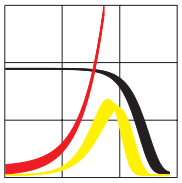

Max-Planck-Institut für demografische Forschung
Max Planck Institute for Demographic Research
Konrad-Zuse-Strasse 1 · D-18057 Rostock · GERMANY
Tel +49 (0) 3 81 20 81 - 0; Fax +49 (0) 3 81 20 81 - 202;
http://www.demogr.mpg.de

MPIDR WORKING PAPER WP 2006-021
AUGUST 2006

On engineering reliability concepts and biological aging

Maxim Finkelstein (FinkelM@sci.uovs.ac.za)

This working paper has been approved for release by: James W. Vaupel (jwv@demogr.mpg.de)
Head of the Laboratory of Survival and Longevity.

ON ENGINEERING RELIABILITY CONCEPTS AND BIOLOGICAL AGING

Maxim Finkelstein

Department of Mathematical Statistics
University of the Free State
PO Box 339, 9300 Bloemfontein, Republic of South Africa
(e-mail: FinkelM@sci.uovs.ac.za)
and
Max Planck Institute for Demographic Research,
Rostock, Germany

ABSTRACT

Some stochastic approaches to biological aging modeling are studied. We assume that an organism acquires a random resource at birth. Death occurs when the accumulated damage (wear) exceeds this initial value, modeled by the discrete or continuous random variables. Another source of death of an organism is also taken into account, when it occurs as a consequence of a shock or of a demand for energy, which is a generalization of the Strehler-Mildwan's model (1960). Biological age based on the observed degradation is also defined. Finally, aging properties of repairable systems are discussed. We show that even in the case of imperfect repair, which is certainly the case for organisms, aging slows down with age and eventually can even fade out. This presents another possible explanation for the human mortality rate plateaus.

Keywords: damage accumulation, redundant systems, degradation of organisms, aging distributions, mortality rate, biological age.

1. INTRODUCTION

The literature on numerous biological theories of aging is quite extensive. Various stochastic mortality models are reviewed, for instance, in Yashin *et al.* (2000). Most authors agree that the nature of aging is in some "biological wearing" or "wear and tear". Reliability theory possesses the well-developed tools for modeling wear in technical systems; therefore it is rather natural to apply this technique to biological aging. (Finkelstein, 2005). As even the simplest organisms are much more complex than the technical systems usually considered in reliability analysis, these analogies should not be, however, interpreted too literally. Therefore, the implications of the corresponding stochastic modeling should be considered rather carefully.

Besides organism's structural complexity of all kinds and on all levels, populations of biological objects, unlike populations of technical devices, evolve in accordance with evolutionary theory. Various maintenance and repair problems (including those with limited resources) had been intensively studied by reliability theory, but the crucial for biodemography notion of reproduction was obviously mostly out of sight**,** although the birth and death processes can certainly be useful for the corresponding modeling. On the other hand, popular evolutionary theories (e.g., Kirkwood's "disposable soma" concept (Kirkwood, 1977, 1997)) try to link mortality, fertility, maintenance and repair, but do not yet possess the sufficient biological knowledge, analytical tools and 'machinery' for considering appropriate stochastic models of repair and maintenance in a proper evolutionary context. This means that existing and to be investigated reliability models can enrich biological aging theory and *vise versa*, as, for instance, a kind of a disposable soma concept can be really helpful for optimal allocation of spare parts in some 'structurally homogeneous' engineering systems.

It is worth noting that evolutionary theories tend toward a rather controversial view that all damage in principle is repairable, that natural selection can shape the lifetime trajectory of damage and repair, constrained only by physical limitations of available resources (Steinsaltz and Goldwasser, 2006). However, not all damage in organisms can be reversed, for instance, damage to central nervous system and heart tissue is usually irreversible. In any case, importance of different repair mechanisms for survival of organisms is evident, which brings into play stochastic modeling of all types of repairable sys-

tems: perfectly, minimally and imperfectly repairable ones. This topic had been studied in reliability theory, but still there are many open problems.

Most likely, the future general theory of biological aging should be built out of some 'blocks' connected and shaped by the evolutionary principles (and not necessarily in the current version), and 'reliability block' and maybe even reliability-based network will be an important part of this scheme. Some interesting discussion on general "quality management" of organisms and *pros* and *contras* of exploiting the existing reliability approaches for biological aging are presented in Steinsaltz and Goldwasser (2006). Meanwhile helpful for this future general theory reliability considerations (for repairable and non-repairable objects) can be studied and developed, and this is the topic of the current paper.

