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BIOLOGICAL AGING MODELED WITH STOCHASTIC DIFFERENTIAL EQUATIONS

E.J. ALLEN[1] AND B.B.U.P. PERERA[2]

[1]Department of Mathematics and Statistics
Texas Tech University
Lubbock, TX 79409, USA

[2]Department of Mathematics
University of Kelaniya, Dalugama
Kelaniya, 11600, Sri Lanka

ABSTRACT: A family of stochastic differential equation (SDE) models is derived and studied for the aging of biological organisms. The SDE aging models give meaningful mathematical interpretations of the aging process, rate of aging, and maximum age. For the SDE models, the first passage time gives the time to death. Probability densities of first passage times are derived for the SDE models yielding theoretical death event densities. The derived death event probability densities are fitted, using maximum likelihood estimation, to several different mortality table datasets. Mortality data for humans, wild sheep, grasshoppers, and fruit flies are considered. The results of fitting the mortality data indicate that the rate of aging for humans and many other animals undergoes an increase at some point in time.

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1. INTRODUCTION

Biologists have studied many physiological processes of aging as well as the molecular and genetic bases of aging and have investigated various ways to measure the aging process [9, 11, 21]. Such studies indicate, for example, that the aging rate for humans increases with time [31, 36]. As explained below, the conclusion that the biological aging rate increases with time agrees with the well-known mathematical hypothesis of Gompertz who proposed that the death rate has a component that increases exponentially with time [15, 24]. However, the mortality rate for certain species such as Mediterranean fruit flies (*Ceratitis capitata*) does not increase with age [10]. This in turn suggests that the rate of aging for certain species, such as fruit flies, does not increase with time. In the present investigation, a stochastic differential equation (SDE) model is derived for the biological aging process. Then, the rate of aging for several species is studied by fitting mortality data to the SDE model.

A common hypothesis in mathematical studies of aging assumes a Gompertz mortality function [15, 24, 32]. Under this hypothesis, the entire population of individuals experiences the same death rate at each time t where t is the time from birth. The Gompertz mortality function assumes the exponential death rate $m(t) = Ae^{\alpha t}$. This death rate leads to a survival function (or reliability function) of the form $S(t) = e^{\frac{A}{\alpha}(1-e^{\alpha t})}$ where $S(t)$ is the probability of surviving beyond time t. For this survival function, the probability density for a death event, $-\frac{dS(t)}{dt}$, is equal to

$$p_G(t; A, \alpha) = Ae^{\alpha t} e^{\frac{A}{\alpha}(1-e^{\alpha t})}.$$

In addition, if the Gompertz distribution is generalized to include a mortality component that is independent of age, then the Gompertz-Makeham distribution results [19].

The SDE model derived in the present investigation for the aging process differs from that of the Gompertz model and is more similar to some models hypothesized in reliability engineering for the degradation of physical systems. An objective in reliability engineering is to estimate the probability that a system will perform its function for a specified period of time. Mathematicians and engineers have hypothesized and studied failure-type models for the degradation process of complex physical systems, with many components,

that ultimately fail with time [3, 13, 14, 30]. In reliability engineering, physical degradation, e.g., wearing or corrosion, gradually occurs with increasing risk of failure of one or more components of the system. Degradation analysis techniques are used to estimate or predict product failure. It is recognized that the biological aging problem is similar to a degradation problem for physical systems [16, 20].

A variety of stochastic techniques have been applied in degradation analysis. Degradation theories, for example, have been built around mean-reverting Ornstein-Uhlenbeck SDEs of the form [1, 13, 39]:

$$dy(t) = a(t)(c(t) - y(t))\ dt + b(t)\ dW(t),$$

where a, b, c are known functions of time and $y(t)$ is the degradation level [13] or a vector of physiological characteristics approximating the organism's condition [39]. For these models, the first-passage time densities are not known analytically but satisfy a Volterra integral equation [13]. In a second stochastic degradation model in reliability engineering, used for studying failure in engineering systems, Wiener diffusion is hypothesized for the degradation process where a monotonic transformation of the time scale is used to account for a time-dependent degradation drift [35, 37, 40]. By assuming a stochastic model of this form, the first-exit time probability distribution becomes a transformed inverse Gaussian [37]. For this model, the degradation level $y(t)$ satisfies the equation

$$y(t) = a\gamma(t) + bW(\gamma(t)),$$

where W is a standard Wiener process, $\gamma(t)$ is defined as a time-dependent degradation drift, and a and b are constants. The SDE model derived in the present investigation for biological aging generalizes this stochastic model for degradation of physical systems.

In the next section, a family of stochastic differential equation models for the aging process is derived. Assuming that the coefficients of the SDE models are independent of age, the first exit time probability densities are analytically derived. In the following section, the derived age models are used to address the question of whether or not the rate of aging increases at some time after birth. The rate of aging is assumed to be either constant or to increase linearly at some point in time. Using maximum likelihood estimation, the two aging

models are fit to mortality data for six datasets, including data for humans, sheep, grasshoppers, and fruit flies. In the final section, the results of the investigation are briefly summarized.

