The Reliability-Engineering Approach to the Problem of Biological Aging

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ABSTRACT: We applied reliability theory to explain aging of biological species and came to the following conclusions: (1) Redundancy is a key notion for understanding aging and the systemic nature of aging in particular. Systems, which are redundant in numbers of irreplaceable elements, do deteriorate (i.e., age) over time, even if they are built of nonaging elements. (2) An apparent aging rate or expression of aging (measured as age differences in failure rates, including death rates) is higher for systems with higher redundancy levels. (3) Redundancy exhaustion over the course of life explains the observed *compensation law of mortality* (mortality convergence at later life) as well as the observed late-life mortality deceleration, leveling-off, and mortality plateaus. (4) Living organisms seem to be formed with a high load of initial damage, and therefore their life span and aging patterns may be sensitive to early-life conditions that determine this initial damage load during early development.

KEYWORDS: redundancy; compensation law of mortality; mortality plateaus; reliability theory

INTRODUCTION

Twenty-five years ago, we first applied the reliability theory to explain aging of biological species.[1,2] Since that time, we continued the development of this theory[3–5] and have come to the following conclusions: (1) Redundancy is a key notion for understanding aging and the systemic nature of aging in particular. Systems, which are redundant in numbers of irreplaceable elements, do deteriorate (i.e., age) over time, even if they are built of nonaging elements. (2) An apparent aging rate or expression of aging (measured as age differences in failure rates, including death rates) is higher for systems with higher redundancy levels. (3) Redundancy exhaustion over the course of life explains the observed *compensation law of mortality* (mortality convergence at later life) as well as the observed late-life mortality deceleration, leveling-off, and mortality plateaus. (4) Living organisms seem to be formed with a high load of initial damage, and therefore their life span and aging patterns may be sensitive to early-life conditions that determine this initial damage load during early

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development. The idea of early-life programming of aging and longevity may have important practical implications for developing early-life interventions promoting health and longevity.

The theory also suggests that aging research should not be limited to studies of qualitative changes (such as age changes in gene expression), because changes in quantity (numbers of cells and other functional elements) could be a more important driving force of the aging process.

DISCUSSION OF THE RELIABILITY-ENGINEERING APPROACH TO THE AGING PROBLEM

There may be several different research strategies in attempts to understand the nature of the aging process. The prevailing research strategy now is to focus on the molecular level in the hope of understanding the proverbial nuts and bolts of the aging process. In accordance with this approach, many aging theories explain aging of organisms through aging of organisms' components. However, this circular reasoning of assuming aging to "explain" aging leads to a logical contradiction, because moving in succession from the aging of organisms to the aging of organs, tissues, and cells, we eventually come to atoms, which are known not to age.

Thus, we come to the following basic question on the origin of aging: How can we explain the aging of a system built of nonaging elements? This question invites us to start thinking about the possible systemic nature of aging and to wonder whether aging may be a property of the system as a whole. In other words, perhaps we need to broaden our vision and be more concerned with the bigger picture of the aging phenomenon rather than its tiny details.

To illustrate the need for a broad vision, consider the following questions. (1) Would it be possible to understand a newspaper article by looking at it through an electronic microscope? (2) Would the perception of a picture in an art gallery be deeper and more comprehensive at the shortest possible distance from it?

A good example of a broad vision of the aging problem is provided by the evolutionary theories of aging.[6–8] Evolutionary perspective helps us to stay focused on a bigger picture, and to avoid being overwhelmed by billions of tiny details. Evolutionary theories demonstrate that taking a step back from too close consideration of the details over "the nuts and bolts" of the aging process helps to gain a broader vision of the aging problem.

The remaining question is whether the evolutionary perspective represents the ultimate general theoretical framework for explanations of aging. Or perhaps there may be even more general theories of aging, one step further removed from the particular details?

The main limitation of evolutionary theories of aging is that they are applicable to reproducing organisms only, because these theories are based on the idea of natural selection and on the declining force of natural selection with age.