Vaupel's (2003) conjecture that "after reproduction ceases, the remaining trajectory of life is determined by forces of wear, tear, and repair acting on the momentum produced by the Darwinian forces operating earlier in life" resulted in reliability modeling of Finkelstein and Vaupel (2006). These authors state: "As the force of natural selection diminishes with age, structural reliability concepts can be profitably used in mortality analysis. It means that the design of the structure is more or less fixed at this stage and reliability laws govern its evolution in time. However, it does not mean that these concepts cannot be used for mortality modeling at earlier ages, but in this case they should be combined with the laws of natural selection".

In accordance with a conventional definition of reliability of a technical object, it is a probability to perform a designed function under given conditions and in a given interval of time (Hoyland and Rausand, 1993). Clearly, this definition can be applied for a probabilistic description of a lifespan of organisms T, where its designed function is just to be alive. For instance, the main demographic model for the lifetime of humans is the Gompertz (1825) law of mortality defined by the exponentially increasing mortality rate $\mu(t)$:

$$F(t) = \Pr(T \le t) = 1 - \exp\left\{-\frac{\alpha}{\beta}[\exp\{\beta t\} - 1]\right\}, \qquad (1)$$

$$\mu(t) = \alpha \exp\{\beta t\}, \quad \alpha > 0, \beta > 0.$$

This is a direct descriptive way to model the lifespan random variable T. It is well known that human mortality data, at least in the age interval from 30-35 to 90-95, perfectly complies with this model.

In accordance with reliability terminology, the Gompertz law belongs to a family of IFR (increasing failure rate) distributions. This is the simplest and the most commonly used in reliability theory aging family for description of various degradation processes in engineering systems (Barlow and Proschan, 1975). There were a number of attempts in the past decades to justify the exponential form of the human mortality rate by some mechanism or model, but most of them exploit additional assumptions, which are explicitly or implicitly equivalent to the desired exponentiality. (Strehler-Mildwan, 1960; Witten, 1985; Koltover,1996; Gavrilov and Gavrilova, 2006).

In what follows we will consider several important applications of reliability-based stochastic reasoning, united by issues of aging and degradation and therefore contributing to the mentioned above reliability block of the future biological aging theory.

2. UNOBSERVED OVERALL RESOURCE

Following Finkelstein (2003), assume that an organism at birth ($t = 0$) acquires an overall unobserved random resource R with a distribution function $F_0(r): F_0(r) = P(R \le r)$. Assume also that the process of organism's aging is described by an increasing, deterministic for simplicity cumulative damage function $W(t)$ ($W(0) = 0$) to be called wear. The wear increment in $[t, t+dt)$ is defined as $w(t) + o(dt)$. Let additionally $W(t) \to \infty$ as $t \to \infty$. Under these assumptions we arrive at the well-known in reliability theory accelerated life model (ALM):

$$P(T \le t) \equiv F(t) = F_0(W(t)) \equiv P(R \le W(t)), \qquad (2)$$

$$W(t) = \int_0^t w(u)du; \quad w(t) > 0; \quad t \in [0, \infty).$$

The death occurs when the wear $W(t)$ reaches R.

Substituting the deterministic wear $W(t)$ in (2) by the increasing stochastic process $W_t, t \ge 0$ leads to the following relation (Finkelstein, 2003):

$$F(t) = P(T \le t) = P(R \le W_t) = E[F_0(W_t)], \tag{3}$$

where the expectation is taken with respect to $W_t, t \ge 0$. As the mortality rate is a conditional characteristic, one cannot obtain it from (3) as a simple expectation: $\mu(t) = E[w_t \mu_0(W_t)]$ and the proper conditioning should be performed (Yashin and Manton (1997)):

$$\mu(t) = E[w_t \mu_0(W_t) \mid T > t], \tag{4}$$

where w_t denotes the stochastic rate of diffusion: $dW_t \equiv w_t dt$, and the baseline mortality rate $\mu_0(t)$ is defined by the distribution $F_0(t)$.

A good candidate for $W_t, t \ge 0$ is the gamma process, which, according to definition, has stationary independent increments and $W_t - W_s$ $(t > s)$ has the gamma density with scale 1 and shape $(t - s)$. The Levy process, as a more general one, is often suitable for this purpose as well. The Weiner process can be also sometimes used for modeling wear but it does not possess the monotonicity property, which is natural for the processes of wear.

