Law of universal mortality

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Mortality is arguably the best statistically quantified biological phenomenon. This allows for a physical approach to its study. I establish that in well protected populations, a dominant fraction of mortality at a given age depends on a single parameter only. Such invariance to any other time and space changes is known only in general relativity. It is so mathematically restrictive that, with no other knowledge of experimental data, it is sufficient to predict the exact law. It is universal for species as remote as humans and flies. The law unravels its biologically nonspecific thermodynamic mechanism. It implies that within a couple of years human mortality may be reset to its value at a much younger age. The reversal (albeit not yet as rapid) is consistent with demographic data. For instance, Swedish females, born in 1916, at 48 yr restored their mortality rate 28 yr earlier. The law and its other predictions and implications are also verified. The universal law suggests that a dominant fraction of mortality in well protected populations is just a by-product, which may be eliminated. Total mortality can be significantly decreased.

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I. DERIVATION OF THE LAW

I apply the concept of invariance to mortality. This yields an exact law of the nature of the invariant mortality. Contrary to all existing theories of mortality [1–3], the law is biologically nonspecific (i.e., independent of genotypes, phenotypes, life history, old age diseases, and all other relevant factors, describing the population and its environment from conception to the age of death). Such a law and its mechanism could arguably be discovered with a physical approach only.

Mortality is extensively quantified in demographic ''life tables'' [4], which use accurately registered human birth and death records. The so-called ''period'' tables contain the mortality rates $q_x(t,r)$, i.e., the probabilities to die from age x to $x+1$ [5] in a given calendar year t, for a given sex and country or its specific group r (over 50 000 data items for Sweden alone). The rates depend on a multitude of unquantified factors [5] describing all kinds of relevant details about the population and its environment, from conception to the age of death. Female mortality rates $q_{40}(t,r)$ and $q_{80}(t,r)$ versus $q_0(t,r)$ in countries as different as Japan, Sweden, and Australia have been plotted in Fig. 1. Their different history and living conditions yield rates which may be very different in the same year, close in the years separated by half a century (e.g., in 1877 Sweden and 1947 Japan), and change almost 300-fold with country, time, and age. Nevertheless, all data in Fig. 1, as well as those for other ages, fall close to the universal curves. Demographers noticed that infant mortality is a sensitive barometer of environmental conditions, established strong correlation between mortality rates at different ages, and presented their regularities in similar sets. Demographers also observed that these similarities are often violated by significant fluctuations over time, country, and age. To accurately estimate and forecast mortality, they developed over 15 specific approximations (e.g., Sweden and Italy yield two different approximations each). I chose a different approach. I maintain that as long as parameters which affect mortality are not quantified and taken explicitly into account, our ability to accurately study mortality and its biology is limited to only their universal fraction, i.e., that fraction which is related to the infant mortality only, and to this accuracy is independent of all other factors. I verify that the universal fraction dominates for males and females in 16 developed countries, over a century of their history, albeit in some cases to a lower accuracy than in Fig. 1.

To state the observed universality in a precise fashion, female mortality rate is presented as

$$q_x(t,r) = Q_x + D_x(t,r).$$

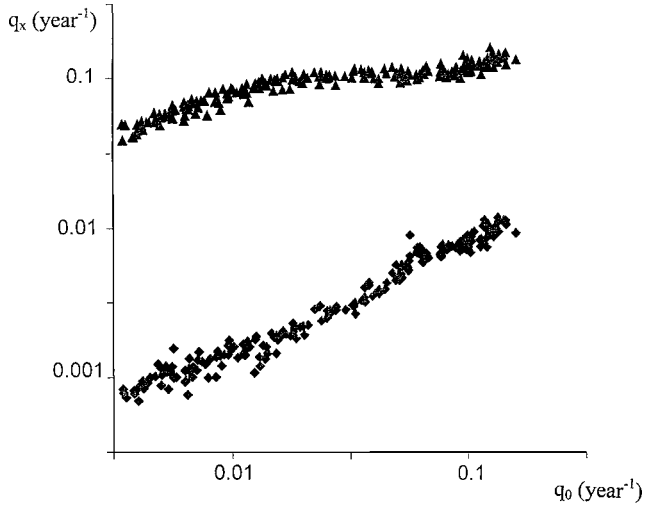

FIG. 1. Universality of human mortality. Logarithms of female mortality rates $q_x(t,r)$, at age x in the year t and country r, vs $q_0(t,r)$ (horizontal axis) for $x=40$ (bottom), and 80 (top), in 1861–1999 Sweden, 1891–1996 Japan, 1909–1997 Australia, and their subgroups. The only significant deviation (Sweden, $q_0=0.009\,04$) is related to the 1918 flu pandemic in Europe. Note that infant mortality changes almost 100-fold.

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The dominant universal component Q_x satisfies universality exactly, i.e., depends only on the infant mortality Q_0 in the same calendar year and country, and provides the minimal relative mean squared deviation from $q_x(t,r)$. (Figure 1 demonstrates that the noninvariant D_x is small compared to Q_x.) These statements mathematically accurately determine the universal fraction and yield its exact law $Q_x(Q_0)$. The derivation is most transparent for the survival probability $l_x(t,r)$ to age x for a (hypothetical) life span under the conditions which existed at time t. In the period life tables $l_x(t,r)$ is calculated as $l_x(t,r)=p_0(t,r)p_1(t,r)\cdots p_{x-1}(t,r)$, where $p_y(t,r)=1-q_y(t,r)$ is the probability to survive in a given case from y to $(y+1)$ in the year t. The universal mortalities yield the universal fraction f_x of the total survivability l_x. It depends on f_1 only. As seen in Fig. 1, the infant mortality $q_0=1-l_1$ changes 50-fold over time, due to a strong dependence on living conditions that vary with time. Living conditions of different (e.g., urban/rural) subgroups $G=1,2,...$ (which are included in Fig. 1) in a given country differ even at the same time t (see Ref. [5]). The population l_x is the average $\langle l_x^G\rangle$ of the survivabilities l_x^G of its constituent subgroups $G=1,2,...$. Indeed, $l_x=N_x/N_0$, where the number N_x of survivors up to the age x is their sum over the subgroups, and $l_x^G=N_x^G/N_0^G$. Since the probabilities l_x, l_x^G are $\geqslant 0$ but $\leqslant 1$, their boundaries $l_x=0$ and $l_x=1$ are reached only when all subgroups simultaneously reach $l_x^G=0$ and $l_x^G=1$. This implies homogenization of survivability in an entire population when $l_x\to 0$ or $l_x\to 1$.

