ON ENGINEERING RELIABILITY CONCEPTS AND BIOLOGICAL AGING

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ABSTRACT

In this study, various stochastic approaches to biological aging modeling are discussed. We assume that an organism acquires a random resource at birth. Death occurs when the accumulated damage (wear) exceeds this initial value. 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-Mildvan's model. Biological age, based on the observed degradation, is also defined. Finally, aging properties of imperfectly repaired systems are discussed. We show that aging slows down with age in this case. This presents another possible explanation for human mortality rate plateaus.

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

1. INTRODUCTION

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

Populations of biological organisms – unlike populations of technical devices – evolve in accordance with evolutionary theory. Various maintenance and repair problems (including those with limited resources) have been intensively studied by reliability theory. However, the notion of reproduction, which is crucial for bio-demography, has not been considered – although stochastic birth and death processes can certainly be useful for the corresponding odelling. 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 and mathematical tools for considering appropriate stochastic models of repair and maintenance in a proper evolutionary context. This means that existing and future reliability models could enrich biological aging theory and *vise versa*: for example, a disposable soma concept can be helpful for the optimal allocation of spare parts in some "structurally homogeneous" engineering systems.

It is worth noting that evolutionary theories tend towards a rather controversial view in that all damage, in principle, is repairable and 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 example, damage to the central nervous system and heart tissue is usually irreversible. In any case, the importance of different repair mechanisms for the survival of organisms is evident, which brings into play stochastic odelling of all types of repairable systems: perfectly, minimally and imperfectly repairable ones. This topic has been partially studied in reliability theory, but there are still many problems.

The future general theory of aging will probably be built on the basis of future unified biological theories that will use stochastic reliability approaches as an important analytical tool. Some interesting discussion on general "quality management" of organisms and the pros and cons of exploiting the existing reliability approaches for biological aging are presented in Steinsaltz and Goldwasser (2006).

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 the reliability odelling 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 odelling at earlier ages, but in this case they should be combined with the laws of natural selection".

In accordance with a conventional definition, reliability of a technical object is the probability of performing a designed function under given conditions and in a given interval of time (Hoyland and Rausand, 1993). 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 example, 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 for adults, perfectly comply with this model.

In accordance with reliability terminology, the Gompertz law belongs to a family of increasing failure rate (IFR) distributions. This is the simplest and most commonly used in reliability theory aging family of distributions. It is widely used for description of various degradation processes in engineering systems (Barlow and Proschan, 1975). There were a number of attempts in the past to justify the exponential form of the human mortality rate by some mechanism or model, but most of these exploited additional assumptions, either explicitly or implicitly equivalent to the desired exponentiality. (Strehler and Mildvan, 1960; Witten, 1985; Koltover,1997; Gavrilov and Gavrilova, 2001).

In what follows, we consider several important applications of reliability-based stochastic reasoning, unified by concepts of aging and degradation. This is partially a review paper of relevant approaches that are mostly developed or generalized by the author in the field of engineering reliability, but modified and adjusted to the description of biological aging.

In Section 2, the resource-based models are considered – an organism at birth acquires some random resource (vitality) and the death occurs when this resource is 'consumed'. For the first time, we use here the unified approach to deal both with the cases of continuous and discrete

resources. Specifically, we show that the reliability theory of aging (Gavrilov and Gavrilova, 2001) is a simple particular case of our more general model and, moreover, does not necessarily result in the Gompertz law.

Section 3 is devoted to the definition of the virtual age of a degrading object. We consider this topic as being one of the most important for the future research, as it creates the possibility of comparing life spans of organisms in different environments.

In Section 4, we suggest a new generalization of the Strehler and Mildvan (1960) vitality model with shocks, and show that the necessary condition that is omitted in original and subsequent publications is the assumption of the Poisson property of the shock process.

Finally, Section 5 deals with aging in repairable systems (imperfect repair). The results of this section are based on our recent mathematical findings (Finkelstein, 2007). An important interpretation for biological aging is that under certain assumptions, aging can slow down for individuals of advanced ages, which is already observed for human populations (mortality plateau).