Example 1. As a specific case of the unobserved reserve model, consider now a discrete resource $R = N$ with a distribution: $F_0(n) \equiv P(N \le n)$. The following simple reliability interpretation is meaningful: Let N be a random number of initially (at $t = 0$) operable i.i.d. components with constant failure rates λ. Assume that these components form a parallel system, which, according to Gavrilov and Gavrilova (2001) can model the lifetime of an organism (the generalization to the series-parallel structure is straightforward). In each realization $N = n, n \ge 1$ our degradation process $W_t, t \ge 0$ for this setting is just a counting process for the corresponding process of pure death: when the number of events (failures of components) reaches n, the death of an organism occurs. The transitions rates of the corresponding Markov chain are: $n\lambda, (n-1)\lambda, (n-2)\lambda, \ldots$ Denote by $\mu_n(t)$ the mortality rate, which describes T_n - the time to death random variable for the fixed $N = n, n = 1,2,\ldots.$ ($n = 0$ is excluded, as there should be operable components at $t = 0$).

Similar to (4), the mortality rate is given as the following conditional expectation with respect to N:

$$\mu(t) = E[\mu_N(t) \mid T > t]. \tag{5}$$

Note that for small t:

$$\mu(t) \approx E[\mu_N(t)] = \sum_{n=1}^{\infty} P_n \mu_n(t), \tag{6}$$

where $P_n \equiv P(N = n)$, but the limiting transition, as $t \to 0$, should be performed in this case carefully. It is clear that as $t \to \infty$:

$$\mu(t) \to \lambda, \tag{7}$$

As the conditional probability (on condition that the system is operable) that only one component is operable, tends to 1.

Assume that N is Poisson-distributed with parameter η. Taking into account that the system should be operable at $t = 0$:

$$P_n = \frac{\exp\{-\eta\}\eta^n}{n!(1-\exp\{-\eta\})}; n = 1,2,....$$

It is clear that

$$\begin{aligned} F(t) = P(T \le t) &= \sum_{n=1}^{\infty} \frac{\exp\{-\eta\}\eta^n}{n!(1-\exp\{-\eta\})}\left(1-(1-\exp\{-\lambda t\})^n\right) \\ &= \frac{1-\exp\{-\eta\exp\{-\lambda t\}\}}{1-\exp\{-\eta\}}. \end{aligned} \tag{8}$$

The corresponding mortality rate is

$$\mu(t) = \frac{F'(t)}{1-F(t)} = \frac{\eta\lambda\exp\{-\lambda t\}}{\exp\{\eta\exp\{-\lambda t\}\}-1}. \tag{9}$$

It can be seen that the mortality plateau (7) takes place for the mortality rate (9) as well. This function is very far from the exponentially increasing Gompertz law (Steinsaltz and Evans, 2004). In fact, the Gompertz law can erroneously result, if approximation (6) is used formally, as in Gavrilov and Gavrilova (2001).

It turns out that simple reliability models of wear of the described type are helpful for lifespan modeling. This will be illustrated in the next section while defining the virtual age of an organism.

3. DEGRADATION AND VIRTUAL (BIOLOGICAL) AGE

The reasoning of the previous section is helpful for discussing an important and challenging notion of virtual (biological) age. Assume for simplicity, as previously, that deterioration of an organism can be modeled by a single, predictable, increasing stochastic process with independent increments $W_t, t \geq 0$. Observing its state at time t can give under certain assumptions an indication of a 'true' age defined by the level of the observed deterioration. We shall call this characteristic an *information-based virtual (biological) age* of a system or of an organism. If for, instance, someone of 50 years old looks like and has vital characteristics (blood pressure, level of cholesterol etc) are as of an 'ordinary' 35 years old one, we can say that this observation indicates that his virtual (biological) age can be estimated as 35. This is, of course, a rather vague statement, which can be made more precise for some simple, specific model settings and under certain assumptions.

Example 2. Consider a system of $n+1$ components (one initial component and n cold standby identical ones) with constant failure rates λ. Note, that in the previous example we had described a system with a hot (loaded) redundancy. The failure occurs when the last component fails. Thus $W_t, t \geq 0$ in this case is just a counting process (number of failed components) for the stopped Poisson process with rate λ. A possible biological interpretation: the limited number of repairs (Vaupel and Yashin, 1987) or cell replications. When, for instance, a cell divides, one of the daughter cells will have a maintained telomere length, the other will have a shorter length (Olofsson, 2000). When this length is shorter than some critical value, the cell stops dividing. The mortality rate of the described system is an increasing function of the form (Hoyland and Rausand, 1993):

$$\mu(t) = \frac{\lambda \exp\{-\lambda t\}(\lambda t)^n / n!}{\exp\{-\lambda t\} \sum_0^n \frac{(\lambda t)^i}{i!}}. \qquad (10)$$

