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Key Terms

- ♦ Aging
- ♦ Breakday
- ♦ Evolutionary Theory of Aging
- ♦ Gompertz Equation
- ♦ Late-Life Mortality Rate
- ♦ Physiology

Late Life Physiology in *Drosophila melanogaster*

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Abstract

Aging has been commonly viewed as an inevitable and persistent process. Recently, however, age-specific mortality rates in a variety of organisms, including humans, have been found to decelerate or plateau at late adult ages, suggesting that aging may slow down or stop later in life. It is unknown what physiological changes occur in organisms when mortality rates plateau. In this study, six populations of *Drosophila melanogaster* were tested for physiological differences between early and late adulthood. The characteristics tested were desiccation resistance, time spent in motion, negative geotactic ability, and starvation resistance. All six populations of *D. melanogaster* displayed the same physiological changes during late life: both starvation and desiccation resistance declined at a significantly slower rate, time in motion plateaued, and negative geotaxis plummeted drastically. These results demonstrate that late life is physiologically different from early adult life, with some characteristics stabilizing, some declining at a slower rate and some declining at a faster rate in late life compared to early adult life. Furthermore, our results suggest that aging is not continuous throughout the lifespan. Understanding lifelong physiological trends in fruit flies will inevitably shed light on the intricate process of aging in humans, which is important as more people live to later ages now than ever before.

Faculty Mentor



That aging can stop is an amazing recent biological discovery, and we have been working on the explanation and meaning of this fact for the last 15 years. This paper summarizes the results of a study of the physiology underlying the cessation of aging led by my graduate student, Parvin Shahrestani, with the help of the massive “POLLA” team of undergraduates. The study has revealed the functional complexity of the cessation of aging in fruit flies. In people, aging stops at about 100 years of age, a landmark that the majority of Americans born in the twenty-first century may achieve. This makes the period after aging stops hugely important for their future.

Michael R. Rose

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Introduction

Before the 1990s, biologists and demographers widely agreed that cohort mortality rates increase exponentially with increasing age until death. Demographic aging was most commonly described by an age-specific mortality equation:

$$\mu(x) = Ae^{ax} \quad (1)$$

In this equation, known as the “Gompertz equation” (Gompertz, 1825), x is age, $\mu(x)$ is age-specific mortality rate, and the positive-valued parameters A and a are background mortality and aging rate, respectively. The values of A and a are estimated from observed mortality data in a population.

The prediction of exponentially increasing mortality rates offered by the Gompertz equation was generally accepted despite demographic studies in which human mortality rates were found to decelerate at later ages (Gavrilov and Gavrilova, 1991; Greenwood and Irwin, 1939). The deceleration of human mortality rates at advanced ages was dismissed for years as the result of advances in medical care, improved living standards of the elderly, and deaths due to war in early adulthood (Smith et al., 1999). In 1992, however, controlled laboratory experiments using medflies (Carey et al., 1992) and fruit flies (Curstinger et al., 1992) definitively showed that cohort mortality rates decelerate and sometimes plateau in late adulthood. Since then, studies using medflies, fruit flies, wasps, nematodes, and yeasts have corroborated the existence of mortality rate deceleration and mortality rate plateaus at late adult ages (Brooks et al., 1994; reviewed in Charlesworth and Partridge, 1997; Fukui et al., 1993; Rose et al., 2002; Tatar et al., 1993; Vaupel et al., 1998). The increasing evidence of mortality rate plateaus defies our preconceived notions of aging. Until now, aging has been defined as physical deterioration that persists until death (Rose et al., 2006). The fact that mortality rates of populations level off later in life introduces the possibility that organisms stop aging at a certain point in life.