The universal law is the same for the population, $f_x=f_x(f_1)$, and its subgroups, $f_x^G=f_x(f_1^G)$. The population universal survivability $f_x=\langle f_x^G\rangle$ is the average of its subgroups; in particular, $f_1=\langle f_1^G\rangle$. (Note that only group survivabilities, rather than, e.g., their mortality rates are additive.) Thus, on the one hand, $f_x=f_x(f_1)=f_x(\langle f_1^G\rangle)$; on the other hand, $f_x=\langle f_x^G\rangle=\langle f_x(f_1^G)\rangle$. So, additivity of the group survivabilities yields a transparent equation:

$$\langle f_x(f_1^G)\rangle=f_x(\langle f_1^G\rangle). \tag{1}$$

The averages in Eq. (1) depend on the mortalities and the fractions of population in the groups. However, no change in the universal subgroups and their mortalities with time and place affects $f_x(f_1)$. In physics such invariance to arbitrary changes with time t and space r is known only in general relativity. In mathematics such an invariant solution, independent of the corresponding changes in the equation, exists only in very special cases, but then the invariance itself is sufficient to yield the solution with no other knowledge of mortality data. Remarkably, Eq. (1) is the case. A general solution to Eq. (1) is piecewise linear. Thus, in each linear interval it may be reduced to the universal values $f_x(F^{(s)})$ and $f_x(F^{(s+1)})$ at the interval boundaries $F^{(s)}$ and $F^{(s+1)}$ ($s=0,1,2,...$ is the ordinary number of the interval):

$$f_x(f_1^G)=cf_x(F^{(s)})+(1-c)f_x(F^{(s+1)}) \quad \text{if} \quad F^{(s)}\leqslant f_1^G\leqslant F^{(s+1)}. \tag{2}$$

Special cases of a single linear segment, or of their infinite number which allows for an arbitrary function $f_x(f_1^G)$, are ruled out in the following section. The value of c is age independent and may be related to the survivability at any age. For instance, the age $x=1$ yields $c=(F^{(s+1)}-f_1^G)/(F^{(s+1)}-F^{(s)})$. The boundaries $F^{(s)}$ of each linear interval are independent of age, while $f_x(F^{(s)})\equiv F_x^{(s)}$ depends on age, and (since f_x is universal) for a given s on age only. Clearly, f_1, the average of such a set of f_1^G, is restricted to a given interval, and as long as all f_1^G stay in the interval, Eq. (1) is satisfied. Equation (2) may be presented in the age invariant form

$$f_x(c)=cF_x^{(s)}+(1-c)F_x^{(s+1)}, \tag{3}$$

where $F_x^{(s)}\leqslant f_x(c)\leqslant F_x^{(s+1)}$. Here $F_x^{(s)}\equiv f_x(F^{(s)})$ is the universal survivability at a boundary, $0\leqslant c\leqslant 1$ reduces to the universal survivability at any given age (e.g., to f_1^G), and $F_1^{(s)}\equiv F^{(s)}$. Since only live newborns are considered, and since nobody lives forever,

$$l_0=f_0=1, \quad l_\infty=f_\infty=0 \tag{4}$$

at any c, so

$$F_0^{(s)}=1, \quad F_\infty^{(s)}=0. \tag{5}$$

The universal mortality equals

$$Q_x(Q_0)=1-f_{x+1}(f_1)/f_x(f_1), \quad \text{where} \quad f_1=1-Q_0. \tag{6}$$

Equations (3) and (6) describe the dynamics of universal mortality. To make it more explicit, note that the age x is the time since birth, i.e., the ''eigentime'' in the reference system of an individual. The universal life expectancy E_x is the mean ''distance'' to death at a given eigentime x. In virtue of Eq. (3) and Ref. [6], in a general case of an arbitrary nonstationary and heterogeneous population, it yields the conservation law

$$[G_x^{(s+1)}-E_x]/[G_x^{(s+1)}-G_x^{(s)}]=c, \quad \text{where} \quad 0\leqslant c\leqslant 1. \tag{7}$$

Here $G_x^{(s)}$ is the universal life expectancy at the sth universal intersection. A constant c is independent of x. It reduces, by Eq. (7), to the initial distance to death E_0, or by Eqs. (3) and (6) to the infant mortality Q_0. The value Q_0 of the infant mortality depends on the population genotypes and phenotypes [1,5,7,8], but within less than 2 yr (from the $Q_0=1-f_1$ conception). Thus, the relaxation time in Eqs. (2), (3), (6), and (7) is less than 2 yr. By Eqs. (3) and (7), the universal mortality dynamics reduces to the set of universal functions of one variable, i.e., it is much simpler than the dynamics of a frictionless sphere (which reduces to five nonuniversal functions of 12 variables). This elucidates the power of invariance. The total survivability $l_x(t,r)$ depends on r, which stands for an unspecified number of nonquantified variables. The invariant survivability $f_x(f_1)$ is a function of two variables ($f_1=1-Q_0$ and x). Invariance to population

transformations reduces it to a set of universal functions (''branches'' in mathematics, ''phases'' in physics—see below) $F_x^{(s)}$ of a single variable (and to the linear dependence on c).

