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Metastability of Life¶

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Abstract—The physical idea of the natural origin of diseases and deaths has been presented. The fundamental microscopical reason is the destruction of any metastable state by thermal activation of a nucleus of a irreversible change. On the basis of this idea the quantitative theory of age dependence of the death probability has been constructed. The obtained simple Death Laws are very accurately fulfilled almost for all known diseases. *© 2000 MAIK "Nauka/Interperiodica".*

All of us will die, as well as all other living organisms and plants. Each and every machine or construction will break. Mountains will fall down or earthquakes will happen.

Why? Physics gives the general answer – all of these systems are not in full equilibrium, but represent metastable states. In other words: (1) they are stable against small external influences, but (2) each of them, the worst ones, as well as the best ones, has a finite probability to be spontaneously destroyed without any external influence even in the ideal environment and at perfect conditions. According to Gibbs [1], the fundamental reason of the destruction of metastable equilibrium is the thermal activation of a critical nucleus of irreversible change in the system.

Let us consider a simple example: a stretched ideal monocrystal string. If we wait a sufficiently long time, the temperature fluctuations will produce a critical Griffith's crack [2] at some place and the string will break. It is possible that the critical crack will appear earlier if there are some defects in the crystal. Such a nucleation process occurs in different ways for different cases (activation of point defects in the crystals, condensation in a super saturated solution, nucleation of a new phase in a first order phase transition) and it is well studied in condensed matter physics.

The described phenomena can also take place in any living organism, even if the latter are much more complicated. The thermal activation of a critical nucleus is the last and unremovable killer. [Last—if we exclude all other origins of diseases and deaths. Unremovable, but, one can hope, not unanalyzable.]

I want to stress here that the known qualitative and quantitative facts for the majority of diseases can be understood from the point of view of theoretical physics in terms of metastability and the activation of a critical nucleus. So, I think that the thermodynamic killer works, and that it is the main killer.

Gompertz [3] discovered that the probability $D(x)$ to die at the age x in the time interval dt exponentially increases with age

$$D \propto \exp\left(\frac{x}{a}\right). \tag{1}$$

According to modern mortality statistics, Gompertz law is valid in the age range from 30–70 years, while an even stronger increase appears in older age groups. The exponential age dependence of D, from my point of view, is the most crucial sign of the microorigin nature of diseases leading to death.

I have no answer for many questions one can ask about the details of the relationship between a given disease and the proposed idea of their natural microorigin. Nonetheless, I believe that the age dependence of the death rate can be interpreted in terms of the probability of formation of critical nuclei of irreversible change that cause the collapse of metastable equilibrium states. In the following, I present a theory that relates the probability of the arising of a critical nucleus to the age of the system in which it takes place.

Unremovable point defects on a molecular (and macromolecular) scale can arise due to the process of oxidation [4]. Thermal fluctuations can produce configurational transformations of individual molecules [5]. The same effect can be caused also by some external agents (photons, impurity atoms or molecules, elementary particles). If a concentration of those point defects is small, then the probability of the arising of new defects does not depend upon the interaction between them. It means that the concentration of point defects should be simply proportional to the age x. This linear law is known in an absolutely analogous situation, the Zeldovich stage of nucleation in I order phase transition [6]. It is quite natural to assume that, at any age, the

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dimensionless molecular concentration of the point defects remains small, so that this law is valid at any age.

A growing concentration of the point defects gives rise to small changes of the physical parameters of the body structures on a macroscopic scale (membranes, cells, as well as higher level structures). One can imagine that some functionally significant defects are thermally activated on this scale (as, e.g., the arising of a Griffith-like critical crack in a microcapillary, periodically stressed by oscillating blood pressure) or that point defects will tend to precipitate into a condensed state (as it is in supersaturated solutions), or even that some type of a structural phase transition occurs at some critical value of defect concentration. Some such types of spontaneous changing in the body can have serious functional consequences leading to diseases, and death.

The probability W of such microdamages arising is governed by the Gibbs law

$$W \propto \exp\left(-\frac{U}{T}\right), \tag{2}$$

where U is the minimum energetic barrier of the irreversible change (critical nucleus), and T is the temperature. Usually, it is possible to expand the energy of the critical nucleus in the small concentration, or equivalently in age: $U = U_0 + U'x$, and if U' is negative, the barrier diminishes with the age, we obtain the exponential law, equation (1). If U' is positive, one has the growth of the barrier, and the stability of the body increases. It is possible that the decreasing age of infant mortality is partly related to this circumstance.

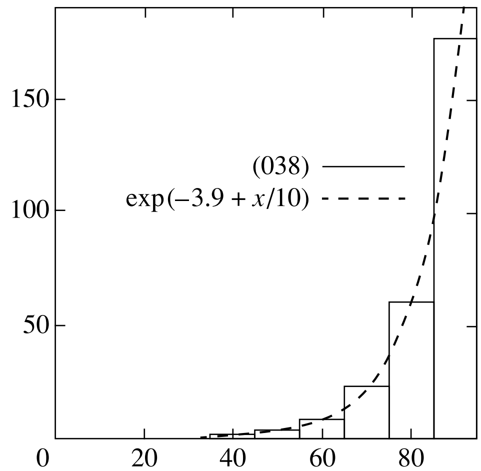

Fig. 1. Septicemia (038). Death rate.

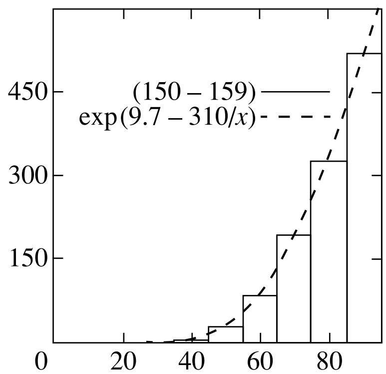

Fig. 2. Malignant neoplasms of digestive organs and peritoneum (150–159). Death rate.