2. A FAMILY OF SDE MODELS FOR BIOLOGICAL AGING

In this section, a family of simple but biologically reasonable stochastic differential equation models are derived for the aging process. As the wear of electronic or mechanical devices is similar to the aging process in biology, the SDE models may also be applicable to problems in reliability engineering such as the wear of physical systems [5]. As the first exit time for the SDE aging models is equal to the time at death, the SDE exit-time probability density corresponds to the death event density which also, after integration, describes the survival function.

To derive SDE models for aging, simple discrete stochastic models are first described for the aging process. These models lead directly to a family of stochastic differential equation models which have approximately the same probability densities as the discrete stochastic models. The first passage time probability densities are derived for special cases of these SDE models, thus producing theoretical death event densities. These exit-time densities are a form of modified Wald (or inverse Gaussian) probability densities. In the third section, the derived exit-time densities are fit using maximum likelihood estimation to several different mortality datasets.

2.1. GENERAL MODEL FOR BIOLOGICAL AGING

The aging process is assumed to be inherently random in nature. It is hypothesized that as each individual ages, the rate of aging of the individual randomly changes with time. A stochastic approach is considered where each individual in the population experiences a different aging trajectory with time. This leads to a stochastic differential equation model for the dynamics of the aging process. Death of an individual occurs when the age reaches a specified maximum age. To describe the mathematical model, let $y(t)$ be the age of an individual at time t. Specifically, age $y(t)$ is a stochastic process and depends

on time since birth t. To derive the stochastic model, let β be a small change in age for a small interval of time Δt. It is assumed that for each interval of time Δt, the age either remains constant or changes by β. Let the probability of a change β be defined as $\hat{g}(t, y)\Delta t$, specifically, the probability is proportional to Δt and may depend on time since birth as well as age. A discrete stochastic model for age is inferred by this discussion. In particular, as the probability of a change of age β is equal to $\hat{g}(t, y)\Delta t$ for a small time interval Δt, a discrete stochastic model for age $y(t)$ is summarized in Table 1.

Change Δy	Probability of change in time interval Δt
β	$\hat{g}(t, y)\Delta t$
0	$1 - \hat{g}(t, y)\Delta t$

Table 1: Age changes and probabilities for a small time interval

For the discrete model of Table 1, let $g(t, y) = \beta\hat{g}(t, y)$. Given the age $y(t)$ at time t, the expected change in age for time interval Δt is $\mathbb{E}(\Delta y) = g(t, y)\Delta t$ and $\mathbb{E}(\Delta y)^2 = \beta g(t, y)\Delta t$. This discrete stochastic model leads, in turn, to an Itô stochastic differential which has approximately the same probability distribution as the discrete stochastic model [4, 7]. The SDE model has the form

$$dy(t) = g(t, y)\ dt + c\sqrt{g(t, y)}\ dW(t) \tag{1}$$

with $y(0) = 0$, $y(t_e) = y_e$, $c = \sqrt{\beta}$, and $W(t)$ a standard Wiener process. It is assumed that exit (death) occurs when the age reaches y_e. Equation (1) forms a family of SDE models for the aging process that depends on the particular form of the rate of aging function $g(t, y)$.

For simplicity, in the remainder of the paper, it is assumed that $g(t, y)$ is independent of age y. In this case, (1) becomes

$$dy(t) = g(t)\ dt + c\sqrt{g(t)}\ dW(t) \tag{2}$$

with $y(0) = 0$, $y(t_e) = y_e$ where y_e is the maximum age or age at death. Furthermore, it is assumed that the mean instantaneous rate of change of aging, $g(t)$, is a monotonic function of time t. With this simplification, an analytic expression for the first exit time density can be determined. To determine the probability density of exit times, t_e, it is useful to consider the backward

Kolmogorov differential equation corresponding to (2) [6, 18, 22, 23, 30]. This equation has the form

$$\frac{\partial R(y,t)}{\partial t} = g(t)\frac{\partial R(y,t)}{\partial y} + \frac{c^2 g(t)}{2}\frac{\partial^2 R(y,t)}{\partial^2 y}, \tag{3}$$

where $R(y,t)$ is the reliability function. That is, $R(y,t)$ is the probability that trajectories starting at age y do not exit before time t. Equation (3) can be written in terms of a new time variable $\tau = \int_0^t g(u)du = G(t)$, where $d\tau = g(t)dt$, as

$$\frac{\partial R(y,\tau)}{\partial \tau} = \frac{\partial R(y,\tau)}{\partial y} + \frac{c^2}{2}\frac{\partial^2 R(y,\tau)}{\partial^2 y}. \tag{4}$$

