# **COMPLEX SYSTEMS BIOPHYSICS**

# Comparative Analysis of Methods for Estimating the Rate of Population Aging

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Abstract—The essence of aging is a decline in total vitality with age, being basic personal characteristics of human potential. Viability (v) is defined as the probability of surviving through one year. Mortality (m) is defined as the probability of dying within the course of the year and, therefore, has an opposite meaning to the term viability but can be an adequate index to estimate the degree of aging of the organism. For the quantitative analysis of aging, a Gompertz—Makeham model (a traditional approach) has been widely used for a long time in describing the phenomenon of exponential increase in mortality rate with age rather well. The other approach to assessing the aging process is to calculate the rate of increment to the mortality rate with age (d(m)), which characterizes the rate of the aging process. The aim of this work is to compare the informativeness, accuracy, and convenience of these approaches to solve the problem of estimating the rate of human aging based on the analysis of age-specific mortality rate in an age group of the human population. It is shown that d(m) is the most accurate, easy to calculate, and mathematically and biologically adequate indicator of the aging rate. This indicator is seen as important to estimate historical changes in the characteristics of the aging of the human population: constancy in the aging rate in history and decline in the aging rate since the middle of the 20th century for middle and older ages as well as the preservation of a reduced aging rate for centenarians.

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The higher proportion of elderly people in the populations of all developed countries of the world is the most important demographic feature of the present time and determines the increased interest in the problem of aging [1-4]. At the same time, one of the important questions is the quantitative measurement of aging rate.

The essence of aging is the age-related decrease in overall vitality, which is the main characteristic of personal potential.

Vitality (v) is defined as the probability of surviving through one year; mortality (m) is defined as the probability dying within a year and, therefore, has an opposite meaning but can be an adequate index to estimate the degree of aging of the organism. Another approach to estimation of aging is the calculation of the increment to the mortality rate with age: d(m), which directly characterizes the rate of aging.

Almost 200 years ago, B. Gompertz showed that the age-related change in mortality rate is well described by the exponential function [5], and the Gompertz formula with W.M. Makeham's correction characterizing the mortality from external causes has been widely used since then to describe the age dynamics of mortality. The Gompertz–Makeham formula, which mathematically models the change in mortality rate with age, is as follows:

$$m(t) = R_0 \exp(kt) + A,$$

where m(t) is the mortality rate for age t; k is the exponent; A and  $R_0$  are the age-independent constants. Constant  $R_0$  is often given the meaning of "the initial level of aging" [6].

The aim of the work was to compare the two abovementioned methods for estimating the aging rate and their correspondence to the essence of aging.

# MATERIALS AND METHODS

In gerontology, it is conventional to measure the mortality rate as an indicator of aging; for this purpose, there are tables of survival rate for a standard cohort with the calculated statistical indices, also including the mortality rate value, m, which character-

izes the level (degree) of aging of cohort members of a given age [6, 7]. These tables make it possible to estimate the aging rate d(m) in the simplest way: by calculating the difference of the neighboring m values divided by the age step used for compiling the tables (usually, it is 1 year).

The methods for assessing the aging rate were compared using the survival tables for the standard cohort (The Human Mortality Database, http://www.mortality.org) with the already calculated statistical indices, including the mortality rate value *m* [8]; the values of the Gompertz–Makeham formula were calculated by the generally accepted method described in [6].

#### **RESULTS AND DISCUSSION**

The analysis of mathematical features of the formulas describing aging shows the following.

The Gompertz–Makeham formula calculates the *absolute* values of the force of mortality *m* for a certain age; therefore, to compare the *rate* of aging of different populations averaged over the period of human life, we have to resort to comparing the *slopes* of the curves of the age dependence of *m*, which assumes, in particular, the uniformity of changes in the indicator throughout the entire period of life. The aging rate of an individual population is often assessed simply by the general view of this graph.

In addition, the biological (i.e., determined by the internal processes of body aging) component of aging is calculated by the Gompertz-Makeham formula using the m - A index: the difference between the total force of mortality and the external environmental component of mortality, which is believed to be dependent not on age but only on the external living conditions and is taken as a constant (which is not true even theoretically). A direct estimate of aging rate can be obtained by calculating the increment to the mortality rate, d(m), based on the survival tables for standard cohorts.

