Medical Hypotheses (2007) **69,** 441–447

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A statistical analogy between collapse of solids and death of living organisms: Proposal for a 'law of life'

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Received 20 October 2006; accepted 22 October 2006

Summary In this paper we present a statistical analogy between the collapse of solids and living organisms; in particular we deduce a statistical law governing their probability of death. We have derived such a law coupling the widely used Weibull Statistics, developed for describing the distribution of the strength of solids, with a general model for ontogenetic growth recently proposed in literature. The main idea presented in this paper is that cracks can propagate in solids and cause their failure as sick cells in living organisms can cause their death. Making a rough analogy, living organisms are found to behave as ''growing'' mechanical components under cyclic, i.e., fatigue, loadings and composed by a dynamic evolutionary material that, as an ineluctable fate, deteriorates. The implications on biological scaling laws are discussed. As an example, we apply such a Dynamic Weibull Statistics to large data collections on human deaths due to cancer of various types recorded in Italy: a significant agreement is observed.

Introduction: Weibull and West–Brown–Enquist approaches

Weibull Statistics [1] has been derived on the hypothesis of the weakest link theory and describes the statistical distribution for the strength of solids. Weibull derives the cumulative probability of failure P_f for a solid of volume V and subjected to a uniaxial local stress $\sigma(\bar{x})$, a function of the position vector $\bar{x}$, as $P_f = 1 - \exp\left[-\int_V \left(\frac{\sigma(\bar{x})}{\sigma_{0V}}\right)^m dx^3\right]$, where σ_{0V} and m are, respectively, Weibull's scale and shape parameters, governing the mean value and the standard deviation of the distribution. The former presents anomalous physical dimension and is related to the mean value of the distribution, whereas the latter is dimensionless and related to its standard deviation. For solids with surface-flaws that are dominating with respect to volume-flaws, e.g., at small size-scales where the ratio surface over volume tends to diverge, the surface S of the structure must replace its volume V.

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0306-9877/$ - see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.mehy.2006.10.067

For uniform uniaxial stress σ, thus coincident with the applied load, e.g., the case of a fiber in tension, the probability of failure P_f becomes:

$$P_f = 1 - \exp\left[-V\left(\frac{\sigma}{\sigma_{0V}}\right)^m\right] \quad (1)$$

The presence of the volume (or of the surface) in Eq. (1) is crucial: Weibull assumed a number of potential ''critical'' defects in the solid, as statistically proportional to its volume V (or to its surface S). The impact on Materials Science of this pioneer Weakest Link Theory, a by-product of the general Statistics of the Extremes [2], has been tremendous.

This suggests to make an analogy between Physics and Biology: we can treat a living organism as a solid (e.g., a mechanical component), the pre-existing defects in the structure corresponding to biological defects in the organism, e.g., potential sick cells. Correspondingly, a instable crack propagation will cause the failure of the specimen as well as a fully propagation of the biological defect will cause the death of the organism. Even if Weibull Statistics is currently applied in Biology [3–10] we demonstrate in this paper the importance of considering dynamic Weibull parameters, and thus a new Dynamic Weibull Statistics. Finally, we apply such a statistics to treat human cancer deceases. The new statistics could reveal itself to be a new useful tool, with respect to classical mesoscopic modeling [11–15].

Starting from this analogy, there are three questions that we have to answer before trying to develop a general statistical law of life: (i) which parameter plays the role of the stress in life? (ii) is the Weibull's modulus m a constant for a living organism or it presents a dynamic evolution as the organism itself? Finally, (iii) is the probability of death of a living organism related to its ''growing'' volume (or mass M), or to its surface or to what else?, and if the growing process plays a role, how we can take into account a ''universal'' growing of the living organisms?

The answer to question (i) seems to be unquestionable: it is the time t. Regarding this point we note that the Weibull Statistics, in which the stress is replaced by the time, is widely used also for describing the statistics of the times to failure for mechanical components under cycling loads [1]. Thus, living organisms would behave as mechanical components under fatigue. A cycle can be considered as a biological characteristic period, as for example a day. We will demonstrate that the answer to question (ii) is that the Weibull's modulus is in general evolutionary as the living organism itself. To give an answer to question (iii) would require to describe in a ''universal'' manner the growing process of the living organisms, i.e., the mass-time dependence $M(t)/M_\infty$, regardless to their asymptotic mass M_∞, that spans 21 orders of magnitude, from microbes to whales [16].