It follows that equation (4) corresponds to the SDE exit-time problem

$$dy(\tau) = d\tau + c\, dW(\tau) \tag{5}$$

with $y(0) = 0$, $y(\tau_e) = y_e$, $W(\tau)$ a standard Wiener process, and death at τ_e when the age reaches y_e. The exit time density for equation (5) is the well-known Wald or inverse Gaussian density and has the form [17, 25]

$$p_W(\tau_e;\mu,\lambda) = \left(\frac{\lambda}{2\pi\tau_e^3}\right)^{1/2} \exp\left(\frac{-\lambda(\tau_e-\mu)^2}{2\mu^2\tau_e}\right), \tag{6}$$

where $\mu = y_e$ and $\lambda = y_e^2/c^2$. In the original time variable, the density of exit times then satisfies

$$p_{exit}(t_e;\mu,\lambda) = p_W(G(t_e);\mu,\lambda)g(t_e). \tag{7}$$

A probability density of this form has been previously hypothesized for the failure density of physical degradation in reliability engineering [35, 37, 40] and a probability density similar to (7) has been studied for the human health state [33].

As the mean rate of aging with respect to time is equal to $g(t)$, that is, $d\mathbb{E}(y(t))/dt = g(t)$, it is assumed that the mean rate of aging with respect to time at birth is equal to unity, i.e., $g(0) = 1$. In addition, for simplicity, it is assumed that $g(t)$ depends on at most two parameters a and b. Specifically, $g(t) = g(t;a,b)$, $G(t) = G(t;a,b)$, and the death event probability density $p_{exit}(t_e;\mu,\lambda) = p_{exit}(t_e;\mu,\lambda,a,b)$.

For a given dataset, maximum likelihood estimation (MLE) is applied in the present investigation to estimate the parameters μ, λ, a, b and hence the

probability density $p_{exit}(t_e; \mu, \lambda, a, b)$. The parameters c and y_e can then be calculated given μ, λ, a, b. Suppose that t_i for $i = 1, \ldots, N$ are data values for the exit time. If a and b are estimated, then the values $\tau_i = G(t_i; a, b)$ are known for $i = 1, \ldots, N$ and the MLE estimates of μ and λ can be readily calculated using appropriate formulas. In particular, if a and b are estimated, using standard MLE applied to the Wald distribution (6) then $\mu \approx \hat{\mu} = \sum_{i=1}^{N} \tau_i/N$ and $\lambda \approx \hat{\lambda} = N/(\sum_{i=1}^{N}(1/\tau_i - 1/\hat{\mu}))$. (See, e.g., [38].) Therefore, it follows that the problem of estimating the four parameters μ, λ, a, b reduces to simply estimating the two parameters a and b. Estimation of a and b can be performed in various ways, for example, by a numerical procedure such as the Nelder-Mead simplex method [28] or by searching a grid of values in a and b which is the robust procedure used in the present investigation.

2.2. COMPARISON WITH GOMPERTZ MODEL

Before continuing, it is interesting to compare the Gompertz death event probability, p_G, and the exit-time death event probability, p_{exit}. The Gompertz model is based on a certain form for the death rate while the exit-time model (7) is based on a certain form for the rate of aging. In a Gompertz-like model, the death event probability satisfies $p_G(t) = m(t) \exp\left(-\int_0^t m(z)\, dz\right)$, in particular, the death rate $m(t) = A \exp(\alpha t)$ in the original Gompertz model. In the SDE model of (7), the aging of individuals satisfies random trajectories with death occurring when the age reaches a maximum value. It is not straightforward to see how the two models are related. It is reasonable to suppose, though, that the two death event densities may be similar based on proper selection of the death and aging rates, $m(t)$ and $g(t)$. As an example, it is assumed that realistic forms are taken for the death and aging rates, yet simple forms so that exact formulas for the moments can be determined. Specifically, it is assumed that the death rate is zero until a certain time and then increases linearly with time and the aging rate is constant up to a maximum age, that is,

$$m(t) = \begin{cases} 0 & \text{for} \quad t < t_c \\ \beta(t - t_c) & \text{for} \quad t > t_c \end{cases} \qquad \text{and} \quad g(t) = k \ \text{ for age } \ y(t) < y_e.$$

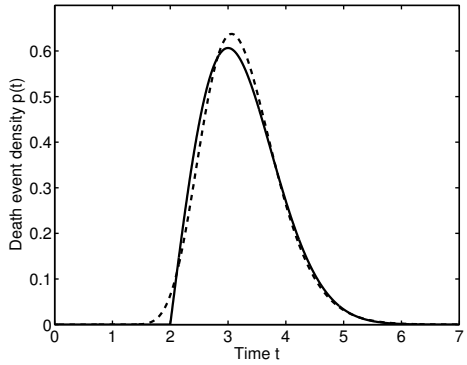

Figure 1: Death event probability densities for a Gompertz-like model (solid line) and an exit-time model (dashed line)