Universal survivability is also demonstrated [9] in the analysis of data [7] on protected laboratory populations of medflies and fruitflies. This implies Eq. (1), and thus Eq. (3). A dominant fraction of mortality is universal for species as remote as humans and flies, i.e., the appropriately scaled functions $F_x^{(s)}$ are the same [9] for flies and for humans. Only fly cohorts (hatched the same day) were studied, thus the universality of their survivability is established in various genetically homogeneous populations in different (in particular, stationary) conditions.

II. PREDICTIONS AND VERIFICATIONS

The same functional form of the human and fly universal laws allows for their accurate reduction to the same law by the appropriate scaling [9]. The fraction of universal mortality, which is common to humans and flies, is less than the universal fraction for each of them. The exact universal law, which crosses a big taxonomic boundary from humans to flies, is highly surprising. Flies have a neural ganglia, spiracles rather than lungs, a body composed primarily of terminally differentiated cells. That is to say, bodies where cell replacement and diseases like cancer cannot really occur. They have radically different life history strategies. Other than being DNA based, there is very little similarity in their basic biology. Laddled on top of all this are stochastic events such as where free radicals generated from metabolism go, whether they cause damage, and whether that damage is repaired. Thus, universal mortality is biologically unusual. At any age the universal law reduces it to the first year (for humans) or day (for flies) mortality. The latter is biologically specific and related to certain intrinsic (e.g., genetic) and extrinsic (e.g., environmental) factors. (To amplify that universal mortality yields the universal law but is not universal and is specific, one may denote it as ''canonic'' mortality.) So, at any age universal mortality also reduces to specific fractions of both intrinsic and extrinsic mortality. (The rest of mortality depends on all relevant factors [5].) Yet, it yields the exact law, which is biologically nonspecific (i.e., independent of genotypes, phenotypes, life history, population, environment), for species as remote as humans and flies. It must be related to biologically nonspecific mechanism. (That is why biologists overlooked it. Possibly, some of their conclusions may be refined or even reconsidered.) Its universality implies a uniquely common genetic legacy of ancient ancestors. It also suggests that, in contrast to the rest of total mortality, universal mortality is just a by-product of certain biologically nonspecific, thus very general, processes (see below), which may be eliminated. The universal law is established in a statistical study of large populations in different environments. Better verification of the law, especially in old age, calls for a comprehensive study of larger nonhuman populations in changing well protected conditions.

The derived law is not the universal law of mortality. It is the exact law of universal mortality, which disregards all nonuniversal deviations, and is derived from its invariance to arbitrary time-place transformations. In this aspect it is similar to physical laws. (For example, no car runs without fuel, whose consumption depends on a road. Yet, the universal inertia law is valid, in virtue of invariance, imposed by the space homogeneity.) Nonuniversal mortality is uncontrollable in humans and is amplified by insufficient statistics in animal populations. That is why I consider the most qualitative and unanticipated predictions. They may be verified with mortality curves, but in some cases they are most explicit in the survivability.

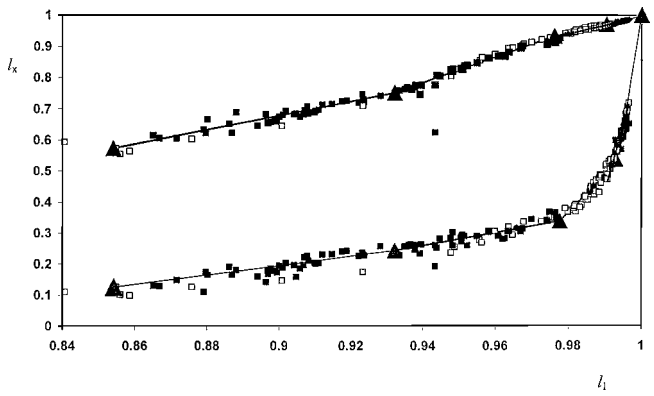

FIG. 2. Universality of human survivability. Survival probabilities $l_x(t,r)$ up to ages $x=40$ (top) and 80 in the year t, vs $l_1(t,r)$ (horizontal axis), according to the law $f_x(f_1)$ of universal survivability (solid lines; black triangles are the limiting values of linear intervals), and period life tables for 1861–1996 Swedish (empty squares) and 1891–1996 Japanese (black squares) females. The only significant deviation (Sweden, $l_1=0.94$) from the universality is related to the 1918 flu pandemic in Europe; a smaller one (Sweden, $l_1=0.84$) to the 1868 crop failure.

Universal slope jumps and natural selection. The universal law (2) predicts graphically transparent piecewise linear dependence of f_x on f_1. Its linear segments intersect, and their slopes jump. The jumps are simultaneous for all ages x, i.e., for all generations, born at different times $(t-x)$, independent of their different life history.

The agreement between the universal law and demographic data is good. It is most graphic in the survivability $l_x=p_0p_1\cdots p_{x-1}$, which smears out age specific fluctuations in $p_0,p_1,\ldots,p_{x-1}$, accumulates their slope jumps, and amplifies them. I have started with Swedish and Japanese females, see Fig. 2. The predicted piecewise linearity, slope jumps, and their increase in advanced age are very explicit in, and quantitatively agree with, the life table survivabilities. The plot of $l_{80}(l_1)$ clearly demonstrates more than one linear segment. Then Eq. (2) predicts a constraint on the heterogeneity of any population which yields universal mortality: all its f_1^G values are restricted to distinct universal intervals $[0,F^{(1)}]$, $[F^{(1)},F^{(2)}],\ldots$. The implication of this statement is that the averages in Eq. (1) are taken only over populations G for which $F^{(s)}\leqslant f_1^G\leqslant F^{(s+1)}$, and that as long as different populations remain in the same interval, the survivability of their arbitrary mixture is dominated by the universal survivability. This allows one to comprehensively verify Eq. (2) with extensive demographic data for different countries.