Let us further make a theoretical comparison of the convenience, accuracy, reliability, and biological essence of both methods of aging rate estimation.

1. In practice, the calculation of d(m) is much simpler and more accurate than the calculation of the coefficients of the Gompertz-Makeham formula.

2. The d(m) index represents the rate of aging for a specific age rather than the average values for a wide range of ages given by the Gompertz–Makeham formula because it is precisely the parameter of rate in essence of calculation.

3. The d(m) index directly estimates the *rate* of aging, whereas the Gompertz-Makeham model shows the *absolute* values of m, which do not indicate the aging rate directly and require drawing the slope lines of the graph.

4. The d(m) index has only one biological meaning: aging rate. The Gompertz-Makeham formula includes the parameters that are not directly related to the aging process: the age independent "external environmental" parameter A and the coefficient  $R_0$  with a not quite clear biological meaning, which is vaguely referred to as the "initial aging level." The only coefficient directly representing the process of aging is the exponential factor k; however, minor changes in this factor lead to significant age-related changes in the aging rate, which, in turn, results in the low accuracy of experimental estimates of the differences in aging rates, e.g., for different countries. The presence of coefficient A in the Gompertz–Makeham formula leads to abrupt changes in the graph shape at high A values, especially at a young age (Fig. 1a), which results in deviation of the graph from the straight line in the semilog coordinates for younger ages. For the ages of long-livers, in view of the very high mortality at these ages that is almost entirely dependent on the aging process, the (m - A) and m values are nearly the same. All these aforementioned effects distort the basic law of aging (the exponential growth of mortality) at young and old ages and represent it adequately only for the middle age. Meanwhile, the d(m) index remains linear over a much longer age period, in fact, throughout the entire period of aging following the period of growth and development of the human organism.

5. The presence of several coefficients in the Gompertz–Makeham formula leads to the fact that they turn out to be related to each other during the calculation, which makes it very difficult to compare the aging rate in several populations or in different historical periods.

6. The d(m) index represents the aging rate for each age, while the Gompertz-Makeham formula is based on averaged values. As a result, the model plot based on the calculated Gompertz-Makeham coefficients does not coincide with the real plot of *m* in the initial and final areas of age.

7. It is sufficiently clear from general considerations that coefficient A of the Gompertz–Makeham formula taken as a constant will not be the same for different ages because environmental factors are obviously different for young and old people, just as responses of the body to these factors, since the essence of aging is a substantial age-related increase in vulnerability of the body to all impacts. The constant A for *the closest* age values is almost the same for the d(m) parameter and, hence, the value of parameter A has actually no effect on the aging rate value.

8. The d(m) index is less in the absolute value and spread than m (by an order of magnitude or more), which makes this parameter more accurate and the graph more clear, sensitive, and demonstrative, reflecting the minor changes in aging rate in different age periods and when comparing different periods and historical epochs. The consequence of this, however, is the sensitivity of this parameter to random noise,

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which makes the d(m) graph not smooth like the *m* graph but notched if the calculations for each year are used. Nevertheless, it can be easily avoided by using a step of 3–5 years or smoothing the graph over three to five points.

9. As can be seen (Fig. 1b), the d(m) index clearly and conspicuously shows the changes in aging rate at the middle age, whereas these changes are not detectable to the eye in the *m* and (m - A) graphs. In addition, the d(m) graph shows persistence of the phenomenon of decrease in the aging rate for long-livers from the middle of the last century to the present time, whereas we can see the reversion of this process for *m* and (m - A): the seeming acceleration of aging for long-livers. This reversion can be accounted for by a rapid increase in life expectancy, which statistically shifts more and more individuals with the normal aging rate to the area of long-livers.