In this case, the Gompertz-like model satisfies a translated Weibull density and the exit-time death event probability satisfies a Wald density with a time scale transformation, i.e.,

$$p_G(t;\beta,t_c) = \begin{cases} 0 \quad \text{for} \quad t < t_c \\ \beta(t-t_c)\exp(-\beta(t-t_c)^2/2) \quad \text{for} \quad t > t_c, \end{cases} \tag{8}$$
$$p_{exit}(t) = p_W(kt,\mu,\lambda)k.$$

Furthermore, if it is assumed that the two densities satisfy the same mean and variance, then the parameters in the two densities (8) are related by the formulas:

$$\frac{y_e}{k} = \sqrt{\frac{\pi}{2\beta}} + t_c \quad \text{and} \quad \frac{y_e c^2}{k^2} = \frac{(2-\pi/2)}{\beta}$$

as $\mu = y_e$ and $\lambda = y_e^2/c^2$. If the maximum age y_e and the time t_c are fixed, then when k increases, the value of β increases. So, for these simple models, the death rate increases as the rate of aging increases, a reasonable result. In Figure 1, a comparison of the two probability densities is illustrated when $t_c = 2, \beta = 1$, and $k = 0.5$. From Figure 1, it is clear that the two densities are approximately identical.

Finally, for the case that $m(t) = A\exp(\alpha t)$ as in the original Gompertz model, then $-\dot{p}_G(t)/p_G(t) = -\dot{m}(t)/m(t) + m(t) = -\alpha + A\exp(\alpha t)$. However, by (7), $-\dot{p}_{exit}(t)/p_{exit}(t) \approx -\dot{g}(t)/g(t) + \lambda g(t)/2\mu^2$ for large t. Assuming then that $g(t) \approx \exp(\alpha t)$ and $A \approx \lambda/(2\mu^2)$, the two densities are similar for large

time t. This can also be seen by substituting $\exp(\alpha t)$ for $g(t)$ directly into (7). Therefore, the Gompertz model agrees with current biological results in that the rate of aging increases with time since birth.

3. COMPARISON OF TWO AGING RATES FOR DATASETS A-F

Two different hypotheses about the aging process are compared for several different datasets. In the first hypothesis, the mean aging rate for individuals is assumed to be constant with respect to time t and so $g(t) = 1$. In this case, the age $y(t)$ for an individual in the population satisfies

$$dy(t) = dt + c\, dW(t) \tag{9}$$

with $y(0) = 0$, $y(t_e) = y_e$, and $W(t)$ is a standard Wiener process. The exit time density or probability density of death time (7) is the Wald density

$$p_{exit}(t_e; \mu, \lambda) = \left(\frac{\lambda}{2\pi t_e^3}\right)^{1/2} \exp\left(\frac{-\lambda(t_e - \mu)^2}{2\mu^2 t_e}\right), \tag{10}$$

where $\mu = y_e$ and $\lambda = y_e^2/c^2$. For a set of exit times in a dataset, t_i for $i = 1, \ldots, N$, the MLE estimates of μ and λ are given directly by the formulas $\mu \approx \hat{\mu} = \sum_{i=1}^{N} t_i/N$ and $\lambda \approx \hat{\lambda} = N/(\sum_{i=1}^{N}(1/t_i - 1/\hat{\mu}))$.

In the second hypothesis, the mean aging rate for individuals is assumed initially to be constant but, then at time $t = a$, the aging rate increases linearly. In particular, under this hypothesis, the aging rate for individuals is assumed to be a continuous piecewise linear function with respect to time t of the form

$$g(t) = \begin{cases} 1 \quad \text{for} \quad t < a \\ 1 + b(t - a) \quad \text{for} \quad t > a \end{cases} \tag{11}$$

where $a, b \geq 0$ are two parameters. In this case, $G(t)$ is given by

$$G(t) = \begin{cases} t \quad \text{for} \quad t < a \\ t + b(t - a)^2/2 \quad \text{for} \quad t > a \end{cases} \tag{12}$$

and the age $y(t)$ of an individual in the population satisfies

$$dy(t) = g(t)\, dt + c\sqrt{g(t)}\, dW(t) \tag{13}$$

with $y(0) = 0$, $y(t_e) = y_e$, and $W(t)$ a standard Wiener process. The exit time density or probability density of death times for this aging rate is the modified Wald density

$$p_{exit}(t_e; \mu, \lambda, a, b) = g(t_e) \left(\frac{\lambda}{2\pi G^3(t_e)} \right)^{1/2} \exp\left(\frac{-\lambda(G(t_e) - \mu)^2}{2\mu^2 G(t_e)} \right) \qquad (14)$$

where $\mu = y_e$ and $\lambda = y_e^2/c^2$. For a set of exit times in a dataset, t_i for $i = 1, \ldots, N$, and estimated values for a and b, the MLE estimates of μ and λ are given by the formulas $\mu \approx \hat{\mu} = \sum_{i=1}^{N} G(t_i)/N$ and $\lambda \approx \hat{\lambda} = N/(\sum_{i=1}^{N}(1/G(t_i) - 1/\hat{\mu}))$. To maximize the likelihood, a search is performed on a two-dimensional grid for the values of parameters a and b.