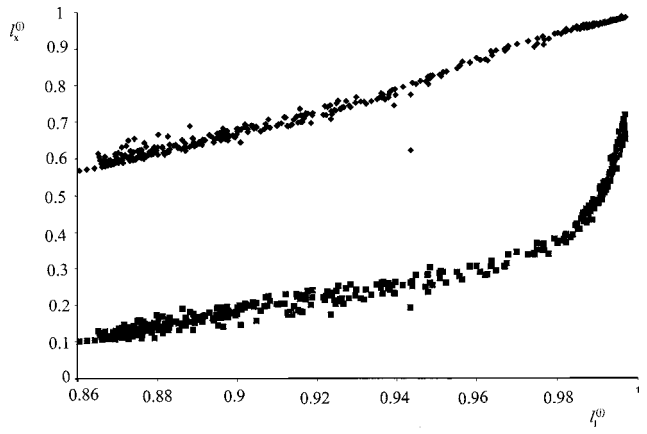

FIG. 3. Same as in Fig. 2, but complemented with the survival probabilities for the formal mixtures of Swedish (S) and Japanese (J) populations: $l_x^{(j)}=jl_x(S)+(1-j)l_x(J)$ for $j=0.25$, 0.5, 0.75 and $x=40$, 80. The mixed populations include all calendar years in Fig. 1, except those in the narrow vicinity of the crossover between linear segments, the Swedish 1918 (flu) and 1868 (failure of crops) years.

Consider, e.g., artificial mixtures of Swedish and Japanese female populations, which are both inside a single interval between successive jumps in Fig. 2, but otherwise are arbitrary (i.e., belong to any calendar years). Although the mixed populations are vastly different (e.g., 1926/1930 Japanese and Swedish females are at the opposite ends of the interval, and their mixtures cover almost the entire interval), all their data in Fig. 3 are very close to the universal curves. This implies Eq. (1), where the subscript G is substituted with the time t and country r. Then the values of f_1^G in each of the considered intervals may be arbitrary. The only function that satisfies Eq. (1) in a general case of such an arbitrarily heterogeneous population is linear [10]. Thus, Fig. 3 implies that the number of linear intervals is finite. Equation (2) is comprehensively (albeit with lower accuracy than in Fig. 2) verified in Fig. 4 for 16 developed countries [4] and their subgroups, three races on four continents, 1529 period life tables, over 200 000 data points total, for males and females alike [11]. In all cases, the slopes exhibit rapid changes, which strongly depend on age, are the highest and most ''beneficial'' for the elderly, and are approximately constant between the jumps. The slopes quantify the rates df_x/df_1 of the f_x adjustment to f_1. From Eq. (2), for any given age, the rates jump at the universal f_1 points, and are constant between them. Thus, until the postreproductive period, Eq. (2) complements natural selection with the rapid adjustment of a given genotype's survival to the current living conditions, according to its age and the value of its infant mortality in a given calendar year only, and independent of its previous life history.

The jumps are consistent with significant declines of old age mortality in the second half of the 20th century [12], discovered by demographers and interpreted as ''epidemiological transitions,'' characterized primarily by the reduction of mortality from cardiovascular diseases. However, the jumps are universal for humans and flies alike, simultaneous at all ages, and occur at the values of $f_1=F^{(s)}$, which are

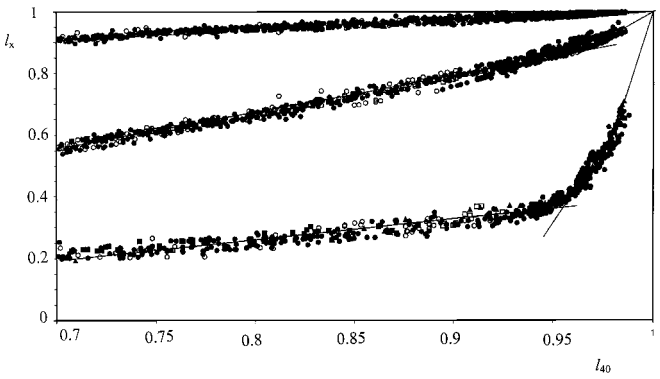

FIG. 4. Survivability probabilities $l_x(t,r)$ vs $l_{40}(t,r)$ (horizontal axis) for $x=1$ (top), $x=60$ (middle), $x=80$ (bottom), according to the universal law (solid lines) and for all male and female cases [5] in 16 developed countries [4] (those in Fig. 1, black squares, complemented with 1880–1998 Austria, 1880–1998 Belgium, 1950–1987 Canada, 1851–1998 England and Wales—courtesy of Dr. Steve Smallwood, 1881–1998 Finland, 1898–1995 France, 1871–1994 Germany, 1841–1998 Iceland, 1925–1992 Ireland, 1846–1998 Norway, 1830–1982 Scotland, 1878–1993 Switzerland, 1990–1995 U.S., white, black, and total populations). To amplify invariance and piecewise linear dependence, some of the linear segments are slightly rotated and shifted. (This does not violate piecewise linearity, black circles.) Empty signs denote years 1914–1919 and 1939–1947.

independent of genotypes and phenotypes. This suggests that medical progress just shifts f_1 to the universal jump.

Linear regressions (similar to those in Figs. 2–4) of the survivability determine the functions $F_x^{(s)}$—see, e.g., $F_x^{(0)}$ and $F_x^{(3)}$ in Fig. 5. Experimental data allow one to quantify the deviations from the universal law (2) and (6)—see Figs. 6 and 7.