To describe the mass evolution, we consider the general model for ontogenetic growth recently proposed [16]. The authors have demonstrated that the growth of the living organisms can be universally described by the following mass/energy balance:

$$\frac{dM}{dt} = aM^p\left[1 - \left(\frac{M}{M_\infty}\right)^{1-p}\right] \quad (2a)$$

where a is a constant related to the metabolic rate of the living organism. These authors argue that a value of $p = 3/4$ has to be considered to describe natural fractal-like energy distribution networks; however this hypothesis can be also relaxed [17]: it would correspond to a different dimension of the fractal set, as demonstrated in a different context, on the strength of solids [18]. Accordingly, a value of p comprised between 2/3 and 1 is expected; $p = 2/3$ would describe surface dominated energy supply mechanisms, whereas for $p = 1$ volume effects prevail.

The universal growth predicted by the previous equation, in dimensionless form, is

$$r = 1 - e^{-\tau}, \quad \text{with } r = (M/M_\infty)^{1-p} \quad \text{and}$$
$$\tau = a(1-p)M_\infty^{p-1}t - \ln(1 - r_0) \quad (2b)$$

where $r_0 = (M_0/M_\infty)^{1-p}$ with $M_0 = M(t = 0)$. Thus, the function $M(t)$ is now ''universally'' quantified. Usually, only the parameter a is unknown. However, we could estimate it by the time at which the organism has reached a conventional ratio M/M_∞. For example if $t_{97\%}$ is defined by $M(t_{97\%})/M_\infty = 0.97$, considering for human individuals $t_{97\%} \approx 25$ years, $M_0 \approx 3$ kg, $M_\infty \approx 80$ kg, and $p = 3/4$ would correspond to $a \approx 2\ \text{kg}^{1/4}$/year. Coupling the Weibull's and West at al.'s approaches, on the basis of the analogy previously presented, a statistical law of the life can be formulated, as described in the next section.

Towards a statistical law of the life

Coupling the Weibull and West–Brown–Enquist approaches, we formulate a statistical law of the life giving the probability of death P_D, or of survival P_S, as suggested by Eqs. (1) and (2):

$$P_D = 1 - P_S = 1 - \exp\left[-kM^{\gamma}(t)\left(\frac{t}{t_0}\right)^{m(t)}\right] \qquad (3a)$$

where $M(t)$ is given by Eq. (2b), $m(t)$ is an evolutionary modulus, k is a constant with anomalous physical dimension and t/t_0 is a dimensionless time, defined by arbitrarily fixing t_0, e.g., $t_0 = 1$ year (note that mathematically $P_D \to 1$ only for $t \to \infty$, but practically $P_D \approx 1$ for realistic finite time).

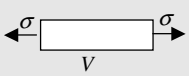
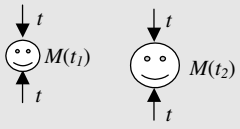
We have considered M^{γ} instead of M since considering the surface instead of the volume (or mass) in Eq. (1) would correspond to replace M with $M^{2/3}$, if individuals belonging to a specified organism family are assumed to be geometrically self-similar. Thus, for generality, a constant γ has to be introduced. To take into account a threshold time t_{th}, we could replace $t \to t - t_{th}$ in the explicit time dependence of Eq. (3a), as suggested by the Weibul's treatment [1]. Note that setting $\gamma = p$ would correspond to assume a direct dependence from the average resting metabolic rate of the organism, derived as proportional to M^p in [16], where $p = 3/4$ was assumed. By setting $\gamma = 0$ we could model an explicit independence from the mass, so that the growing process would be only implicitly modeled by the dynamic evolution of $m(t)$. Negative value of γ would reveal an inverse mass dependence, unrealistic for solids but perhaps plausible for living organisms (note that lower and upper bounds exist for the mass of mammals). Formally, the parameter γ allows one to consider any interesting function into Eq. (3a): if for example we want to consider the growing rate dM/dt instead of M^{γ}, it would correspond to $\gamma = \ln(dM/dt)/\ln M$. This would imply a probability of finding potential critical cells as proportional to the growing rate that, according to Eq. (2b), presents a maximum for $M/M_{\infty} = p^{1/(1-p)}$. The proposed physics/biology analogy is summarized in Table 1. Finally, we note that as Eq. (1) has been adapted for treating the statistics of living organisms, Eq. (2) can be used to describe the evolution of the damaged zone (of mass M) in a solid (of mass M_{∞}). In fact, such an energy balance states that the average resting metabolic rate/fragmentation energy (proportional to M^p [16,18]) is spent in creating new cells/damaged zones (proportional to dM/dt) and in maintaining the pre-existing cells/in friction on pre-existing cracks (proportional to M).