Two main types of theory—lifelong heterogeneity theory and evolutionary theory—have been offered to explain the mortality rate plateaus. Lifelong heterogeneity theory is based on the assumption that some subcohorts within a population are more robust than others, either through genetic or environmental advantages (Carnes and Olshansky, 2001). Essentially, the theory assumes that these robust individuals possess lifelong advantages that

allow them to age at a slower rate. The more feeble subcohorts, on the other hand, die at younger ages and therefore become underrepresented at later ages. Consequently, the population's overall mortality rate appears to approach a plateau at late ages. Lifelong heterogeneity theory presumes that aging continues to increase exponentially until death for all individuals in a cohort, albeit occurring at different rates according to the robustness of each subcohort. The major criticism of this theory is that the robustness characteristic underlying lifelong heterogeneity is unspecified; studies attempting to identify the “true” robustness characteristic have failed to provide sufficient evidence for its existence (e.g. Drapeau et al., 2000; Khazaeli et al., 1995; reviewed in Rose et al., 2002).

Unlike the heterogeneity theory, which lacks strong experimental support, the evolutionary theory for late life continues to collect supporting evidence (reviewed in Shahrestani et al., 2009). The evolutionary theory for late life is based on the force of natural selection, which is the underlying cause of the observed mortality rate pattern in populations (Hamilton, 1966). Natural selection functions to prevent harmful alleles from being passed on to future generations (Rose, 1991). As a population reaches its first reproductive age, it is able to pass on harmful alleles to future generations; consequently, mortality rates increase as the population ages. When the population passes its last age of reproduction, natural selection no longer acts on the individuals in that population because they no longer have a chance of passing on their genes to the next generation. As a result, the force of natural selection plateaus at a value of zero after the last age of reproduction, which is theoretically expected to lead to a plateau in mortality rates at these same ages (Mueller and Rose, 1996; Rose and Mueller, 2000). Rose *et al.* have found that mortality rate plateaus evolve according to the last age of reproduction in the evolutionary history of *D. melanogaster* populations (2002). Overall, these experiments strongly indicate that natural selection is the underlying force of mortality patterns.

Mortality rates in adulthood are now modeled by two-stage Gompertz equations (as described in the methods below) that allow for a period in late adulthood, called “late life,” during which mortality rates stabilize. Evolutionary biologists consider aging and late life two separate phases of adult life. Using the two-stage Gompertz model, the age that separates aging and late life, called the breakday, can be estimated (Mueller and Rose, 1996). Demographic aging occurs during the aging phase of adulthood and stops in late life when mortality rates stop increasing. This suggests that individuals in cohorts may actually stop aging at advanced

ages in physiological terms. Biologists have for many years studied the physiology of the aging phase (e.g. Finch, 1990), and physiological function, such as resistance to stress for example, generally deteriorates gradually during aging (e.g. Minois and Le Bourg, 1999; Rose et al., 2004). What happens to physiology during late life is not yet understood. Investigating the physiology of late life is especially important now because humans are living much longer than in the past (Kirkwood, 2002); thus, more people are reaching late life. Furthermore, understanding the driving force behind aging could help us develop methods to combat the effects of aging.

In this study, we test whether physiology is different in late life compared to the aging period. Given the difference in mortality rates between aging and late life, we expect that the physiology of late life is different from the physiology of aging. This difference could follow one of two patterns: (a) in late life, changes in physiological characteristics may stabilize, much as mortality rates do; or (b) late life physiology may be more complex, such that physiological characteristics vary with respect to their continued deterioration, stabilization, or even partial recovery. For example, a particular phenotype might deteriorate with age during the aging phase and then improve during the late life phase. Alternatively, a physiological characteristic might continue to worsen with age even during the late life phase, perhaps deteriorating at a more rapid rate. It is then possible that the overall effects of physiological characteristics changing in opposite directions could partially balance, representative of an evolutionary trade-off pattern. We cannot differentiate between the likelihood of these possibilities because a study like ours has not been done before.