Restricted heterogeneity and homogenization of populations. Consider a population for which Eq. (2) holds. The range of values that infant survivability f_1^G can take in such a population is restricted. As f_1 varies (with living conditions, which are, in particular, a function of time), the *distribution* of the values of f_1^G also changes. A striking consequence of

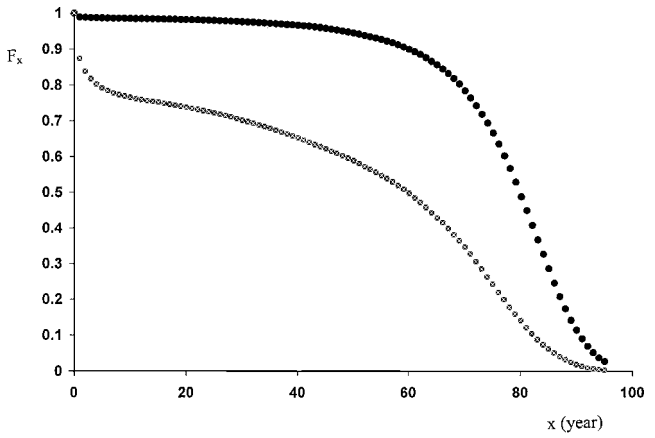

FIG. 5. Universal survivabilities $F_x^{(0)}$ (lower) and $F_x^{(3)}$ (upper curve) vs x at the intersections of linear segments.

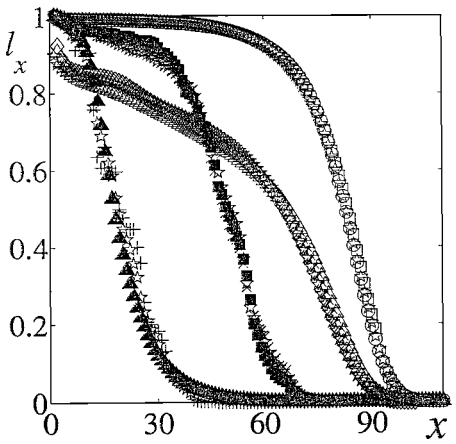

FIG. 6. Survival curves l_x vs age x for 1895 Swedish (△) and 1947 Japanese (◇); 1980 Japanese (○) and 1994 German (□) females, x in years; genetically heterogeneous female medflies (▲) in overcrowded cages and genetically homogeneous male fruitflies (+) in vials; different crosses of male fruitflies (■ and x), x in days; and l_x vs x according to the invariant law (☆). Note the proximity of the very different cases with close values of q_0.

the relation $f_x=\langle f_x\rangle$ is that as living conditions improve, and f_1 reaches one of the limiting values of its interval, $F^{(s)}$, the values of f_1^G which are also restricted to the same interval must homogenize and become equal to $F^{(s)}$ for all constituent subgroups G of the population (cf. the homogenization at $l_1=0$ and $l_1=1$, which was demonstrated earlier), and thereafter heterogenize again. Different countries reach $F^{(s)}$ at different times, which are neither singular nor even specific for the population and its heterogeneity. Thus, homogenization manifests vanishing susceptibility of the universal mortality to different living conditions at $f_1=F^{(s)}$. Correspondingly, all phenotypes simultaneously reach the point (''attractor'') at which the universal survivabilities become equal to $F^{(s)}$, and there change their slope df_x/df_1. Consider subgroups of males and females, and quantify the population heterogeneity by the relative difference $\delta_x=(l_x^F-l_x^M)/l_x^F$ of the female and male survivabilities at age $x=80$. The latter, l_x^F and l_x^M, are measured for genetically different populations, significantly change with living conditions, and are listed in all life tables. The choice $x=80$ was made since for old age the crossover is most pronounced (see Fig. 2). The weight of the nonuniversal fraction of δ_{80} is significantly higher than in l_{80}, thus its fluctuations are also higher. So, I looked for data with relatively low noise. Since the survivability fluctuations are lower in Sweden, I plotted in Fig. 8, δ_{80} vs the female l_1 in Sweden. The nonuniversal fraction of δ_{80} depends on many factors (besides l_1), shifts the δ_{80} minimum from $f_1=F^{(s)}$, and yields $\min(\delta_{80})\neq 0$. However, a sufficiently deep minimum survives. Indeed, in agreement with the predictions, δ_{80} in Fig. 8 exhibits a deep (albeit broad) minimum at a value of l_1 in the vicinity of the main crossover between linear segments in Fig. 2, and after a maximum decreases towards $l_1=1$. The small minimal value of the male/female survivability difference and the final decrease confirm the predicted homogenization of the population.

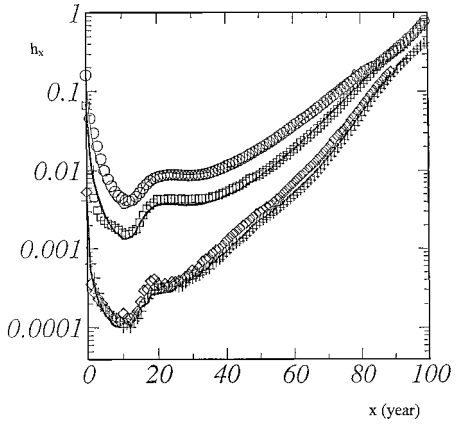

FIG. 7. Agreement between theoretical and life table mortality force [6] $h_x=\ln(l_x/l_{x+1})$ vs x (in all cases the age x is in years) for 1891/1898 Japanese (○) and 1928 Swedish (□) males; 1992/1994 German (◇) and 1990 (+) Japanese females. The universal law calculations are presented by solid lines.