Consider the following conditional expectation:

$$D(t) \equiv E[N(t) \mid N(t) \le n] = E[N(t) \mid T > t]$$
$$= \frac{\exp\{-\lambda t\}\sum_{0}^{n} i\frac{(\lambda t)^i}{i!}}{\exp\{-\lambda t\}\sum_{0}^{n}\frac{(\lambda t)^i}{i!}} \tag{11}$$

where $N(t)$ is the number of events in the interval $[0,t]$ for the Poisson process with the rate λ. As we observe an operable system, relation (11) defines the expected value of the number of its failures (measure of degradation) on condition of survival in $[0,t]$. The function $D(t)$ is monotonically increasing, $D(0) = 0$ and $\lim_{t\to\infty} = n$. This function defines an average degradation curve for the defined system. Denote the corresponding information-based virtual age by $V(t)$. *Our definition* for this specific model is:

$$V(t) = D^{-1}(k), \tag{12}$$

where $D^{-1}(t)$ is an inverse function to $D(t)$. If $k = D(t)$, then: $V(t) = D^{-1}(D(t)) = t$. Similar:

$$k < D(t) \Rightarrow V(t) < t, \quad k > D(t) \Rightarrow V(t) > t.$$

Thus, in this example, the information-based virtual age is obtained via the average degradation curve $D(t)$. If n is sufficiently large. Then $D(t) = \lambda t$ and in accordance with (12):

$$V(t) = \frac{k}{\mu}.$$

A general case of degrading objects can be considered in the same way. Let D_t be an increasing, smoothly varying (predictable) stochastic process of degradation with a mean $D(t)$. Assume for simplicity that this is a *process with independent increments*, and therefore it possesses the Markov property. Similar to (12), observation, d_t at time t defines the information-based virtual age. Formally:

Definition. *Let D_t be an increasing, predictable, with independent increments stochastic process of degradation with a mean $D(t)$, and let d_t be an observation at time t.*

Then the information-based virtual age is defined as

$$V(t) = D^{-1}(d_t).$$

Thus, considering degradation in a simple reliability structure resulted in a rather general definition and in a helpful for studying of aging approach.

4. SHOCK MODELS AND DEGRADATION

Technical systems and organisms are usually subject to shocks-random in time and magnitude harmful events that can cause a failure or death, respectively. We assume for simplicity that durations of shocks are negligible. In mechanical and electronic systems, for instance, shocks occur when the applied load exceeds the strength. Diseases, viruses, heart attacks, or more generally,-demands for energy, as in the Strehler-Mildwan model to be discussed in this section, can be interpreted as shocks for organisms. The stochastic theory of shocks was extensively studied in reliability literature, although there are still a lot of opened questions from theoretical and practical points of view. Traditionally, two basic cases, cumulative shock model and extreme shock model were considered. The former means that the system fails when the cumulative shock magnitude enters some critical region (Sumita and Shantikumar, 1985). The latter means that the system breaks down as soon as the magnitude of an individual shock goes into some given critical region (Shantikumar and Sumita, 1983). In what follows in this section, we shall revisit the Strehler-Mildwan model in more general assumptions and justify this approach from the probabilistic point of view, proving that it is valid only under the additional assumption that the shocks (demands for energy) occur in accordance with the Poisson process.

Consider a univariate first passage-type model with shocks. Let, as previously, $W_t, t \geq 0$ denote an increasing stochastic process of damage accumulation (e.g. the gamma process) and $R(t)$ be a function that defines a corresponding boundary. In Section 2 it was a random constant: $R(t) \equiv R$. Assume for simplicity that $R(t)$ is deterministic.

Let $P_t, t \geq 0$ be a point process of shocks with rate $\lambda(t)$ and independent from $W_t, t \geq 0$. Assume that each shock, independently from the previous ones, results in death with probability $\theta(t)$ and is 'survived' with the complementary probability $1-\theta(t)$. This can be interpreted in the following way: each shock has a random magnitude $Y_i = Y, i = 1,2,...$ with a distribution function $\Psi(y)$. The death at age t occurs when this magnitude exceeds the margin: $R(t) - w(t)$, where $w(t)$ denotes the increasing sample path of the process of degradation. Therefore:

$$\theta(t) = \Pr(Y > R(t) - w(t)) = 1 - \Psi(R(t) - w(t)).$$

In the original Strehler-Mildvan (1960) model, which was widely applied to human mortality data, our $R(t) - w(t)$ has a meaning of organisms vitality. It was also supposed that this function linearly decreases with age and that the distribution function $\Psi(y)$ is exponential (Yashin *et al*, 2000). We do not need these stringent assumptions for the forthcoming considerations.

