängande evolutionära teorierna om åldrande föreslogs av August Weismann (1891). Weismann föreslog att alla celler hos en organism kan separeras i könscellinjer och kroppscelllinjer (Weismann 1892, 1893). De celler som utgör kroppen kommer till slut att dö (vid organismens död), men deras huvudsakliga syfte genom livet är att hålla könscellerna i gott skick och medan kroppscellerna åldras är könscellerna på sätt och vis odödliga. Weismanns sammanhängande teori som förklarar varför åldrandet finns och hans forskning har styrt forskningen inom fältet i årtionden. Många evolutionära teorier har föreslagits och reviderats sedan dess. Haldane (1941) var den första som observerade att det naturliga urvalet är svagare vid senare livsstadier, eftersom det då finns färre individer i en population kvar som inte dött av externa faktorer, såsom predation, olyckor eller parasitism (”yttre dödlighet”). Därefter föreslog Medawar (1952) att åldrandet uppstår eftersom negativa mutationer som inte framträder förrän sent i livet inte kan elimineras effektivt av selektionen (mutationsackumulering teori). Williams

gav en alternativ förklaring och föreslog att åldrande har utvecklats på grund av förekomsten av gener som gynnas av det naturliga urvalet eftersom de har fördelaktiga effekter tidigt i livet, även om de också har skadliga effekter senare i livet (antagonistisk pleiotropi teori).

Williams (1957) centrala och mest testade hypotes (”Williamshypotesen”) säger att höga nivåer av yttre dödlighet bör leda till evolutionen av snabbt åldrande och därmed en kortare livslängd. I en miljö med hög dödlighet kommer färre individer i populationen att nå ålderdomen, jämfört med populationer från miljöer med låg dödlighet. Detta resulterar i en bredare "selektionsskugga" i slutet av livet, där selektionen eliminerar färre sent verkande skadliga gener. Om dessa populationer skulle studeras i en skyddad miljö (dvs. ett laboratorium), kommer populationer som tagits från naturliga miljöer med höga yttre mortalitetsnivåer att uppvisa en kortare livslängd än populationer som tagits från miljöer med låg yttre mortalitetsrisk. Även om det har finns väsentligt empiriskt stöd för denna hypotes, har ”Williamshypotesen” nyligen utmanats, med ett ökande antal vetenskapliga studier som rapporterar motstridiga mönster (dvs. att hög yttre dödlighet leder till lång livslängd). Dessutom föreslår nya teoretiska studier att Williams hypotes endast är giltig när yttre dödlighet drabbar alla medlemmar i en population slumpmässigt och i samma utsträckning. Vi vet emellertid att detta inte kan vara fallet eftersom individer kan variera i sin kondition (eller kvalité) och individer med låg kondition kan löpa större risk att dö än individer med hög kondition. Det naturliga urvalet kan gynna individer av hög kondition och därmed bidra till evolutionen av ett senare åldrande. För att överbrygga klyftan mellan teori och empiriskt stöd för detta begrepp utförde Chen och Maklakov (2012) en experimentell evolutionstudie på den tvåkönade nematodmasken *Caenorhabditis remanei*, där de manipulerade både dödlighetens frekvens (hög och låg dödlighet) och källa (slumpmässig och konditionsberoende dödlighet). Till stöd för den nya teorin utvecklade populationer under ökad konditionsberoende yttre dödlighet ett försenat åldrande, samtidigt som ett tidigare åldrande utvecklades i populationer med hög slumpmässig yttre dödlighet, i enlighet med Williams hypotes. Därför är konditionsberoende en viktig komponent som kan forma åldrandemönster och konditionsberoende dödlighet kan leda till evolutionen av en längre livslängd. Dessutom fann Chen och Maklakov (2012) också fördelar, eftersom honor från testpopulationerna som evolverat under hög konditionsberoende dödlighet producerade fler ägg. Ändå leder detta till frågan varför naturliga populationer inte utvecklar en längre livslängd och ökar reproduktionen (dvs. supernematoder), eftersom yttre dödlighet i naturen ofta är konditionsberoende? För att svara på den frågan fokuserade jag på livshistorieav-vägningar och könsskillnader. Som jag visar i **artikel I**, hade hanar som utvecklats under hög yttre konditionsberoende dödlighet längre livslängd, men drabbades också av minskad reproduktion tidigt i livet och totalt över livet. Detta tyder på att det hos hanar sker en kompromiss mellan kondition och reproduktion, och därför kan denna sexuellt antagonistiska