Scaling laws in physics and biology

Let us consider solids composed by a given material but having different size-scales. It is well-known that Eq. (1) implies a scaling for their (nominal) failure stresses according to $\sigma_f^m V \approx \text{const}$ [1]; this can be deduced by setting $P_f = \text{const}$ (=0.63, it being the value of the probability defining the nominal stress). The size-scale effect $\sigma_f \propto V^{-1/m}$ suggests that *smaller is stronger* as nowadays well-known in Physics [18,19]. This represents the reason why nanostructures, such as nanotubes or nanowires, show tremendous high strength: it is a consequence of the reduced probability of finding critical defects in their minimal volume [20].

Similarly, a scale-time effect is deduced according to Eq. (3a) as $kM^{\gamma}(t_D)(t_D/t_0)^{m(t_D)} \approx \text{const}$. Since $M(t_D) \approx M_{\infty}$, a biological time scaling law $t_D \propto k^{-1} t_0^{m(t_D)} M_{\infty}^{-\gamma/m(t_D)}$ between t_D and M_{∞} is finally derived. Consequently, some information on the parameter γ can in principle be obtained by matching well-known biological scaling laws with our prediction. For example, generalizing for a generic value of p the biological scaling laws reported in [21] (that assume $p = 3/4$), metabolic rate scales as M_{∞}^p, radii of mammalian aortas and tree trunks as $M_{\infty}^{p/2}$, mammalian heart and respiratory rates as M_{∞}^{p-1}, as well as circulation times for blood of

Table 1 Statistical analogy between Weibull approach applied to solids and the statistical law of the life applied to living organisms

Probability of failure of a mechanical component	Probability of death of a living organism
	
Stress σ	Time t
V or S = time-independent	$M^{\gamma}(t)$ = time-dependent
m = time-independent	$m(t)$ = time-dependent

mammals and sap of trees scale as M_∞^{1-p}. Such a scaling is expected for most biological times, including those of respiratory and cardiac cycles and gestation, postembryonic development and life span. Accordingly, $t_D \propto M_\infty^{-\gamma/m} \propto M_\infty^{1-p}$ gives an additional information on the constants involved in Eq. (3a), and in particular seems to suggest slightly negative values for γ. Furthermore, as a consequence of the small value of the exponent $1-p$, the time-scale effect seems to be negligible in this context, i.e., $\gamma \approx 0$, as observed in the next section by the data treatment.

However, as $\sigma_f \propto V^{-1/m}$ in Physics, $t_D \propto M_\infty^{1-p}$ in Biology. The parameter p, as previously discussed, is in general expected to be comprised between 2/3 and 1 [18], as a consequence of the dimension $D = 3p$ [22] of the fractal domain in which the energy exchanges occur, always comprised between those of an Euclidean surface ($D = 2$) and volume ($D = 3$). This is confirmed by the experimental observations that reveal p not identical but only close to 3/4 for all the analyzed living organism families and slightly increasing with the size- [21] and time-scales [22], indicating a transition from surface- to volume-dominated mechanisms [23]. We show here that this transition could be quantified considering the simplest (i.e., with unitary modulus) Weibull size-frequency distribution, i.e., $V(<r)/V_0 = 1-\exp(-r/r_0)$, where V is a total volume of cluster cells, having size smaller than r; the subscript ''0'' refers to characteristic values. In fact, by comparing the last law with its fractal counterpart, i.e., $V(<r)/V_0 = (r/r_0)^{3-D}$ [18], we find ($D = 3p$) the following p-scaling:

$$p = 1 - \frac{\ln(1-\exp(-r/r_0))}{3\ln(r/r_0)} \tag{4}$$

At large size-scales (or time-scales if $r \to t$) $r/r_0 \to \infty$ and $p \to 1$, whereas at small size-scales $r/r_0 \to 0$ and $p \to 2/3$; this spatial-temporal scaling for p is observed in mammalian [21] or tumoral growths [22], suggesting a universal range (and transition) rather than an universal value for p. Biological scaling laws can thus be better described in the light of the deduced p-scaling.