It is worth noting that the rate $\lambda(t)$ does not define an arbitrary point process. However, it can be defined via its complete intensity function (Cox and Isham, 1980):

$$\lambda(t; H_t) = \lim_{\Delta t \to 0} \frac{\Pr\{N(t, t+\Delta t) = 1 \mid H_t\}}{\Delta t},$$

where H_t specifies the point process up to time t (history). Thus $\lambda(t; H_t)dt$ can be interpreted as the probability of a shock occurrence in $[t, t+dt)$, given the process history up to t. Therefore, the conditional mortality rate in our model is:

$$\mu_c(t, H_t)dt = \Pr\{T \in [t, t+dt) \mid H_t, T(H_t) \geq t\} = \theta(t)\lambda(t, H_t)dt, \qquad (13)$$

where condition $T(H_t) \geq t$ means that all shocks in $[0, t)$ were survived. It is clear from the definition of the *Poisson process* that *only for this specific case* equation (13) reduces to the usual, not history-dependent mortality rate $\mu(t)$ (unfortunately Strehler-Mildwan (1960) model did not consider this crucial assumption):

$$\mu_c(t, H_t) = \theta(t)\lambda(t) = \mu(t). \tag{14}$$

Therefore, the conventional exponential representation for the corresponding survival function is

$$\overline{F}(t) = \exp\left\{-\int_0^t \theta(u)\lambda(u)du\right\} \tag{15}$$

and this completes the proof for the specific case of the Poisson process of shocks for the case when shocks are the only source of death. The technical proof of this fact can be found, e.g., in Brown and Proschan (1983). Another meaningful interpretation of this result is via the thinning of the initial Poisson process with rate $\lambda(t)$, which results in the Poisson process with rate $\theta(t)\lambda(t)$. Therefore, the survival function till the first event in this process (death) is given by equation (15).

Coming back to our setting, when formally death can also result from crossing the increasing $w(t)$ with the boundary $R(t)$, equation (15) is obviously modified to:

$$\overline{F}(t) = \begin{cases} \exp\left\{-\int_0^t \theta(u)\lambda(u)du\right\}, & t \le t_r \\ 0, & t > t_r \end{cases},$$

where t_r is defined as the minimal solution of equation $R(t) = w(t)$. If the curves do not cross, then $t_r = \infty$. Humans and other organisms do not usually dye directly from accumulated damage, which is a slowly increasing process. Therefore, we can assume that formally $t_r = \infty$ and relations (14) and (15) hold.

We have derived equations (14) - (15) for the sample paths $w(t)$ and deterministic $R(t)$. A general case of the processes $W_t, t \ge 0$ and $R_t, t \ge 0$ can be also considered under reasonable assumptions. Then probability $\theta(t)$ turns to a stochastic process $\theta_t, t \ge 0$, whereas mortality rate $\mu(t)$ also starts to be stochastic and conditioning similar to those in equations (4) and (6) should be used.

Equation (14) states that the resulting mortality rate is just a simple product of the rate of the Poisson process and of the probability $\theta(t)$. Therefore, its shape can be easily ana-

lyzed. When $R(t)-w(t)$ is decreasing, the probability of death $\theta(t)$ is increasing with age, which goes in line with the conventional accumulation of degradation reasoning. If, additionally, the rate of shocks $\lambda(t)$ is not decreasing, or decreasing not faster than $\theta(t)$ is increasing, the resulting mortality rate $\mu(t)$ is also increasing. In conventional settings $R(t)$ is usually assumed to be a constant, therefore $R-w(t)$ is decreasing automatically. On the other hand, it can be easily seen that in principle certain reasonable combinations of shapes of functions $\theta(t)$ and $\lambda(t)$ can result in decreasing or ultimately decreasing mortality rates (negative senescence). For instance, $R(t)$ can increase faster than $w(t)$ - an organism is 'earning or obtaining' additional vitality in the course of life.

The considered in this section approach, in fact, deals with two dependent sources of death: degradation and shocks as specific case of traumatic events. More generally, the mortality rate process due to a traumatic part is $\mu(W_t)$ and under the assumption that there are no deaths due to degradation as such, it is the only part. Conditioning similar to (4) should be used in order to arrive at the mortality rate $\mu(t)$.