selektion upprätthålla genetisk variation för livslängd och kondition i denna population. Variation i kondition är en viktig populationskomponent som kan förutsäga övergripande åldrandemönster och individuell variation i kondition kan leda till betydande skillnader i fenotyp och fitness. "Kondition" har definierats som den totala mängden metaboliska resurser som finns tillgängliga för en individ och beror på både den genetiska kvaliteten hos individen (dvs. närvaron av "bra" gener som förbättrar fitness) och kvaliteten på individens miljö (dvs. resurstillgänglighet eller stressfaktorer). I synnerhet den tidiga livsmiljön kan få djupa konsekvenser för den individuella konditionen. Individer i en population kan uppleva olika stressfaktorer under sin utveckling, såsom ökad populationstäthet, temperaturavvikelser eller begränsad resurstillgänglighet. Dessa stressfaktorer kan orsaka skadliga fitnesseffekter genom att begränsa utvecklingen av en optimal fenotyp. Kvaliteten på utvecklingsmiljön i det tidiga livet kan således få betydande konsekvenser för senare livslängd. individer som är uppvuxna i högkvalitativa miljöer är ofta i ett bättre skick än individer som växer upp i en lågkvalitativ miljö och kommer därför att ha mer metaboliska resurser för att fördela till fitnessförbättrande egenskaper ("silverskedeffekten" – Grafen 1988). Samtidigt möter alla individer samma livshistorieavvägningar gällande resursallokering (på grund av den begränsade mängden resurser), individer av olika kondition kan därför anamma olika livshistoriestrategier för att maximera sin fitness. Till exempel kommer en ökning av investeringen av resurser i reproduktionen att minska de tillgängliga resurserna för underhåll av kroppen och kommer därför att påverka överlevnaden negativt. Samtidigt kommer inga av de begränsade resurserna som tilldelas reproduktionen, att finnas tillgängliga för underhålls- och reparationsmekanismer (Disposable soma-teorin - Kirkwood 1977). Därför måste varje individ, beroende på sin kondition, hitta den optimala investeringen av resurser i kroppsunderhåll för att maximera sin fitness. Individer fördelar inte bara om sina begränsade resurser mellan olika egenskaper som påverkar fitness, utan också mellan olika livsfaser (dvs. investeringar mellan nutida och framtida uttryck av en egenskap). Således är en viktig fråga som återstår, hur konditionen i slutändan kan påverka uttrycket av olika egenskaper med ökande ålder? Till exempel, kan individer med hög kondition antingen upprätthålla en hög reproduktion under hela livet (eftersom reproduktionen speglar konditionen) eller offra lång livstid för överinvestering i reproduktion tidigt i livet. För att belysa förhållandet mellan kondition och livshistoria manipulerade jag, i **artikel II, III** och **IV**, resurstillgängligheten i den tidiga livsmiljön, både indirekt, genom manipulering av kullstorleken (**artikel II**) och direkt genom manipuleringar av näringsinnehållet hos dieter under uppväxten (**artikel III** och **IV**). Sammantaget mätte jag hur känsligt uttrycket av olika livshistorieegenskaper var för förändringar i miljökvaliteten i tidiga livsstadier och jag undersökte framväxande avvägningar mellan egenskaper som beror på konditionen. I **artikel II**, undersökte jag de långsiktiga effekterna av miljön under det tidiga livet på reproduktion och överlevnad

hos honor i en naturlig population av halsbandsflugsnappare (*Ficedula albicollis*). Jag använde långsiktiga övervakningsdata som samlats in mellan 1983 och 2009 från Gotland i Östersjön. Avkommor fick växa upp i kullar som experimentellt hade antingen förstorats (låg kondition) eller förminskats (hög kondition). Jag fann att den reproduktiva framgången hos honor med låg kondition ökade i slutet av livet, då honorna med hög kondition redan hade en kraftig reproduktiv nedgång och drabbades av högre dödlighet. Mina resultat visar att "silverskedseffekter" kan öka honors tidiga produktivitet på bekostnad av snabbare reproduktivt åldrande och ökad dödlighet senare i livet. Dessa fynd stöder disposable soma-teorin om åldrande och föreslår att tidiga livsvillkor formar individens åldrande i naturen.

Jag undersökte sedan dessa effekter i en mer kontrollerad miljö, jag utförde laboratorieexperiment, som beskrivs i **artiklar III** och **IV**, med hjälp av neriidflugan *Telostylinus angusticollis*. Hanar av denna art ökar sin reproduktiva framgång när de investerar i sekundära sexuella egenskaper, som ornament, vapen och uppvisningsbeteenden. Sådana egenskaper är dock kostsamma att producera och underhålla, vilket resulterar i ett konditionsberoende uttryck. I **artikel III**, undersökte jag därför hur konditionsberoende investeringar i sekundära sexuella egenskaper påverkar hanars livshistoriestrategier och specifikt om det finns en kompromiss med investeringar i kroppens underhåll. Med hjälp av en fullständig faktoriell design manipulerade jag hanars tidiga livsförhållanden genom varierande näringsinnehåll i larvdieten och därefter manipulerade jag möjligheterna för vuxna hanar att interagera med rivaliserande hanar. Jag fann att hanar med hög kondition utvecklades snabbare och nådde sin reproduktiva topp tidigare i livet, men de upplevde också snabbare reproduktivt åldrande och dog snabbare än hanar av låg kondition. Däremot minskade interaktioner med rivaliserande hanar hanens egen livslängd men påverkade inte deras reproduktiva åldrande. Ökad tidig livskvalitet är därför associerad med snabbt åldrande hos hanar av *T. angusticollis*, även i avsaknad av skadliga han-han-interaktioner. Dessa resultat visar att rikliga resurser under ungdomsfasen används för att påskynda tillväxt och utveckling och förbättra reproduktiva prestationer tidigt i livet på bekostnad av prestation och överlevnad i slutet av livet, vilket visar en tydlig koppling mellan hanars kondition och åldrandet.