In the following subsections, Model 1 refers to the first SDE model (9) for which a constant rate of aging is assumed. Model 2 refers to the second SDE model (13) for which a continuous piecewise linear rate of aging is assumed. In each dataset, some values associated with death before a particular age were eliminated to help correct for deaths unrelated to age. Less than 13% of the data values were eliminated from any dataset except for the Dall mountain sheep data, dataset C, but only data for the youngest age group were removed from this dataset.

3.1. DATASET A

The first dataset is on the number of survivors by age for the United States for 2010 and is taken from Table B of the National Vital Statistics Reports of the U.S. Department of Health and Human Services [8]. The life table data for males is compared with that for females using the two hypothesized aging rates. The dataset values were modified to eliminate deaths of males and females before the age of 50 years. This reduced the dataset to 92,822 values for males and 95,798 for females. Computed maximum likelihood estimates for the death event densities are summarized in Tables 2 and 3 and displayed in Figure 2. Also listed in the tables are values of the Akaike information criterion (AIC) [2] that measures the quality of the models taking into account the number of parameters. AIC is equal to $\text{AIC} = 2k - 2\log(\hat{L})$ where k is the number of parameters and $\hat{L}$ is the maximum value of the likelihood function. The model considered of highest quality has the smallest value of AIC. For

this example, the best fit is achieved by Model 2 which assumes a continuous piecewise linear aging rate.

In considering the results for this example, by comparing the values of parameter a in Model 2 for men and women, the results indicate that men begin to have an aging rate increase at year $a = 75$ about 5 years earlier than that for women. However, the "maximum age" y_e is approximately 90 for both men and women.

SDE Model	a	b	c	y_e	$\log(\hat{L})$	AIC
Model 1	NA	NA	1.84	81.18	-376137.	752278.
Model 2	75.	0.14	2.58	88.98	-362725.	725458.

Table 2: MLE parameter values for the two models for the data for men

SDE Model	a	b	c	y_e	$\log(\hat{L})$	AIC
Model 1	NA	NA	1.33	83.17	-373690.	747385.
Model 2	80.	0.15	2.02	89.50	-361757.	723522.

Table 3: MLE parameter values for the two models for the data for women

3.2. DATASET B

The second dataset is for the mortality of people with mild/moderate intellectual disability in California with Down syndrome for 1986-1991 [34]. Similar to dataset A, deaths before the age of 40 years were eliminated from dataset B to help correct for deaths unrelated to age. This reduced the set to 87,017 values. Computed maximum likelihood estimates for the parameters in the death event probability densities are summarized in Table 4 and displayed in Figure 3. The best fit is achieved by Model 2 which assumes a piecewise linear rate of aging. In comparing the results of this dataset with the dataset A, it is clear that the lifespan is lower for people with mild/moderate intellectual

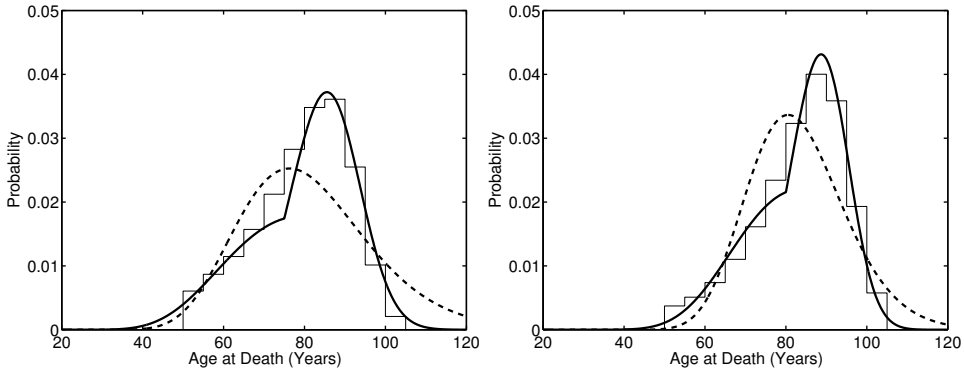

Figure 2: Death event probability densities for men (left) and women (right), dashed line for Model 1 (constant aging rate), solid line for Model 2 (piecewise linear aging rate), histogram for data

disability with Down syndrome than for the general population.

SDE Model	a	b	c	y_e	$\log(\hat{L})$	AIC
Model 1	NA	NA	1.23	61.24	-319206.	638416.
Model 2	71.	0.37	1.35	61.91	-314853.	629714.