10. Finally, if we compare the slope angle for the m and (m - A) graphs for the past (50–70 years ago) and the present, it often turns out that the slope of the curves has increased in the present, which formally indicates an increase in the aging rate! However, all gerontological studies show that 70-year-old people, with respect to all physiological parameters, social activity, general appearance, general state and mortality statistics, at present correspond to 50-60-year-old people in the earlier historical periods, i.e., there is an undoubted comparative rejuvenation of middle-aged and elderly people, which, in turn, can only be achieved due to a decrease in the aging rate. The change in the angle of slope of the *m* and (m - A)graphs is inevitable in case of very significant changes in the average life expectancy in history and very insignificant changes in the maximum life expectancy, i.e., the age of complete extinction of a standard cohort. This is not surprising because mortality at the final stages of life increases so rapidly that the changes in the aging rate at the earlier ages have hardly any effect on the aging rate of the final stages of life: the endpoints of the graph cannot shift significantly due to the very high mortality rate of elderly people. On the contrary, the drastic changes in mortality at young and middle age significantly reduce the initial values of the graph, giving the appearance of an abrupt change in the slope of the graph. In addition, as has been mentioned above, the method of determining the slope of the graph assumes its linearity over the entire age period, which is clearly not the case. All the above is absent in the graph of the d(m) index, which adequately shows the rate of aging and it changes for a given age and does not depend on the mean values and constant coefficients as in the Gompertz-Makeham formula.

The d(m) index makes it possible to describe the peculiarities of aging in a clear and strict way, in particular, the historical changes in aging rate: the rate of aging in history and the decrease in aging rate since the

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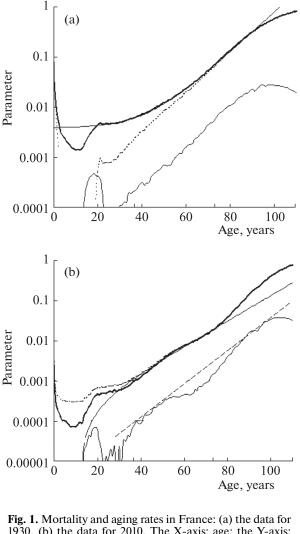


Fig. 1. Mortality and aging rates in France: (a) the data for 1930, (b) the data for 2010. The X-axis: age; the Y-axis: rates (logarithmic scale). The plots of true force of mortality m (bold line), the model curve by the Gompertz–Makeham formula (thin line), the true mortality without an external component (m–A) (dotted line), the increment to the force of mortality d(m) for one year (smoothed by three points, the lower line) are presented. The dotted line in (b) is a theoretical straight line for visual representation of the deviation (decrease) of the aging rate from the straight line at middle and older ages. The parameters of the Gompertz–Makeham formula were calculated according to Gavrilov et al. [6].

middle of the 20th century for middle-aged people as well as the maintenance of the lower aging rate for long-livers [4, 7].

The d(m) formula is, in the essence of calculation (the difference of values divided by time), exactly the rate parameter and, therefore, is adequate specifically to the rate of aging; its main role is to analyze the available statistical material. The index has no predictive power, though the latter can be extrapolated from the previous values of d(m); it does not seem productive to calculate the aging rate according to the Gompertz– Makeham formula because the Gompertz–Makeham graph has already been smoothed and all peculiar features of aging rate in the age aspect have already been eliminated.

The present article is, in essence, a "letter to the editor" and has been written in response to the request of the reviewer of our previous paper [7] to compare more thoroughly and to explain the two methods of aging rate calculation. The detailed analysis and comparison of the methods by the example of several tens of countries and within several centuries had been presented previously [7] and is not the subject of the article; all peculiarities of changes in the aging rate for different countries, at different times, at different ages, as well as their probable causes, are the subjects of our extensive articles written earlier [4, 7], where we also discussed in detail the specifics of behavior of individual components of aging indicators at different ages in different historical epochs [7].

#### CONCLUSIONS

The paper presents the results of a comparative analysis of the two approaches to quantitative description of aging rate at the population level: the Gompertz–Makeham equation for mortality rate m (the traditional approach) and calculation of the aging rate by measuring the difference in mortality rate for adjacent age groups: d(m), using life expectancy tables. It has been shown that the d(m) index is a more accurate, easy-to-calculate, and mathematically and biologically more adequate indicator of aging rate, which reflects the rate of aging at a particular age and allows the study of historical regularities of aging rate in the human population. This index made it possible to detect persistence of the aging rate in history and the decrease since the middle of the 20th century for middle and older ages as well as persistence of the lower aging rate for long-livers [4].

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## COMPLIANCE WITH ETHICAL STANDARDS

The authors declare that they have no conflicts of interest. This article does not contain any studies involving animals or human participants performed by any of the authors.

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