Effekten av utvecklingsmiljön under det tidiga livet kan ha ihållande effekter på den enskilda livshistorien och kan till och med bestå i flera generationer. Sådana transgenerationella föräldraeffekter är en del av icke-genetiskt arv, som kan definieras som effekterna på avkommans fenotyp som orsakas av överföring av faktorer som inte är DNA från föräldrarna. Föräldrar kan forma avkommans fenotyp, genom att antingen direkt överföra sin kondition till sina avkommor ("konditionsöverföringseffekter") eller genom att justera sina investeringar i avkomman utifrån miljömässiga signaler ("förväntade effekter"). I **artikel IV** undersökte jag dessa adaptiva föräldrastrategier, genom att manipulera miljön när föräldrarna själva var

larver (för att få föräldrar med hög och låg kondition) och testa hur det påverkade både reproduktivt och kroppsligt åldrande hos dem själva och deras avkommor. Jag fann att fäder som fått en diet av hög kvalité visade en snabb utveckling men drabbades av snabbt reproduktivt och kroppsligt åldrande, medan deras söner hade en liknande snabb reproduktiv nedgång utvecklades långsammare, var mer långlivade och hade långsammare kroppsligt åldrande än hanar som fått en diet av låg kvalité. Döttrar från hanar som fått en diet av hög kvalité hade också långsammare kroppsligt åldrande men deras reproduktion var opåverkad. Mödrar som fått en diet av hög kvalité utvecklades snabbare och hade bättre överlevnad i det tidiga livet men lägre överlevnad i slutet av livet jämfört med mödrar som fått en diet av låg kvalité. I skarp kontrast till effekter på faderssidan, utvecklades söner till mödrar som fått en diet av hög kvalité snabbare, drabbades inte av snabbt reproduktivt åldrande, men visade högre dödlighet senare i livet jämfört med söner från mödrar som fått en diet av låg kvalité. Anmärkningsvärt var att moderns diet hade liten effekt på döttrarnas åldersspecifika livshistorier. Dessa resultat stöder inte fullständigt hypotesen att föräldrar överför sin egen kondition till sina avkommor, men föreslår istället att föräldrarnas diet interagerar med både förälderns kön och avkommans kön för att påverka avkommans livshistoria. Föräldraeffekter kan spela en viktig roll för att forma mellan-individuell variation i reproduktivt och kroppsligt åldrande.

Sammantaget behandlar jag i denna avhandling konditionsberoende hos livshistorieegenskaper och deras effekter på åldrandemönster från olika perspektiv. Genom att kombinera olika studiesystem utnyttjar jag både laboratoriemodellorganismer (**artiklar I, III och IV**) och naturliga populationer (**artikel II**) för att ytterligare belysa vikten av konditionen för livshistorieavvägningar och i slutändan för evolutionen av åldrande (**artikel I**). Ett sådant holistiskt tillvägagångssätt behövs, eftersom tidigare studier har visat att experimentella resultat kan bero på huruvida organismer studeras i vilda eller under laboratoriebetingelser.

Översättning av/ translation by Elisabeth Bolund

Περίληψη στα ελληνικά

Η γήρανση είναι ένα ευρέως διαδεδομένο βιολογικό φαινόμενο, το οποίο διαδραματίζει σημαντικό ρόλο στη διαμόρφωση των χαρακτηριστικών του κύκλου ζωής σε όλους τους οργανισμούς. Μπορεί να οριστεί ως η προοδευτική φυσιολογική φθορά που εμφανίζεται με την ηλικία και οδηγεί στη μείωση της ικανότητας αναπαραγωγής και επιβίωσης. Παρά την αρνητική της επίδραση στους οργανισμούς, η γήρανση δεν έχει εξαλειφθεί από τη φυσική επιλογή ενώ αποτελεί αντικείμενο ενδιαφέροντος και μελέτης από την αρχαιότητα. Σύμφωνα με τον μεγάλο αρχαίο Έλληνα φιλόσοφο Αριστοτέλη:

> «Επί του παρόντος δε περί των ζώων εξηγήσαμεν την αιτίαν της μακροβιότητος και της ολιγοβιότητος αυτών. Υπολείπεται δε να εξετάσωμεν ακόμη περί νεότητος και γήρατος και περί ζωής και θανάτου. Και όταν ταύτα πραγματευθώμεν, θα λάβη τέλος η περί των ζώων μελέτη ημών».
>
> [Αριστοτέλης, Μικρά Φυσικά: Περί μακροβιότητος και βραχυβιότητος, 350 π.Χ. Μετάφραση Π. Γρατσιάτου]

