Metastability of life

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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 nonreversible change. On the basis of this idea the quantitative theory of age dependence of death probability has been constructed. The obtained simple Death Laws are very accurately fulfilled almost for all known diseases.

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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 a full equilibrium. All the systems are metastable, it means: 1) they are stable against small external influences, but 2) each of them, as 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 the perfect conditions. According to Gibbs the fundamental reason of the destruction is the thermal activation of critical nucleus of nonreversible change in the system.

Let us consider a simple example - a stretched ideal monocrystal string. If we wait sufficiently long time the temperature fluctuations will produce a critical Griffith’s crack 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.

Any living organism is a much more complicated system, but the described phenomena should occur in it also. The thermal activation of 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 untreatable.

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

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

$$D \propto \exp \left( \frac{X}{a} \right).$$

According to modern mortal statistics Gompertz law is valid at the age range $30 \div 70$ years, and even more strong increase appears at older ages. Exponential age dependence of $D$, from my point of view, is the most crucial sign on the nature of micro origin of diseases leading to death.

I have no answer for many questions one can ask about details of the relationship between a given disease and the proposed idea of their natural micro origin. Only I can do for the moment is to present a theory of age dependence of probability of arising of the nucleus.

On a molecular (and macromolecular) level there are few reasons of arising of almost non removale point defects, for example, due to the process of oxidation. Thermal fluctuations should produce configurational transformations of individual molecules. 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 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 analogies situation. Zeldovich stage of nucleation in I order phase transition. It is quite natural to assume, that at any age the dimensionless molecular concentration of the point defects remains small, so at any age this law is valid.

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

The probability $W$ of arising of such micro damages is
governed by Gibbs law

\[ W \propto \exp \left( -\frac{U}{T} \right) \],

where \( U \) is the minimum energetic barrier of the irreversible change (critical nucleus), and \( T \) is the temperature. Usually it is possible to expand energy of 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, Eq.(1). If \( U' \) is positive, one has the growth of the barrier, and the stability of the body increases. It is possible that the age decreasing of the infant mortality is partly related to this circumstance.

The expansion of \( U \) in concentration is impossible in the case of condensation in a supersaturated gas with 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 \( U \sim x^{-1} \), corresponding to the second exponential law

\[ W \propto \exp \left( -\frac{b}{x} \right) \],

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

\[ W \propto \exp \left( -\frac{c}{x^2} \right) \].

Let us consider the US-97 death statistics specified by selected causes [7]. If one plots \( \ln(D_i) \) v.s. \( x \), or, v.s. \( 1/x \), and \( 1/x^2 \) it is easy to find that almost all cases have a clearly distinguishable age behaviors: 20 cases of Gompertz exponential law, Eq.(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 the age dependence. Examples of the clearly detectable exponential age behavior of death rate presented in Fig.1-4.

Death rate here is the number of 1997 year deaths per 100,000 population of specified age groups 0-5, 5-14, ... 75-84, 85 years and over. There are a lot of intriguing coincidences of parameters \((a, b)\) for different diseases. It possibly means, that a number of discussed different micro origins is substantially smaller than a number of diseases. Some of diseases arise presumably as a combined effect of two different micro origins. This analysis is in progress.
FIG. 4. Acute myocardial infarction (410). Death rate.

The characteristic magnitude of function $D$ in cases with Gompertz law (1) at $x = 0$ is $\exp(-13 \div -22)$ per year, or $\exp(-30 \div -39)$ per second. Let us compare this value with Eq.(2). One should introduce some pre-exponent value. Its most simple estimate is the characteristic frequency of oscillations of atoms in condensed matter $\omega \sim k \theta / \hbar$, where $\theta \sim 10^2 K$ is a Debye temperature, $k$ - Boltzmann’s constant, $\hbar$ - Planck’s constant. One should introduce an additional factor, an 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 estimation of barriers $U \sim (1.2 \div 1.4) \times 10^4 K + T \ln N$, or $U \sim 1.1 \div 1.3 eV$ if $N \sim 1$, and only $U \sim 3 eV$ even if $N$ is equals to total amount of molecules in a body, this effective number is of course unrealistic, and I want just to note here that in any case the barrier estimation gives value usual in condensed matter physics.

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

In the framework of presented picture the small difference in barriers of the order of $0.02 eV$ for male and female corresponds to known ratio $D_m / D_f \sim 2$, and can be directly related to the difference 1/23 in chromosome compositions. The variation of parameters on 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 experimental data are observably dependent on sample preparation conditions.

Note, that there is no real contradiction between presented idea and the fact that there is a lot of diseases casad by viruses and bacteria. The age dependence of those diseases should be related to some micro origin of the destruction of the immune system.

I think also, that discussed thermal activations should play not the last role in a generation of congenital anomalies.

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