Table 4: MLE parameter values for people with mild/moderate intellectual disability with Down syndrome

3.3. DATASET C

The third dataset is a well-known dataset for Dall sheep mortality collected by Murie [26] and studied, e.g., by Deevey [12]. Murie collected the skulls of 608 Alaskan Dall mountain sheep and determined each sheep's age at death by the number of annual rings on the horns. The dataset values were modified to eliminate deaths before the age of one year. This reduced the number of data values to 487. Computed maximum likelihood estimates for the parameters in the death event probability densities are summarized in Table 5 and displayed in Figure 4. The best fit is achieved by Model 2 which assumes a piecewise

linear rate of aging.

For comparison purposes, a Gompertz-like death event density is also fit to this data. In particular, a translated Weibull density involving a piecewise linear death rate is studied. The death rate $m(t)$ and the death event probability have the specific forms:

$$m(t) = \begin{cases} 0 \quad \text{for} \quad t < t_c \\ \beta(t - t_c) \quad \text{for} \quad t > t_c \end{cases} \quad \text{and}$$

$$p_G(t; \beta, t_c) = \begin{cases} 0 \quad \text{for} \quad t < t_c \\ \beta(t - t_c) \exp(-\beta(t - t_c)^2/2) \quad \text{for} \quad t > t_c. \end{cases}$$

The computed MLE values for this model are $\beta = 0.0333$, $t_c = 1.3$, $\log(\hat{L}) = -1216.4$, and AIC= 2436.8. The quality of the fitted density is similar to that of Model 1 but not as good as that of Model 2. The MLE death event density for this Gompertz-like model is also shown in Figure 4.

SDE Model	a	b	c	y_e	$\log(\hat{L})$	AIC
Model 1	NA	NA	1.16	8.703	-1251.	2506.
Model 2	8.1	5.14	3.54	16.71	-1048.	2105.

Table 5: MLE parameter values for Dall mountain sheep

3.4. DATASET D

The fourth dataset is from a well-known dataset on common fruit fly (*Drosophila melanogaster*) mortality for five groups of 25 male fruit flies [29]. In group 1, each male was kept with eight sexually uninterested (pregnant) females; in group 2, each male was kept with no females; in group 3, each male was kept with one sexually uninterested female; in group 4, each male was kept with one sexually interested (virgin) female; in group 5, each male was kept with eight sexually interested females. The results of the experiment indicated that sexual activity reduces the lifespan of male fruit flies [29].

Computed maximum likelihood estimates for the death event densities for Models 1 and 2 are summarized in Table 6 for each of the five groups. As no fruit fly died before 16 days in any group, no data values were removed

Figure 3: Death event densities for people with mild/moderate intellectual disability with Down syndrome, dashed line for Model 1, solid line for Model 2, histogram for data

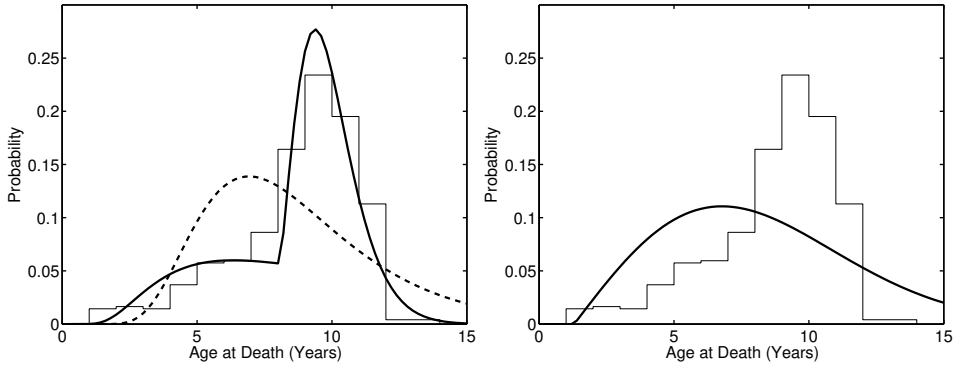

Figure 4: Displayed left are death event densities for Dall mountain sheep, dashed line for Model 1 (constant aging rate), solid line for Model 2 (piecewise linear aging rate), histogram for data; Displayed right is the death event density for a Gompertz-like model

to help correct for deaths unrelated to age. The densities are displayed in Figure 5, for comparison, for groups 1, 3, 4, and 5. For the fruit fly data, the Akaike information criterion values are smaller for Model 2 for three of the data groups but larger for two groups and so it is difficult to justify selection of the more complicated Model 2 for the fruit fly data. Nevertheless, the MLE values of maximum age, y_e, for Model 1 for the five groups are 63.4, 63.6, 64.8, 56.8, and 38.7 days, respectively, which is convincing evidence for the main conclusion of the study, specifically, that sexual activity reduces the lifespan of male fruit flies.