Ενώ η αξιοθαύμαστη ποικιλία των προτύπων γήρανσης έχει αποτελέσει αντικείμενο μελέτης από την αρχαιότητα, η πρώτη συνεκτική εξελικτική θεωρία για το φαινόμενο αυτό διατυπώθηκε στο τέλος του 19ου αιώνα από τον August Weismann (1891). Σύμφωνα με τον τελευταίο, τα κύτταρα των οργανισμών διαιρούνται σε σωματικά και σε γεννητικά ("germ-plasm" theory – Weismann 1892, 1893). Τα σωματικά κύτταρα, τα οποία πεθαίνουν μαζί με τον οργανισμό, κατά τη διάρκεια της ζωής τους χρησιμεύουν στο να διατηρούν τα γεννητικά κύτταρα σε καλή κατάσταση και, ενώ τα πρώτα γερνούν, τα δεύτερα είναι κατά κάποιον τρόπο αθάνατα. Ο Weismann υπήρξε συνεπώς ο πρώτος ερευνητής που διατύπωσε μία συνεκτική θεωρία που εξηγεί γιατί η γήρανση έχει διατηρηθεί εξελικτικά και η έρευνά του αποτέλεσε για δεκαετίες το πρότυπο για αυτό το πεδίο έρευνας.

Η βασική πρόοδος στην έρευνα της γήρανσης έλαβε χώρα κατά την περίοδο 1940-1960. Αρχικά, ο Haldane (1941) παρατήρησε πως η φυσική επιλογή είναι ασθενέστερη κατά τα τελευταία στάδια της ζωής των

οργανισμών, καθώς υπάρχουν λιγότερα άτομα σε έναν πληθυσμό που έχουν καταφέρει να διαφύγουν τον θάνατο από εξωγενείς παράγοντες, όπως η θήρευση, τα ατυχήματα ή τα παράσιτα (εξωγενής θνησιμότητα). Ακολούθως, ο Medawar (1952) πρότεινε πως η γήρανση υφίσταται, επειδή η φυσική επιλογή δεν μπορεί να εξαλείψει ολοκληρωτικά τις επιβλαβείς μεταλλάξεις που εμφανίζονται στα τελευταία στάδια της ζωής (θεωρία της «συσσώρευσης μεταλλάξεων» – Mutation Accumulation theory). Ο Williams (1957) διατύπωσε μία εναλλακτική ερμηνεία, σύμφωνα με την οποία η γήρανση έχει εξελιχθεί και επικρατήσει λόγω της επιλογής των πλειοτροπικών γονιδίων, τα οποία, ενώ προσφέρουν ορισμένα πλεονεκτήματα κατά τα πρώτα στάδια της ζωής, ασκούν επιβλαβή δράση κατά τα τελευταία (θεωρία της «ανταγωνιστικής πλειοτροπίας» – Antagonistic Pleiotropy theory). Τόσο η συσσώρευση μεταλλάξεων όσο και η ανταγωνιστική πλειοτροπία θεωρούνται σήμερα οι κλασικές εξελικτικές θεωρίες της γήρανσης και περιγράφουν διεργασίες που θα μπορούσαν από κοινού να οδηγήσουν στην εξέλιξη της.

Ως προέκταση της θεωρίας της ανταγωνιστικής πλειοτροπίας του Williams (1957), προέκυψαν εννέα υποθέσεις, οι οποίες καθοδήγησαν την έρευνα πάνω στη γήρανση για τα χρόνια που ακολούθησαν. Σύμφωνα με την κεντρική και περισσότερο ελεγμένη υπόθεση (υπόθεση του Williams) τα υψηλά επίπεδα εξωγενούς θνησιμότητας προωθούν την ταχεία γήρανση και κατά συνέπεια τη μικρή διάρκεια ζωής. Τα άτομα ενός πληθυσμού που θα φτάσουν σε μεγάλη ηλικία θα είναι λιγότερα σε περιβάλλον με υψηλή θνησιμότητα απ' ό,τι σε περιβάλλον με χαμηλή. Αυτό θα οδηγήσει σε ευρύτερο παράθυρο «σκίασης επιλογής» αργά στη ζωή, όπου η φυσική επιλογή θα εξαλείφει λιγότερα βλαβερά γονίδια που δρουν σε μεγάλη ηλικία. Συνεπώς, υπό προστατευμένες συνθήκες (π.χ. στο εργαστήριο) οι πληθυσμοί που προέρχονται από περιβάλλον υψηλής θνησιμότητας αναμένεται να εμφανίσουν μικρότερη διάρκεια ζωής σε σύγκριση με όσους προέρχονται από περιβάλλοντα χαμηλής εξωγενούς θνησιμότητας. Παρά την επιβεβαίωση της παραπάνω υπόθεσης από πλήθος εμπειρικών δεδομένων, ένας αυξανόμενος αριθμός μελετών την αμφισβητούν παρουσιάζοντας τα αντίθετα αποτελέσματα (δηλ. η υψηλή εξωγενής θνησιμότητα οδηγεί σε μεγαλύτερη διάρκεια ζωής). Σύμφωνα με μία πρόσφατη θεωρητική προσέγγιση, η υπόθεση του Williams ισχύει μόνο όταν οι εξωγενείς παράγοντες θνησιμότητας επηρεάζουν εξίσου και με τυχαίο τρόπο όλα τα μέλη ενός πληθυσμού. Αυτό όμως δεν μπορεί να ισχύσει αφού τα άτομα ενός πληθυσμού διαφέρουν μεταξύ τους ως προς τη φυσική τους κατάσταση, με εκείνα που βρίσκονται σε κακή κατάσταση να έχουν περισσότερες πιθανότητες να πεθάνουν από όσα βρίσκονται σε καλή. Η φυσική επιλογή μπορεί συνεπώς να ευνοήσει τα τελευταία, προωθώντας έτσι την καθυστέρηση της γήρανσης. Για να καλύψουν το κενό μεταξύ της εμπειρικής και της θεωρητικής υποστήριξης της παραπάνω υπόθεσης, οι