However, aging is a very general phenomenon—it is also observed in technical devices (such as cars), which do not reproduce themselves in a sexual or any other way and that are, therefore, not subject to evolution through natural selection. Thus, there may exist a more general explanation of aging, beyond the evolutionary theories.

The quest for a general explanation of aging (age-related increase in failure rates) applicable both to technical devices and biological systems invites us to consider the general theory of systems failure known as reliability theory.[1–5] Interestingly, the reliability theory suggests that we reevaluate the old belief that aging is somehow related to limited economic or evolutionary investments in systems' longevity. The theory provides a completely opposite perspective on this issue: that aging is a direct consequence of investments into systems reliability and durability through enhanced redundancy. This is an important statement, because it helps to explain why the expression of aging (age-associated differences in failure rates) might be more profound in more complicated redundant systems, designed for higher durability.[5]

The theory also suggests that research on aging should not be limited to the studies of qualitative changes (such as age-related changes in gene expression), because changes in quantity (numbers of cells and other functional elements) could be an important driving force of the aging process. In other words, aging might be largely driven by a process of redundancy loss.[5,9]

Reliability theory predicts that a system may deteriorate with age even if it is built from nonaging elements with constant failure rates.[3–5] The key issue here is the system's redundancy for irreplaceable elements, which is responsible for the aging phenomenon. In other words, each particular step of system destruction or deterioration may seem to be random (no aging, just occasional failure by chance), but if a system failure requires a sequence of several such steps (not just a single step of destruction), then the system as a whole may have an aging behavior. Why is this conclusion important? Because the significance of beneficial health-promoting interventions often is undermined by claims that these interventions are not proved to delay the process of aging itself, but instead that they simply delay or cover up some particular manifestations of aging.

In contrast with these pessimistic views, reliability theory says that there might be no specific underlying elementary aging process; instead, aging might be largely a property of a redundant system as a whole, because it has a network of destruction pathways, each being associated with particular manifestations of aging (types of failure). Therefore, we should not be discouraged by only partial success of each particular intervention, but instead we can appreciate that we might have many opportunities to oppose aging in numerous different ways.

Thus, the efforts to understand the routes and early stages of age-related degenerative diseases should not be discarded as irrelevant to understanding true biological aging. On the contrary, attempts to build an intellectual firewall between biogerontological research and clinical medicine are counterproductive. After all, the main reason why people are really concerned about aging is because it is related to health deterioration and increased morbidity. The most important age-related changes, with respect to quality of life, are those that make older people sick and frail.

Reliability theory suggests general answers to both the "why" and the "how" questions about aging. It explains why aging occurs by identifying the key determinant of aging behavior: system redundancy in numbers of irreplaceable elements. Reliability theory also explains how aging occurs, by focusing on the process of redundancy loss over time as the major mechanism of aging. It is perfectly compatible with evolutionary theories of aging, and it helps to identify key components, which might be important for the evolution of species reliability and durability (longevity): initial redundancy levels, rate of redundancy loss, and repair potential. Moreover, reliability theory helps evolutionary theories to explain how the age of onset of deleterious mutations could be postponed during evolution, which could be easily achieved by a simple increase in initial redundancy levels. From the reliability perspective, the increase in initial redundancy levels is the simplest way to improve survival at particularly early reproductive ages (with gains fading at older ages). This matches exactly with the higher fitness priority of early reproductive ages emphasized by evolutionary theories. Evolutionary and reliability ideas also help in understanding why organisms seem to "choose" a simple but short-term solution of the survival problem through enhancing the systems' redundancy, instead of a more permanent but complicated solution based on rigorous repair (with the potential of achieving negligible senescence). Thus, there are promising opportunities for merging the reliability and evolutionary theories of aging.

Aging is a complex phenomenon, and a holistic approach using reliability theory may help to analyze, understand, and perhaps control it. We suggest therefore that reliability theory should be added to the arsenal of methodological approaches applied in research on aging.

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