Materials and Methods

Study System

The laboratory fruit fly, *Drosophila melanogaster*, is an ideal organism for studies of aging and late life because of its short generation time and ease of maintenance. The genetics and physiology of *D. melanogaster* during the aging phase has been extensively studied, further adding to the value of this model organism. Moreover, fruit flies can provide information invaluable to further understanding of human physiology. For instance, fruit flies and humans have comparable genetics; approximately 75% of known human disease genes have been identified in the *D. melanogaster* genome (Reiter et al., 2001). Both human and fruit fly populations experience similar mortality rate plateaus in late life (Gavrilov and Gavrilova, 1991; Curtsinger 1992). Thus, understanding the mortality plateau phenomenon in

D. melanogaster should provide insight into human mortality trends.

Six *D. melanogaster* populations, known as the IV and B₁₋₅ populations, were used in this study. The IV population is an ancestral line established by Philip Ives in South Amherst, Massachusetts, in 1975 (Ives, 1975). From the IV population, Rose (1984) derived the five replicate baseline (B₁₋₅) populations. The IV and B₁₋₅ populations are maintained under identical conditions at 23–25 °C, 24-hour illumination, and 14-day generation cycles. The flies are fed with abundant banana-molasses medium at densities above 1,000 adults per generation.

Prior to the experimental assays, the six populations (IV and B₁₋₅) underwent two generations of controlled density rearing to eliminate any parental and grandparental effects on phenotype. At the start of each experiment, adult flies (fourteen days old from egg) from each replicate population were divided into thirteen population cages at densities of 300 males and 300 females per cage. A total of 46,800 flies were used in this experiment. Testing of the six populations was staggered in time such that the populations were tested at different times over twelve months due to the substantial amount of work this large-scale experiment required.

Estimating Age-Specific Mortality Rates and Mortality Breakdays

Four of the thirteen cages used for each replicate population were set aside and used to estimate age-specific mortality rates. The other nine cages for each replicate population were used as a source of flies for the physiological assays described below. The mortality cages were maintained in an identical environment to all other cages allowing for mortality estimates of each replicate population.

Mortality was recorded by removing dead flies from the mortality cages three times each week (Mondays, Wednesdays and Fridays) and recording the number of dead males and females. Using maximum-likelihood statistics, the observed mortality data was used to predict the breakday using a two-stage Gompertz equation as follows:

$$\text{For } x < d, \mu(x) = A_1 e^{ax} \quad (2)$$

$$\text{For } x > d, \mu(x) = A_2 \quad (3)$$

Age d marks the mortality breakday which separates adult life into the aging and late life phases. At ages x less than d , age-specific mortality rates are modeled by the continu-

ous time Gompertz equation and set equal to $A_1 e^{ax}$, where A_1 is the age-independent rate of mortality and a is the age-dependent rate of mortality. For ages greater than d , mortality rates are set to equal a constant value A_2 , which is independent of age but differs from A_1 . The two-stage Gompertz equation does not force a plateau onto the observed data because the estimated value of d can be arbitrarily large. If age-specific mortality does not plateau in a particular population, the estimated breakday will be at an age greater than the last age of survival, and the mortality rate will be modeled by the first part of the two-stage Gompertz, which is a traditional Gompertz model with exponentially increasing mortality rates.

Testing for Physiological Differences Between Aging and Late Life

Four physiological characteristics involved in *D. melanogaster* survival and fitness were tested three times each week (Tuesdays, Thursdays and Saturdays) throughout the entire adulthood of a population, which includes both the aging and late life phases. The physiological characteristics analyzed were time in motion, negative geotaxis, starvation resistance, and desiccation resistance. These characteristics have been well studied in the aging phase (Rose et al., 2004), but had not been previously studied in the late life phase.

Desiccation Resistance. Desiccation resistance was measured by the amount of time a fly survived in the absence of water and food. Sample flies were removed from the cages three times each week using light carbon dioxide anesthesia. Twenty-four males and twenty-four females from each population were tested for desiccation resistance three times each week during adulthood. Flies were placed in 8-dram vials—each vial contained four flies of the same sex. A sponge was used to create a barrier between the flies and 3.0g of desiccant. The vials were then sealed with two layers of parafilm to prevent outside moisture from entering the vial. The number of dead flies in each vial was recorded every hour until all flies were dead. The desiccation resistance data was analyzed using mixed linear regression models in R, a programming language used for statistical analysis (www.r-project.org).