Chen και Maklakov (2012) διεξήγαγαν μία πειραματική μελέτη σε πληθυσμούς του δίοικου νηματώδους *Caenorhabditis remanei*, ελέγχοντας ταυτόχρονα τον ρυθμό (υψηλό vs. χαμηλό) αλλά και την πηγή (τυχαία vs. εξαρτώμενη από τη φυσική κατάσταση) της θνησιμότητας που εφάρμοσαν σε αυτούς. Υποστηρίζοντας τις προβλέψεις της νέας θεωρίας, οι πληθυσμοί που βρίσκονταν υπό αυξημένη και εξαρτώμενη από τη φυσική κατάσταση θνησιμότητα εμφάνισαν καθυστερημένη γήρανση, ενώ ταυτόχρονα οι πληθυσμοί υπό υψηλή αλλά τυχαία εφαρμοσμένη εξωγενή θνησιμότητα εμφάνισαν ταχεία γήρανση σε συμφωνία με την υπόθεση του Williams.

Κατά συνέπεια, η φυσική κατάσταση παίζει σημαντικό ρόλο στη διαμόρφωση των εξελικτικών προτύπων της γήρανσης και μπορεί να οδηγήσει στην επιμήκυνση της διάρκειας ζωής των οργανισμών, μέσω της αλληλεπίδρασής της με τη θνησιμότητα. Επιπλέον, σύμφωνα με τη μελέτη των Chen και Maklakov (2012), η καλή φυσική κατάσταση ευνοεί την αναπαραγωγή, καθώς σε συνθήκες στις οποίες η θνησιμότητα δεν ήταν τυχαία αλλά εξαρτώμενη από αυτήν, τα θηλυκά σε καλή κατάσταση γεννούσαν περισσότερα αυγά. Τα αποτελέσματα αυτά εγείρουν το ερώτημα γιατί οι φυσικοί πληθυσμοί δεν εμφανίζουν εκτεταμένη διάρκεια ζωής και αυξημένη αναπαραγωγική ικανότητα («superworms») παρότι η εξωγενής θνησιμότητα εξαρτάται συνήθως από τη φυσική κατάσταση των διαφορετικών ατόμων. Για να απαντήσω στο παραπάνω ερώτημα, εστιάστηκα στις αντισταθμιστικές σχέσεις των κύκλων ζωής και στις φυλετικές διαφορές. Όπως φαίνεται στη **Κεφάλαιο Ι**, σε αντίθεση με τα θηλυκά (Chen και Maklakov 2012), τα αρσενικά που εξελίχθηκαν σε περιβάλλον με υψηλά επίπεδα θνησιμότητας, εξαρτημένης από τη φυσική τους κατάσταση, εμφάνισαν χαμηλότερο ρυθμό γήρανσης και ταυτόχρονα μειωμένη αναπαραγωγική ικανότητα τόσο στα πρώτα στάδια της ζωής τους όσο και αργότερα. Το αποτέλεσμα αυτό φανερώνει ότι η καλή κατάσταση και η μακρά διάρκεια ζωής αντισταθμίζονται από την αναπαραγωγική επιτυχία στα αρσενικά αλλά όχι στα θηλυκά, και υπογραμμίζει τη σημασία της φυλετικής ανταγωνιστικής επιλογής στη διατήρηση της γενετικής ποικιλότητας που σχετίζεται με τη διάρκεια ζωής και την αρμοστικότητα στον πληθυσμό αυτό.

Η ποικιλία της φυσικής κατάστασης μεταξύ των διαφορετικών ατόμων αποτελεί σημαντική πληθυσμιακή παράμετρο, η οποία μπορεί να οδηγήσει σε διαφορές ως προς τον φαινότυπο και την αρμοστικότητα, και κατ' επέκταση στα πρότυπα γήρανσης. Ως «φυσική κατάσταση» έχει ορισθεί η συνολική ποσότητα μεταβολικών πόρων που είναι διαθέσιμοι σε ένα άτομο και εξαρτάται τόσο από τη γενετική ποιότητα του ατόμου (δηλ., την παρουσία «καλών» γονιδίων που αυξάνουν την αρμοστικότητα) όσο και από την ποιότητα του περιβάλλοντος (δηλ., τη διαθεσιμότητα πόρων ή παραγόντων πίεσης). Το περιβάλλον κατά τα πρώτα στάδια της ζωής, ιδιαίτερα, μπορεί να έχει μεγάλες συνέπειες στη φυσική κατάσταση του