Example 3. Following our previous examples, assume that the degradation process is given by the counting measure of the Poisson process with rate λ and that there are no deaths due to direct degradation. On the other hand, let the traumatic mortality rate be constant for the degradation level n (number of events in the Poisson process): $\mu_n, n=0,1,2,\ldots$. It is reasonable to assume that mortality rates are increasing with degradation: $\mu_0<\mu_1<\mu_2<\ldots$. Then the stochastic mortality rate (the mortality rate process) can be compactly written via the corresponding indicator function as:

$$\mu_t=\sum_{n=0}^{\infty}\mu_n I(S_n\le t<S_{n+1});\ t\ge 0,$$

where S_n is the time of the nth event arrival, $S_0=0$. The observed (marginal) mortality rate $\mu(t)$ can be in principle obtained from this equation by direct integration on condition that there were no deaths in $[0,t)$, but the resulting formula is rather cumbersome.

4. AGING OF REPAIRABLE SYSTEMS

Although it is widely admitted by the evolutionary and non-evolutionary theories of aging that repair and repair mechanisms on all levels play a crucial role in senescence, very little had been done in terms of stochastic repair modeling in organisms. On one hand, it is clear that different theories require different 'machinery', on the other, there are certain general principles and approaches developed (or to be developed) by reliability theory and the theory of stochastic processes that can be applied to various biological setting.

Consider some hypothetical repairable object, to be called for convenience a component, which starts functioning at $t = 0$. Assume, as usually in renewal theory, that repair is perfect (after the repair a component is as good as new. Then the sequence of independent, identically distributed inter-arrival times $\{T_i\}_{i\geq 1}$ with a common distribution function $F(t)$ forms a standard renewal process. The repair times in this case are given by the sequence $T_1, T_1 + T_2, T_1 + T_2 + T_3, \ldots$ Assume that the generic $F(t) \in$ IFR, which means that the corresponding failure rate $\lambda(t)$ is not decreasing. Therefore $F(t)$ is an aging distribution. What can be said about the aging properties of the renewal process? It is reasonable to conclude, that as the repair is perfect, there is no aging in this process, as after each perfect repair the age of a component is 0. Thus, the perfect repair clearly does not lead to accumulation of damage in the described sense. But this is not so when the repair is not perfect, which is definitely the case in nature and in most technical systems. Note, that even the complete overhaul of a system, which is usually considered as a perfect repair, is not such, as even switched off standby items also age.

We have two major possibilities. The first one is when the imperfect repair reduces wear only of the last cycle. It is clear that in this case the overall wear increases and under some reasonable assumptions this operation only decreases the rate of accumulation of wear for the process. This ant-aging mechanism is described in Finkelstein (2003). Situation starts to be much more interesting, at least from the modeling point of view, when the current repair reduces the overall accumulated wear. We shall model this setting in the following way: Assume now that the repair at $t = t_1$ (realization of T_1) decreases the age of a system not to 0 as in the case of a perfect repair, but to $v_1 = qt_1, 0 < q < 1$, and the system starts the second cycle with this initial age in accor-

dance with the distribution of the remaining lifetime $1-\overline{F}(v_1+t)/\overline{F}(v_1)$. The constant q defines the quality of repair. The forthcoming results can be generalizes to the cases of random quality of repair (the time-dependent $q(t)$ can be also considered).

Thus, the reduction of wear is modeled by the corresponding reduction in age after the repair. Note that, as the failure rate of a component $\lambda(t)$ is increasing, the described operation also decreases its value and the failure rate at the beginning of the new cycle is smaller, than it was at the end of the previous one. The forthcoming cycles are defined in a similar way to form a *process of general repair* (Kijima, 1989; Finkelstein, 1992, 2000). The sequence of ages after the i th repair $\{V_i\}_{i\geq 0}$ in this model is defined as

$$V_0=0; V_1=qT_1; V_2=q(V_1+T_2),....,V_i=q(V_{i-1}+T_i),.... \tag{16}$$

and distributions of the corresponding inter-arrival times for realizations v_i are given by:

$$\overline{F}_i(t)=\frac{\overline{F}(v_{i-1}+t)}{\overline{F}(v_{i-1})}, i\geq 1.$$