We are convinced that mathematical, reliability-based modeling of aging is an important part of biological aging research. We show how straightforward stochastic approaches can work, in principle, for some settings. These approaches are probably oversimplified and should be developed in the future to more closely match the real biological situation.

N. UNOBSERVED OVERALL RESOURCE

Following Finkelstein (2003), we assume that an organism at birth ($t = 0$) acquires an overall unobserved random resource R with a distribution function $F_0(r): F_0(r) = P(R \le r)$. We also assume that the process of an 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 $w(t) + o(dt)$. Additionally, let $W(t) \to \infty$ as $t \to \infty$. Under these assumptions, we arrive at the well-known in reliability theory the accelerated life model (ALM):

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

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

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 relationship (Finkelstein, 2003):

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

where the expectation is defined with respect to $W_t, t \ge 0$. As the mortality rate is a conditional characteristic, it cannot be obtained 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 Wiener process can also sometimes be used for odelling 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 independent and identically distributed (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: $n\lambda, (n-1)\lambda, (n-2)\lambda, ...$ Denote by $\mu_n(t)$ the mortality rate, which describes T_n - the time to death random variable for the fixed $N = n, n = 1,2,...$. ($n = 0$ 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 carefully in this case. It is clear that as $t \to \infty$:

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

This is because 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 can be shown that (Steinsaltz and Evans, 2004):

$$F(t) = P(T \le t) = \frac{1-\exp\{-\eta \exp\{-\lambda t\}\}}{1-\exp\{-\eta\}}. \tag{8}$$

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) exists for the mortality rate (9) as well. This function is far from the exponentially increasing Gompertz law. In fact, the Gompertz law can erroneously result, if approximation (6) is used formally, as in Gavrilov and Gavrilova (2001).

O. DEGRADATION AND VIRTUAL (BIOLOGICAL) AGE

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 $W_t, t \ge 0$. Observing its state at time t can give, under certain assumptions, an indication of a 'true' age, which is 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 example, someone of 50 years old looks like and has vital characteristics (blood pressure, level of cholesterol, etc) that

are of an 'ordinary' 35- year-old individual, we could say that this observation indicates that his virtual (biological) age can be estimated as 35 years. This is, of course, a rather vague statement, which could 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 (mortality) rates λ, which starts operating at $t=0$. 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. The mortality rate of the described system is an increasing function of the form (Hoyland and Rausand, 1993):

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

Consider the following conditional expectation:

$$D(t) \equiv E[N(t) \mid N(t) \leq n] = \frac{\exp\{-\lambda t\}\sum_0^n i\frac{(\lambda t)^i}{i!}}{\exp\{-\lambda t\}\sum_0^n \frac{(\lambda t)^i}{i!}} \tag{11}$$

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, relationship (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. Assume that at time t we observe k failed components. This is the measure of observed degradation in our system. Denote the corresponding (information-based) virtual age by $V(t)$. Our definition of $V(t)$ for this specific model is:

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

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

When the observed degradation k at time t is less than the expected $D(t)$, then the corresponding virtual age is less than a calendar age t and vise versa.

If n is sufficiently large, then $D(t) = \lambda t$ and in accordance with (12):

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

Equivalently, as the function $D(t)$ is linear in this specific case, the virtual age $V(t)$ is equal to the expected age at which the number of observed failures is k.

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 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 virtual age is defined as:

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

Alternatively, the virtual age can be defined as the mean age for the process to reach the level d_t. Usually, obtaining $D(t)$ is easier then obtaining the mean time to reach the threshold d_t and, therefore, the foregoing definition is more convenient.

Thus, considering degradation in a simple reliability structure resulted in a general definition and in a helpful for studying of aging notion of virtual age. Note that, the approach of this section is heuristic and further mathematical justification will be published elsewhere.