ατόμου. Τα άτομα ενός πληθυσμού μπορεί να βιώνουν διαφορετικούς παράγοντες πίεσης εξαιτίας της περιβαλλοντικής στοχαστικότητας, όπως αυξημένη πληθυσμιακή πυκνότητα, θερμοκρασιακές αποκλίσεις ή περιορισμένη διαθεσιμότητα πόρων. Οι παράγοντες πίεσης αυτοί μπορεί να έχουν επιβλαβείς συνέπειες στην αρμοστικότητα, περιορίζοντας την ανάπτυξη ενός βέλτιστου φαινοτύπου. Έτσι, η ποιότητα του περιβάλλοντος κατά τα πρώτα στάδια της ανάπτυξης μπορεί να καθορίσει τη φυσική κατάσταση του ατόμου.

Άτομα μεγαλωμένα σε περιβάλλον υψηλής ποιότητας κατά τα πρώτα στάδια της ζωής τους («φαινόμενο χρυσών κουταλιών» – "silver spoon effects", Grafen 1988) βρίσκονται συχνά σε καλύτερη φυσική κατάσταση από άτομα που μεγάλωσαν σε χαμηλής ποιότητας περιβάλλον και, ως εκ τούτου, μπορούν να επενδύσουν περισσότερους πόρους σε χαρακτηριστικά που αυξάνουν την αρμοστικότητα. Παρότι όλα τα άτομα αντιμετωπίζουν τις ίδιες αντισταθμιστικές σχέσεις στον κύκλο της ζωής τους όσον αφορά την επένδυση των πόρων (εξαιτίας των περιορισμένων ποσοτήτων τους), άτομα με διαφορετική φυσική κατάσταση μπορεί συνεπώς να υιοθετήσουν διαφορετική στρατηγική διαβίωσης ώστε να μεγιστοποιήσουν την αρμοστικότητά τους. Έτσι, η ατομική αρμοστικότητα εξαρτάται από τη σχετική διακύμανση στην πρόσκτηση (δηλ. τη συσσώρευση) και την επένδυση των πόρων. Για παράδειγμα, μια αύξηση στην επένδυση των πόρων στην αναπαραγωγή θα μειώσει εκείνη στη διατήρηση του σώματος και, συνεπώς, θα επηρεάσει αρνητικά την επιβίωση. Ταυτόχρονα, όποιοι από τους περιορισμένους πόρους επενδυθούν στην αναπαραγωγή δεν θα είναι διαθέσιμοι στους μηχανισμούς διατήρησης και επιδιόρθωσης (θεωρία του «αναλώσιμου σώματος» – Disposable Soma theory, Kirkwood 1977). Συνεπώς, ανάλογα με τη φυσική του κατάσταση, κάθε άτομο πρέπει να βρει ποια είναι η βέλτιστη επένδυση των πόρων στη διατήρηση του σώματος που θα μεγιστοποιήσει την αρμοστικότητά του.

Τα άτομα δεν αντισταθμίζουν μόνο τους περιορισμένους πόρους τους μεταξύ των διαφορετικών χαρακτηριστικών που βελτιώνουν την αρμοστικότητα αλλά και μεταξύ των διαφορετικών σταδίων της ζωής τους (δηλ., επένδυση στην έκφραση σημερινού ή μελλοντικού χαρακτηριστικού). Συνεπώς, παραμένει το μείζον ερώτημα πώς μπορεί εντέλει η φυσική κατάσταση να επηρεάσει την έκφραση χαρακτηριστικών όσο αυξάνεται η ηλικία; Για παράδειγμα, εστιάζοντας στη σχέση μεταξύ αναπαραγωγής και συντήρησης του σώματος, τα άτομα με πολύ καλή φυσική κατάσταση μπορούν είτε να διατηρήσουν υψηλή αναπαραγωγική απόδοση για όλη τη διάρκεια της ζωής τους (αφού ο αναπαραγωγικός ρυθμός θα αντανακλά τη φυσική κατάσταση) ή να θυσιάσουν τη μακροβιότητα υπέρ της υπερεπένδυσης στην πρώιμη αναπαραγωγή. Με σκοπό την περαιτέρω διερεύνηση της σχέσης μεταξύ φυσικής κατάστασης και κύκλου ζωής, στα **Κεφάλαια II, III και IV**, χειρίστηκα τη διαθεσιμότητα των πόρων σε

περιβάλλοντα κατά την πρώιμη ανάπτυξη τόσο έμμεσα, μέσω χειρισμού του μεγέθους γέννας (**Κεφάλαιο ΙΙ**) όσο και άμεσα, μέσω χειρισμών του θρεπτικού περιεχομένου της διατροφής (**Κεφάλαια ΙΙΙ και ΙV**). Συνολικά, μέτρησα την ευαισθησία της έκφρασης χαρακτηριστικών του κύκλου ζωής σε μεταβολές της ποιότητας του περιβάλλοντος κατά την πρώιμη ανάπτυξη και διερεύνησα τις αντισταθμιστικές σχέσεις μεταξύ των χαρακτηριστικών που εμφανίζονται εξαιτίας της εξάρτησης από τη φυσική κατάσταση.