Time in Motion. The time in motion assay determines the amount of time a fly spends in spontaneous motion. Twenty-four males and twenty-four females were removed from the cages using light carbon dioxide anesthesia. The flies were placed individually in 8-dram glass vials and were forced to the bottom 1 cm of the vial using a sponge. With a stopwatch, the fraction of a 2 min time interval in which the fly was moving was recorded. Each fly's time in motion

was measured twice by two different experimenters and the average of the two trials was used in the data analysis. Linear regression models in R were used to analyze the time in motion data.

Negative Geotaxis. Fruit flies naturally tend to fly upward against gravity, a trait known as negative geotaxis. The negative geotaxis assay tests for the escape response of the fly. The same twenty-four male and twenty-four female flies at each age that were used for the time in motion assays were used for the geotaxis assays. These flies were already in 8-dram glass vials following the time in motion assay. The sponge keeping them at the bottom 1 cm of the vial was moved up the vial to allow 8 cm of vertical space. The vials were tapped onto the bench top to make the flies fall to the bottom of the vials. The flies were then given 1 min to move up to the 8 cm mark. The number of flies that made it to the top of the vial was recorded and analyzed using mixed linear regression models in R.

Starvation Resistance. The starvation resistance assay determines the amount of time a fly can survive in the absence of food. The same twenty-four males and twenty-four females that were used in both the time in motion and negative geotaxis assays were used for the starvation resistance assays. Since the starvation resistance assay requires the flies to die in order to record how long they can survive in the absence of food, it was performed after the negative geotaxis and time in motion assays. A cotton ball moistened by 5 mL of distilled water was placed above the sponge that enclosed the flies inside each vial. The vials were then sealed with two layers of parafilm to keep the moisture inside the vial in order to prevent death from desiccation. The number of dead flies was recorded every four hours until all the flies were dead. The starvation resistance data was analyzed using mixed linear regression models in R.

Results

Age-specific mortality rates of males and females were similar, and therefore combined in the analyses. Mortality breakdays for each of the six replicate populations (Table 1) were calculated using the two-stage Gompertz equation described above (Equations 2 and 3). The mortality breakdays divide adult life into the aging and late life phases, allowing for a comparison of physiology between these phases. Because the mortality data of the populations was combined, the data between the first and last breakday among the six populations was excluded from the analysis to allow for a clear division of adult life into the aging and late life phases (Figure 1). Ages before the first mortality

breakday among the six populations are considered to be part of the aging phase; ages after the last breakday are considered to be the late life phase.

Table 1

The breakday, the age which separates the aging and late life phase, for each population as estimated by the parameter d from the two-stage Gompertz equations (Equations 2 and 3).

Population	B ₁	B ₂	B ₃	B ₄	B ₅	IV
Breakday	30.02	37.92	40.98	38.03	35.32	31.79

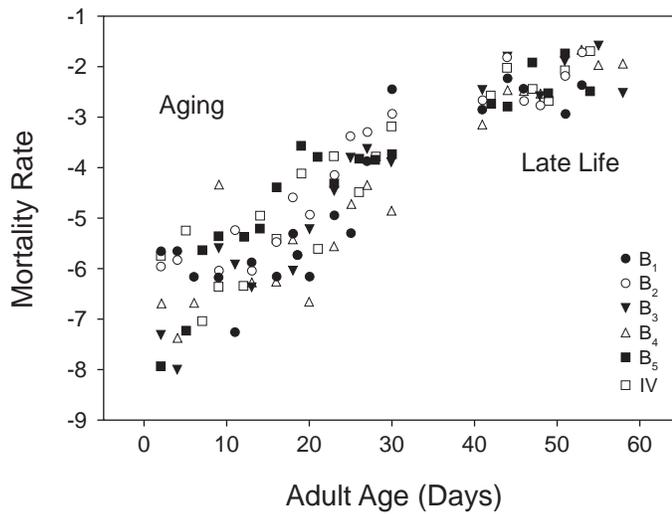


Figure 1

The natural log of age-specific mortality rates were plotted against adult age. Mortality was recorded on 2,400 flies per population (half male and half female). The mortality data between age 30 and age 40 has been eliminated from the graph. Ages before the first breakday in the six populations (before age 30) are considered the aging phase, and ages after the last breakday in the six populations (after age 40) are considered the late life phase.