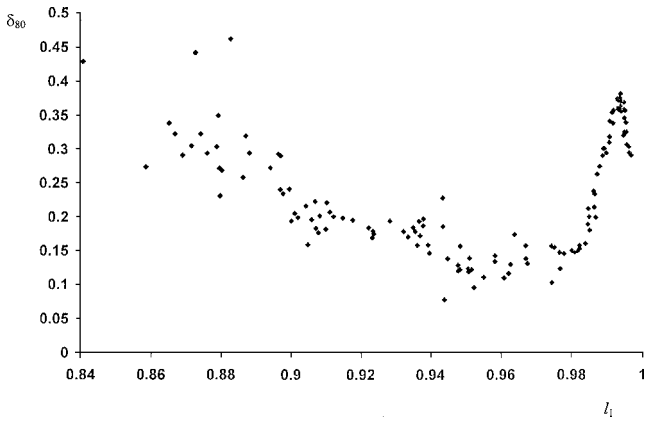

FIG. 8. The relative difference δ_{80} (vertical axis) of female and male probabilities to survive up to 80 yr vs the female l_1 (horizontal axis). The largest fluctuations correspond to the years 1866–1869 (extremely bad crops), 1918 (flu), and 1922. The nonuniversal fluctuations are significantly higher than those of l_{80} in Fig. 2.

Mortality reversal. Undoubtedly, the most intriguing prospect resulting from the analysis presented above is that of reversing the trend of increasing mortality. According to common wisdom, the life expectancy of an age group as measured in the year t, is larger than that of the same group measured, say, τ years later: an older person is less likely to survive. Reversal of this trend (due to an induced decrease of mortality, which is independent of the previous life history) runs contrary to this wisdom. The law implies that at any age x and time t the universal survivability f_x and mortality Q_x are completely governed by the infant mortality [13] $Q_0=1-f_1$, *measured at the same time t*, as exemplified in Fig. 9. This implies that the universal mortality is reversible: when Q_0 comes back to the same value, at any age Q_x and f_x also do. So, e.g., a group of elderly Jews who survived many years in the Nazi concentration camp, after a while, accurately restored the universal survivability of their French compatriots and contemporaries. (Any irreparable, and thus

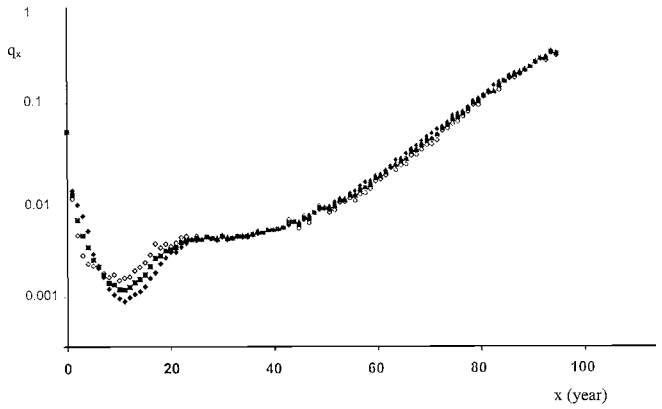

FIG. 9. Proximity of the mortality curves $q_x = 1 - l_{x+1}/l_x$ vs age x (in years) on a semilogarithmic scale for 1923 Swedish (empty diamonds) and 1951 Japanese (black diamonds) females with very close values of infant mortality (0.051 75 and 0.051 20), but very different life histories. The vertical and horizontal axes present the mortality rate and age (in years) correspondingly. Consistent with the experiments, the law of universal mortality (black squares) predicts its age dependence at any age, in particular, its minimum at 10 yr and deceleration in old age.

irreversible, damage to their health reduces their *nonuniversal* life expectancy.) While there is no comprehensive statistics on the survivors, Fig. 1, where $q_0(t,r)$ often changes nonmonotonically with time, verifies the reversibility of the universal mortality. The infant mortality $q_0(t,r) = 1 - l_1(t,r)$ preserves no memory of the life history of a phenotype beyond 2 yr from the infant's conception. The fact that the value of f_x, independent of its life history, is determined by a quantity with such short ''memory'' implies that the current values of survivability l_x can be increased, and of mortality rate q_x can be decreased, by changes in q_0, which are administered in the span of a few years, and reversed to their values at a much earlier age. Remarkably, this agrees with the data. Consistent with the predicted mortality changes (yet not as rapidly), Swedish females, born in 1916, at 48 yr *restored* their mortality rate 28 yr earlier; Japanese females, born in 1927, from 1947 till 1955 *increased* their remaining life expectancy. The limits of mortality reversal may be estimated according to Eq. (2). Each invariant segment uncovers the previous and forecasts the next ones. For instance, the first linear segment in Fig. 2 yields $f_{80} = 0$ when $f_1 = 0.8$. Unless there are no survivors beyond 80 yr (which never happened), this implies the jump to a smaller slope at its left boundary. The first segment also yields $f_{80} = 0.367$ when $f_1 = 1$. Unless there always exists the universal upper limit on the fraction f_{80} of survivors up to 80 yr, this implies the jump to a higher slope at its right boundary, which is consistent with the figure. Figures 2 and 4 suggest the ultimate $f_x = 1$. Then at *any age, everybody* survives to any age and *nobody* dies. This implies that universal mortality may be completely eliminated and total mortality reduced to its nonuniversal fraction. Since currently universal mortality dominates (Fig. 1), the corresponding decrease in mortality and increase in survivability may be significant (yet terminated by nonuniversal mortality. Of course, the extrapolation assumes that there are no more intersections in its way). The possibility to eliminate universal mortality is consistent with its being just a by-product of a ''nonbiological'' mechanism. The ultimate nonuniversal mortality may be a quantitative limit on the decline in physiological functions, increase in the pathology burden, etc., which are compatible with perfectly protected life. Mortality decrease runs contrary to a stable schedule of age specific death rates associated with intrinsic biological causes of death. At present, this schedule is only being modified by medical interventions that delay death by dealing with the symptoms rather than the underlying cause. In other words, it is being treated with geriatric medicine rather than modified by biogerontological technologies that modify the rate of aging. In the absence of meaningful intervention, the biological intrinsic mortality schedule remains unchanged. Yet, the predicted nonbiological mortality decrease is consistent with demographic data. In the last 30 yr (1965–1995) Japanese females almost halved their mortality at 90 yr, and increased their period probability to survive from 60 to 90 yr 4.5-fold to a remarkable 33% of survivors. However, beyond 90 y their mortality increases so rapidly that although from 1965 till 1995 the life expectancy at 90 yr increased by 50%, its absolute increase was from 3 to 4.6 yr only. This may or may not signal a close ultimate limit. A 50% increase in life expectancy of very old (40 days.) well protected flies may suggest the latter case.