Στο **Κεφάλαιο ΙΙ**, διερεύνησα τα μακροπρόθεσμα αποτελέσματα του περιβάλλοντος πρώιμης ανάπτυξης στην αναπαραγωγή και την επιβίωση θηλυκών ενός φυσικού πληθυσμού του κρικομυγοχάφτη (*Ficedula albicollis*). Χρησιμοποίησα δεδομένα πολύχρονων καταγραφών που συλλέχθηκαν μεταξύ 1983 και 2009 από το νησί Γκότλαντ της Σουηδίας στη Βαλτική. Οι νεοσσοί ανατράφηκαν πειραματικά σε τεχνητά αυξημένες (κακή φυσική κατάσταση) ή μειωμένες (καλή φυσική κατάσταση) γέννες. Βρήκα ότι η αναπαραγωγική επιτυχία των θηλυκών με κακή φυσική κατάσταση κορυφωνόταν σε προχωρημένο στάδιο της ζωής τους, όταν τα θηλυκά με καλή φυσική κατάσταση βρίσκονταν ήδη σε αναπαραγωγική μειωτική τάση και υφίσταντο υψηλότερη θνησιμότητα. Τα αποτελέσματά μου, δείχνουν ότι τα φαινόμενα «χρυσών κουταλιών» μπορούν να αυξήσουν την επίδοση των θηλυκών κατά τα πρώιμα στάδια της ζωής τους με κόστος την ταχύτερη αναπαραγωγική γήρανση και την αυξημένη θνησιμότητα σε προχωρημένη ηλικία. Τα ευρήματα αυτά στηρίζουν τη θεωρία του αναλώσιμου σώματος για τη γήρανση και υποδηλώνουν ότι οι συνθήκες κατά τα πρώτα στάδια ανάπτυξης διαμορφώνουν την ατομική γήρανση στη φύση.

Κατόπιν διερεύνησα το φαινόμενο αυτό σε περισσότερο ελεγχόμενο περιβάλλον, διεξάγοντας εργαστηριακά πειράματα, όπως περιγράφεται στα **Κεφάλαια ΙΙΙ και ΙV**, χρησιμοποιώντας το δίπτερο *Telostylinus angusticollis* (Neriidae) ως σύστημα μελέτης. Τα αρσενικά αυξάνουν την αναπαραγωγική τους επιτυχία όταν επενδύουν σε δευτερεύοντα φυλετικά χαρακτηριστικά, όπως οι διακοσμήσεις, τα όπλα και οι συμπεριφορές επίδειξης. Τα χαρακτηριστικά αυτά, όμως, έχουν μεγάλο κόστος παραγωγής και διατήρησης, με αποτέλεσμα η έκφρασή τους να εξαρτάται από τη φυσική κατάσταση. Στο **Κεφάλαιο ΙΙΙ** εξέτασα, συνεπώς, πώς επηρεάζονται οι στρατηγικές διαβίωσης των αρσενικών *T. angusticollis* (ιδίως η επένδυση στη διατήρηση του σώματος) από την εξαρτώμενη από τη φυσική κατάσταση επένδυση στα δευτερεύοντα φυλετικά χαρακτηριστικά. Χρησιμοποιώντας έναν πλήρως παραγοντικό σχεδιασμό, χειρίστηκα τη φυσική κατάσταση κατά την πρώιμη ανάπτυξη αρσενικών, μεταβάλλοντας το θρεπτικό περιεχόμενο της διατροφής των προνυμφών και, στη συνέχεια, τις ευκαιρίες των ενήλικων αρσενικών να αλληλοεπιδράσουν με αντίπαλα αρσενικά. Βρήκα ότι τα αρσενικά με πολύ καλή φυσική κατάσταση αναπτύχθηκαν ταχύτερα και έφθασαν στην αναπαραγωγική τους κορύφωση σε πιο πρώιμο στάδιο της ζωής τους αλλά, επίσης, υπέστησαν γρηγορότερη

αναπαραγωγική γήρανση και πέθαναν συντομότερα από τα αρσενικά με κακή φυσική κατάσταση. Αντιθέτως, οι αλληλεπιδράσεις με αντίπαλα αρσενικά μείωσαν τη διάρκεια ζωής των αρσενικών αλλά δεν επηρέασαν την αναπαραγωγική τους γήρανση. Η βελτιωμένη ποιότητα του περιβάλλοντος στα πρώτα στάδια της ζωής ως εκ τούτου σχετίζεται με την ταχύτατη γήρανση στα αρσενικά *T. angusticollis*, ακόμα και υπό την απουσία βλαπτικών αλληλεπιδράσεων μεταξύ αρσενικών. Τα αποτελέσματα αυτά δείχνουν ότι η αφθονία των πόρων κατά την ανήλικη περίοδο χρησιμοποιείται για την επίσπευση της αύξησης και της ανάπτυξης, και την ενίσχυση της πρώιμης αναπαραγωγικής επίδοσης εις βάρος της επίδοσης σε όψιμα στάδια της ζωής και της επιβίωσης, δείχνοντας σαφή σύνδεση μεταξύ της φυσικής κατάστασης και γήρανσης στα αρσενικά.