P. SHOCK MODELS AND DEGRADATION

Technical systems and organisms are usually subject to shocks, which are harmful events that occur randomly in time and magnitude, and that can cause a failure or death, respectively. We assume for simplicity that durations of shocks are negligible. In mechanical and electronic systems, for example, shocks occur when the applied load exceeds the strength. Diseases, viruses, heart attacks or, more generally, demands for energy (as in the Strehler-Mildvan 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 open questions from theoretical and practical points of view. Traditionally, two basic cases – the cumulative shock model and the 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 will revisit the Strehler-Mildvan 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 model (Strehler and Mildvan, 1960), which was widely applied to human mortality data, our $R(t) - w(t)$ has a meaning of vitality of organisms. 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) did reduce to the usual, non-history-dependent mortality rate $\mu(t)$ (unfortunately, the Strehler-Mildvan model did not consider this crucial assumption):

$$\mu_c(t,H_t)=\theta(t)\lambda(t)=\mu(t). \qquad (14)$$

Therefore, the conventional exponential representation for the corresponding survival function ($\overline{F}(t)\equiv 1-F(t)$) is

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

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, for example, in Brown and Proschan (1983). Another meaningful interpretation of this result is via the thinning of the initial Poisson process with the rate $\lambda(t)$, which results in the Poisson process with the rate $\theta(t)\lambda(t)$. Therefore, the survival function up to the first event in this process (death) is given by equation (15).

We have derived equations (14) and (15) for the sample paths $w(t)$ and deterministic $R(t)$. A general case of the processes $W_t, t\geq 0$ and $R_t, t\geq 0$ can be also considered under reasonable assumptions. The probability $\theta(t)$ turns to a stochastic process $\theta_t, t\geq 0$, whereas the 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 analyzed. When $R(t)-w(t)$ is decreasing, the probability of death $\theta(t)$ is increasing with age, which is consistent 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 example, $R(t)$ can increase faster than $w(t)$ - an organism is 'earning or obtaining' additional vitality in the course of life. This approach, in fact, deals with two dependent sources of death: degradation and shocks.

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): $\mu_n, n = 0,1,2,....$ It is reasonable to assume that mortality rates are increasing with degradation: $\mu_0 < \mu_1 < \mu_2 < ....$ 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 cumbersome.

Q. 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, little had been done in terms of stochastic repair odelling in organisms. On the 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 usual, that repair is perfect (after the repair a component is as good as new. The sequence of independent, identically distributed inter-arrival times $\{T_i\}_{i\ge1}$ with a common distribution function $F(t)$ forms a standard renewal process. The repair times in this case are given by the sequence $T_1, T_1 + T_2, T_1 + T_2 + T_3, ...$ 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.

Let us call a period between two successive repairs a 'cycle'. We have two major possibilities. The first is when the imperfect repair reduces wear of the last cycle only. 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). The 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 accordance 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 generalized 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, 2007). The sequence of ages after the i th repair $\{V_i\}_{i\geq 0}$ in this model is defined as:

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

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

$$A^S_{i+1}(v) = A^E_i(v/q)), i = 1,2,...$$

This can be easily seen, as

$$A^S_{i+1}(v) = \Pr(V^S_{i+1} \leq v) = \Pr(qV^E_i \leq v) = \Pr(V^E_i \leq v/q),$$

where V^S_{i+1} is a random age at the start of $(i+1)$ th cycle, whereas V^E_i -is a random age at the end of the previous one. The following results (Finkelstein, 2007) 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:*

$$\overline{A}^E_{i+1}(v) > \overline{A}^E_i(v), (\overline{A}^S_{i+2}(v) > \overline{A}^S_{i+1}(v)), t > 0; v > 0, i = 1,2,.... \quad (17)$$

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

$$\lim_{i\to\infty} A^E_i(v) = A^E_L(v), (\lim_{i\to\infty} A^S_i(v) = A^S_L(v)). \quad (18)$$

The corresponding interpretation is 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. This is usually 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 the failure rates of inter-arrival times are also increasing functions. The process can be described as "stochastic sliding' to the right along the generic failure rate $\lambda(t)$, which can definitely 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, for example, 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 the 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 previously.

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 IFR 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.

R. CONCLUSIONS

Under a conventional assumption that the process of biological aging is a process of "wear and tear" we consider several approaches that are useful for odelling and odelling the lifetimes of organisms. All these approaches are united by the accumulation of damage concept, which allows the incorporation and generalization of 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 odellin 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 the obtained results, we plan to combine them in future work with optimization under constraints tools, developed in reliability theory, in a suitable evolutionary-theory-based manner.

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