Desiccation Resistance. Females of all populations and at all ages were more resistant to desiccation stress than males (data not shown). However, males and females showed similar trends of change in desiccation resistance with age. Therefore, the male and female data was combined for the statistical analyses. To combine the data from males and females, the highest value of desiccation resistance in each sex was set equal to one and all other data points were transformed according to the highest value.

Mean desiccation resistance was lower in late life compared to aging ($p < 0.001$) reflecting the overall decline in desiccation resistance with increasing age (Figure 2). More importantly, the slope of decline in desiccation resistance decelerated in late life as compared to aging ($p < 0.001$). In other

words, desiccation resistance in late life did not deteriorate as quickly with age as it did during the aging phase.

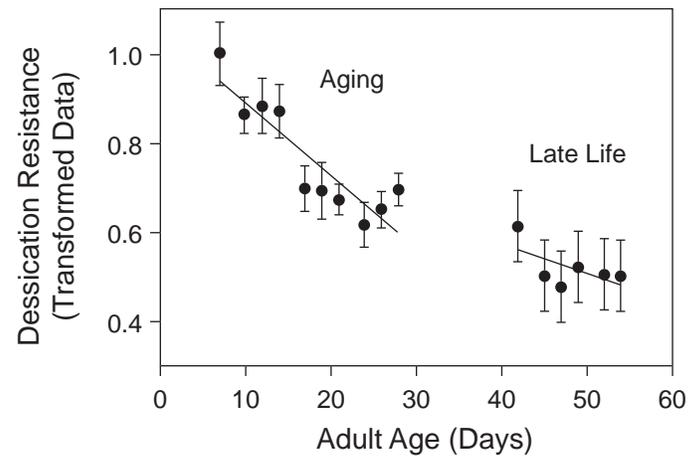


Figure 2

Resistance to desiccation stress measured in hours is transformed such that the highest desiccation resistance is set equal to 1 and all other values are a fraction of 1. Each point represents the average data from all flies (male and female) from all populations (B1–5 and IV) tested at that age. The error bars are standard error of the mean between the six populations. Before age 30, the data points are in the aging phase, after age 40, the points represent late life phase. Desiccation resistance deteriorates at a faster rate during aging compared to late life.

Starvation Resistance. Similar to the results of the desiccation resistance assay, females of all populations and at all ages

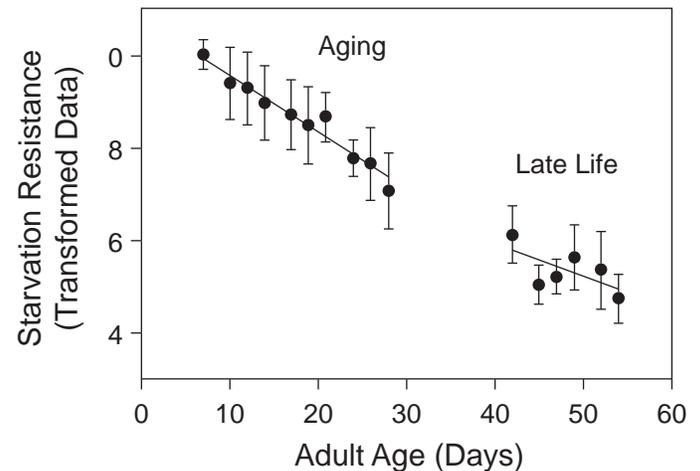


Figure 3

Resistance to starvation stress measured in hours was transformed such that the highest starvation resistance value was set equal to 1 and all other values are a fraction of 1. Each point represents the average data from all flies (male and female) from all populations (B1–5 and IV) tested at that age. The error bars are standard error of the mean between the six populations. Before age 30, the data points are in the aging phase, after age 40, the points represent late life phase. Starvation resistance deteriorates at a significantly slower rate in late life compared to the decline in aging.