Deterioration as ineluctable fate

Let us consider cancer data. In particular we refer to the tables of mortality due to cancers of various types recorded in Italy [24]. The age of the individuals deaths are divided into time-intervals, 1–4, 5–9, ..., i-(i+4), ..., 75–79 years. For each time-interval i the number N_i of the observed deceases, for a specified year and in Italy, is reported. We consider the deaths related to the time-interval i as arising at its mean value t_i and we calculate the cumulative probability of death as $P_D(t_i) = \frac{\sum_{j=1}^{i} N_j - 1/2}{N}$ [25], where N is the total number of deceases (i.e., $N = \sum_j N_j$): thus, we are here considering relative probabilities. Alternatively, we could also refer to the total number of individuals $N = N_{TOT}$, that is the population in Italy in the investigated year: in this case the probabilities would be absolute. Referring to the time between onset of cancer and death, rather than to the age at death, would give different information, but since onset and diagnosis are not coincident these data are not of easy derivation and thus are not usually available.

In Fig. 1 the data related to the year 1990 for males and females [24], deceased as a consequence of cancer of various types, are treated by assuming m = const in Eq. (3a), and alternatively $\gamma = 1$ (explicit mass dependence), $\gamma = \ln(dM/dt)/\ln M$ (explicit growing rate dependence) or $\gamma = 0$ (explicit independence from the growing process). We have fixed $t_0 = 1$ year.

Note that Eq. (3a) could be put in the following form:

$$\ln(\ln(1/(1-P_D))) - \gamma\ln(M) = \ln(k) + m\ln(t/t_0) \tag{3b}$$

Thus, if m = const and an explicit linear dependence ($\gamma = 1$) from the mass are reasonable hypotheses, in the diagram of Fig. 1, the squares should fall on a straight line, as predicted by Eq. (3b). This clearly does not happen. At the same manner the triangles in Fig. 1 should fall on a straight line if m = const and independence from the growing pro-

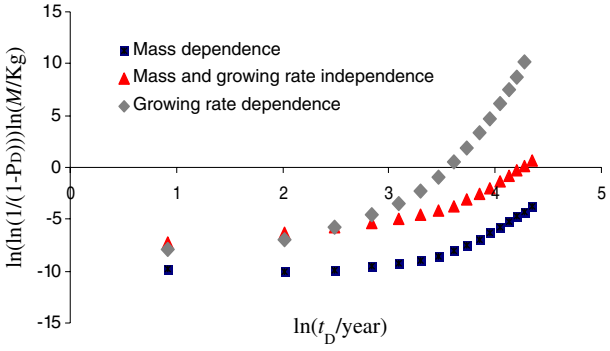


Figure 1 Eq. (3) with m = const, applied to human individuals deceased as a consequence of cancer (of various types) in the year 1990 in Italy: triangles ($\gamma = 0$), squares ($\gamma = 1$) and rhombs ($\gamma = \ln(dM/dt)/\ln M$); $M_0 \approx 3$ kg, $M_\infty \approx 80$ kg, $a \approx 2\ \mathrm{kg}^{1/4}$/year ($p = 3/4$).

cess ($\gamma = 0$) are reasonable assumptions. Again, this is not the case. The same curved trend is observed for an explicit dependence from the growing rate ($\gamma = \ln(dM/dt)/\ln M$, $m = \text{const}$, rhombs). A similar trend is observed also considering $\gamma = -1$. Such curved trends suggest that for human cancer the mass M or its growing rate dM/dt has not an explicit crucial role here, in contrast to what happens in the biology scaling laws; thus, we can treat these data by setting here $\gamma = 0$. On the other hand, the discrepancy from straight lines observed in Fig. 1, emphasizes the importance of considering an evolutionary behaviour for m, related to the slopes of the curves in Fig. 1. Such evolution can be physically clarified noting that, according to reliability theory, a Weibull distribution with $m > 1$ characterizes a life system that increasingly deteriorates [3]. On the other hand, if the shape parameter is smaller then unity ($m < 1$), there is a reliability growth as the failure rate of the system decreases with time [3]. Thus, since the slopes of the curves in Fig. 1 increase, the corresponding life systems tend, as an ineluctably fate, to deteriorate. The simplest assumption is to consider the linear dependence $m = t/t_m$, where t_m is a biological characteristic time. Considering other hypotheses, such as $m \propto \sqrt{t}$ or $m \propto t^2$ would make the fit strongly worse. The physical meaning of the parameter t_m is clear: for $t < t_m$ no deterioration occurs, whereas for $t > t_m$ a catastrophic deterioration is expected. In these hypotheses, the more general Eqs. (3a) and (3b) become:

$$P_D = 1 - P_S = 1 - \exp\left[-k\left(\frac{t}{t_0}\right)^{t/t_m}\right] \tag{5a}$$

$$\ln(\ln(1/(1-P_D))) = \ln(k) + (t/t_m)\ln(t/t_0) \tag{5b}$$

If nature follows, for human cancer diseases, the statistical law of Eq. (5a), the same data reported in Fig. 1 should fall in the diagram of Fig. 2 on a straight line, as suggested by Eq. (5b). A significant agreement is observed (see the coefficient of correlation R^2), suggesting that such a statistic could represent a kind of general biological law. In addition, the best fit gives in a simple manner the two

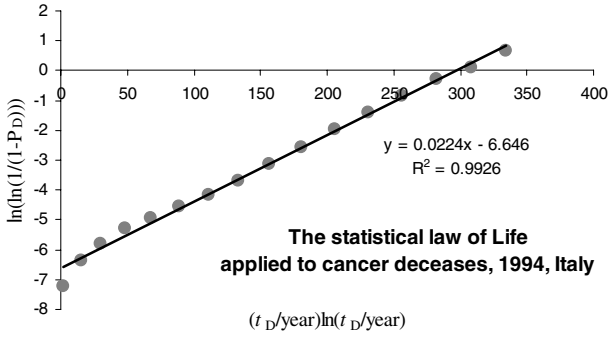


Figure 2 Eq. (5) applied to human individuals deceased as a consequence of cancer (of various types) in the year 1990 in Italy. The observation of a straight line seems to confirm the statistical law of Life here derived.

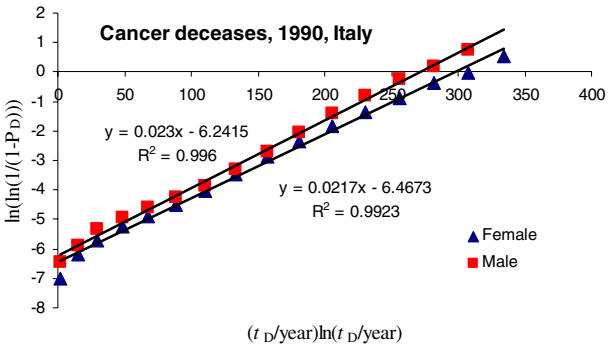


Figure 3 Eq. (5) applied to human individuals deceased as a consequence of cancer (of various types) in the year 1990 in Italy. Males (squares) and females (triangles) are treated separately.

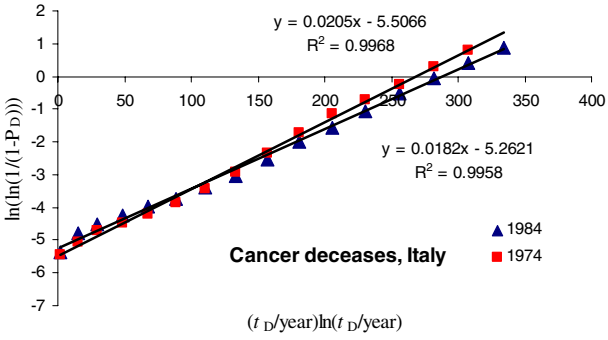


Figure 4 Eq. (5) applied to human individuals deceased as a consequence of cancer (of various types) in the years 1974 (squares) and 1984 (triangles).

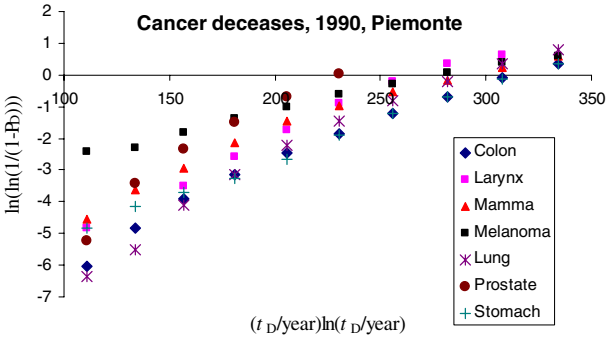


Figure 5 Eq. (5) applied to human individuals deceased as a consequence of cancer of different types (colon, larynx, mamma, melanoma, lung, prostate, stomach) in the year 1990 in Piemonte, a region of Italy.