SDE Model	a	b	c	y_e	$\log(\hat{L})$	AIC
Group 1, Model 1	NA	NA	2.02	63.36	-103.84	211.69
Group 1, Model 2	67.	0.22	2.72	68.59	-100.33	208.66
Group 2, Model 1	NA	NA	2.08	63.56	-104.48	212.97
Group 2, Model 2	66.	0.03	2.34	65.25	-104.13	216.26
Group 3, Model 1	NA	NA	1.96	64.80	-103.37	210.74
Group 3, Model 2	61.	0.03	2.34	67.51	-102.88	213.77
Group 4, Model 1	NA	NA	2.29	56.76	-105.20	214.40
Group 4, Model 2	34.	0.14	6.94	107.5	-102.65	213.30
Group 5, Model 1	NA	NA	2.21	38.72	-98.94	201.89
Group 5, Model 2	39.	0.15	3.05	43.67	-96.59	201.19

Table 6: MLE parameter values for five groups of fruit flies

3.5. DATASET E

The fifth dataset is from a well-known set of data on the mortality of 1,203,646 adult Mediterranean fruit flies (*Ceratitis capitata*) in a laboratory setting [10]. The fruit flies were given a diet of water and sugar and each day dead flies were removed and counted. For this dataset, deaths of medflies before age 5 days were disregarded to help correct for deaths unrelated to age and 1,174,502 medflies survived beyond the fifth day. For this data, there is an extremely long tail that strongly influences the MLE calculation. Indeed, although only 1% of the medflies survived until 50 days, 0.1% survived until 64 days, 0.01%

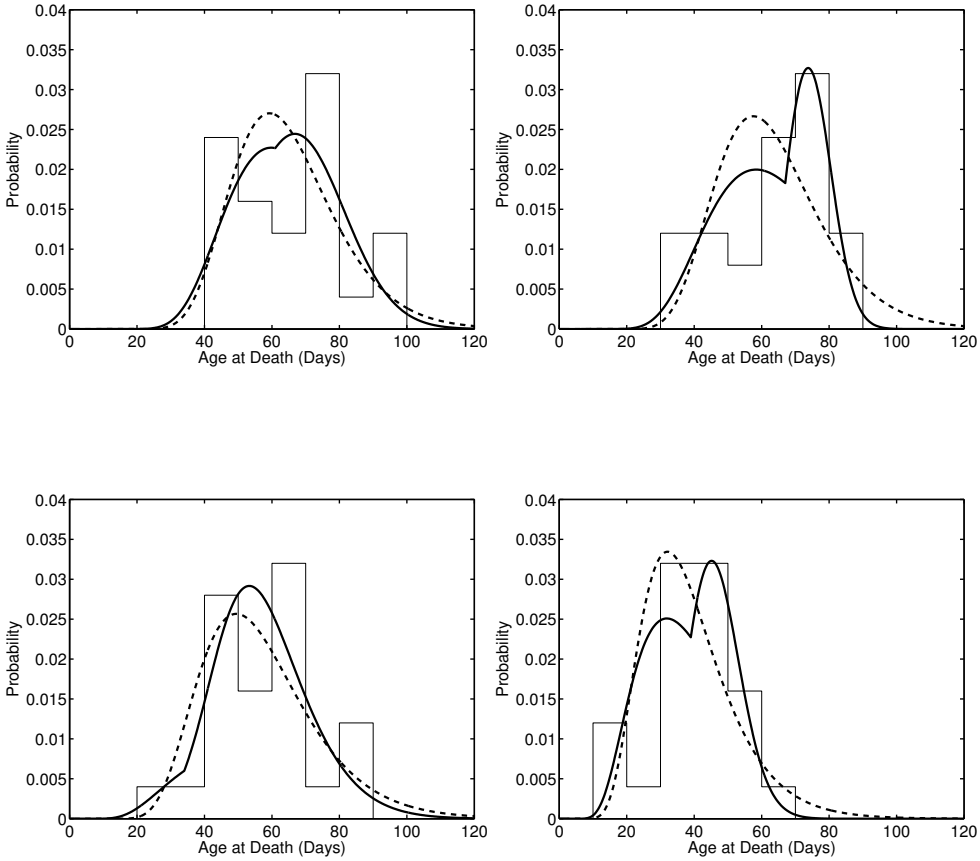

Figure 5: Death event probability densities for fruit flies, Group 3 at upper left, Group 1 at upper right, Group 4 at lower left, Group 5 at lower right, dashed line for Model 1 (constant aging rate), solid line for Model 2 (piecewise linear aging rate), histogram for data

survived until 86 days, and 0.001% survived until 146 days. Maximum likelihood estimates for the parameters in the death event probability densities for Models 1 and 2 are given in Table 7. The probability densities of the two models are indistinguishable in Figure 6 making it is difficult to justify selection of the more complicated Model 2.