Thus, the law of the universal mortality complements demographic approximations. The latter may be better than the universal fraction estimating the mortality rate in a certain country at a certain period in its history, and provides important empirical observations. However, only an exact law may yield unanticipated verifiable predictions, uncover the underlying molecular mechanism of mortality, and suggest the possibility to direct it.

III. MORTALITY THEORIES AND UNIVERSAL MORTALITY AS A BY-PRODUCT

Natural mortality is mostly due to accidental extrinsic hazards. As a rule, wild animals do not live long enough to grow old. Semelparous animals, e.g., salmon and mayflies, do not show any signs of aging or age-associated increase in mortality [1]. Yet, all animals die even in perfect living conditions. Why? The first answer came half a century ago, and was appropriately titled ''An unsolved problem of biology.'' Medawar [14] suggested that the force of selection progressively weakens with the increasing age of few surviving wild animals, and mutations with late-acting deleterious effects accumulate [1,15]. Mutation accumulation allows for a semiquantitative theory [16(a)] and was extensively studied numerically [3]. It is consistent with experiments [1,16(a)]. Other theories of cumulative damage relate mortality to telomers, oxygen consumption, and free radicals [see Ref. [16(b)]]. Cumulative damage is remarkably universal. Every animal consumes about 20 oxygen molecules per body atom per maximal lifespan [17]. Experimental data verify it for dozens of species in all taxons, from invertebrates to mammals, and even for oxygen consuming bacteria (per maximal fission time for a given species). The mean error is by a factor of 1.7. For some species it is higher, but always very

low compared to the 10^{20}-fold change in the number of body atoms from a bacteria to a whale. However, it is much too high to accurately estimate the maximal lifespan. The error is related to experimental inaccuracy (up to fivefold for the oxygen consumption rates and the maximal lifespan of fish and reptiles), and theoretical assumptions (which may be refined). Gradual irreparable damage (to DNA, cells, tissues, and organs) is inevitable and universal for all animals. It implies a persistent mortality increase with age (which is indeed observed in the advanced age) and the resulting maximal lifespan. This is hardly consistent with the sudden death of semelparous animals (e.g., salmon and mayfly). It is inconsistent with the mortality decrease in early age, its deceleration in humans [12], and decrease in flies [7] and nematods [18] in old age. Partially, this may be related to damage repair and robustness of survivors to old age. However, the former hardly significantly improves in old age, while the latter is unlikely to be sufficiently large in pure lines in identical stationary laboratory conditions. Thus, inevitable cumulative damage yields only a fraction of the total mortality, and provides too high a limit on the maximal life span.

Williams [19] suggested that genes with good early effects may be favored by selection, although these genes had bad effects, including senescence and death, at later ages (antagonistic pleiotropy theory). This implies a life-history trade-off in the Kirkwood [20] disposable soma theory, which is based on optimal allocation of metabolic resources between somatic maintenance and reproduction. The theory predicts strong correlation between mortalities $q_x(t,r)$ at old ages x and $q_y(t-x+y,r)$ at young ages y of the same generation (born in $t-x$). Such correlation was indeed verified in extensive studies [1]. However, the dominant universal mortality Q_x at any age x does not depend on the life history and accurately reduces to the universal infant mortality Q_0 at the same time t. Cumulative damage is irreversible (or at least imperfectly reversible, since any biological repair declines with age) and implies a monotonic mortality increase with age. Meanwhile, from Eqs. (2) and (6), universal mortality is perfectly reversible at any age. Thus, existing theories should be complemented with a new one, to account for the law of universal mortality. Life-history trade-off considers mortality dependence on the younger age living conditions, while universal mortality depends on the current conditions only. (This allows one to distinguish them experimentally.) Cumulative damage explains monotonic mortality age dependence, but only universal mortality yields its decrease in early age, and deceleration (see, e.g., Fig. 7) and decrease in old age. During the last 130 years infant mortality has decreased 45-fold, the deviations from the universal law are relatively low, and universal mortality dominates in these (certainly evolutionary unprecedented) living conditions.

Universal thermodynamic mechanism of mortality. Dynamics of universal mortality, which is much simpler than dynamics of a frictionless sphere; its independence of genotypes and of the phenotype life history; perfect and rapid reversibility that does not decrease with age; mortality homogenization at the universal points; universal and accurate dependence on a single parameter for species as complex as humans and as diverse as humans and flies over an almost 300-fold change in the mortality rate; simultaneous for different generation jumps (most beneficial for the elderly) in the universal rate df_x/df_1 of the survivability change with the environment, are biologically unusual. Rather, they are characteristic of a physical law.