were more resistant to starvation stress than males (data not shown). However, because males and females showed similar trends in the change of starvation resistance with age, the data for the sexes was combined in the analyses by first transforming the data as explained above for desiccation resistance. Mean starvation resistance in late life was lower than mean starvation resistance in aging ($p < 0.001$) reflecting the overall decline in starvation resistance with increasing age (Figure 3). Notably, starvation resistance declined at a slower rate in late life compared to aging ($p < 0.001$).

Time in Motion. Males and females had similar time in motion values and trends (data not shown) and were therefore analyzed jointly without any transformation of data. The mean time in motion value in late life was lower than the mean time in motion value in aging ($p < 0.001$) reflecting the overall deterioration of this characteristic with age (Figure 4). However, while time spent in motion decreased with age in the aging phase, it stopped decreasing in the late life phase ($p < 0.001$). 95% confidence intervals of time in motion in late life showed that the slope was not different from zero.

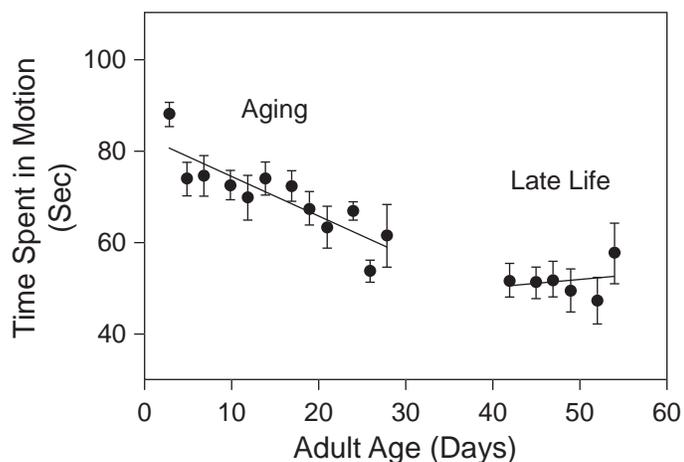


Figure 4

Time spent in motion in a two minute time interval, measured in seconds, is plotted against adult age. Each point represents the average data from all flies (male and female) from all populations (B1-5 and IV) tested at that age. The error bars are standard error of the mean between the six populations. Before age 30, the data points are in the aging phase, after age 40, the points represent late life phase. Time spent in motion declines during the aging phase, but plateaus in the late life phase.

Negative Geotaxis. Male and female negative geotaxis data were combined without any data transformations because the data for males and females was similar (data not shown). Although the negative geotaxis characteristic declined overall with age as indicated by mean differences between late life and aging for this characteristic ($p < 0.001$), this decline

was almost entirely in the late life phase (Figure 5). The negative geotactic ability declined very slowly during aging, but then declined rapidly in late life ($p < 0.001$ for difference in slope between aging and late life).

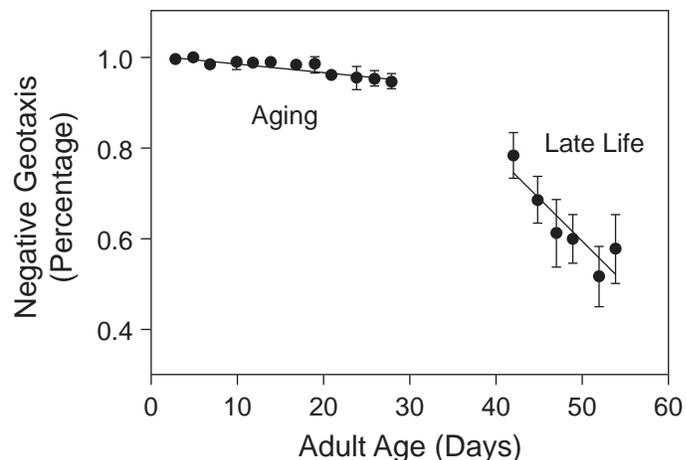


Figure 5

Negative geotactic ability, measured as the percentage of flies that made it to the top of an 8-cm glass vial in one minute, is plotted against adult age. Each point represents the average data from all flies (male and female) from all populations (B1-5 and IV) tested at that age. The error bars are standard error of the mean between the six populations. Before age 30, the data points are in the aging phase, after age 40, the points represent late life phase. Negative geotactic ability declined more rapidly in the late life phase compared to the aging phase.