The expansion of U in the concentration is impossible in the case of condensation in a supersaturated gas with a small concentration (as well as in the vicinity of I order phase transition). In a two-dimensional condensation of supersaturated gas, the energy of the critical nucleus is inversely proportional to the concentration, or in our case $U \propto x^{-1}$, corresponding to the second exponential law

$$W \propto \exp\left(-\frac{b}{x}\right). \tag{3}$$

In a three-dimensional condensation, there should be $U \propto x^{-2}$, and the third exponential law is

$$W \propto \exp\left(-\frac{c}{x^2}\right). \tag{4}$$

Let us consider the US-97 death statistics specified by selected causes [7]. If one plots $\ln(D_i)$ versus x, or versus $1/x$, and $1/x^2$, it is easy to find that almost all cases have a clearly distinguishable age behavior: 20 cases of Gompertz exponential law, equation (1); 14 cases of second exponential law (3); 4 cases with more complicated behavior, but the laws (1) or (3) are valid there in a wide age range, and some strange crossover occurs to some other behavior; 24 cases are not related with aging. Only in 3 cases statistics does not permit to make a definite conclusion on the type of age dependence. Examples of the clearly detectable exponential age behavior of the death rate are presented in Fig. 1.

The death rate here is the number of deaths per 100000 population of specified age groups 0–5, 5–14, …, 75–84, 85 years and over in 1997. There are a lot of intriguing coincidences of the parameters (a, b) for different diseases. This possibly means that a number of discussed different microorigins is substantially smaller than a number of diseases. Some of the diseases arise presumably as a combined effect of two different microorigins. This analysis is in progress.

The characteristic magnitude of function D in cases with Gompertz law (1) at $x = 0$ is exp(–13)…exp(–22) per year, or exp(–30)…exp(–39) per second. Let us compare this value with equation (2). One should introduce some preexponential value. Its simplest estimate is the characteristic frequency of oscillations of atoms in condensed matter $\omega \sim k\Theta/\hbar$, where $\Theta \sim 10^2$ K is Debye temperature; k, Boltzmann constant; $\hbar$, Planck's constant. One should introduce an additional factor, an

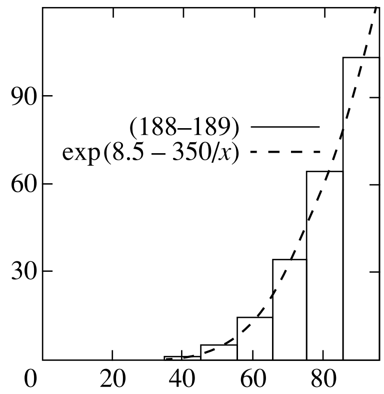

Fig. 3. Malignant neoplasms of urinary organs (188–189). Death rate.

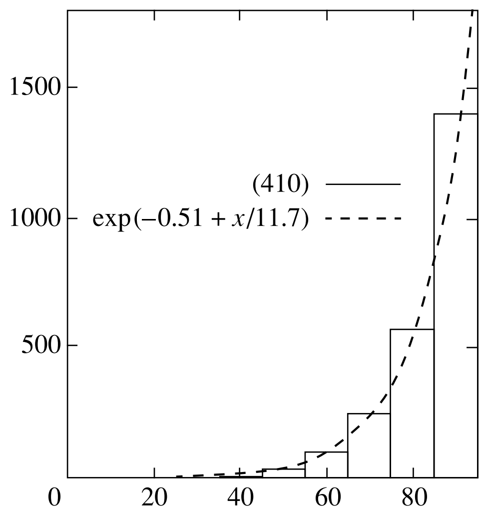

Fig. 4. Acute myocardial infarction (410). Death rate.

effective number N of possible places where the given critical nucleus can arise. The temperature of the body is $T = 273 + 36.6 \approx 310$ K. The comparison gives a reasonable estimate of barriers $U \sim (1.2–1.4) \times 10^4$ K + $T\ln N$, or $U \sim 1.1–1.3$ eV if $N \sim 1$, and only $U \sim 3$ eV even if N is equal to the total amount of the molecules in the human body (this effective number is of course unrealistic). It is noteworthy to say here that the estimated barrier values are comparable to those typically encountered in condensed matter physics for the processes mentioned in the previous pages.

In order to estimate the age change of barriers, one does not need to know the preexponential factor in the expression (2). Typical 90 years increasing factor of D_i is exp(8). It corresponds to the diminishing of barriers $\delta U \sim 8T$, this value is also reasonable $\delta U \sim 0.2$ eV $\ll U$. Two parameters $\delta U/U \ll 1$ and $U/T \gg 1$ are the main parameters of the theory.

In the framework of the presented picture, the small difference in barriers of the order of 0.02 eV for males and females corresponds to the known ratio $D_m/D_f \sim 2$, and can be directly related to the difference 1/23 in chromosome compositions. The variation of the parameters with time and specific groups of population, countries, races, etc., should be of the same order of magnitude. The situation is similar to the usual one in condensed matter physics, where the experimental data are observably dependent on the sample preparation conditions.

Note, that there is no real contradiction between the presented idea and the fact that there are a lot of diseases caused by viruses and bacteria. The age dependence of those diseases can be related to the microorigin of the destruction of the immune system.

Moreover, I think that the discussed thermal activation mechanism could play a role in the generation of congenital anomalies.

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