SDE Model	a	b	c	y_e	$\log(\hat{L})$	AIC
Model 1	NA	NA	1.92	22.78	-4136567.	8273139.
Model 2	33.	0.002	1.92	22.79	-4136539.	8273086.

Table 7: MLE parameter values for the medfly data

3.6. DATASET F

The sixth dataset is for the mortality of an Asian pest grasshopper *Ceracris nigricornis laeta* (Bolivar). Data for the mortality of 275 male and 265 female adult grasshoppers were collected in a laboratory setting [27]. The dataset is applied in the present investigation to study the death event probability densities for male and female grasshoppers. Deaths before the age of 90 days were eliminated reducing the number of data values to 208 and 265 for male and female grasshoppers, respectively. Maximum likelihood estimates for the parameters in the death event probability densities were computed and are given in Table 8 and displayed in Figure 7. For this example, the best fit is achieved by Model 2, a piecewise linear rate of aging, for both male and female grasshoppers. In comparing Model 2 for male mortality with female mortality, it is observed that y_e, the maximum age, is much less for males than for females, specifically, 134.95 days and 161.28 days for males and females, respectively. Although the time until the death rate increase, $a = 151$ days, is the same for both males and females, the aging rate slope $b = 0.27$ for males and $b = .14$ for females indicates a more rapid rate of aging increase for males than for females after $a = 151$ days.

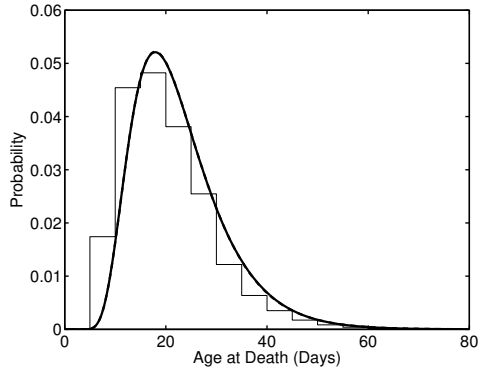

Figure 6: Death event probability densities for medflies, dashed line for Model 1 (constant aging rate), solid line for Model 2 (piecewise linear aging rate), histogram for data

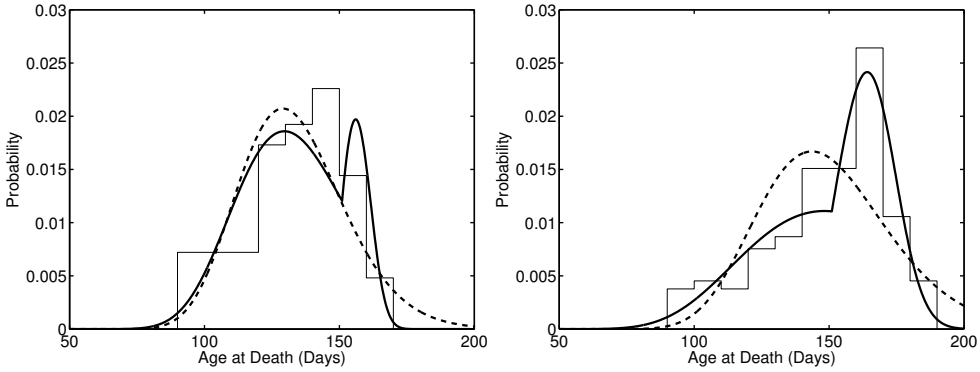

Figure 7: Death event probability densities for male grasshoppers (left) and female grasshoppers (right), dashed line for Model 1 (constant aging rate), solid line for Model 2 (piecewise linear aging rate), histogram for data

SDE Model	a	b	c	y_e	$\log(\hat{L})$	AIC
Males, Model 1	NA	NA	1.71	133.37	-912.21	1828.43
Males, Model 2	151.	0.27	1.90	134.95	-897.52	1803.03
Females, Model 1	NA	NA	2.02	149.57	-1220.24	2444.48
Females, Model 2	151.	0.14	3.02	161.28	-1175.23	2358.45

Table 8: MLE parameter values for male and female grasshoppers

4. SUMMARY

A family of stochastic differential equations is derived for the biological aging process. It is pointed out that the SDE models generalize some stochastic models hypothesized in reliability engineering for predicting product or system failure in physical degradation processes. The first exit times of the SDE aging models give the death event probability densities for the organisms. The SDE models are simplified by assuming that mean aging rates depend only on time from birth and are independent of age. This simplification allows derivation of an analytic form for the death event probability density. Two aging rates, constant and piecewise linear, are studied for six different datasets for humans, fruit flies, grasshoppers, and mountain sheep. It is shown, except for fruit flies, that the piecewise linear aging rate fits the mortality data better than a constant aging rate. In particular, the mortality data indicates that the rate of aging for humans and many other animals undergoes an increase at some point in time.

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