Το περιβάλλον κατά την πρώιμη ανάπτυξη μπορεί να έχει επίμονα προσαρμοστικά αποτελέσματα στον κύκλο ζωής του ατόμου που μπορεί ακόμα και να διαρκέσουν για αρκετές γενιές. Αυτές οι διαγενεακές γονικές επιδράσεις είναι συνιστώσες της μη γενετικής κληρονομικότητας, η οποία μπορεί να ορισθεί ως τα αποτελέσματα στον φαινότυπο των απογόνων που προκαλούνται από τη μεταβίβαση μέσω των γονέων μη-DNA παραγόντων. Τέτοιοι παράγοντες μπορεί να είναι επιγενετικοί (δηλ., η μεθυλίωση του DNA και οι τροποποιήσεις ιστονών), κυτταροπλασματικοί (δηλ., μικρά RNA και πρωτεΐνες) ή σωματικοί (δηλ., θρεπτικά και ορμόνες). Η γνώση των εγγύς μηχανισμών της μεταβίβασης, όμως, δεν είναι αναγκαία για την κατανόηση των προσαρμοστικών συνεπειών των μη γενετικών γονικών επιδράσεων. Οι γονείς μπορεί να διαμορφώσουν τον φαινότυπο των απογόνων είτε μεταδίδοντας άμεσα τη φυσική τους κατάσταση στους απογόνους τους («επιδράσεις μεταφοράς κατάστασης» – "condition-transfer effects") είτε ρυθμίζοντας τη γονική τους επένδυση στη βάση περιβαλλοντικών ερεθισμάτων («προβλεπτικές επιδράσεις» – "anticipatory effects"). Στο **Κεφάλαιο IV** διερεύνησα αυτές τις προσαρμοστικές γονικές στρατηγικές μέσα από τον χειρισμό του προνυμφικού περιβάλλοντος των γονέων (δημιουργώντας γονείς καλής και κακής κατάστασης) και ελέγχοντας το πώς αυτό επηρέασε την αναπαραγωγική και τη σωματική γήρανση αυτών και των απογόνων τους. Βρήκα ότι οι πατεράδες με πλούσια διατροφή επέδειξαν ταχεία ανάπτυξη αλλά υπέφεραν από ταχεία αναπαραγωγική και σωματική γήρανση, ενώ οι γιοί τους επέδειξαν παρόμοια γρήγορη αναπαραγωγική παρακμή αλλά αναπτύσσονταν βραδύτερα, ζούσαν περισσότερο και είχαν βραδύτερη σωματική γήρανση από τους αντίστοιχους φτωχής διατροφής. Οι κόρες των πλούσιας διατροφής πατεράδων επίσης είχαν βραδύτερη σωματική γήρανση αλλά η αναπαραγωγή τους δεν επηρεάστηκε. Οι μητέρες με πλούσια διατροφή αναπτύχθηκαν ταχύτερα και είχαν υψηλότερη επιβίωση στα πρώιμα στάδια αλλά χαμηλότερη επιβίωση σε μεταγενέστερα στάδια σε σύγκριση με τις μητέρες φτωχής διατροφής. Σε έντονη αντίθεση με τις πατρικές επιδράσεις,

οι γιοί των πλούσιας διατροφής μητέρων αναπτύχθηκαν ταχύτερα, δεν υπέφεραν από ταχεία αναπαραγωγική γήρανση αλλά επέδειξαν υψηλότερη θνησιμότητα στα μεταγενέστερα στάδια του κύκλου ζωής σε σύγκριση με τους γιους των μητέρων φτωχής διατροφής. Αξίζει να σημειωθεί ότι η μητρική διατροφή είχε ελάχιστη επίδραση στα ειδικά κατά ηλικία χαρακτηριστικά του κύκλου ζωής των θυγατέρων τους. Τα αποτελέσματα αυτά δεν υποστηρίζουν πλήρως την υπόθεση ότι οι γονείς μεταδίδουν τη δική τους φυσική κατάσταση στους απογόνους τους αλλά, αντιθέτως, υποδηλώνουν ότι η διατροφή των γονέων αλληλοεπιδρά με το φύλο των γονέων και των απογόνων, επηρεάζοντας τον κύκλο ζωής των τελευταίων. Οι γονικές επιδράσεις μπορεί να διαδραματίσουν σημαντικό ρόλο στη διαμόρφωση της ποικιλομορφίας στην αναπαραγωγική και τη σωματική γήρανση μεταξύ των ατόμων.

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Inga, many thanks for hosting me during these years! Living with you made me feel like I had a family away from home. And this was something that made it difficult to move out. I will always cherish our many conversations and I was always happy to discover that you were home and keen to have a chat about our daily lives. I am looking forward to spend more fika's together now this thesis is finally finished and I hope we can also watch that final episode of Bron! Also, I think it is time for our garden, don't you think? This year will be just wonderful! ☺

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που είμαι τώρα και σε ευχαριστώ πολύ. Ένα κομμάτι αυτού του διδακτορικού, σου ανήκει! ☺

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