The number of independent parameters in the universal law is much less than in any dynamic law. It is the same as in a thermodynamic equation of state. The piecewise linear form (2) of the universal survivability is reminiscent of the manner in which intensive quantities behave in the coexistence region of two thermodynamically stable phases [21]. The set of phases $s=0, 1, 2,...$ is universal at least for a given species. The survivability in the phase s is $F_x^{(s)}$; it depends on age only. The universal survivability can be in a coexistence region only, i.e., it is a mixture of only two different phases s and $s+1$, where the value of f_x, restricted to the interval $F_x^{(s)} \leqslant f_x \leqslant F_x^{(s+1)}$, controls the concentrations c, $1-c$ of two coexisting phases. In fact, Eq. (3) with its piecewise linearity, singularities, and homogenization at the universal points is arguably unique for phase coexistence under certain conditions. Thus, together with the fact that adiabatic changes in the equilibrium state of a system are the only known reversible processes of macroscopic systems, Eq. (3) is suggestive of the universal mortality being governed in a homeostatic animal by some kind of phase equilibrium in a cell, which may be manipulated by externally induced changes in, e.g., cell chemistry. Possibly, this is true even for death from diseases, since their mortality, and even the strongly tubercular mortality patterns in Japan prior to 1949 and in 1890–1940 in Finland, does not violate universal scaling predominantly. Presumably, phases are related to different configurations of certain molecules in a cell [10]. Such a mechanism of universal mortality explains the origin of its extraordinary dynamics, exact piecewise linear law, and other predictions. In particular, the mechanism allows one to rapidly direct mortality. It suggests that universal mortality is just a by-product of certain processes in a cell. The specific biological nature of the mechanism may be established in experiments on animals in well protected conditions.

IV. COMMENTS

Mortalities of weakly interacting populations are little correlated, thus they may be distributed outside a single linearity interval (e.g., in 1958, the Japanese $q_0=0.032\,29$ is 2.4 times higher than the Swedish one in the same year, and their l_1 belong to different linear intervals in Fig. 2). Then the subgroup distribution function $g(f_1^G, f_1)$ and Eq. (2) allow one to calculate the survivability of the entire population. The resulting $l_x(l_1)$ is not universal, its crossovers are shifted and smeared out. Nonuniversal changes are relatively small when only a relatively small fraction of the population is outside a single linearity interval. This agrees with Figs. 2–4 and implies a sufficiently strong interaction between subgroups.

Mortality depends on a genotype [6,7]. As a result, in nonstationary conditions genetic heterogeneity is age specific. The resulting mortality nonuniversality is relatively

small when the genetic composition of the population changes relatively little during the mean lifespan, and the distribution function of f_1^G in the population with $\langle f_1^G \rangle = f_1$ little depends on age. The distribution function, together with Eq. (2), allow for the calculation of the population mortality.

Thus, mortality accurately yields the universal law (rather than its averaging with the distribution function) in any homogeneous nonstationary population. This implies its validity in any population which is restricted to a single linearity interval.

V. SUMMARY

A physical approach to mortality data establishes an exact biological law, suggests its mechanism and the possibility to direct it. An accurately defined (universal) fraction of human survivability up to a given age x is a piecewise function of the infant mortality in the same calendar year. This law is universal for species as remote as humans and flies, and dominates in their protected populations. Its slopes jump simultaneously for all generations. The jumps are most beneficial for the elderly. Infant mortality depends on the environment and phenotypes in the population. In a prereproductive age, very rapid (within a couple of years) adjustment of a given genotype's survival to the current living conditions complements natural selection. The mortality of an entire population homogenizes in the narrow vicinity of the jumps. Universal mortality is reversible and independent of the life history. Undoubtedly, the most intriguing prospect resulting from the analysis of universal mortality (and, according to the previous examples, consistent with demographic data) is that of reversing the trend of human mortality (its increase in advanced and old age). Within a couple of years, at any age universal mortality may be reset to its value at a younger age. All these predictions are verified with demographic data, and suggest that universal mortality is related to a certain phase equilibrium in a cell, which changes universally with age and adiabatically with time. Different mechanisms significantly contribute to mortality, but the dominant one changes with living conditions. In the wild, intrinsic mortality is mostly related to the life-history trade-off. Human and protected population mortalities are predominantly universal, which allows for rapid life extension. Ultimate inevitable death is determined by mutation accumulation and other kinds of irreparable cumulative damage. (For more details see Ref. [22].)

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[5] The rate $q_x = (N_x - N_{x+1})/N_x$, where N_x is the number of survivors up to age x. It significantly changes with the country (in 1947 the female infant mortality q_0 was three times higher in Japan than in Sweden), time (in Japan q_0 halved from 1947 till 1955), age specific factors (from 1851 till 1900 English female mortality decreased 2.6 times for 10 yr olds and by 5% for breast fed infants, prevented from contaminated food and water), deceases (the 1918 flu pandemic in Europe increased

Swedish female mortality threefold at 28 yr, but changed it little for newborns and elderly), wars (French male mortality at 40 yr was 2.5 times higher in 1915 than in 1913), genotype and its life history (acquired components yield significantly different mean lifespans of even genetically identical populations in a uniform environment [1,7,8]), and genetic and environmental heterogeneity. Mortality rates in the same calendar year and country are significantly different for different population subgroups (e.g., in 1891/1900 Swedish female q_0 was almost twice higher in Stockholm than in the rural area).

[6] Everywhere in this paper, I escape any adjustment by using "raw" life table variables, e.g., an integer age x (in years for humans and in days for flies), the mortality rate $q_x=1-l_{x+1}/l_x$ [and mortality force $h_x=\ln(l_x/l_{x+1})$] rather than $q_x=-d\ln l_x/dx$; the life expectancy $e_x=\Sigma_{y=x}^{\infty}y(l_y-l_{y+1})$ at age x rather than $e_x=\int_x^{\infty}y\,dl_y$. All universal quantities are related to f_x rather than to l_x. Note that only f_x and E_x are piecewise linear in f_1 and E_0. The only normalization condition is $l_0=1$, it implies $\Sigma q_x l_x=1$.

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