Discussion

Experiments done on wasps, yeasts, nematodes, medflies, and fruit flies have shown that age-specific mortality rates decelerate or plateau at very late ages (Brooks et al., 1994; reviewed in Charlesworth and Partridge, 1997; Fukui et al., 1993; Gavrilov and Gavrilova, 1991; Greenwood and Irwin, 1939; Vaupel et al., 1998). Therefore, we expected age-specific mortality rates to plateau in the six *D. melanogaster* populations used in this study. As predicted, all six populations followed the pattern of mortality described by the two-stage Gompertz equation (Equations 2 and 3) such that mortality rates exponentially increased with age in early adulthood and then stabilized in late life (Figure 1). Mortality data from males and females was combined in all of the analyses.

The age that marks the start of the mortality rate plateau, known as breakday, was estimated separately for each of the six populations (Table 1). The breakdays occurred at different ages in the six populations, which could be because the six replicate populations have been maintained in genetic isolation of each other since 1980, and may have

diverged in some respects as a result of random genetic drift. Additionally, the six populations were tested at different times of the year and any variations in the laboratory environment may have played a role in their age-specific mortality patterns.

Our general finding was that physiology is different in the two phases of adulthood. In late life, some physiological characteristics declined at a slower rate, some stopped declining, and some declined at a faster rate compared to aging. For example, desiccation resistance declined at a slower rate in late life compared to aging (Figure 2). Female resistance to desiccation stress was greater than that of males because female *D. melanogaster* are larger than males and, therefore, have the ability to store more water (Ashburner, 1989; Dukas, 2005). Despite the difference between females and males in absolute resistance to desiccation, the pattern of change in desiccation resistance during aging and late life was the same for both sexes.

The decline in desiccation resistance with age during the aging phase corroborates the findings of studies that show that water loss rates increase with age in *D. melanogaster* (Fairbanks and Burch, 1970) and that longer-lived populations of flies have lower rates of water loss than shorter-lived flies (Nghiem et al., 2000). These findings suggest that loss of resistance to desiccation stress is involved in the aging process. Interestingly, in late life, there was a decrease in the deterioration of desiccation resistance with age, meaning that very old adult flies do not deteriorate as quickly as younger adult flies with regards to this characteristic.

The results for the starvation resistance assay were similar to those of the desiccation resistance assay in that the deterioration in starvation resistance slowed down in the late life phase compared to the aging phase. The larger body size of females and their ability to store more lipids led to higher resistance to starvation stress compared to males (Wang et al., 2005; Wigglesworth, 1949). Despite the differences between males and females in terms of absolute resistance to starvation, the pattern of change in starvation resistance with age was similar in both sexes.

We found that starvation resistance declined with age during the aging phase; this result corroborates the work of Drapeau *et al.* (2000) among others (*e.g.* Minois and Le Bourg, 1999). Fat reserves of *D. melanogaster* have been shown to decrease with age in studies of aging (Baldal et al., 2006), which explains the deterioration of the starvation resistance characteristic with age during the aging phase. In

late life, starvation resistance does not decline as much with age as it does during aging.

Time spent in motion, which is a measure of muscle activity in flies, is known to decline with age during the aging phase (Le Bourg, 1987; Service, 1987). It is expected that a fly's level of activity decreases with age due to deterioration of various organ systems (Minois and Le Bourg, 1999). For instance, cardiac functions have been observed to diminish as a fly ages, decreasing the fly's ability of prolonged movement (Paternostro et al., 2001). Interestingly, age-specific decline in time spent in motion stopped in late life (Figure 4). During late life, time in motion stabilized and showed no decline with increasing age. This result suggests that the physiological deterioration associated with aging does not continue throughout all of adulthood; instead, for some characteristics, physiological deterioration stops in late life.