Table 2 Critical characteristic time t_m (in years) and toughness dimensionless parameter k^{-1} from the best fits of the different cancer typologies analyzed in Fig. 5

	Colon	Larynx	Mamma	Melanoma	Lung	Prostate	Stomach
t_m (years)	36.2	34.3	44.6	69.9	31.1	23.7	42.6
k^{-1}	4665.2	2694.6	658.7	56.2	11,185.8	11,599.3	1627.0

characteristic constants k, t_m for the analysed case: we find $k^{-1} \approx 769.7$ and $t_m \approx 44.6$ years. About the physical interpretation of the former parameter, we note that the larger the value of k the lower the toughness against the considered decease, as suggested by Eq. (5) considering $t = \text{const}$; thus k^{-1} represents a toughness dimensionless parameter. The latter represents the time corresponding to the beginning of a catastrophic deterioration, thus t_m is a critical characteristic time. This allows one to classify the considered living organism family against the considered kind of death in a simple but rigorous manner: from such parameters, statistical biological predictions could be easily obtained by applying Eq. (5a). Moreover, our method, capable of discriminating between even slightly different statistical experimental data, could become an interesting tool for evaluating the efficiency of different therapy strategies and thus their optimization.

Cancer data analysis

We choose to treat other data on cancer deaths [24] to further test the statistics of Eq. (5a). In Fig. 3 we still refer to the year 1990 but considering separately males and females. Females ($k^{-1} \approx 643.7$ and $t_m \approx 46.1$ years) are found to be slightly stronger (larger k^{-1}, t_m) than males ($k^{-1} \approx 513.8$ and $t_m \approx 43.5$ years) against cancer. In Fig. 4 a comparison between the years 1974 ($k^{-1} \approx 246.3$ and $t_m \approx 48.8$ years) and 1984 ($k^{-1} \approx 192.9$ and $t_m \approx 54.9$ years) is reported. The influence of the time, related to the different cancer aggressiveness and available therapies, is clearly observed: catastrophic behavior has been successfully retarded (t_m increases with time), even if cancer seems to become more aggressive (k^{-1} decreases). In Fig. 5 different cancers (colon, larynx, breast, melanoma, lung, prostate, stomach) are treated separately for the year 1990, as observed in Piemonte, a region of Italy. In all these cases the statistical law of life of Eq. (3a) in its particular version of Eq. (5a) shows an interesting agreement; however we note that the reduced data availability for such cases [24] and the presence of a threshold time (some of these cancer types do not appear below a given age) yield these data sets statistically less significant. In Table 2 the parameters t_m and k^{-1} are reported as deduced from the best fits of the data in Fig. 5, as a rigorous purpose of classification.

Conclusions

Summarizing, the proposed statistical law of the life could represent an interesting tool for classifying and deducing statistical predictions on the natural deaths of living organisms, as here demonstrated for cancer in human individuals. Further investigations may reveal the necessity of considering the more general Eq. (3a) rather then its simplified version of Eq. (5a), or a different statistics. As the Weibull Statistics can be applied for predicting the probability of failure of a given family of structures, the Dynamic Weibull Statistics could be useful for treating the most important causes of human deaths (e.g., car accidents, HIV virus, heart attack, etc.). The universally accepted importance of the Weibull Statistics for describing the strength of solids would suggest that our statistics may have an interesting role in Biophysics, Biology and Medicine. Note that Weibull Statistics alone ($m = \text{const}$) has been demonstrated to be in general unable to catch the reality in the context of living organisms. An evolutionary parameter m, intrinsically related to the deterioration process of the living organisms, seems to be crucial for correctly describing the statistics of the life. Furthermore, the spatial-temporal scaling deduced in Eq. (4) suggests a universal range (and transition) rather than an universal value for p in the related biological scaling laws. However, $p = 3/4$ as proposed by West et al. [16] remains a good compromise.

Acknowledgement

The author would like to thank P.P. Delsanto and F. Pugno for discussion, as well as Diane Dijak for the English grammar supervision.

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