Denote the distribution of age at the start of the $(i+1)$th cycle by $A_{i+1}^S(v)$, $i=1,2,....$ ($v=0$ at the start of the first cycle) and by $A_i^E(v), i=1,2,...$ the corresponding age distribution at the end of the previous i th cycle. It is clear that in accordance with our model (16):

$$A_{i+1}^S(v)=A_i^E(v/q)), i=1,2,...$$

This can be easily seen, as

$$A_{i+1}^S(v)=\Pr(V_{i+1}^S\leq v)=\Pr(qV_i^E\leq v)=\Pr(V_i^E\leq v/q),$$

where V_{i+1}^S is a random age at the start of $(i+1)$ th cycle, whereas V_i^E -at the end of the previous one. The following results (Finkelstein, 1992, 2000) state that the age processes under consideration are stochastically increasing and are tending to a limiting distribution.

a. *Random ages at the end (start) of each cycle in the general repair model (16) form the stochastically increasing sequences:*

$$\overline{A}_{i+1}^{E}(v) > \overline{A}_{i}^{E}(v),\ (\overline{A}_{i+2}^{S}(v) > \overline{A}_{i+1}^{S}(v)), t > 0; v > 0, i = 1,2,\ldots. \qquad (17)$$

b. *There exist limiting distributions for ages at the start and at the end of cycles:*

$$\lim_{i\to\infty} A_i^E(v) = A_L^E(v), (\lim_{i\to\infty} A_i^S(v) = A_L^S(v)). \qquad (18)$$

The proof of these results is rigorous but the interpretation is very simple and meaningful. Indeed, as the ages at the start (end) of the cycles are random, they should be compared stochastically. The simplest and the most natural ordering is the ordering of the corresponding distribution functions at every point of support, which is called stochastic ordering or stochastic dominance. It follows from (17) that the sequences of the corresponding mean ages at the start (end) of each cycle are also increasing. Thus, the process as a whole is aging, because the ages at the start (end) of the cycles are stochastically increasing with i and besides the failure rates of inter-arrival times are also increasing functions. On can loosely describe the process as 'stochastic sliding' to the right along the generic failure rate $\lambda(t)$, which is definitely can be qualified as aging. On the other hand, it follows from (18) that the sequences of ages have a finite limit, which means that aging of the process slows down and asymptotically vanishes!

If the repair process in parts of organisms decreases the accumulated wear and not only the wear of the last cycle, then the mortality rate (as a function of degradation) of these parts and of an organism as a whole, slows down at advanced ages and can even tend to a constant t (mortality plateau). Therefore, our model can explain the deceleration of human mortality at advanced ages (see, e.g., Thatcher (1999)) and even approaching the mortality plateau. It is worth noting that another possible explanation of the mortality deceleration phenomenon is via the concept of population heterogeneity (see Vaupel *et al* (1979) for basic facts and Finkelstein and Esaulova (2006) for mathematical details in a general frailty model).

It can be shown under reasonable assumptions that in case of a minimal repair, which does not reduce wear, or when repair reduces the damage only of the last cycle, the corresponding point process can be described by inter-arrival times of a non-homogeneous Poisson process with increasing rate. The ages at the start (end) of the cycles in this process tend to infinity as $i \to \infty$. Thus this model shows a different asymptotic behavior than the one considered before.

Example 4. The reduction of accumulated damage was modeled via the reduction of age (or the decrease in the failure rate). This is a reasonable approach, as under some assumptions, the process of damage accumulation can be 'translated' into the corresponding increasing failure rate model. In order to illustrate the limiting behavior of our model in a time-free, direct damage-based reasoning, consider the following simplified setting. Assume that each event from the orderly (without multiple occurrences) point process results in a unit damage which is immediately reduced by the repair mechanism to $q, 0 < q < 1$. Therefore, accumulation of damage in this model is given by the following series: after the first repair it is q; after the second repair it is $q(q+1) = q + q^2$; after the third repair it is $q(q(q+1)+1) = q + q^2 + q^3$,….Therefore, the accumulated damage increases with each cycle and tends to the limiting, stable value:

$$D_l = \frac{q}{1-q},$$

which defines the accumulated damage plateau.

5. CONCLUSIONS

Under a conventional assumption that the process of biological aging is a process of "tear and wear" we consider several approaches useful for modeling and analyzing lifetimes of organisms. All these approaches are united by the accumulation of damage concept, which allows incorporating and generalizing engineering-reliability thinking to a wider class of objects. Aging is an extremely complex biological process, but it does not mean that it cannot be modeled by some relatively simple stochastic tools.

Repairable and non-repairable systems are considered. We prove that even in the case of imperfect repair the resulting process of aging under reasonable assumptions slows down with time and asymptotically fades out. This gives another possible explanation of the human mortality rate plateau.

Using obtained results we plan to combine them in future work with optimization under constraints tools, developed in reliability theory, in a suitable for the evolutionary theory way.