The negative geotaxis assays offered yet another unforeseen finding. In the case of negative geotaxis, age-specific deterioration occurred more rapidly in late life than in aging. Negative geotactic ability decreased only slightly during the aging phase, but after the transition to the late life phase this ability declined very quickly (Figure 5). This finding suggests that there are physiological characteristics that decline more rapidly during the period when mortality rates have plateaued compared to the period when mortality rates are increasing exponentially. Interestingly, the time in motion data obtained in this experiment demonstrated that the flies' ability to move did not deteriorate during the late life phase (Figure 4). Thus, age-related decline of movement cannot be attributed to the rapid degeneration of negative geotactic ability. Further experimentation would be needed to determine the underlying cause of the plummet in negative geotaxis observed in late life.

Comparisons between aging and late life for the four physiological characteristics tested show that aging and late life are different in terms of age-specific changes in physiology. Late life physiology appears to be complex in that some physiological characteristics decline at a slower rate in late life, some stop declining altogether, and some decline at a faster rate in late life compared to aging. An important corollary of this result is that the process of aging, as defined by physical deterioration, does not continue throughout the entire lifespan. This finding is in agreement with evolutionary theory of late-life mortality plateaus because it shows that aging and late life are distinct phases of adulthood.

Most previous studies of adulthood have focused only on the aging phase (*e.g.* Fiskin et al., 1994). Given that adult-

hood is composed of more than just an aging phase, a complete understanding of adult life requires studying the late life phase. Our study is the first large-scale replicated study of late life physiology. Our finding that physiology changes in late life has profound implications for future studies in the field of aging because it creates the possibility and necessity for studying the late life phase in greater detail. A better understanding of the complex physiology of late life could help improve quality of life for the elderly.

Author Profiles

Keila Benjamin

During her sophomore year at UCI, Keila Benjamin decided that she wanted to add hands-on experience to her education. She joined in the Rose Lab, and became involved in learning about the physiological aspects of aging and late life. She credits her research experience with helping her develop leadership skill that she'll be able to apply throughout the rest of her education and career. Keila is planning to attend medical school as her next step on the road to practicing medicine.

Ana Garcia

Ana Garcia has had a life-long desire to become a research pharmacist. In pursuing that goal, she found the Rose lab to be a perfect balance between a learning and leadership experience. In the lab, Ana was able to work under the supervision of graduate students while overseeing the work of a number of undergraduates. This experience confirmed her passion for research. Ana is working in a retail/compounding pharmacy exploring the field she loves, applying the etiquette she learned while conducting research: attention, dedication, and persistence.

Heena Kapoor

When Heena Kapoor was looking for an area of research, she was intrigued by the work being done in the Rose lab. Through her two years in the lab, Heena was not only able to do her own work, she also developed her leadership skills by overseeing a team of 25 undergraduate researchers. Heena plans to go to medical school and hopes to become a pediatrician.

Rebecca Post

When she learned of an opportunity to work in Dr. Rose's lab, Rebecca Post seized it eagerly. As a premedical student, she was particularly interested in the research into late life and aging, realizing that a better understanding of the aging process would be a great benefit in her treatment of future patients. Throughout her research process, Rebecca was able

to learn about the research process, manage a project, and lead a team of undergraduate researchers. Rebecca hopes to move on to medical school, specializing in Neurology or Oncology.

Acknowledgments

We would like to thank our mentors, Dr. Michael R. Rose and Parvin Shahrestani, for their continuing support and guidance, and Dr. Laurence Mueller for his invaluable input. Many thanks also go to the undergraduates of the POLLA team that made this project possible. This project was funded by the UCI Undergraduate Research Opportunities Program (UROP) and the National Science Foundation (NSF).

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