REFERENCES

Barlow R., and Proschan F. (1975). *Statistical Theory of Reliability and Life Testing. Probability Models*. New-York: Holt, Rinehart and Winston.

Brown, M., and Proschan, F. (1983). Imperfect repair. *Journal of Applied Probability,* 20, 851-862.

Cox D.R. and Isham V. (1980). Point processes, Chapman and Hall, London.

Finkelstein, M.S., and V. Esaulova, V (2001) "Modeling a failure rate for a mixture of distribution functions," *Probability in the Engineering and Informational Sciences,* 15, 383-400.

Finkelstein, M.S. (2003). A model of biological aging and the shape of the observed hazard rate. *Lifetime Data Analysis,* 9, 93-109.

Finkelstein, M.S. (2005). On some reliability approaches to humans aging. *International Journal of Reliability, Quality and Safety Engineering,* 12, 337-346.

Finkelstein, M.S., an Esaulova V. (2006). Asymptotic behavior of a general class of mixture failure rates. *Advances in Applied Probability,* 38, 244-262.

Finkelstein, M.S., and Vaupel J. (2006). The relative tail of longevity and the mean remaining lifetime (with J. Vaupel). *Demographic Research,* 14/6, 111-138. http://www.demographic-research.org/Volumes/Vol14/7/14-7.pdf

Gavrilov, V.A., and Gavrilova N.S. (2001). The reliability theory of aging and longevity. *Journal of Theoretical Biology,* 213, 527-545

Gompertz, B. (1825). On the nature of the function expressive of the law of human mortality and on a new mode of determining the value of life contingencies. *Philosophical Transactions of the Royal Society,* 115, 513-585.

Hoyland A., and M. Rausand M. (1993). *System Reliability theory. Models and Statistical Methods.* John Wiley: New-York.

Kirkwood, T. (1977). Evolution of aging. *Nature*, 270(5635), 301-304.

Kirkwood, T. B. (1997). The origins of human aging. *Philosophical Transactions of the Royal Society of London-Series B: Biological Sciences*, 352(1363): 1765-1772.

Koltover, V.K. (1997). Reliability concept as atrend in biophysics of aging. *Journal of Theoretical Biology*, 184, 157-163.

Olofsson K. (2000). Branching process model of telomere shortening. *Commun. Stat.-Stochastic Models*, 16, 167-177.

Pletcher, S.D., and Neuhauser, C. (2000). Biological aging-criteria for modeling and a new mechanistic model. *International Journal of Modern physics C*, 11 (3), 525-546.

Shantikumar, J.G., and Sumita, U. (1983). General shock models associated with correlated renewal sequences. *Journal of Applied Probability*, 20, 600-6-14.

Steinsaltz, D., and Evans, S. (2004). Markov mortality models: Implications of quasistationarity and varying initial distributions. Theoretical Population Biology, 65:4.

Steinsaltz, D., and Goldwasser L. Aging and total quality management: extending the reliability metaphor for longevity. Submitted.

Strehler, B.L., and Mildvan, A.S. (1960). General theory of mortality and aging. *Science*, 132, 14-21.

Sumita, U., and Shantikumar, J.G. (1985). A class of correlated shock models. *Advances in Applied probability*, 17, 347-366.

Thatcher, A.R. (1999) "The long-term pattern of adult mortality and the highest attained age." *J. R. Statist. Soc. A*, vol. 162, pp. 5-43.

Vaupel, J.W., Manton K.G., and Stallard E. (1979). The impact of heterogeneity in individual frailty on the dynamics of mortality. *Demography*, 16, 439-454.

Vaupel, J.W., and Yashin, A.I. (1987). Repeated resuscitation: how life saving alters life tables. *Demography*, 4, 123-135

Vaupel, J. W. (2003). Post-Darwinian longevity. In: J. K. Carey and S. Tuljapurkar (eds). *Life Span. Evolutionary, Ecological and Demographic Perspectives. A Supplement to vol.29: Population and Development Review*: 127-151.

Witten, M (1985). A return to time, cells, systems and aging: 3. Gompertzian models of biological aging and some possible roles for critical elements. *Mechanics of Aging and development*,32, 141-177.

Yashin A.I., and Manton, K.G. (1997) "Effects of unobserved and partially observed covariate processes on system failure: a review of models and estimation strategies." *Statistical Science*, vol.12, pp. 20-34.

Yashin, A., Iachin, I., and Begun, A.S. (2000). Mortality modeling: a review. *Mathematical Population Studies*, 8, 305-332.